Synthesis of Functionalized Biaryls, Benzophenones, Phenols, Fluorenones, Fluoroarenes, and Chloroarenes based on formal [3+3] Cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes and 1,3,5-tris(silyloxy)-1,3,5-hexatrienes.

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To Ammi……

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With genuine humility, I acknowledge Allah our Creator who bestowed me the shower of His blessings and selected me in the Ummah of Holy Prophet Muhammad (S.A.W) Without Allah's help this humble writing of mine would have never become a reality.

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I have dedicated this little effort of my life to my mother (Late), due to her prayers I am able to write these words. I have great debt on my life due to tremendous sacrifices of my father for my better future.

Muhammad Adeel

Contents

Abbreviations

Ar	Aromatic
*n*BuLi	*n*-Butylithium
DEPT	Distortionless Enhancement by Polarisation Transfer
EI	Electronic Impact
ESI	Electrospray Ionization
EtOAc	Ethylacetate
HRMS	High Resolution Mass Spectroscopy
IR	Infrared Spectroscopy
LDA	Lithium Diisopropylamide
MS	Mass Spectrometry
Ph	Phenyl
NEt_3	Triethylamine
NMR	Nuclear Magnetic Resonance
HMQC	Heteronuclear Multiple Quantum Coherence
HMBC	Heteronuclear Multiple Bond Correlation
COSY	Correlated Spectroscopy
NOESY	Nuclear Overhauser and Exchange Spectroscopy
Me_3SiOTf	Trimethylsilyl-trifluoromethanesulfonate
Me_3SiCl	Trimethylsilylchloride
mp.	Melting Point
TFA	Trifluoroacetic Acid
Tf2O	Trifluoromethanesulfonic Anhydride
THF	Tetrahydrofurane
TLC	Thin Layer Chromatography
TMS	Trimethylsilane
UV	Ultraviolet Spectroscopy
TfOH	Trifluoromethanesulfonic Acid

Summary

A significant part of this dissertation has recently been published (see list of publications at the end). The work in this dissertation is mainly concerned with Synthesis of functionalized biaryls, benzophenones, phenols, fluorenones, fluoroarenes, and chloroarenes based on formal [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes and 1,3,5-tris(silyloxy)-1,3,5-hexatrienes.

1. This Chapter contains the synthesis of Highly functionalized polyketide-type phenols **(5a-j)** and **(6a-j)** which were prepared by domino ′Michael / retro-Michael / aldol′ reactions of 3-formylchromones (**4a-j)** with 1-ethoxy-1,3,5-tris(trimethylsilyloxy)-1,3,5-hexatriene (**2**) and its synthetic precursor, ethyl 3,5-bis(trimethylsilyloxy)-2,4-hexadienoate (**3**).

2. This cahapter includes the synthesis of Sterically encumbered biaryls (**11a-e**) and (**13a-j**) which were regioselectively prepared based on formal [3+3] cyclocondensations of novel 4-aryl-1,3-bis(trimethylsilyloxy)-1,3-dienes.

3. This chapter contains the synthesis of Functionalized fluorenones (**24**) which were efficiently prepared in four steps. 1-hydroxyfluorenones (**24**) were prepared by [3+3] cyclization of 3-aryl-3-(silyloxy)-2-en-1-ones with 1,3-bis(silyloxy)buta-1,3-dienes and subsequent intramolecular Friedel–Crafts acylation of the 6-arylsalicylates (**23**).

4. This chapter contains the reactions of first fluorine containing 1,3-bis(silyl enol ether) **27**, the reactions of **27** with epichlohydrin, 2,3butenoxide, cyanochromones and phathaloyl dichloride resulted in several novel fluorinated compounds **28**, **32**, **33** and **35a-e** which are not readily available by other methods.

5. This chapter is concerned with reactions of 2-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadienes (**38**) with epibromo and epichlorohydrin, 2,3butenoxide, cyanochromones and DMAD allow a convenient synthesis of chlorinated molecules such as **47**, **48, 51a-d**, and **52** which are not readily available by other methods.

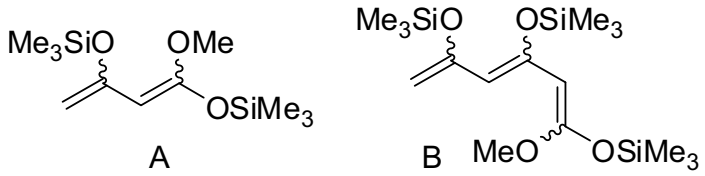
6. This chapter includes the synthesis of chlorinated biaryls (**62a-f**), azaxanthones (**60a-d**), benzotropones (**66**), and isobenzofurans which were prepared by one-pot cyclizations 1-alkoxy-4-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadienes (**55a-b**) with various dielectrophiles.

7. Acetal-protected (2,4-dioxocyclohex-1-yl)-acetic acids (**73a,b**) were prepared by allylation of dilithiated 1,3-cyclohexane-1,3-diones (**67a,b**), protection of the carbonyl groups and oxidation of the alkene moiety. Their reaction with amines afforded the corresponding amides (**76a-v**) which were transformed, by acid-catalyzed cyclization, into various 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles (77a-v). The reaction of the corresponding amides (**76a-v**) with triflic acid resulted in the formation of novel 5,8,9,10-tetrahydro-6H-indolo [2,1-a]isoquinolin-9-ones (**80a-c**).

1. Synthesis of Polyketide-Type Phenols by Domino 'Michael / Retro-Michael / Aldol' Reactions of 3-Formylchromones with Silyl Enol Ethers derived from Ethyl 3,5-Dioxohexanoate.

1.1 Introduction

In recent years, several one-pot cyclization reactions of 1,3-bis(silyloxy)-1,3-butadienes, such as **A**,[1] have been reported (Scheme 1). This includes, for example, cyclizations with oxalyl chloride to give butenolides,[2] formal [3+3] cyclocondensations to give salicylates,[3] syntheses of 2-alkylidenetetrahydrofurans,[4] reactions with iminium salts,[5] and domino reactions with benzopyrylium triflates.[6] In contrast, reactions of 1,3,5-tris(silyloxy)-1,3,5-hexatrienes, such as B, have only scarcely been reported to date. Trienes B contain three rather than only two masked carbonyl groups. Chan and coworkers studied their reaction with acid chlorides to give polyketides which spontaneously underwent an intramolecular aldol reaction to give hydroxylated arenes.[7] The cyclization of **B** with oxalyl chloride has also been reported.[8] Recently, we developed a new synthesis of 4-(2-hydroxybenzoyl)phenols by domino reaction of 1,3-bis(silyloxy)-1,3-butadienes with 3-formylchromones.[9] Herein, we report for the first time the application of this methodology to 1-ethoxy-1,3,5-tris(trimethylsilyloxy)-1,3,5-hexatriene and its synthetic precursor, ethyl 3,5-bis(trimethylsilyloxy)-2,4-hexadienoate. The domino reactions reported herein provide a convenient access to highly functionalized polyketide-type phenols which are not readily available by other methods.

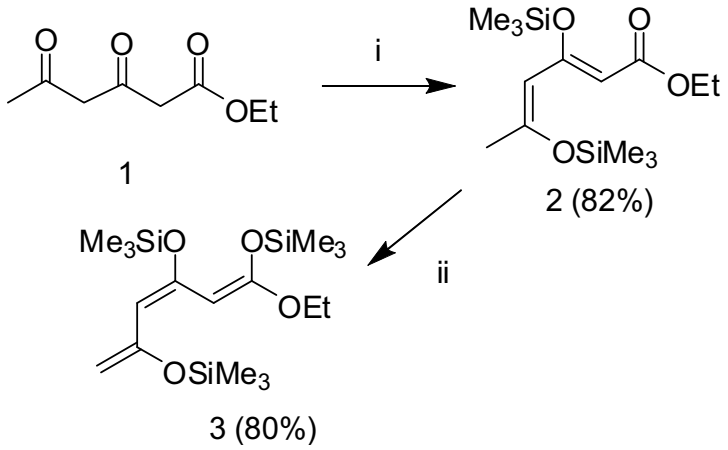


Scheme 1: Structure of 1,3-bis(silyloxy)-1,3-butadiene **A** and of 1,3,5-tris(silyloxy)-1,3,5-hexatriene **B.**

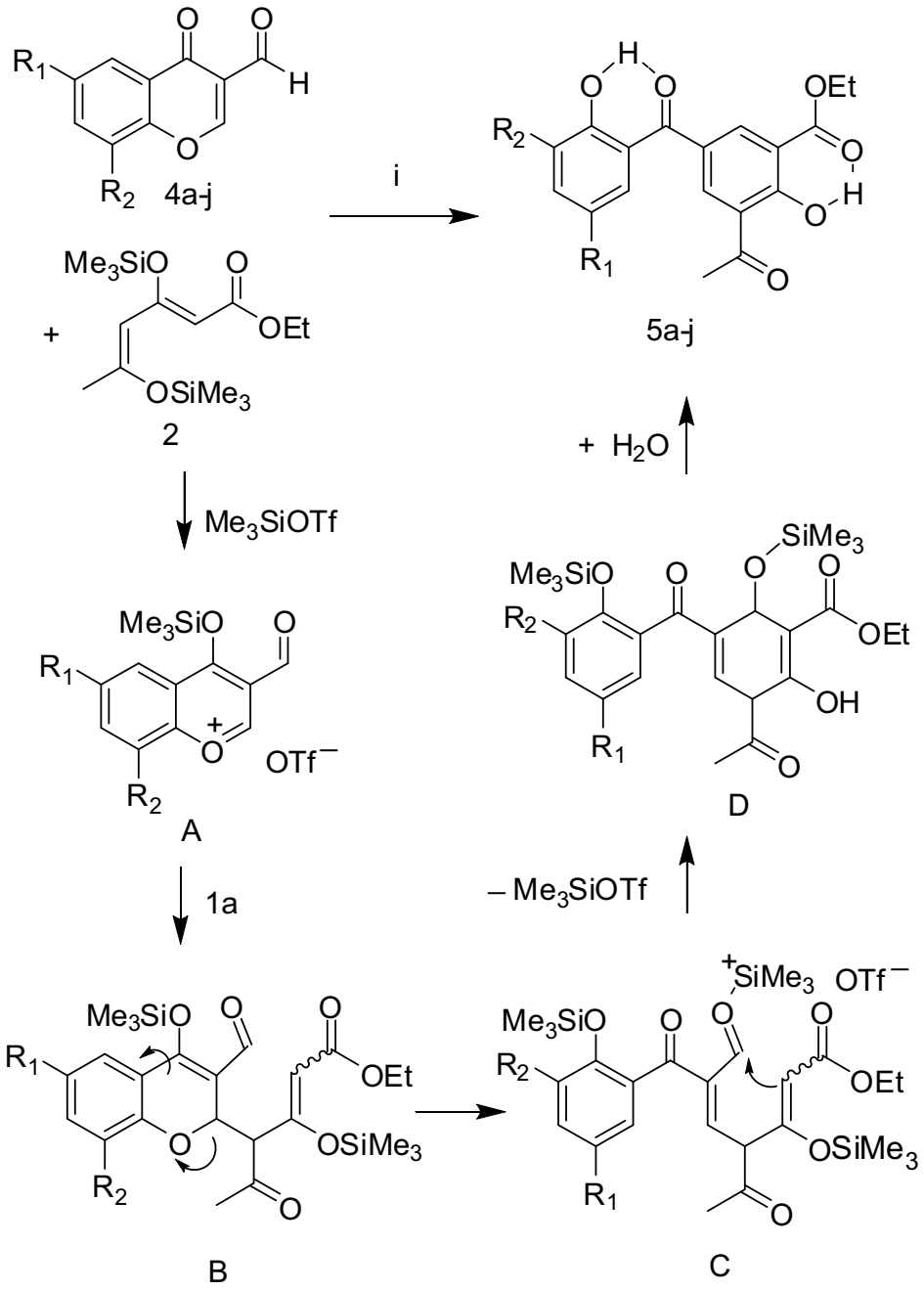
1.2 Results and Discussion

1,3,5-Tris(silyloxy)-1,3,5-hexatriene **3** was prepared, following the procedure reported for the synthesis of the methoxy derivative,[7] in two steps (Scheme 1). The silylation of

ethyl 3,5-dioxohexanoate (**1**) gave ethyl 3,5-bis(trimethylsilyloxy)-2,4-hexadienoate (**2**). Deprotonation of the latter with LDA and subsequent addition of Me_3SiCl gave **3** in 80% overall yield. The reaction of 1,3-bis(trimethylsilyloxy)-1,3-butadiene **2** with 3-formylchromones **4a-j** afforded the functionalized 4-(2-hydroxybenzoyl)phenols **5a-j** (Scheme 3, Table 1). The formation of the products can be explained by a domino ′Michael / retro-Michael / aldol′ reaction: the reaction of **4a-j** with Me_3SiOTf gave pyrylium triflate **A**. The conjugate addition of the diene onto **A** afforded intermediate **B** which underwent a retro-Michael reaction to give intermediate **C**. An aldol reaction of the latter gave intermediate **D** which underwent an elimination of silanolate and aromatization (before or during the aqueous work-up) to give the final product. The best yields were obtained for products **5a, b, h-j** which are derived from the chlorinated and fluorinated chromones **4h-j**, from parent formylchromone **4a** and from **4b**.



Scheme 2. Synthesis of **3**; *i*: Me_3SiCl (3.6 equiv.), NEt_3 (3 equiv.), C_6H_6, 20 °C, 72 h; *ii*: 1) LDA (1.5 equiv.), THF, –78 °C, 1 h; 2) Me_3SiCl (2.5 equiv.), 20 °C, –78 → 20 °C.



Scheme 3. Synthesis of **5a-j**. Reagents and conditions: *i*, 1) **4a-j** (1.0 equiv.), Me_3SiOTf (0.3 equiv), 20 °C, 10 min; 2) **2** (1.3 equiv), CH_2Cl_2, 0→20 °C, 12 h; 3) HCl (10%).

Table 1. Synthesis of **5a-j**

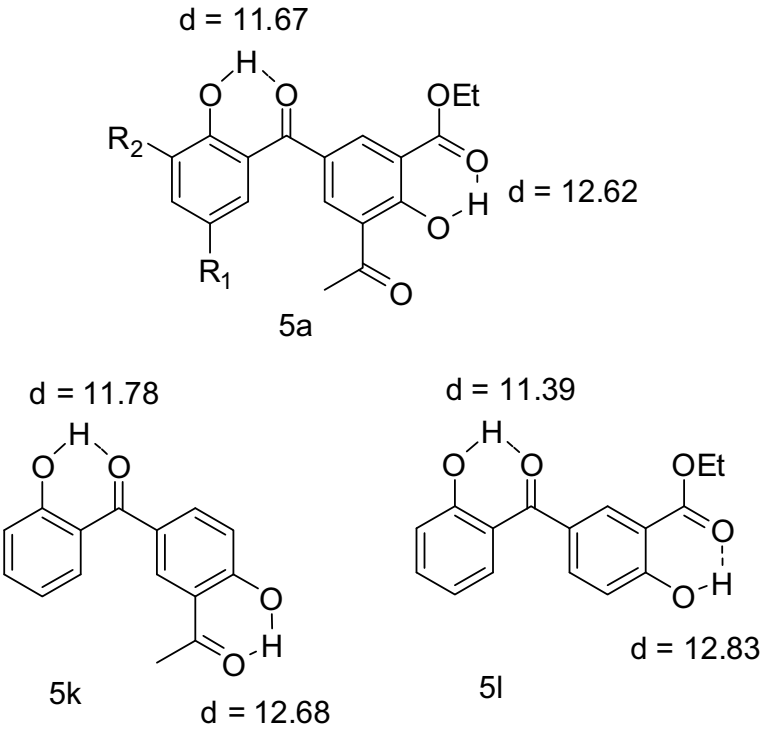
5	R^1	R^2	Yield (%) [a]	δ (O-H) [b]
a	H	H	79	11.67, 12.62
b	Me	H	88	11.47, 12.62
c	Et	H	63	11.48, 12.64
d	*i*Pr	H	52	11.47, 12.65
e	NO_2	H	43	12.28, 12.70
f	Br	H	54	11.55, 12.66
g	Br	Br	56	12.10, 12.68
h	Cl	H	76	11.54, 12.65
i	Cl	Cl	80[c]	11.93, 12.67
j	F	H	79	11.36, 12.63

[a] Yields of isolated products
[b] 1H NMR shifts of OH protons.
[c] Synthesized by Muhammad Nawaz

The structures of all products were established by spectroscopic methods. The structures of **5e**, **5h** and **5j** were independently confirmed by X-ray crystal structure analyses (Figures 1 and 2).[10] All products possess two low field signals (^{1}H NMR, $CDCl_3$) for the protons involved in intramolecular hydrogen bonds O–H···O. The chemical shifts of the hydroxyl proton derived from the chromone moiety are found in the range of δ = 11.36-12.10 ppm and strongly depend on the substitution pattern (Table 1). The most extreme downfield shift is observed for derivative **5e** (δ = 12.28), due to the electron-withdrawing effect of the nitro group. Extreme low field shifts are observed also for compounds **5g** and **5i** containing two halogen atoms.

The signals of the hydroxyl protons of the second phenol moiety (which is derived from the diene **2**) are located in a rather narrow chemical shift range (δ = 12.62-12.70 ppm). This can be explained by the fact that the substitution pattern of this phenol moiety is the same for all derivatives **5a-j**. The chemical shifts of the hydroxyl protons appear in the same range as earlier reported[9] for derivatives **5k** and **5l** (Scheme 4). It is worth to be noted that the hydroxyl proton may participate in a hydrogen bond either to the acetyl or the ester oxygen atom. In the solid state structures of **5e**, **5h** and **5j**, the hydrogen bonds involve the ester group. However, the solution structures might be different. The comparison of the chemical shifts of the low field signals of **5a-j** with those of

derivatives **5k** and **5l**, containing an acetyl and an ester group, do not allow to clearly distinguish the solution structure. However, the ester group is expected to be a better hydrogen bond acceptor than the keto group which is in accordance with the structures observed in the solid state.



Scheme 4. Chemical shifts (^{1}H NMR) of OH protons of **5a**, **5k** and **5l**

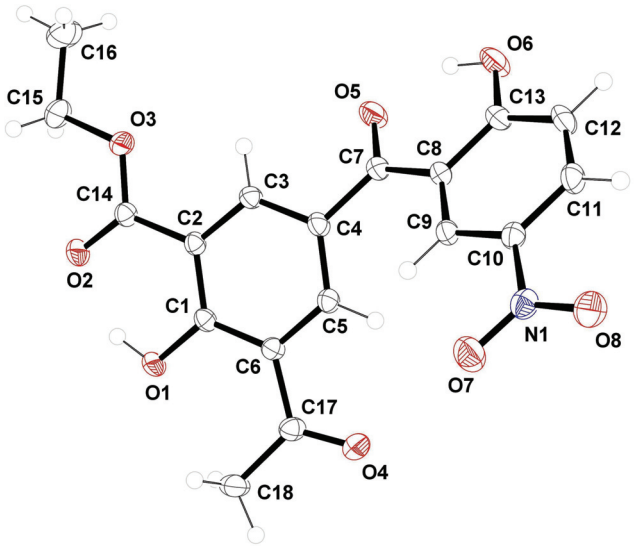


Figure 1. Ortep plot of **5e**

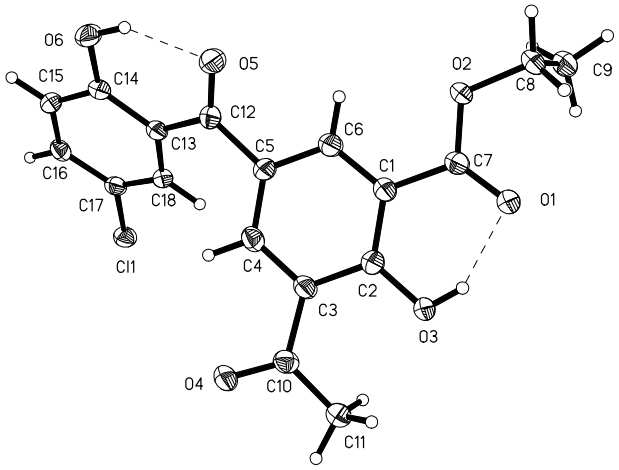


Figure 2. Ortep plot of **5h**

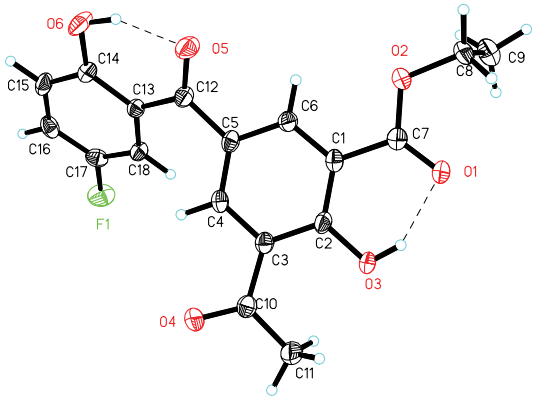
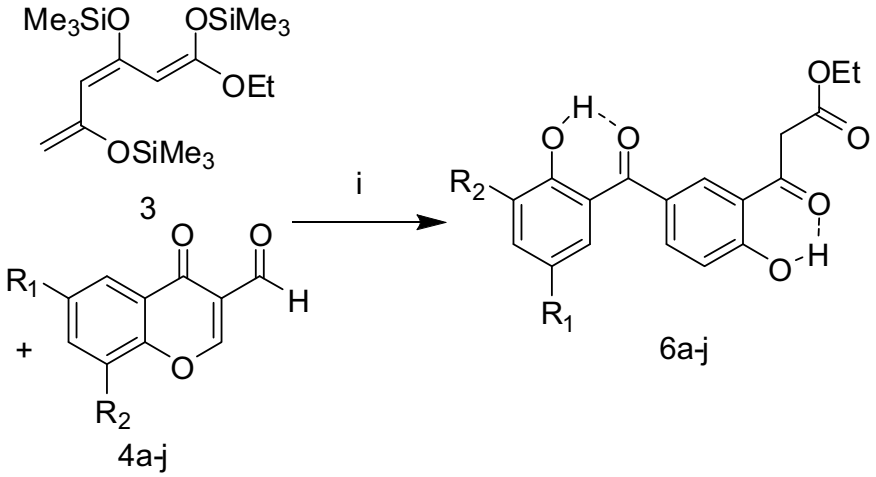


Figure 3. Ortep plot of **5j**

The cyclization of 3-formylchromones **4a-j** with 1,3,5-tris(silyloxy)-1,3,5-hexatriene **3** afforded the 4-(2-hydroxybenzoyl)phenols **6a-j** which represent regioisomers of **5a-j** (Scheme 5, Table 2). The cyclizations involve, as expected, the terminal carbon atom of the triene. Phenols **6a-j** can be regarded as masked polyketides. All products exist in their keto tautomeric form. The yields of **6a-j** are generally lower than the yields of **5a-j**. This can be explained by the unstable nature of triene **3** which results in some decomposition and hydrolysis under the reaction conditions. In fact, a small amount of 3,5-dioxoester **1**

was isolated as side-product in all reactions. Similar to products **5a** and **5i**, relatively good yields are obtained for **6a** and **6i** which are derived from parent formylchromone **4a** and from dichlorinated formylchromone **4i**, respectively. Besides, the trends of the yields of products **5** and **6** are quite different from each other.



Scheme 5. Synthesis of **6a-j**. Reagents and conditions: *i*, 1) **4a-j** (1.0 equiv.), Me_3SiOTf (0.3 equiv), 20 °C, 10 min; 2) **3** (1.1 equiv.), CH_2Cl_2, 0→20 °C, 12 h; 3) HCl (10%).

Table 2. Synthesis of **6a-j**

6	R^1	R^2	Yield (%) [a]	δ (O-H) [b]
a	H	H	43[c]	11.63, 12.14
b	Me	H	36	11.60, 12.29
c	Et	H	45	11.60, 12.30
d	*i*Pr	H	47	11.59, 12.30
e	NO_2	H	30	12.30
f	Br	H	31	11.56, 12.24
g	Br	Br	33	12.13, 12.27
h	Cl	H	37	11.63, 12.33
i	Cl	Cl	59[c]	12.13, 12.27
j	F	H	34	11.39, 12.23

[a] Yields of isolated products
[b] 1H NMR shifts of OH protons.
[C] Synthesized by Muhammad Nawaz

Two low field signals, assigned to hydroxyl protons, are observed also for products **6a-j** (Table 2). The signals assigned to the chromone-derived hydroxyl protons are in the

range of δ = 11.39-12.20 ppm and again depend on the substitution pattern. In contrast, the signals of the other hydroxyl protons are found in a rather narrow range.

1.3 Conclusion:

In conclusion, we have reported the synthesis of highly functionalized polyketide-type phenols by domino ′Michael / retro-Michael / aldol′ reactions of 3-formylchromones with 1-ethoxy-1,3,5-tris(trimethylsilyloxy)-1,3,5-hexatriene and its synthetic precursor, ethyl 3,5-bis(trimethylsilyloxy)-2,4-hexadienoate. These products are not readily available by other methods.

2 Regioselective Synthesis of Functionalized Biaryls based on the First [3+3] Cyclocondensations of 4-Aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes

2.1 Introduction:

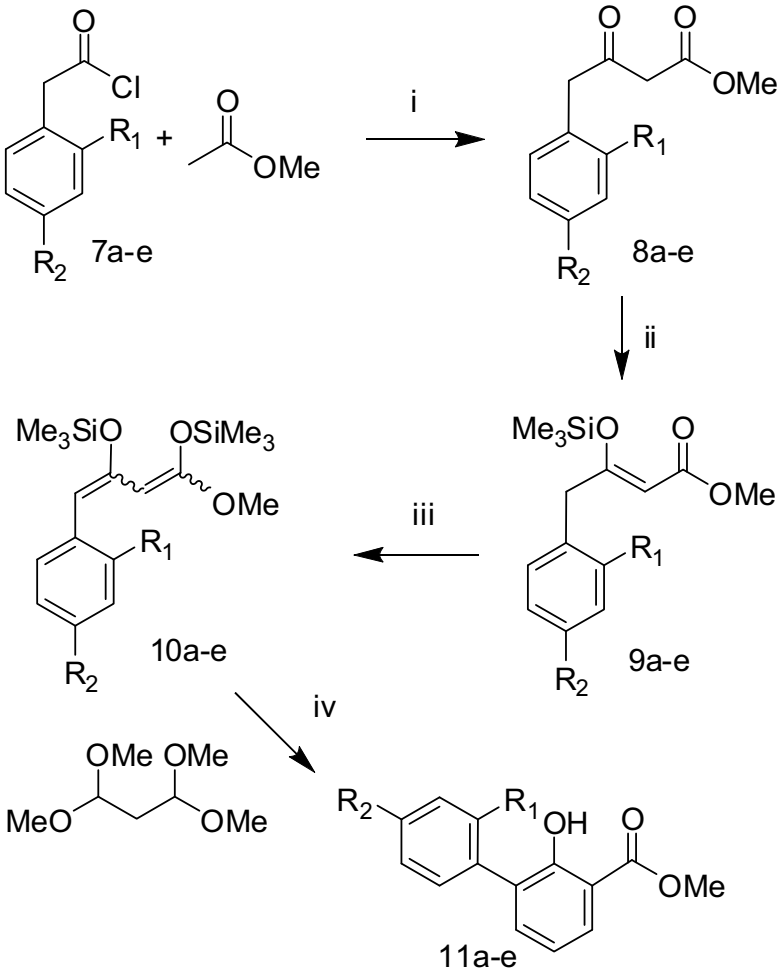
Functionalized biaryls containing a 3-arylsalicylate substructure occur in a variety of pharmacologically relevant natural products. The simple biaryls cynandione A-C have been isolated from many plant sources and show a considerable in vitro activity against hepatocytes, human bladder carcinoma T-24 cells, epidermoid carcinoma KB cells, and human hepatoma PLC/PRF/5 cells.[11] A number of natural products, such as knipholone, 6'-*O*-methylknipholone or (+)-asphodelin, contain an anthraquinone moiety.[12] Other compounds, e. g. secalonic acid A or globulixanthone E, contain a bixanthenyl substructure.[13] 3-Arylsalicylates are also present in many flavones (e. g. 2,3-dihydroamentoflavone,[14a] bartramiaflavone,[14b] robustaflavone,[14c] dichamanetin).[14d,e] For some derivatives, inhibition of the human liver cathepsin B and K has been reported.[14f,g] The natural product anastatin A, which contains a hydroxylated dibenzofuran moiety, shows hepatoprotective activity.[15]

The most important synthetic approach to biaryls relies on palladium(0)-catalyzed cross-coupling reactions.[16] Although these reactions are broadly applicable, the synthesis of sterically encumbered products can be difficult or not possible at all. In addition, the regioselective synthesis of the required aryl halides or triflates can be a very difficult task. Some years ago, Chan *et al.* developed[17] a convenient approach to salicylates by formal [3+3] cyclizations[18] of 1,3-bis(trimethylsilyloxy)-1,3-dienes[19] with 3-trimethylsilyloxy-2-en-1-ones. Recently, we developed a catalytic variant of this transformation.[10] Herein, we report, for the first time, the synthesis of 4-aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes and their application to the synthesis of functionalized biaryls. The sterically encumbered and functionalized biaryls reported herein are not readily available by other methods.

2.2 Results and Discussion

The 4-arylacetoacetates **8a-e** were prepared by LDA-mediated reaction of methyl acetate with the α-arylacetyl chlorides **7a-e** (Scheme 1, Table 1). The silylation of **8a-e** afforded the 3-silyloxy-2-en-1-ones **9a-e**. The novel 4-aryl-1,3-bis(silyloxy)-1,3-dienes **10a-e** were prepared by deprotonation (LDA) of **9a-e** at −78 °C and subsequent addition of trimethylchlorosilane. The Me_3SiOTf-catalyzed cyclization of 4-aryl-1,3-bis(silyloxy)-1,3-dienes **10a-e** with 1,1,3,3-tetramethoxypropane, afforded the 3-arylsalicylates **11a-e**. During the optimization of this reaction, we had to modify the protocol recently reported by us.[20] Noteworthy, the best yields were obtained when the cyclizations were carried out in a highly concentrated rather than in dilute solution.

The structures of all products were established by spectroscopic methods. The structures of **11b, 11c**[21] **13e, 13h and 13i** were independently confirmed by X-ray crystal structure analysis (Figures 1-5).



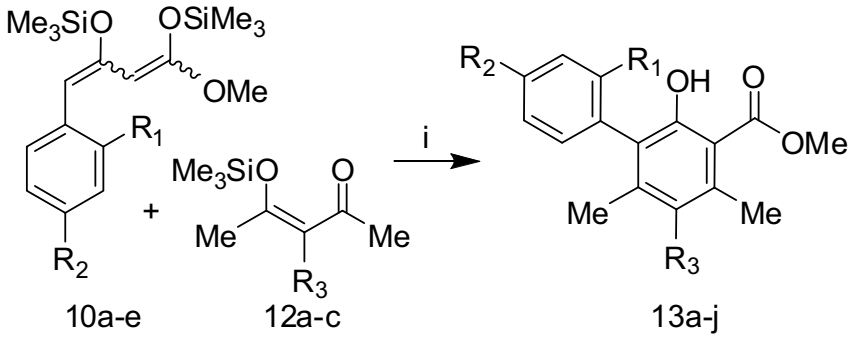
Scheme 6. Synthesis of **11a-e**; *i*: LDA, THF, –78 → 20 °C, 14 h; *ii*: Me_3SiCl, NEt_3, C_6H_6, 20 °C, 72 h; *iii*: LDA, THF, –78 → 20 °C; *iv*: Me_3SiOTf (0.1 equiv.), CH_2Cl_2, –78 → 20 °C, 20 h

Table 3. Synthesis of biaryls **11a-e**

8-11	R^1	R^2	% (**2**)[a]	% (**3**)[a]	% (**4**)[a]	% (**5**)[a]
a	H	H	60	82	80	44
b	H	OMe	56	80	84	50
c	OMe	H	48	75	82	34[b]
d	H	Cl	34	77	85	43
e	H	Me	45	81	86	36[c]

[a] Isolated yields
[b] Synthesized by M.Abid Rashid
[c] Synthesized by Rasheed Ahmad

The $TiCl_4$-mediated [3+3] cyclization of 1,3-bis(silyloxy)-1,3-dienes **10a-e** with 3-silyloxy-2-en-1-ones **12a-c** afforded the 3-arylsalicylates **13a-j** (Scheme 2, Table 2). During the optimization, it proved to be important to carry out the reactions in a highly concentrated solution.



Scheme 7. Synthesis of **13a-j**; *i*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 20 h

Table 4. Synthesis of biaryls **13a-j**

10	**12**	**13**	R^1	R^2	R^3	% (**13**)[a]
a	**a**	**a**	H	H	H	41
a	**b**	**b**	H	H	Cl	40
c	**a**	**c**	OMe	H	H	26[b]
c	**b**	**d**	OMe	H	Cl	30[b]
b	**b**	**e**	H	OMe	Cl	38
b	**a**	**f**	H	OMe	H	37
b	**c**	**g**	H	OMe	Me	38
a	**c**	**h**	H	H	Me	35
d	**b**	**i**	H	Cl	Cl	40
e	**b**	**j**	H	Me	Cl	30[c]

[a] Isolated yields
[b] Synthesized by M.Abid Rashid
[c] Synthesized by Rasheed Ahmad

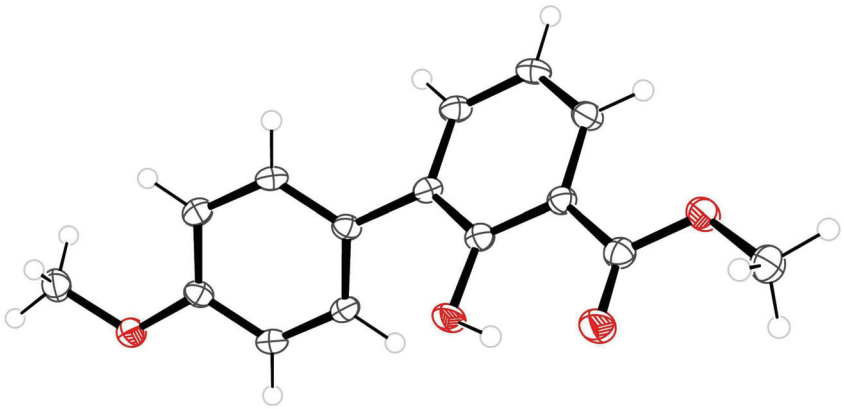


Figure 4. Ortep plot of **11b**

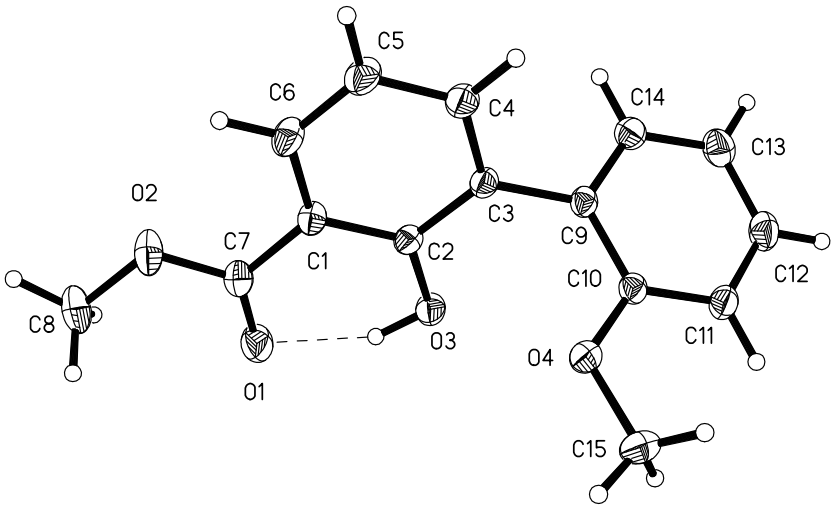


Figure 5. Ortep plot of **11c**

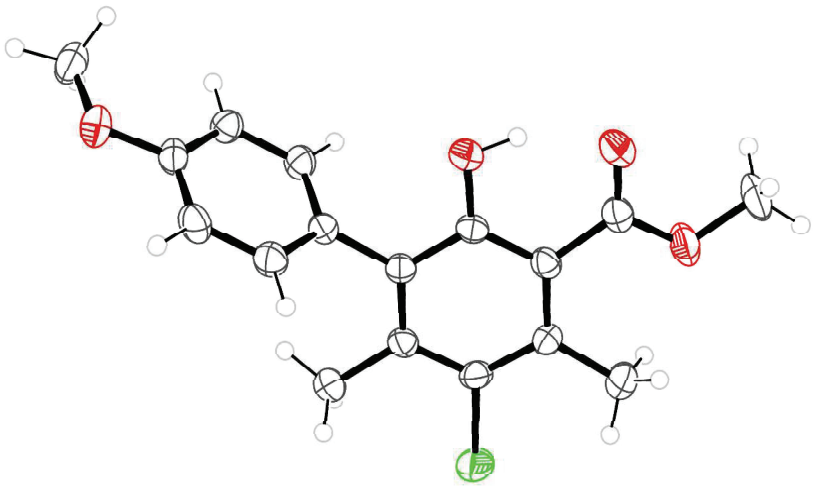


Figure 6. Ortep plot of **13e**

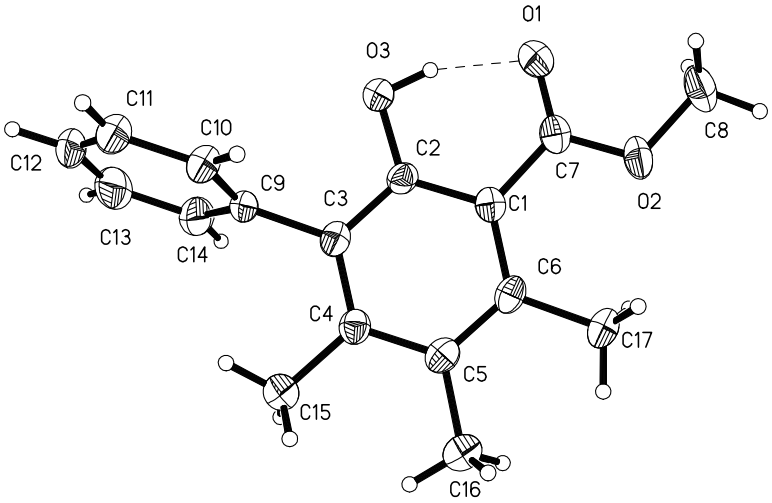


Figure 7. Ortep plot of **13h**

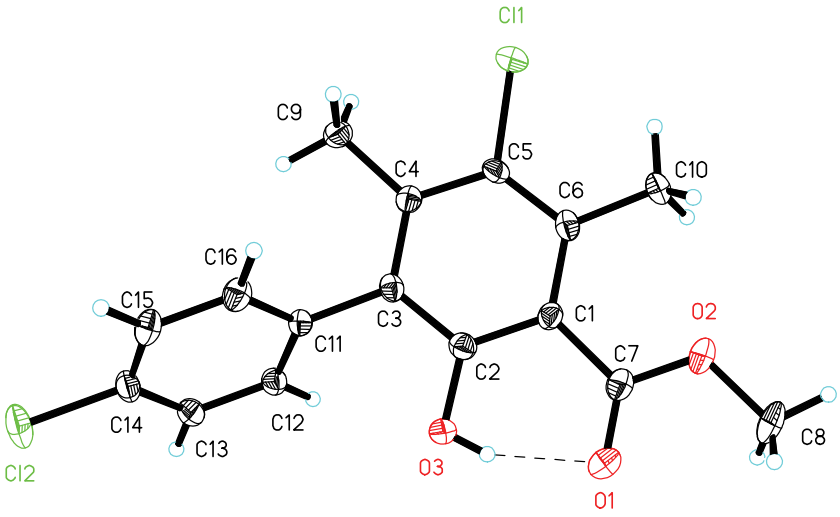
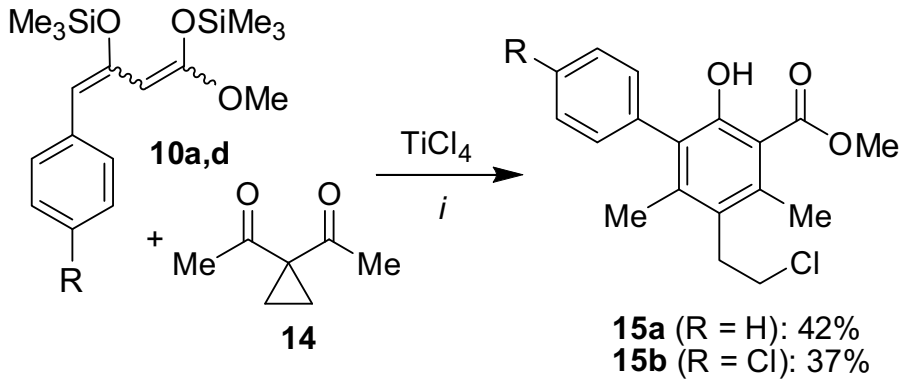


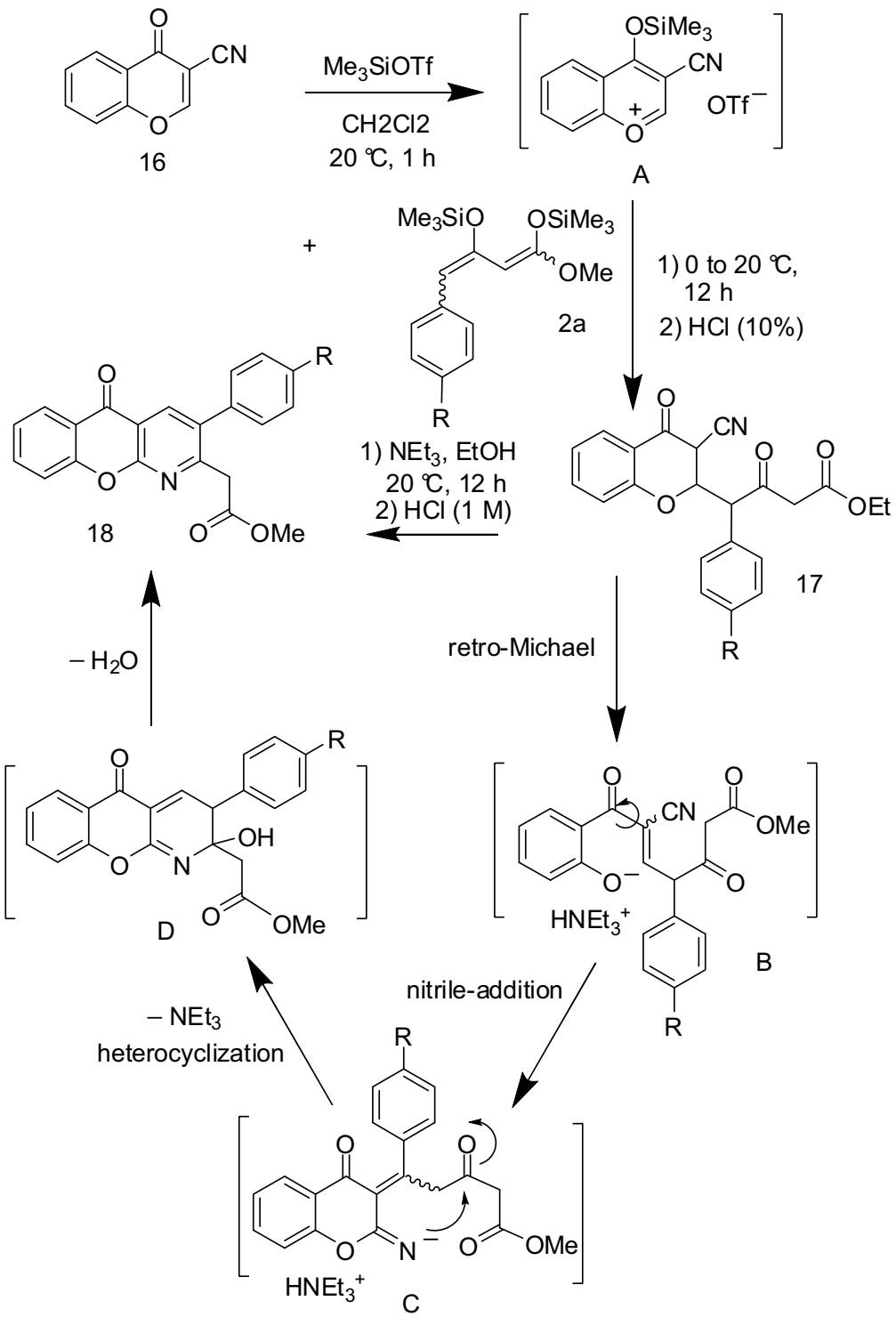
Figure 8. Ortep plot of **13i**

The $TiCl_4$-mediated reaction of 1,3-bis(silyloxy)-1,3-dienes **10a** and **10d** with 1,1-diacetylcyclopropane (**14**) gave the 3-arylsalicylates **15a** and **15b**, respectively (Scheme 3). Products **15a,b** are formed by a domino ′[3+3]-cyclization-homo-Michael′ reaction.[22]



Scheme 8. Synthesis of **15a,b**; *i*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 20 h

The TMSOTf-mediated reaction of 3-cyanochromone (**16**) with 1,3-bis(trimethylsilyloxy)-1,3-butadiene **10a, d, e**, afforded the condensation product **17** by regioselective attack of the terminal carbon atom of **10a, d, e** onto carbon atom C-2 of **16** and subsequent hydrolysis. Treatment of an ethanol solution of crude **17** with triethylamine afforded 1-azaxanthone **18** (Scheme 1). The formation of **18** can be explained by a domino 'retro-Michael-lactonization-aldol' reaction. The base-mediated retro-Michael reaction of **17** gave open-chained intermediate **B**. The attack of the hydroxy group onto the nitrile gave intermediate **C**. The attack of the imino nitrogen atom onto the carbonyl group (intermediate **D**) and subsequent aromatization by extrusion of water afforded **18**. The transformation of **17** into **18** can be regarded as a domino 'retro-Michael / nitrile-addition / heterocyclization' reaction. [23]


Me3SiOTf
CH2Cl2
20 °C, 1 h
16
A
2a
1) 0 to 20 °C, 12 h
2) HCl (10%)
1) NEt3, EtOH
20 °C, 12 h
2) HCl (1 M)
18
17
retro-Michael
– H2O
D
B
HNEt3+
nitrile-addition
– NEt3
heterocyclization
C
HNEt3+

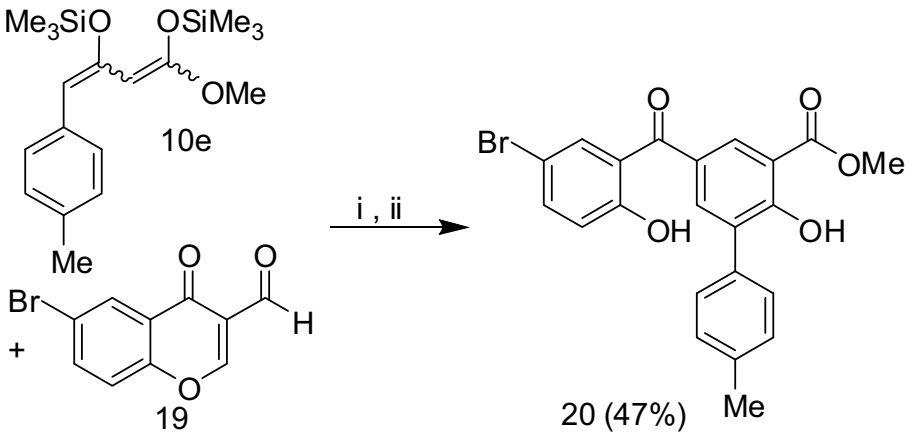
Scheme 9. Synthesis of 3-aryl-1-azaxanthone **18a-c**: *i*: 1) **16**, Me_3SiOTf, 1 h, 20 °C, 2) **10a, d, e**, CH_2Cl_2, 0 → 20 °C, 12 h, 3) HCl (10%); *ii*: 1) NEt_3, EtOH, 20 °C, 12 h, 2) HCl (1 M)

Table 5. Synthesis of 1-azaxanthones **18a-c.**

17,18	R	18[a] (%)
a	H	62
b	Me	63
c	Cl	50

[a] Yield of isolated products.

The Me_3SiOTf-catalyzed reaction of 1,3-bis(silyloxy)-1,3-butadiene **10e** with 3-formylchromone (**19**) afforded the highly functionalized biaryl **20** (Scheme 5). This product is formed by a domino ′Michael–retro-Michael–Mukaiyama-Aldol′ reaction.[24]



Scheme 10. Synthesis of **20**; *i*: Me_3SiOTf (0.3 equiv), 20 °C, 10 min; *ii*: 1) **10e** (1.3 equiv), CH_2Cl_2, 0 → 20 °C, 12 h; 2) HCl (10%)

2.3 Conclusions

In conclusion, we have reported, for the first time, a new and regioselective approach to a variety of sterically encumbered biaryls based on formal [3+3] cyclizations of novel 4-aryl-1,3-bis(trimethylsilyloxy)-1,3-dienes. The products are not readily available by other methods.

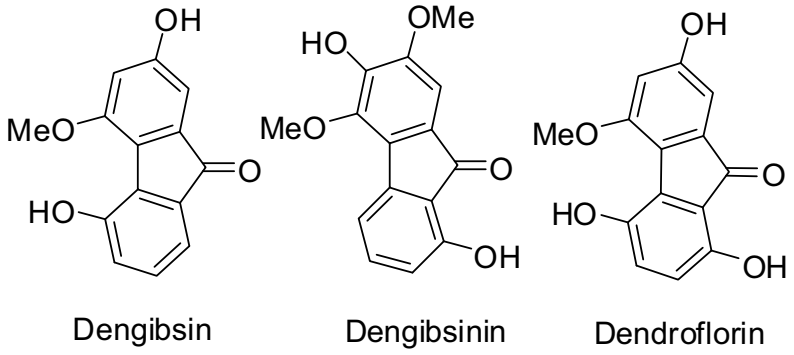
3. Synthesis of Functionalized Fluorenones based on the Combination of Formal [3+3] Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes with Intramolecular Friedel-Crafts-Acylations

3.1 Introduction

Fluorenones occur in a number of natural products. This includes various highly hydroxylated derivatives, such as dengibsin, dengibsinin, or dendroflorin (Scheme 11).[25] The first two fluorenone natural products, dengibsin und dengibsinin, were isolated 1985 by Talapatra et al. from the Orchidee *Dendrobium gibsonii Lindl.*[25a] These products were first prepared by Sargent and coworkers.[25b] Fluorenones are of considerable pharmacological relevance.[26] They have been used as probes for the redox activity of DNA.[27] Amidofluorenone derivatives have been shown to be telomerase inhibitors which is important for the development of anti-cancer agents.[28] In addition, fluorenones represent versatile synthetic intermediates. They have been used, for example, during the synthesis of the antibiotic kinamycin D.[29] Fluorenones are also important compounds in photochemistry.[30]

The most important synthetic approach to fluorenones includes intramolecular Friedel-Crafts acylations of appropriate biaryls.[31] Other syntheses rely on [4+2]-cycloadditions of conjugated enynes[32] and on the oxidation of fluorenes.[33] Snieckus and coworkers reported the synthesis of fluorenones based on remote aromatic metalation.[34] Larock and coworkers reported the synthesis of fluorenones by palladium-catalyzed cyclocarbonylation of 2-halobiaryls.[26] Valesco and Yu reported the synthesis of fluorenones based on the reaction of malonic acid dinitrile with aromatic aldehydes and methylketones.[35] Ciske and Jones prepared fluorenones by Suzuki reaction of boronic acids, generated in situ from benzoic acid amides, with aryl triflates and subsequent cyclization by remote metalation.[36] Fluorenones have been prepared by acid-mediated intramolecular Friedel-Crafts cyclation of 2-methoxycarbonyl-biaryls. Recently, the synthesis of the latter by Suzuki reactions of salicylate-derived enol triflates has been reported.[37]

Salicylates are available by various synthetic strategies. An important approach to salicylates, first reported by Chan and coworkers,[38] relies on the formal [3+3] cyclization of 1,3-bis(silyloxy)-1,3-butadienes[39] with 3-silyloxy-2-en-1-ones. In recent years, we have reported the application of this methodology to the synthesis of a variety of functionalized arenes.[40] Recently, we have reported[41] a convenient four-step synthesis of fluorenones: The [3+3] cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy-2-en-1-ones afforded salicylates which were transformed into their enol triflates. The Suzuki cross-coupling reaction of the latter with arylboronic acids afforded 2-methoxycarbonyl-biaryls which were subsequently transformed into the target molecules by intramolecular Friedel-Crafts acylation. Herein, we report full details of these studies. In addition, we report the synthesis of 1-hydroxyfluorenones by cyclization of 3-aryl-3-silyloxy-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes and subsequent intramolecular Friedel-Crafts acylation of the 6-arylsalicylates thus formed.[42] In this context, the synthesis of novel cyclopenta[*def*]phenanthren-4-ones is reported. The advantage of the two synthetic strategies outlined herein relies on the fact that various substitution patterns are readily available based on a building-block strategy. The products are not readily available by other methods.



Scheme 11. Fluorenone natural products

3.2 Results and Discussion

The reaction of 1,3-bis(silyl enol ether) **21a,c** with 3-silyloxy-2-en-1-one **22h-k**, prepared from arylketones, resulted in regioselective formation of salicylates **23i-m**, which were transformed into fluorenones **24y-ac** (Scheme 2, Table 3). The regioselective formation of **23i-m** can be explained by isomerization of **22h-k** into *iso*-**22h-k** and subsequent cyclization as described above.

The structure of all products was established by spectroscopic methods. The structures of **23j** and **24ab** were independently confirmed by an X-ray crystal structure analysis (Figures 9 and 10). The fluorenone is, as expected, a flat molecules. An intramolecular hydrogen bond is present.

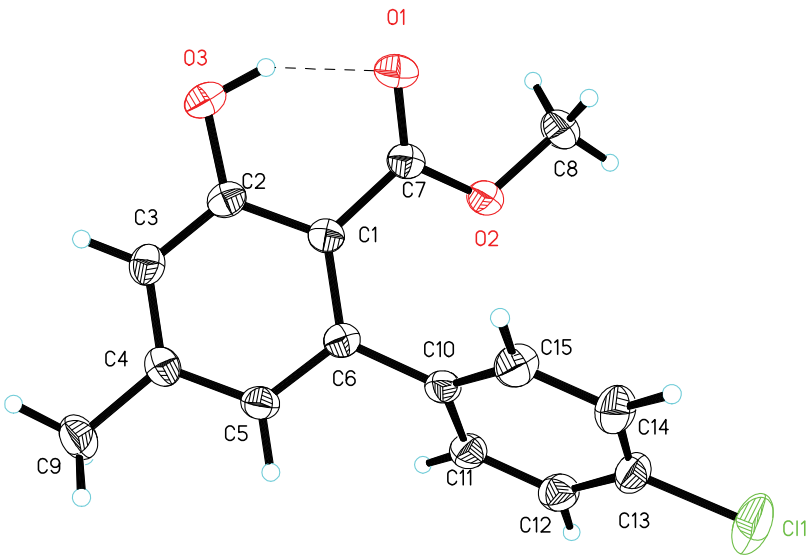


Figure 9: Crystal Structure of **23j**

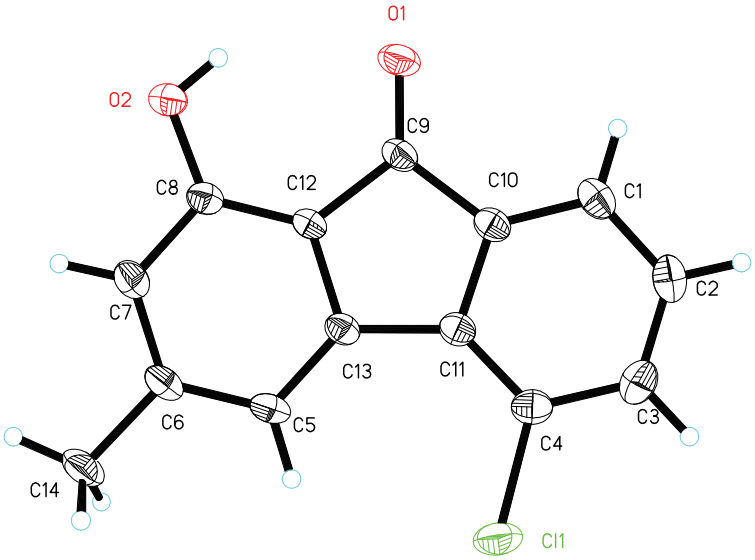
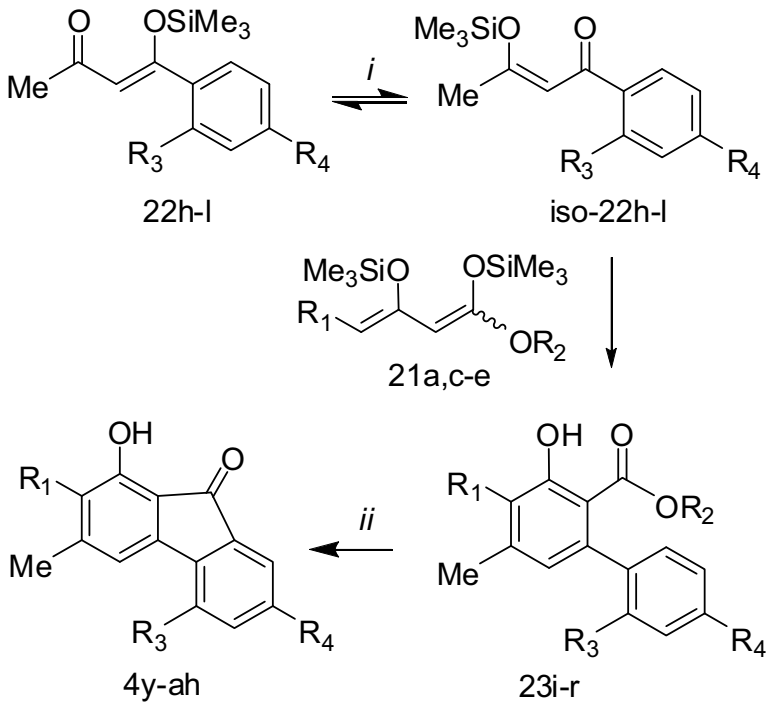


Figure 10. Ortep-Plot of **24ab** (50% probability level)



Scheme 12. Synthesis of fluorenones **24y-ah**, *i*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C; *ii*: conc. H_2SO_4, 1 h

Table 6. Products and yields

21	**22**	**23**	**24**	R^1	R^2	R^3	R^4	% (**23**)[a]	% (**24**)[a]
a	**h**	**i**	**y**	H	Me	Me	H	43	68
a	**i**	**j**	**z**	H	Me	H	Cl	40	83
c	**i**	**k**	**aa**	*n*Hex	Me	H	Cl	34	65
a	**j**	**l**	**ab**	H	Me	Cl	H	37	75
d	**j**	**m**	**ac**	Me	Me	Cl	H	32[b]	80[b]
e	**j**	**n**	**ad**	Et	Et	Cl	H	35[b]	60[b]
a	**k**	**o**	**ae**	H	Me	F	H	44	75
d	**k**	**p**	**af**	Me	Me	F	H	32[b]	51[b]
a	**l**	**q**	**ag**	H	Me	H	F	44[b]	68[b]
e	**l**	**r**	**ah**	Et	Et	H	F	44[b]	76[b]

[a] Yields of isolated products
[b] Synthesized by M.A. Yawer and I. Hussain

3.3 Conclusion:

In conclusion, a method for the synthesis of functionalized fluorenones was developed. The approach relies on the [3+3] cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy-2-en-1-ones to give salicylates. The cyclization of 3-aryl-3-silyloxy-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes afforded 6-arylsalicylates which were subsequently transformed into the products by intramolecular Friedel-Crafts acylation. In this context, the synthesis of novel cyclopenta[*def*]phenanthren-4-ones is reported. The advantage of the synthetic strategy outlined herein relies on the fact that various substitution patterns are readily available based on a building-block strategy. The products are not readily available by other methods.

4 Synthesis and Reactions of the First Fluorine-Containing 1,3-Bis(trimethylsilyloxy)-1,3-butadienes:

4.1 Introduction:

Organofluorine compounds play an important role in drug discovery[43]. They exhibit unique stereoelectronic properties: on the one hand the fluorine atom is fairly small, on the other hand its high electronegativity often results in a great improvement of drug-receptor interactions. The carbon-fluorine bond is chemically and biologically stable which avoids undesired metabolic transformations. In addition, the high lipophilicity of organofluorine compounds improves their *in vivo* transport. They also show a very good solubility in fluorophilic solvents. Therefore, organo-fluorine compounds are used as ligands[44] for catalytic reactions in fluorous biphase systems and supercritical carbon dioxide.[45] The unique electronic properties of fluorinated arenes are widely used for applications in organocatalysis.[46] Last but not least, fluorinated arenes and heteroarenes are versatile building blocks in transition metal-catalyzed cross coupling reactions.[47]

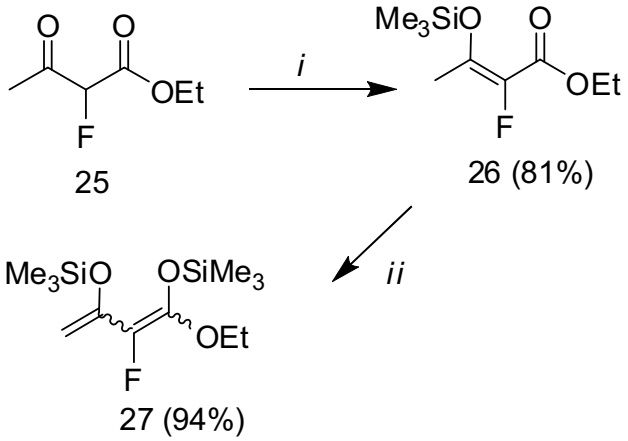
The direct fluorination of arenes, heteroarenes and several open-chained molecules often suffers from several drawbacks, such as low chemo- and regioselectivity or multiple fluorination. An alternative strategy for the regioselective synthesis of organofluorine compounds relies on the use of appropriate fluorine-containing building blocks in condensation and cyclization reactions. For example, aryl fluorides have been prepared by [4+2] cycloaddition reactions of 2-fluoro-1-methoxy-3-trimethylsilyloxy-buta-1,3-diene, 2-fluoro-3-methoxy-buta-1,3-diene and related dienes with alkenes or alkynes.[48] Portella *et al.* reported the synthesis of fluorophenols by annulation reactions of 2,2-difluoro-1,5-diketones which were prepared from trifluoromethyltrimethylsilane, acylsilanes and enones.[49]

1,3-Bis(trimethylsilyloxy)-1,3-butadienes (e. g., Chan's diene)[50, 51] represent important synthetic building blocks which have been used in formal [3+2], [3+3], [4+2] and [4+3] cyclizations and other transformations.[52] Herein, we report the synthesis and reactions of 2-fluoro-1,3-bis(silyloxy)-1,3-butadienes which represent, to the best of our knowledge, the first fluorine-containing 1,3-bis(silyl enol ethers).[53] Their reactions with electrophiles

provide a convenient and regioselective approach to a variety of organofluorine compounds which are not readily available by other methods.

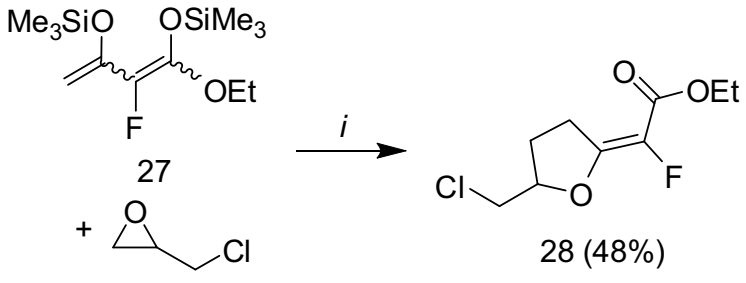
4.2 Results and Discussion:

The silylation of commercially available ethyl 2-fluoroacetoacetate (**25**) afforded silyl enol ether **26**. The latter was transformed, by deprotonation (LDA) at −78 °C and subsequent addition of trimethylchlorosilane, into novel 1-ethoxy-2-fluoro-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**27**) (Scheme 13). Diene **27a** can be stored at −20 °C under inert atmosphere for several weeks.



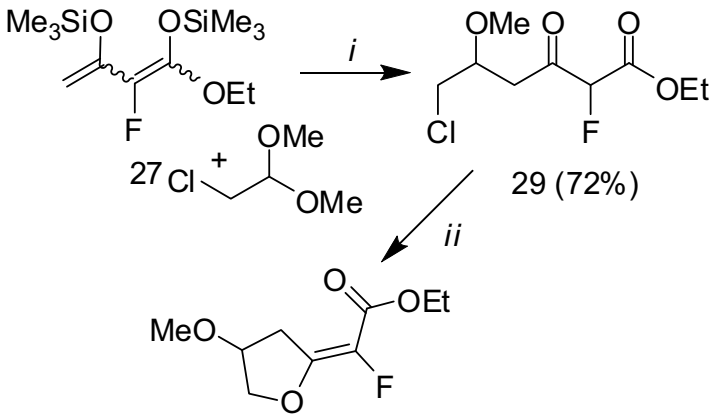
Scheme 13. Synthesis of diene **27**: *i*: Me_3SiCl, NEt_3, benzene, 20 °C, 48 h; *ii*: 1) LDA, THF, −78 °C, 1 h, 2) Me_3SiCl, −78 → 20 °C, 14 h.

The $TiCl_4$-mediated cyclization of **27** with epichlorohydrin, following our recently reported protocol,[54] afforded the halogenated 2-alkylidenetetrahydrofuran **28** (Scheme 14). The exocyclic double bond was formed with excellent *Z*-diastereoselectivity.



Scheme 14. Synthesis of 2-alkylidenetetrahydrofuran **28**: *i*: $TiCl_4$ (2.0 equiv.), CH_2Cl_2, −78 → 20 °C.

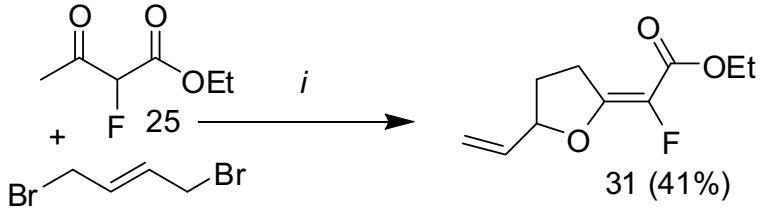
The Me_3SiOTf-catalyzed condensation of **27** with 1-chloro-2,2-dimethoxyethane gave the 2-fluoro-6-chloro-5-methoxy-3-oxo-hexanoate **29** (Scheme 15). The DBU-mediated cyclization[55] of **29** afforded the *E*-configured 4-methoxy-2-alkylidenetetrahydrofuran **30**.



30 (81%)

Scheme 15 Synthesis of **30**: *i*: Me_3SiOTf (0.5 equiv.), CH_2Cl_2, −78 → 20 °C; *ii*: 2.0 equiv. DBU, THF, 20 °C.

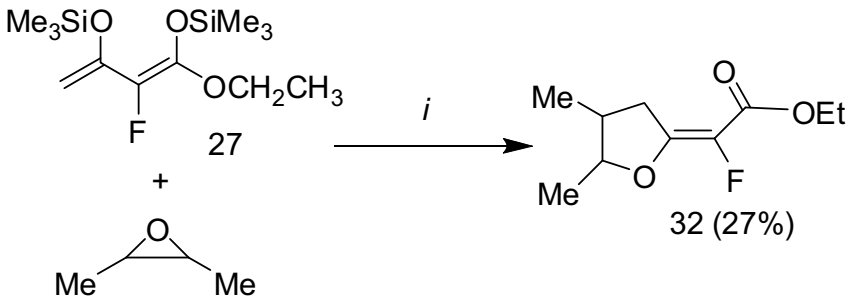
The treatment of **25** with trans-1, 4-dibromobutene gave Z-configured Ethyl 2-fluoro-2-(5-vinyldihydrofuran-2(3H)-ylidene)acetate **31** (Scheme 16)[56].



31 (41%)

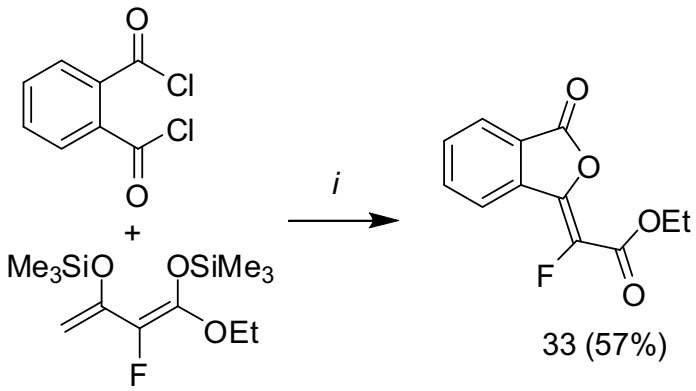
Scheme 16. Synthesis of **31**. *i*: LDA (2.5 Equiv.), THF, **25** (1 Equiv.), $BrCH_2CH=CHCH_2Br$ (1.2 Equiv.), −78 → 20 °C.

The reaction of 1-ethoxy-2-fluoro-1,3-bis(trimethylsilyloxy)-1,3-butadiene **(27)** with 2,3-butenoxide[57] afforded Z-configured **32** in good yield (Scheme17).



Scheme 17. Synthesis of **32**. (*i*) 27 (1 equiv.), 2,3-butenoxide (1 equiv.), $TiCl_4$ (2 equiv.), CH_2Cl_2, Molecular Sieves (4Å), -78ºC (5 h) - 20ºC (12 h).

The reaction of 1-ethoxy-2-fluoro-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**27**) with phthaloyl dichloride, following our recently reported protocol,[58] afforded product **33** (Scheme 18). The best yield was obtained in the presence of any Lewis acid ($TiCl_4$). An unexpected product was formed which was never observed from our previous studies. The structure of **33** was independently confirmed by X-ray crystal structure analysis (Figure 11).



Scheme 18. Synthesis of **33.** *i*: CH_2Cl_2, $TiCl_4$, -78→20°C, HCl (10%).

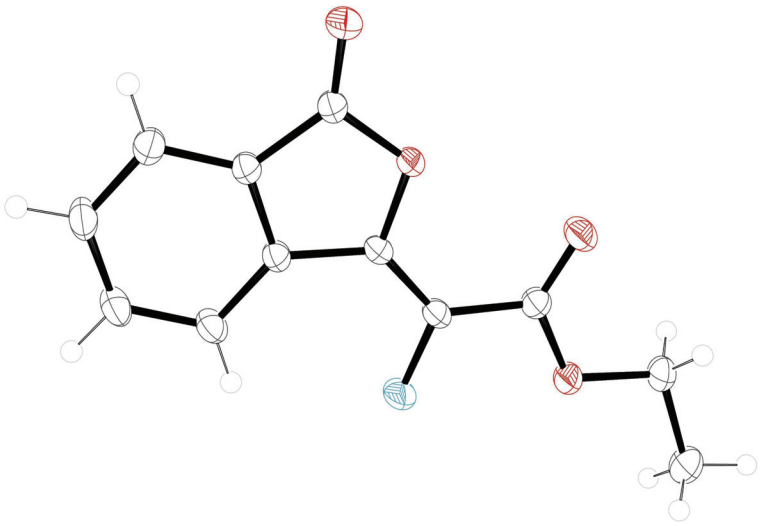
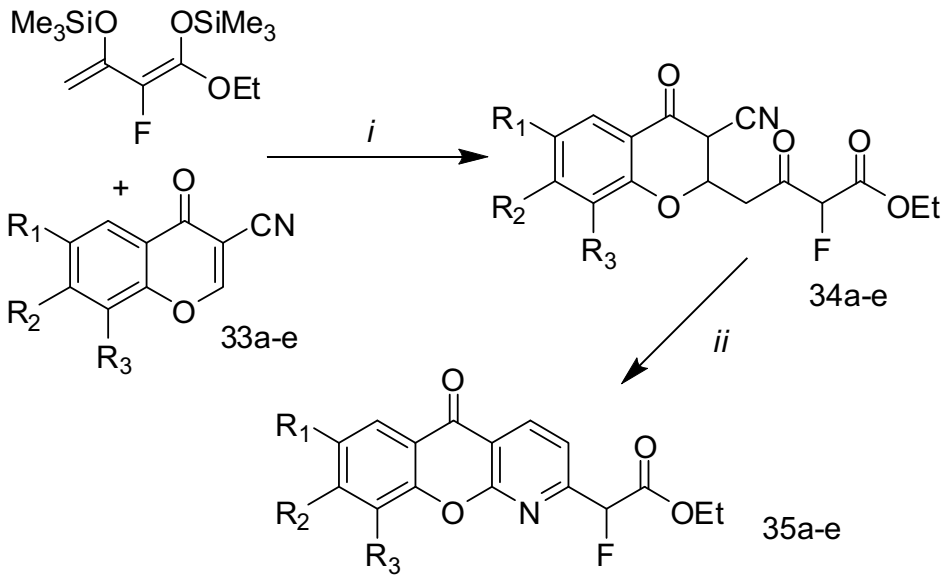


Figure 11: Crystal Structure of **33**

The Me_3SiOTf-mediated reaction of **27** with 3-cyanochromones (**33a-e**) gave condensation products **34a-e**. The latter was formed by regioselective attack of the terminal carbon atom of the diene onto C-2 of the cyanochromone and subsequent hydrolysis upon aqueous work-up. Treatment of an ethanol solution of crude **34a-e** with triethylamine afforded the novel fluorinated 1-azaxanthones **35a-e** (Scheme 19). These types of products are again not available by direct fluorination. The transformation of **33a-e** into **35a-e** can be explained by a domino 'retro-Michael / nitrile-addition / heterocyclization' reaction.[23]



Scheme 19. Synthesis of 1-azaxanthones **35a-e**: (i) (1) **33a-e**, Me_3SiOTf, 1 h, 20 °C, (2) **34a-e**, CH_2Cl_2, 0→20°C, 12 h, (3) HCl (10%); (ii) (1) NEt_3, EtOH, 20°C, 12 h, (2) HCl (10 %).

Table 7. Synthesis of 1-azaxanthones **35a-e.**

33, 34, 35(a-e)	R^1	R^2	R^3	35[a] (%)
a	H	H	H	56
b	Me	Me	H	46
c	Cl	H	H	41
d	Cl	H	Cl	35
e	F	H	H	33

[a] Yield of isolated products.

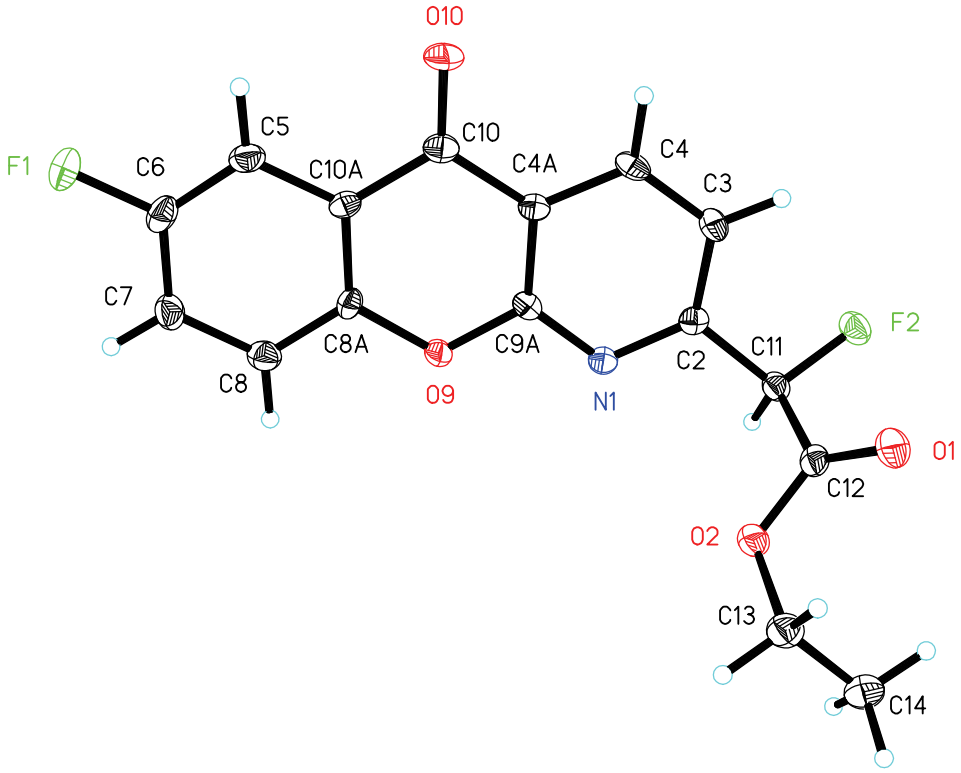
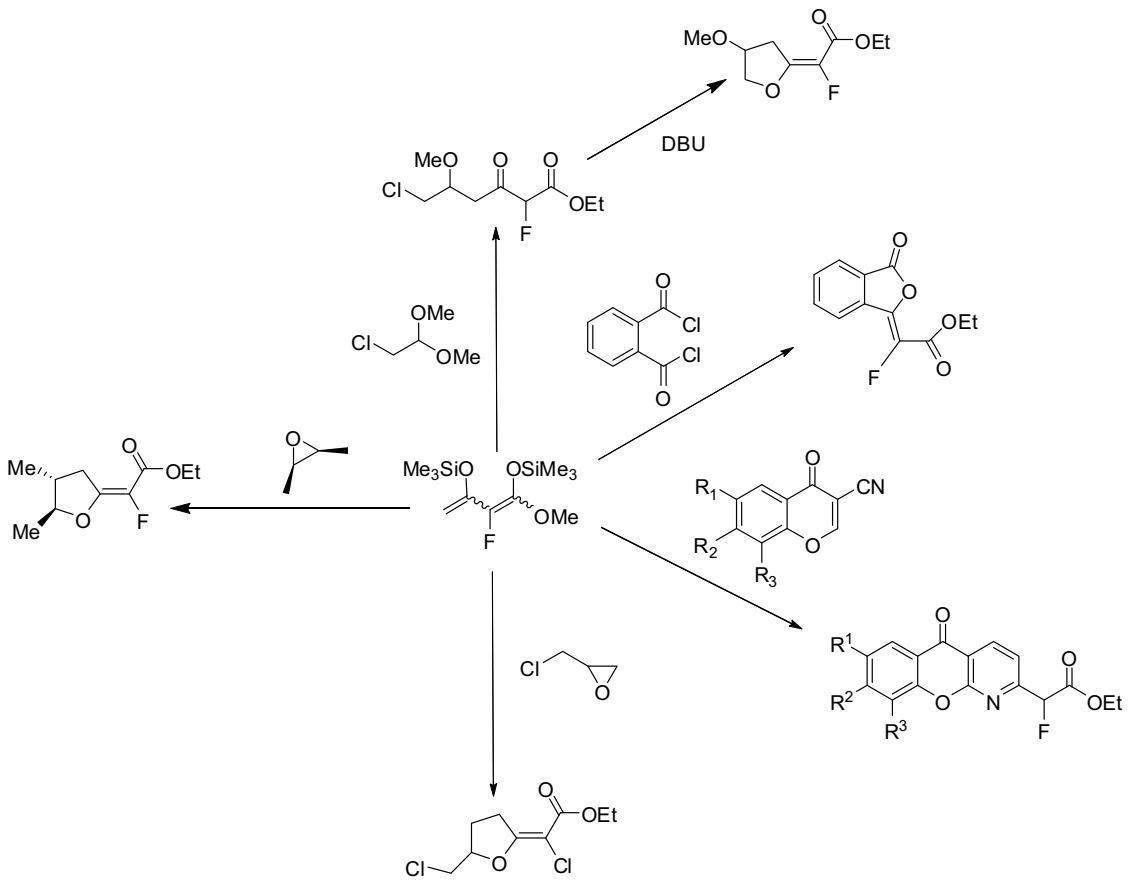


Figure 12: ORTEP-plot of 35e (50% level)

4.3 Conclusion:

In conclusion, we have reported a building block strategy for the synthesis of novel organofluorine compounds based on reactions of 2-fluoro-1,3-bis(trimethylsilyloxy)-1,3-butadienes – the first fluorinated 1,3-bis(silyl enol ethers). The products are not available by direct fluorination reactions.

4.4 Summary:



Scheme 20: Schematic Representation of 1-ethoxy-2-fluoro-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**27**).

5 Synthesis and Reactions of the First 2-Chloro-1,3-bis(trimethylsilyloxy)-1,3-butadienes:

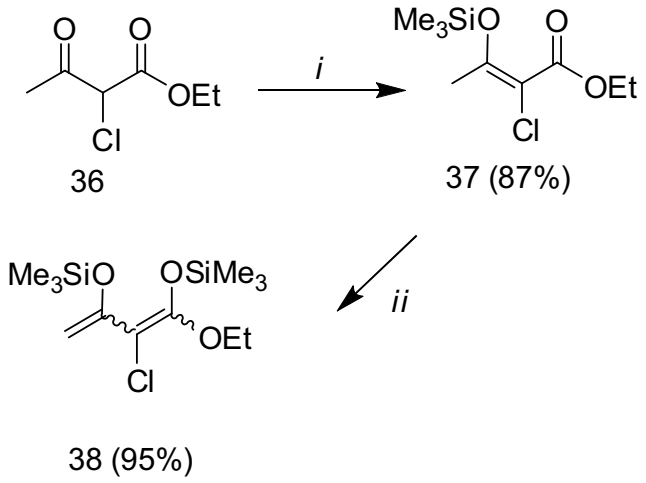
5.1 Introduction:

Chlorinated molecules are of considerable pharmacological relevance and occur in a number of natural products.[59] In fact, arenes and hetarenes containing a chloride group often show a better pharmacological activity compared to their non-halogenated analogues.[60] Chlorinated arenes and hetarenes also represent versatile building blocks in transition metal-catalyzed cross coupling reactions.[61] However, the direct chlorination of arenes, hetarenes and open-chained molecules often suffers from several drawbacks, such as low regioselectivity or multiple chlorination. An alternative strategy for the regioselective synthesis of organochlorine compounds relies on the use of appropriate chlorine-containing building blocks in condensation and cyclization reactions. For example, Manzanares and coworkers reported the synthesis of a 4-chlorophenol by [4+2] cycloaddition of a chlorinated thiophene with dimethyl acetylenedicarboxylate.[62]

1,3-Bis(trimethylsilyloxy)-1,3-butadienes (e. g. Chan's diene)[63,64] represent important synthetic building blocks which have been used in formal [3+2], [3+3], [4+2] and [4+3] cyclizations and other transformations.[65] Herein, we report what are, to the best of our knowledge, the first 2-chloro-1,3-bis(silyloxy)-1,3-butadienes.[66] Their reactions with various electrophiles provide a convenient and regioselective approach to a variety of organochlorine compounds which are not readily available by other methods.

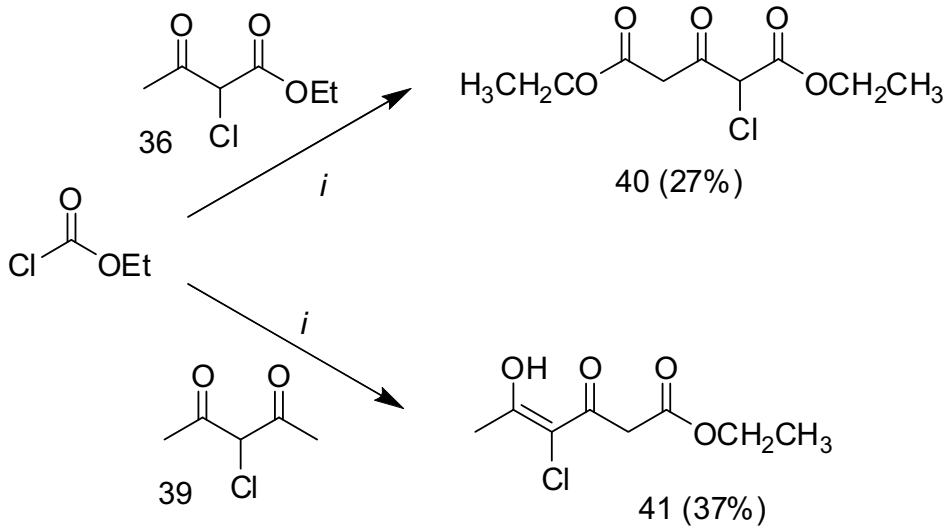
5.2 Results and Discussion:

The reaction of commercially available ethyl 2-chloroacetoacetate (**36**) with Me_3SiCl and triethylamine afforded the silyl enol ether **37** (Scheme 21). The novel 2-chloro-1-ethoxy-1,3-bis(silyloxy)-1,3-butadiene **38** were prepared by deprotonation (LDA) of **37** at −78°C and subsequent addition of trimethylchlorosilane. Noteworthy, the chloride group proved to be compatible with the reaction conditions.



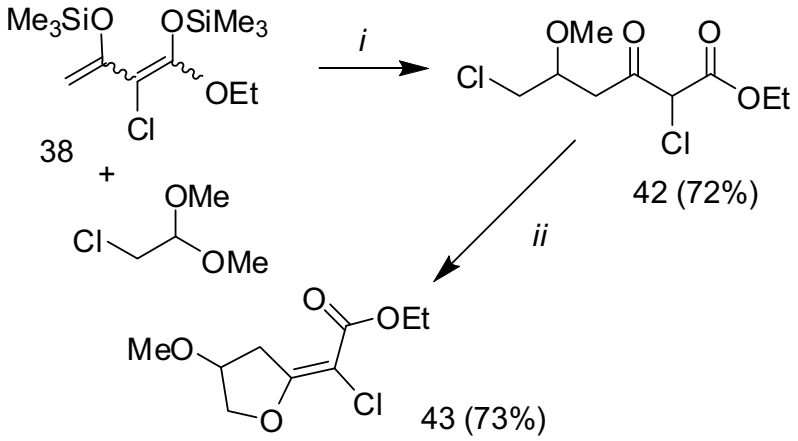
Scheme 21. Synthesis of dienes **36**: *i*: Me_3SiCl, NEt_3, benzene, 20 °C, 48 h; *ii*: 1) LDA, THF, −78, 1 h, 2) Me_3SiCl, −78 → 20 °C, 14 h.

Treatment of **36** and **39** with ethylchloroformate in LDA (2.2Eq) afforded novel tricarbonyl compounds **40** and **41** (Scheme22)[67]. Which can be further used to get variety of novel chlorinated compounds.



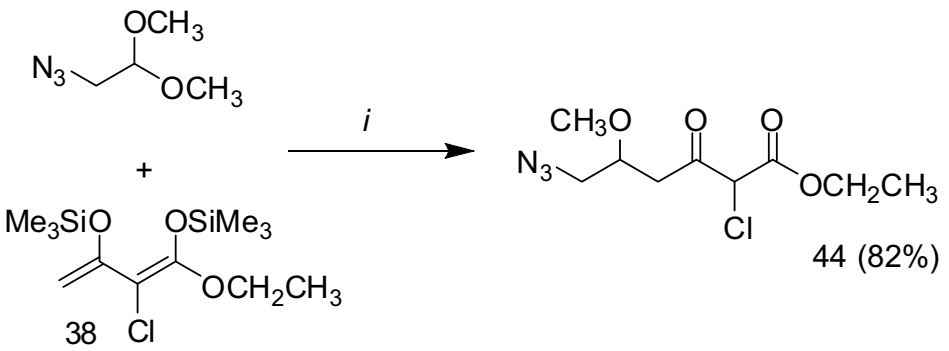
Scheme 22. Synthesis of **40** and **41**. i: **36, 39** (1 equiv.), LDA (2.2 Equvi), THF, Ethyl Chloroformate (1.1 Equiv.),−78 → 20°C, Acetic Acid.

The Me_3SiOTf-catalyzed condensation of **38** with 1-chloro-2,2-dimethoxyethane gave ethyl 2,6-dichloro-5-methoxy-3-oxohexanoate (**42**) in good yield (Scheme 23). The DBU-mediated cyclization[55] of **42** afforded the *Z*-configured 4-methoxy-2-alkylidenetetrahydrofuran **43**.



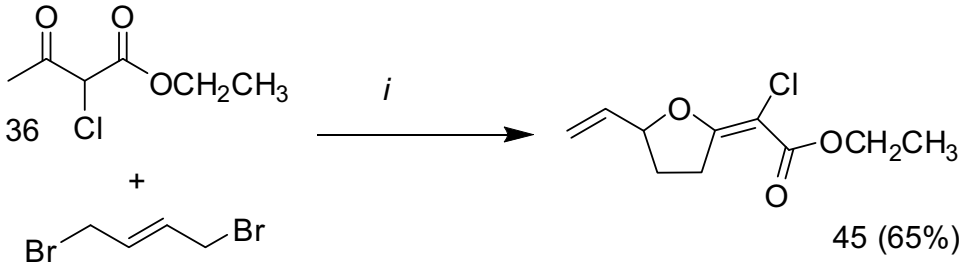
Scheme 23. Synthesis of furan **43**: *i*: **38** (1Equiv.)**,** Me_3SiOTf (0.5 equiv.), 1-Chloro-2,2-dimethoxy ethane (1 Equiv.). CH_2Cl_2, −78 → 20 °C; *ii*: **42** DBU, (2.0 equiv). THF, 20 °C.

The Me_3SiOTf-mediated reaction of 1-ethoxy-2-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**38**) with 1-azido-2,2-dimehtoxy ethane afforded the desired condensation product[68] (44) with good regio- and chemoselectivity (Scheme 24). Several attempts to get the cyclized pyrolidene derivative by treatment of a THF solution of **44** at 45°C with PPh_3 were not successful.



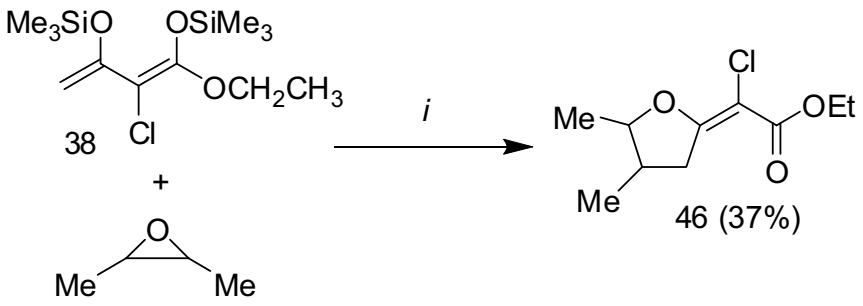
Scheme 24. Synthesis of **13**: *i*: Me_3SiOTf (0.5 equiv.), CH_2Cl_2, −78 → 20 °C.

The treatment of **36** with trans-1, 4-dibromobutene gave Z-configured Ethyl 2-chloro-2-(5-vinyldihydrofuran-2(3H)-ylidene)acetate **45** (Scheme 25)[56].



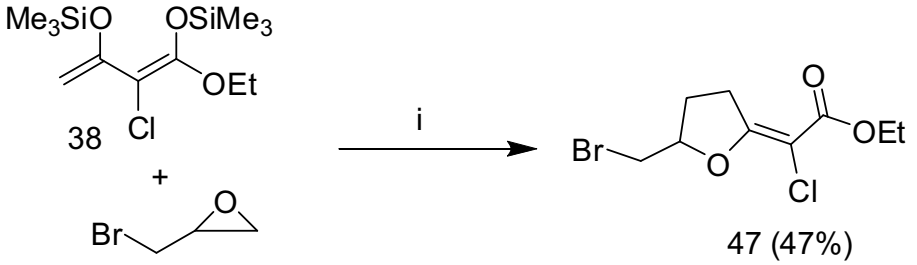
Scheme 25. Synthesis of **45**: *i*: LDA (2.5 Equiv.), THF, **36** (1 Equiv.), $BrCH_2CH_2$=CH_2CH_2Br (1.2 Equiv.), −78 → 20 °C.

The reaction of 1-ethoxy-2-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**38**) with 2,3-butenoxide[57] afforded Z-configured **46** in good yield (Scheme 26).



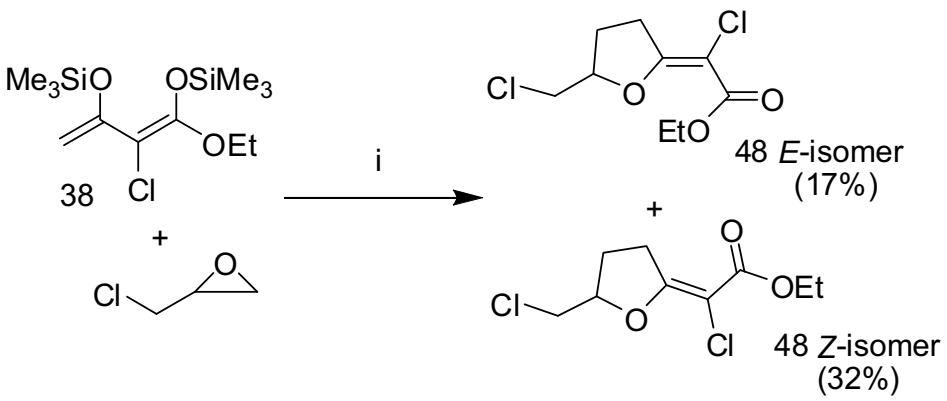
Scheme 26. Synthesis of **46**. (i) **38** (1 equiv.), 2,3-butenoxide (1 equiv.), $TiCl_4$ (2 equiv.), CH_2Cl_2, Molecular Sieves (4Å), -78ºC (5 h) - 20ºC (12 h).

The $TiCl_4$-mediated cyclization of **38** with epibromohydrin, following our recently reported protocol,[54] afforded the halogenated 2-alkylidenetetrahydrofuran **47** (Scheme 27). The exocyclic double bond was again formed with excellent *Z*-diastereoselectivity.



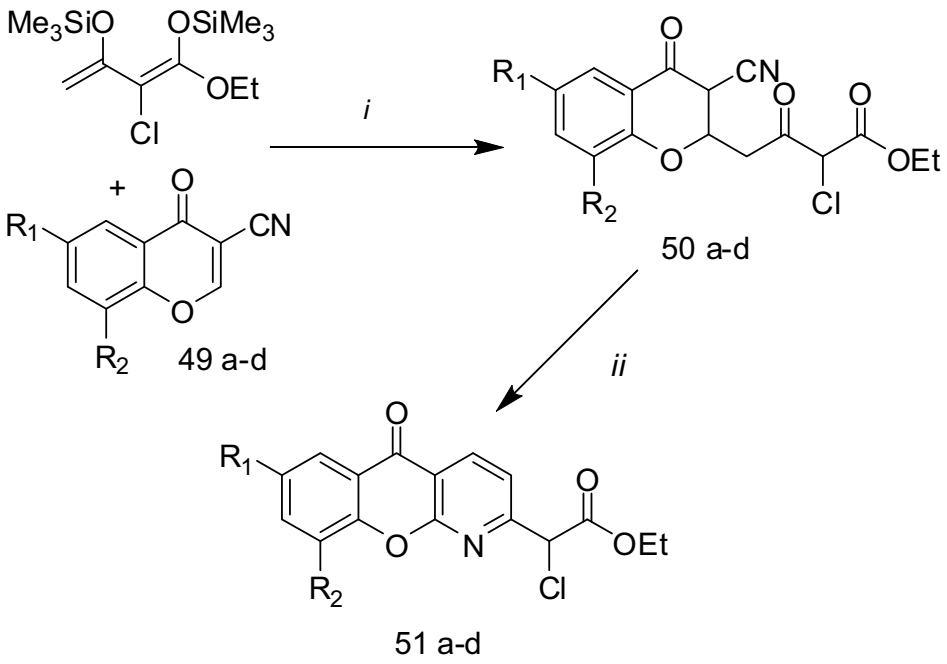
Scheme 27. Synthesis of **47**. (i) 3b (1 equiv.), Epibromohyrin (1 equiv.), $TiCl_4$ (2 equiv.), CH_2Cl_2, Molecular Sieves (4Å), -78ºC (5 h) - 20ºC (12 h).

The $TiCl_4$-mediated cyclization of **38** with epichlrohydrin, following our recently reported protocol,[54] afforded the halogenated 2-alkylidenetetrahydrofuran **48** (Scheme 28). The exocyclic double bond was again formed with excellent *Z*-and *E*-diastereoselectivity. The configuration of **48** *E* and *Z* isomers was confirmed by 2D-NMR studies.



Scheme 28. Synthesis of **48** *E* and *Z*. (i) **38** (1 equiv.), Epichlorohydrin (1 equiv.), $TiCl_4$ (2 equiv.), CH_2Cl_2, Molecular Sieves (4Å), -78ºC (5 h) - 20ºC (12 h).

The Me_3SiOTf-mediated reaction of **38** with 3-cyanochromones (**49a-d**) gave condensation products **50a-d**. The latter was formed by regioselective attack of the terminal carbon atom of the diene onto C-2 of the cyanochromone and subsequent hydrolysis upon aqueous work-up. Treatment of an ethanol solution of crude **49a-d** with triethylamine afforded the novel fluorinated 1-azaxanthones **51a-d** (Scheme 29). These types of products are again not available by direct fluorination. The transformation of **49a-d** into **51a-d** can be explained by a domino 'retro-Michael / nitrile-addition / heterocyclization' reaction.[23]



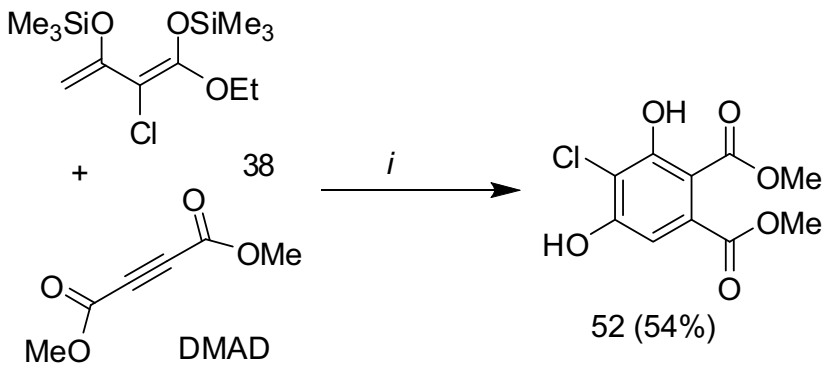
Scheme 29. Synthesis of 1-azaxanthones **51a-d:** (i) (1) **49a-d,** Me_3SiOTf, 1 h, 20 °C, (2) **38**, CH_2Cl_2, 0→20°C, 12 h, (3) HCl (10%); (ii) **50a-d**: NEt_3, EtOH, 20°C, 12 h, (2) HCl (10 %).

Table 8. Synthesis of 1-azaxanthones **51a-d.**

49,50,51a-d	R^1	R^2	51[a] (%)
a	H	H	58
b	Cl	H	60
c	F	H	60
d	Cl	Cl	39

[a] Yield of isolated products.

The solvent free reaction of **38** with **DMAD** at -78°C afforded highly functionalized chlorinated arene **52** in good yield and its structure was independently confirmed by X-ray crystal analysis. **52** will be used for further studies.



Scheme 30. Synthesis of **52** *i*: **38** (1 equiv.), DMAD (1.5 Equiv.), −78 → 20 °C (20h), HCl (10%).

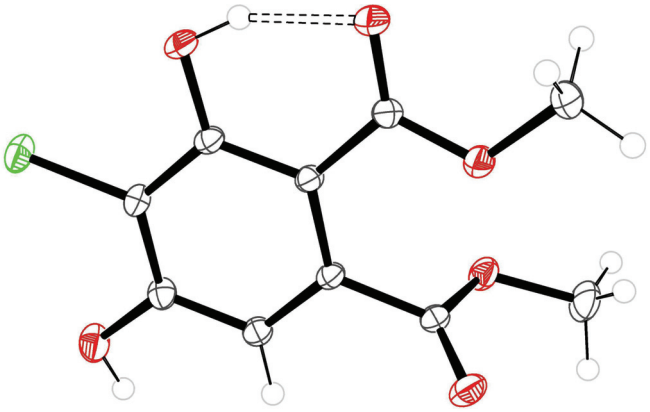
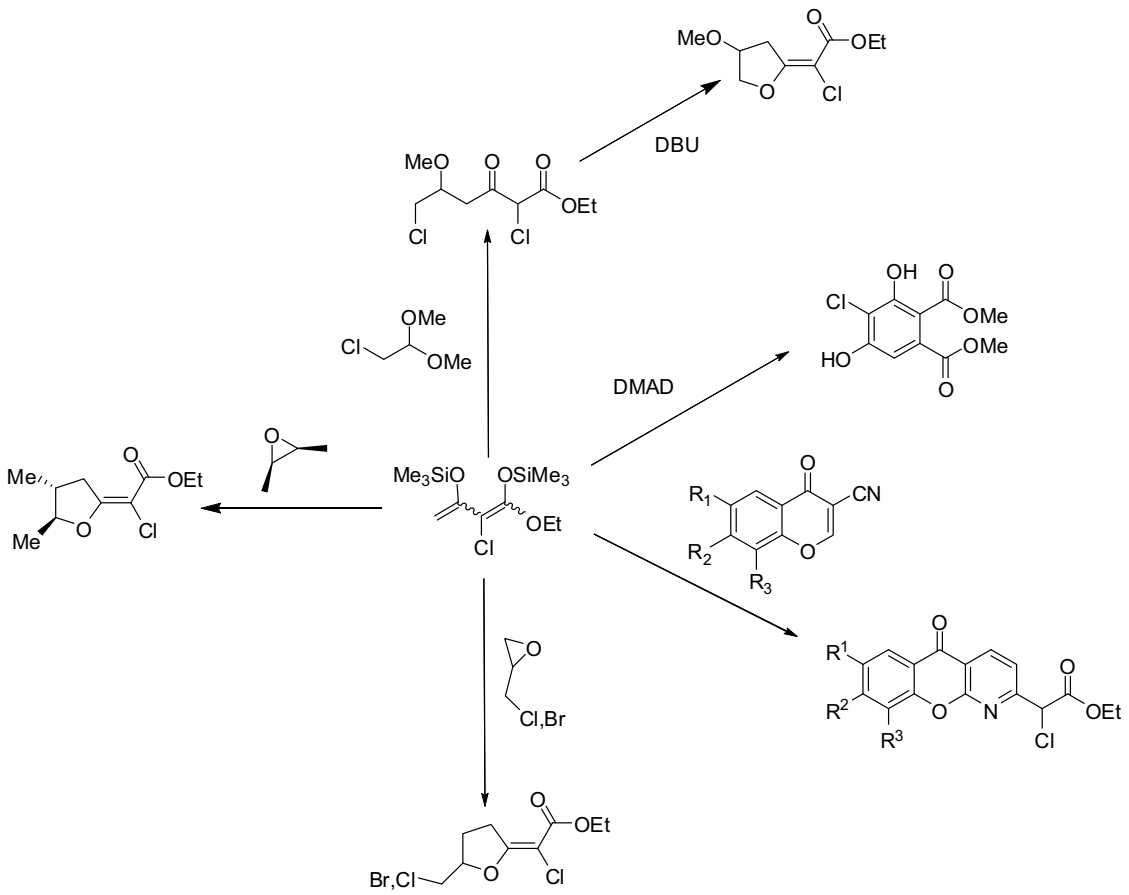


Figure 13: Crystal Structure of **52**

5.3 Conclusion:

In conclusion, we reported a building block strategy for the regioselective synthesis of a variety of chlorinated carba- and heterocycles and of chlorinated dicarbonyl compounds. Novel 2-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadienes were prepared and reacted with various electrophiles. The products are not available by direct chlorination reactions.

5.4 Summary:



Scheme 31: Schematic representation for reactions 1-ethoxy-2-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**38**).

6. Synthesis of Chlorinated Arenes and Hetarenes based on One-Pot Cyclocondensations of 1-Alkoxy-4-chloro-1,3-bis(trimethylsilyloxy) -1,3-butadienes.

6.1 Introduction:

Functionalized chloroarenes are of considerable pharmacological relevance[69] and represent increasingly important building blocks for transition metal-catalyzed cross-coupling reactions.[70] 3-Chlorosalicylates and related compounds are present in a variety of natural products. This includes, for example, dihydronidulin.[71] The spirocyclic griseofulvin[72] and epigriseofulvin[73] have been reported to show clastogenic, cytotoxic and antifungal activity. Polyketide-derived xanthones,[74] geodin[75] and geodinhydrate-methyl ester[76] show, for example, antibacterial and antifungal activity. 7-Chlor-1-*O*-methylemodin has been reported to exhibit antiviral activity.[77] 3-Chlorosalicylates and related compounds are also present in simple arenes, acetophenones (longissiminone B), benzophenones (chloroisosulochrin, pestalone) and diaryl ethers (methyl chloroasterrate),[78] falconensin B,[79] natural chromones,[80] and in 7-chloro-8-hydroxy-6-methoxy-3-methyl-isochroman-1-one.[81]

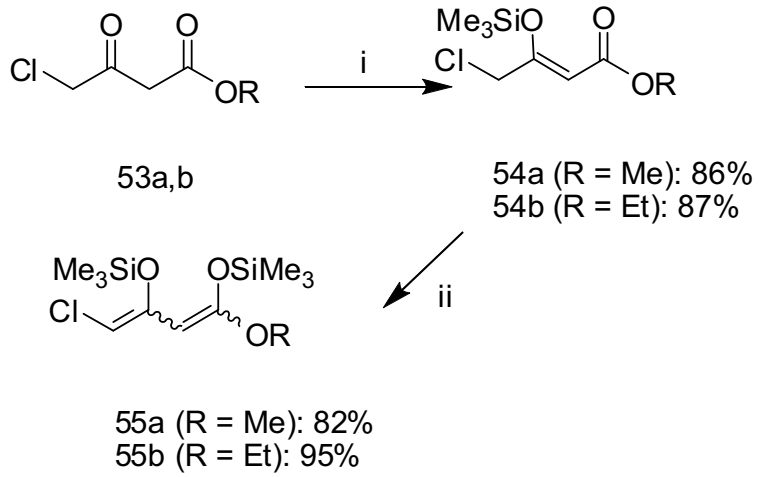
1,3-Bis(trimethylsilyloxy)-1,3-butadienes (e. g. Chan's diene)[82] represent important synthetic building blocks which have been used in formal [3+2], [3+3], [4+2] and [4+3] cyclizations and various other transformations.[83,84] We have recently reported the synthesis of 4-chlorophenols by cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 2-chloro-3-silyloxy-2-en-1-ones[85] and the synthesis of chlorinated hetero- and carbacycles by cyclization reactions of 2-chloro-1,3-bis(silyloxy)-1,3-butadienes.[86] Recently, we have reported[87] the synthesis of 4-chloro-1,3-bis(silyloxy)-1,3-butadienes and their application to the synthesis of chlorinated arenes and hetarenes. Herein, we report full details of these studies and studies related to the scope and limitations.

The one-pot cyclizations reported herein provide a convenient and regioselective approach to various sterically encumbered, heavily substituted chlorinated products which are not readily available by other methods. Classic syntheses of chloroarenes, based on direct chlorinations, suffer from many drawbacks, such as low regioselectivities

and yields. In addition, the synthesis of the required starting materials, highly substituted and functionalized arenes, can be a difficult and tedious task

6.2 Results and Discussion:

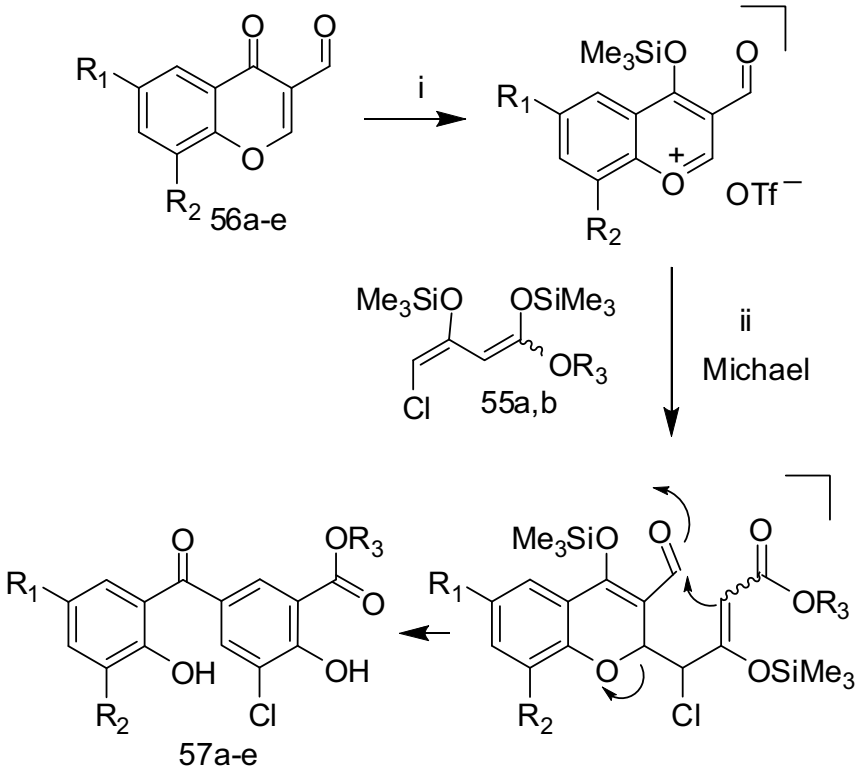
The silylation of commercially available ethyl and methyl 4-chloroacetoacetate **(53a,b)** gave 3-silyloxy-2-en-1-one **54a,b** (Scheme 32). 4-Chloro-1-alkoxy-1,3-bis(silyloxy)-1,3-butadiene **(55a,b)** were prepared by the deprotonation (LDA) of **54** at -78°C and subsequent addition of trimethylchlorosilane. Noteworthy, the chloro group proved to be compatible with the reaction conditions. Diene **55a,b** can be stored at -20°C under inert atmosphere for several weeks.



Scheme 32. Synthesis of dienes **55a, b**: *i*: Me_3SiCl, NEt_3, benzene, 20 °C, 48 h; *ii*: 1) LDA, THF, −78, 1 h, 2) Me_3SiCl, −78 → 20 °C, 14 h.

The Me_3SiOTf-catalyzed reaction of 1,3-bis(silyloxy)-1,3-dienes **55a,b** with 3-formylchromones **57 a-e** afforded the chlorinated 2,4'-dihydroxybenzophenones **57a-e** in good yields (Scheme 32, Table 9). The products are formed by a domino ′Michael–retro-Michael–Mukaiyama-Aldol′ reaction.[88]

The structures of all products were confirmed by spectroscopic studies. The structure of **57a** was independently confirmed by X-ray crystal structure analysis (Figure 14).



Scheme 32. Synthesis of **57a-e**. Reagents and conditions: (i) **56a-e**, Me_3SiOTf (0.3 equiv), 20 °C, 10 min; (ii) (1) **55a, b** (1.3 equiv), CH_2Cl_2, 0→20 °C, 12 h; (2) HCl (10%).

Table 9. Synthesis of 3-chlorosalicylates **57a-e**

56,57	R^1	R^2	R^3	% (**57**)[a]
a	H	H	OEt	42
b	Me	H	OEt	40
c	NO_2	H	OEt	40
d	Br	H	OEt	36
e	Cl	H	OEt	36[b]

[a] Yields of isolated products.

b From Stefanie Reim

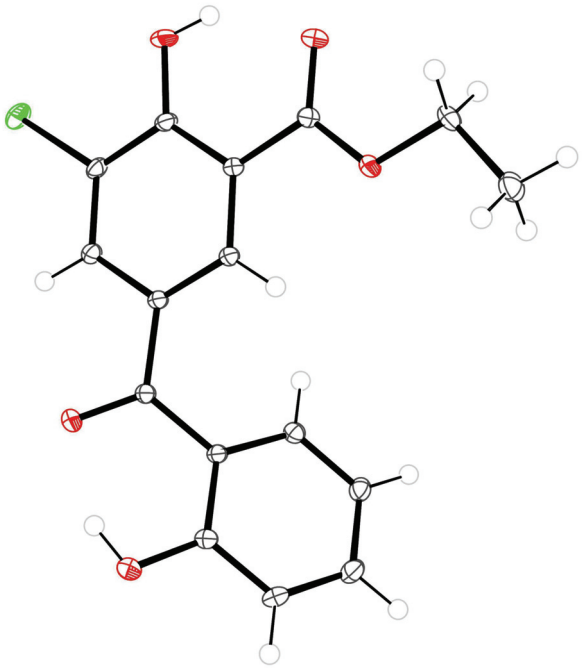
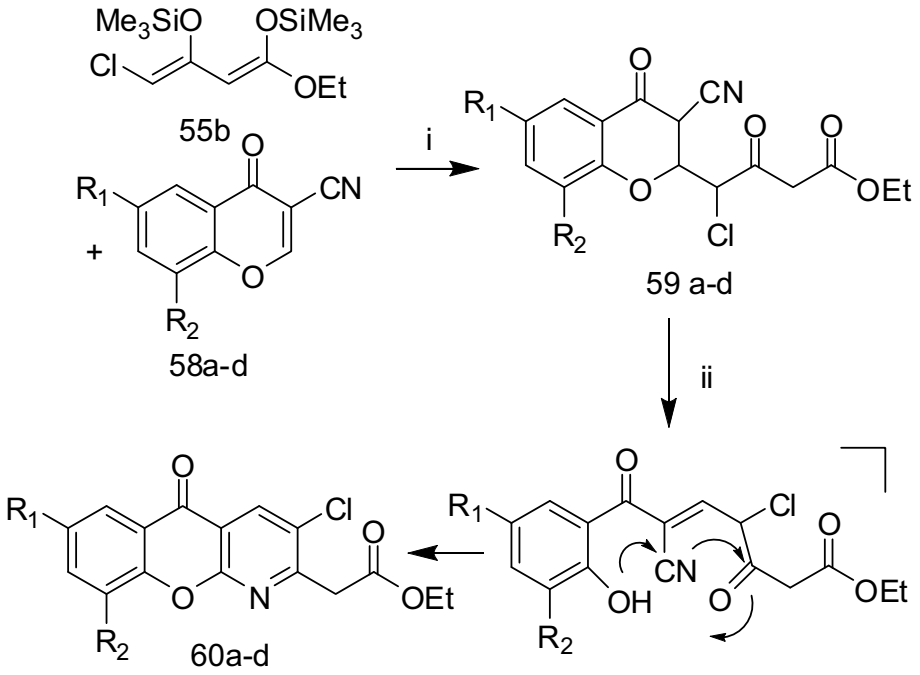


Figure 14. Ortep plot of **57a** (50% probability level)

The Me_3SiOTf-catalyzed reaction of 1,3-bis(silyloxy)-1,3-diene **55b** with 3-cyanochromones **58a-d** afforded products **59a-d** which were transformed, by treatment with triethylamine, into the chlorinated azaxanthones **60a-d** (Scheme 33, Table 10). The formation of the products can be explained that products are formed by a domino ′Retro-Michael / nitrile-addition / heterocyclization′ reaction.[89] The structure of **60c** was independently confirmed by X-ray crystal structure analysis (Figure 15).



Scheme 33. Synthesis of 1-azaxanthones **60a–d**: (i) (1) **58a–d**, Me_3SiOTf, 1 h, 20 °C, (2) **59a–d**, CH_2Cl_2, 0 → 20°C, 12 h, (3) HCl (10%); (ii) (1) NEt_3, EtOH, 20°C, 12 h, (2) HCl (10 %).

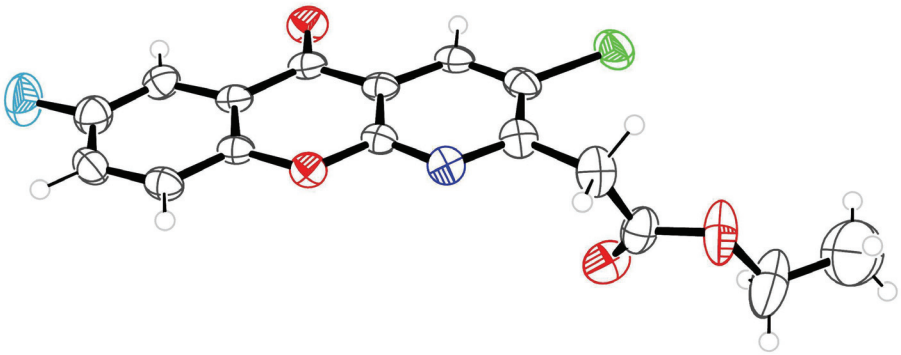


Figure 15. Ortep plot of **60c** (50% probability level)

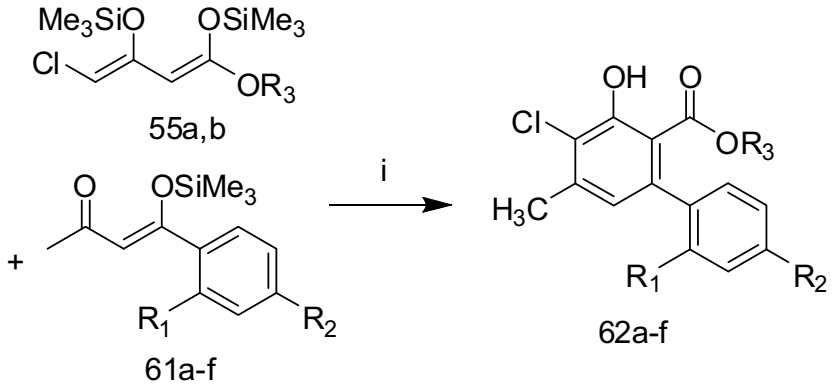
Table 10. Synthesis of 1-azaxanthones **60a–d**

58,59,60	R^1	R^2	% (**60**)[a]
a	H	H	58
b	Me	Me	34
c	F	H	37
d	Cl	H	40

[a] Yields of isolated products (from **58**)

The $TiCl_4$-mediated [3+3] cyclization of 4-chloro-1,3-bis(silyloxy)-1,3-dienes **55a,b** with 3-aryl-3-silyloxy-2-en-1-ones **61a-e**, prepared by silylation of the corresponding benzoylacetones, afforded the chlorinated biaryls **62a-e** (Scheme 34, Table 11). During the optimization, it proved to be important to carry out the reactions in a highly concentrated solution. All products were formed with very good regioselectivity which can be explained, following a mechanism first suggested by Chan *et al.*,[82a, 84] by $TiCl_4$-mediated isomerization of **61a-e**, conjugate addition by attack of carbon atom C-4 of **55** onto **61** and subsequent cyclization.

The structures of all products were confirmed by spectroscopic studies. The structures of **62b**, **62c**, **62d,** and **62f** were independently confirmed by X-ray crystal structure analysis (Figures 16-19).



Scheme 34. Synthesis of **62a–f**. Reagents and conditions: (i) $TiCl_4$, CH_2Cl_2, -78º→ 20ºC, 20 h.

Table 11. Synthesis of 4-chlorobiphenyls **62a-f**

61,62	R^1	R^2	R^3	% (**62**)[a]
a	H	H	Me	42
b	H	H	Et	41
c	H	F	Et	48
d	Cl	H	Et	50
e	Me	H	Et	40
f	F	H	Et	45

[a] Yields of isolated products.

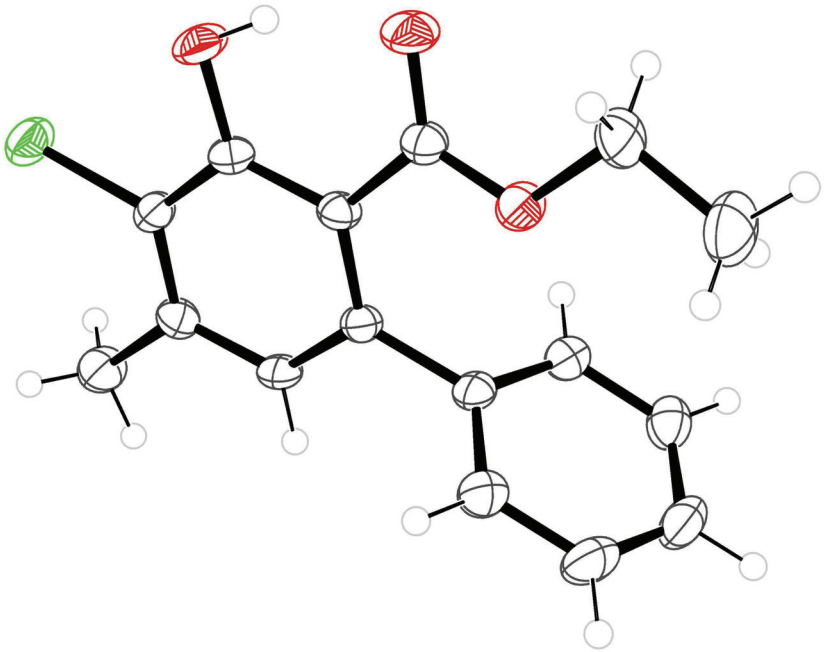


Figure 16. Ortep plot of **62b** (50% probability level)

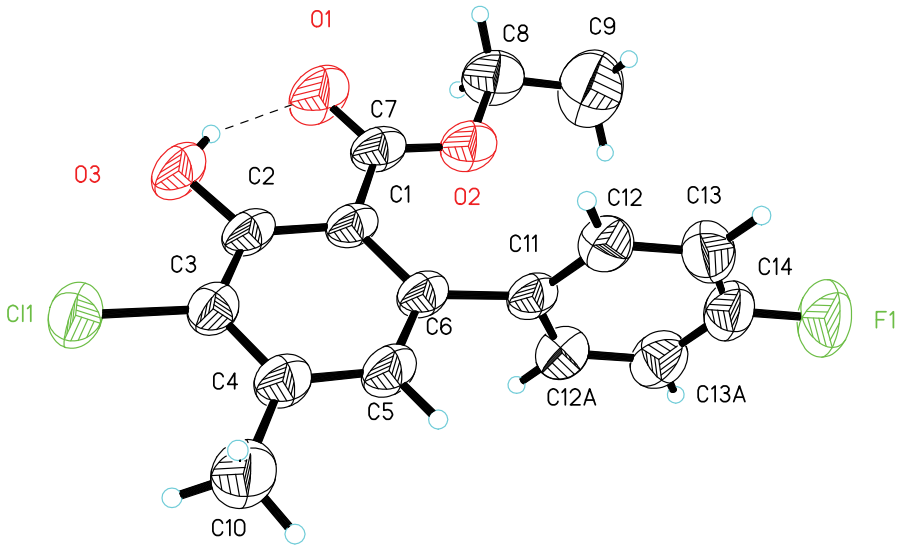


Figure 17. Ortep plot of **62c** (50% probability level)

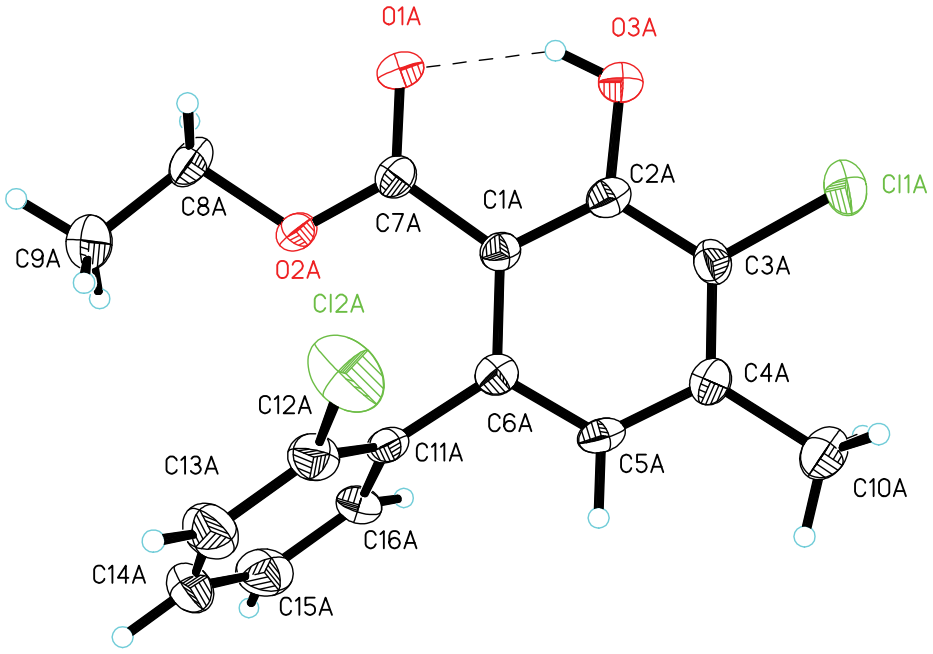


Figure 18. Ortep plot of **62d** (50% probability level)

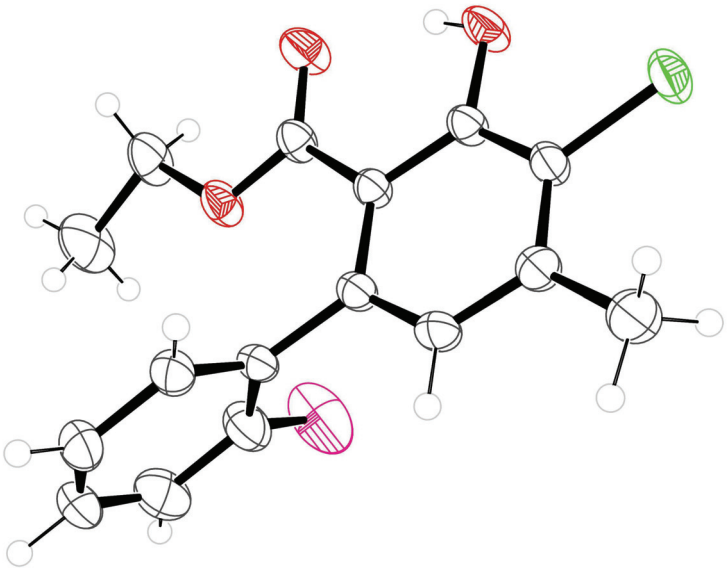
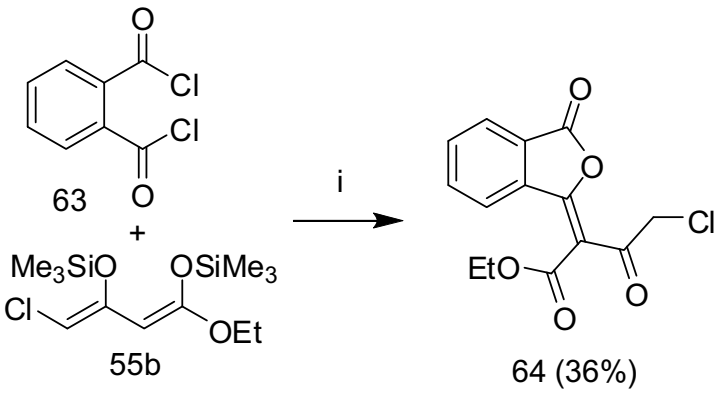


Figure 19. Ortep plot of **62f** (50% probability level)

The reaction of 4-chloro-1,3-bis(silyloxy)-1,3-diene **55b** with phthaloyl dichloride (**63**), following our recently reported protocol,[90] afforded product **64** (Scheme 35). The best yield was obtained in the absence of any Lewis acid. Unexpectedly, the regioisomer derived from attack of the central, rather than the terminal carbon atom of the diene onto **63** was formed. In our previous studies,[90] we have observed this irregular reaction pattern for 1,3-diketone-derived 1,3-bis(silyloxy)-1,3-butadienes. For β-ketoester-derived dienes, those regioisomers derived from attack of the terminal carbon atom onto **63** was usually observed.

The structure of **64** was independently confirmed by X-ray crystal structure analysis (Figure 20).



Scheme 35. Synthesis of **64.** *i*: CH_2Cl_2, -78→20°C.

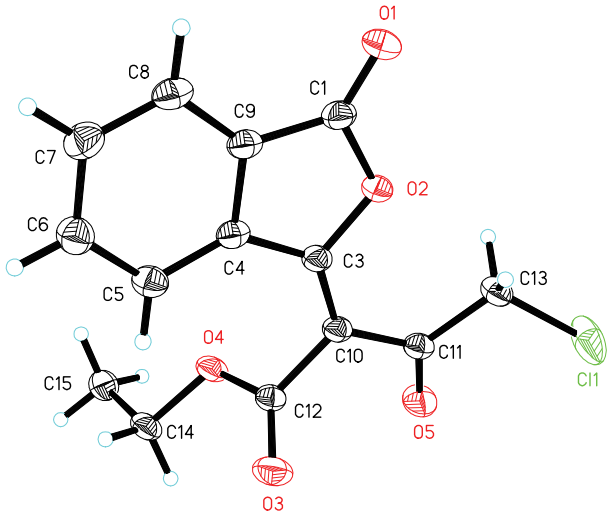
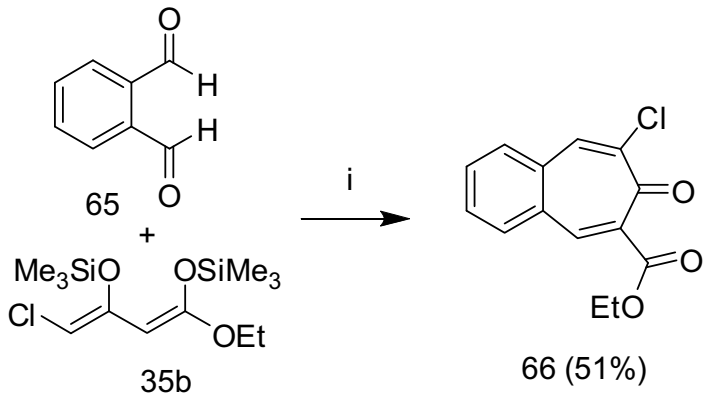


Figure 20. Ortep plot of **64** (50% probability level)

The $TiCl_4$-mediated cyclization of 4-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadiene **55b** with phthalic aldehyde (**65**), following our recently reported procedure,[91] afforded the chlorinated benzotropone **66** (Scheme 36). The structure of **66** was independently confirmed by X-ray crystal structure analysis (Figure 21).



Scheme 36. Synthesis of benzotropone **66**, *i*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C.

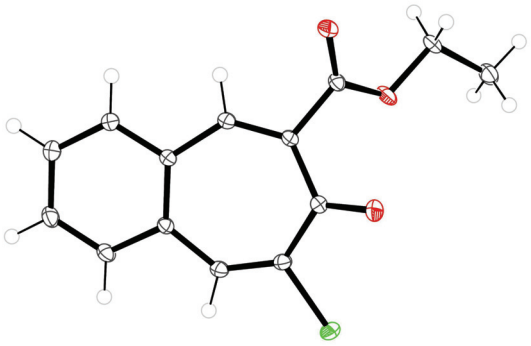
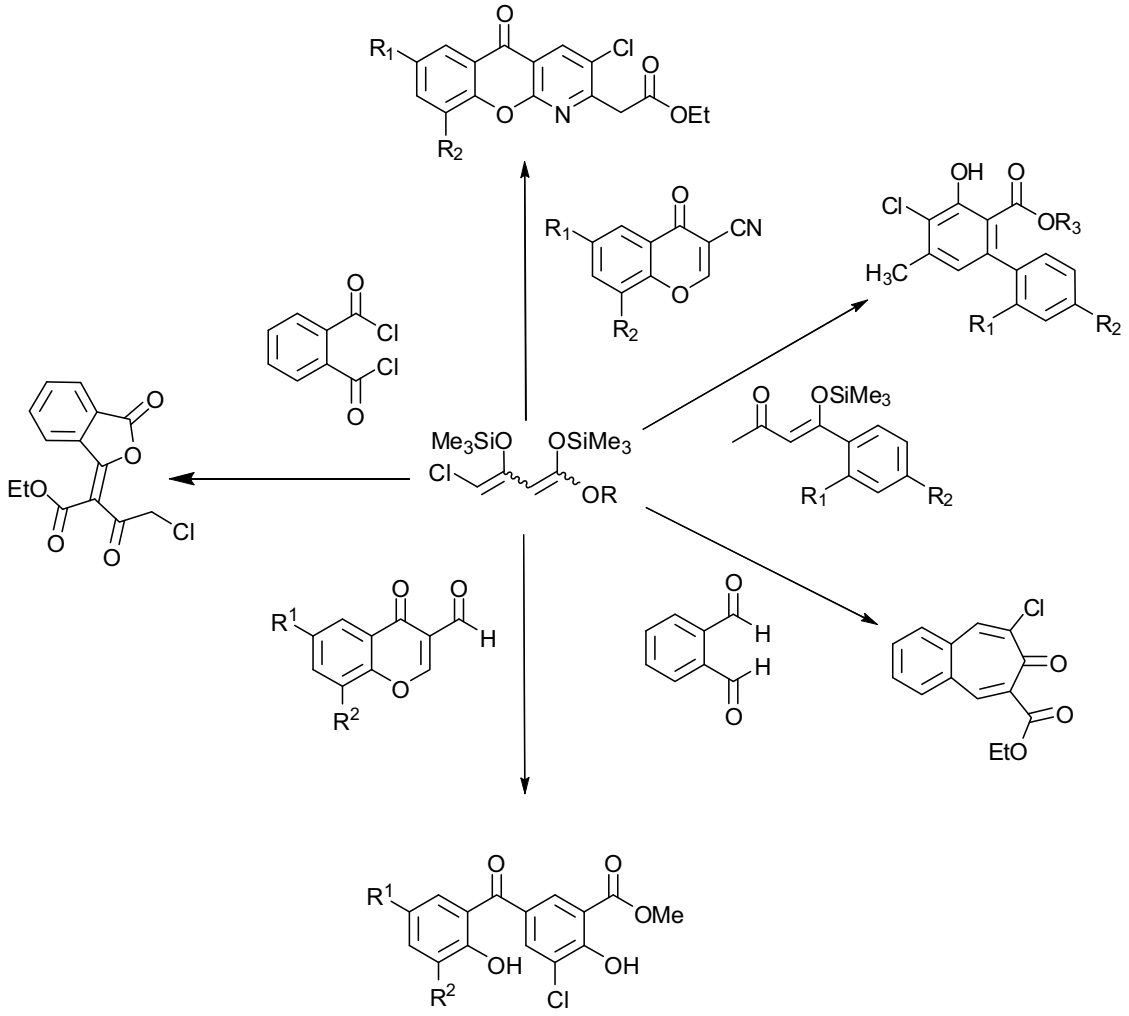


Figure 21. Ortep plot of **66** (50% probability level)

6.3 Conclusion:

In conclusion, a variety of highly substituted chlorinated arenes and hetarenes were regioselectively prepared by one-pot cyclizations of 4-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadienes with various dielectrophiles. The products are not readily available by other methods.

6.4 Summary:



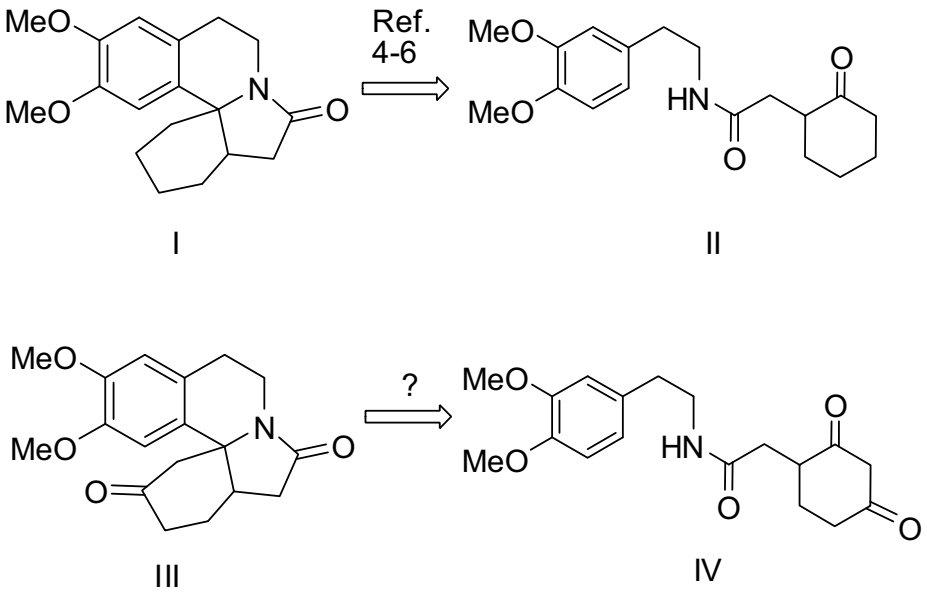
Scheme 37: Schematic representation of reaction of 4-Chloro-1-alkoxy-1,3-bis(silyloxy)-1,3-butadiene (**55a,b**).

7. Synthesis of 2,6-Dioxo-1,2,3,4,5,6-hexahydroindoles by Acid-Catalyzed Cyclization of Acetal-Protected (2,4-Dioxocyclohex-1-yl)acetamides and their Transformation into 5,8,9,10-Tetrahydro-6H-indolo[2,1-a] isoquinolin -9- ones.

7.1 Introduction

E*rythrina* alkaloids occur in various tropical and subtropical plants[92] and show a wide range of interesting biological properties.[93] This includes, for example, curare-like, hypotensive, sedative, anticonvulsive, and CNS-depressive activity.[94] *Erythrina* alkaloids have been prepared, for example, using photochemical [2+2] cycloadditions or Diels-Alder reactions as the key steps.[95] An important strategy for the synthesis of *erythrina* alkaloids relies on the acid-mediated domino reaction of (2-oxocyclohex-1-yl)acetic amides.[95-97] This transformation proceeds by acid-mediated cyclization of the amide to give a *N*-(2-arylethyl)-2-oxo-1,2,3,4,5,6-hexahydroindole which is transformed in situ into the *erythrina*-type spirocyclic product by a Pictet-Spengler reaction. For example, spirocycle **I** has been directly prepared from the amide **II** under various conditions (Scheme xxx). However, the preparative scope of this reaction is very narrow and its success strongly depends on the structure of the substrate (substitution pattern of the aryl group, length of the linker between the aryl group and the nitrogen atom etc.). This is a severe limitation because the synthesis of specific target molecules heavily relies on functional group transformations of the spiro-compounds obtained by the domino process.

To address this problem, we planned to prepare the unknown *erythrina* derivative **III**, which contains an additional carbonyl group, from the corresponding amide **IV** (Scheme 38). The carbonyl group of **III** was expected to be a useful tool for the synthesis of *erythrina*-type natural products and their non-natural analogues. It was planned to prepare the required starting material **IV** from (2,4-dioxocyclohex-1-yl)acetic acid which, therefore, represents an important key intermediate of the present study.



Scheme 38. Strategy for the synthesis of the novel *erythrina*-type spiro-compound **III** containing an additional carbonyl group

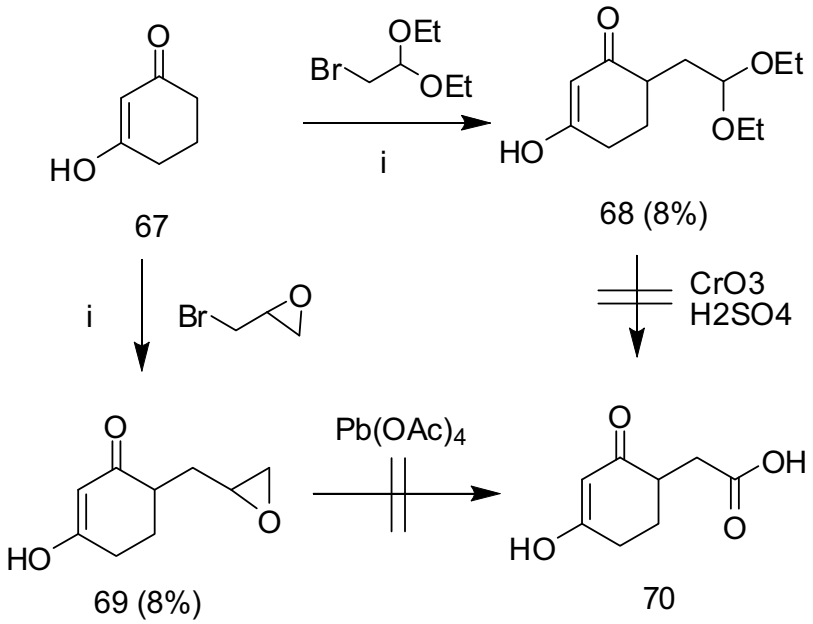
Recently, we have reported[98] our preliminary results related to the synthesis of (2,4-dioxocyclohex-1-yl)acetic amides, such as **IV**. Their reaction with *para*-toluenesulfonic acid (PTSA) resulted in the formation of 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles rather than the expected *erythrina*-type spiro-compounds. Herein, we report a full account of the preparative scope of this methodology which provides, to the best of our knowledge, the yet most general approach to 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles.[99] In addition, we report for the first time the reaction of 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles with triflic acid which results in the formation of novel 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-9-ones.

7.2 Results and Discussion

The synthesis of (2,4-dioxocyclohex-1-yl)acetic acid (**70**) has, to the best of our knowledge, not been reported to date. The synthesis of **70** proved to be very difficult in our hands, despite its structural simplicity. The reaction of the dianion[100,101] of cyclohexane-1,3-dione (**67**) with 1-bromo-2,2-diethoxyethane and epibromohydrin afforded products **68** and **69**, respectively (Scheme 39). The low yield of **68** and **69** can

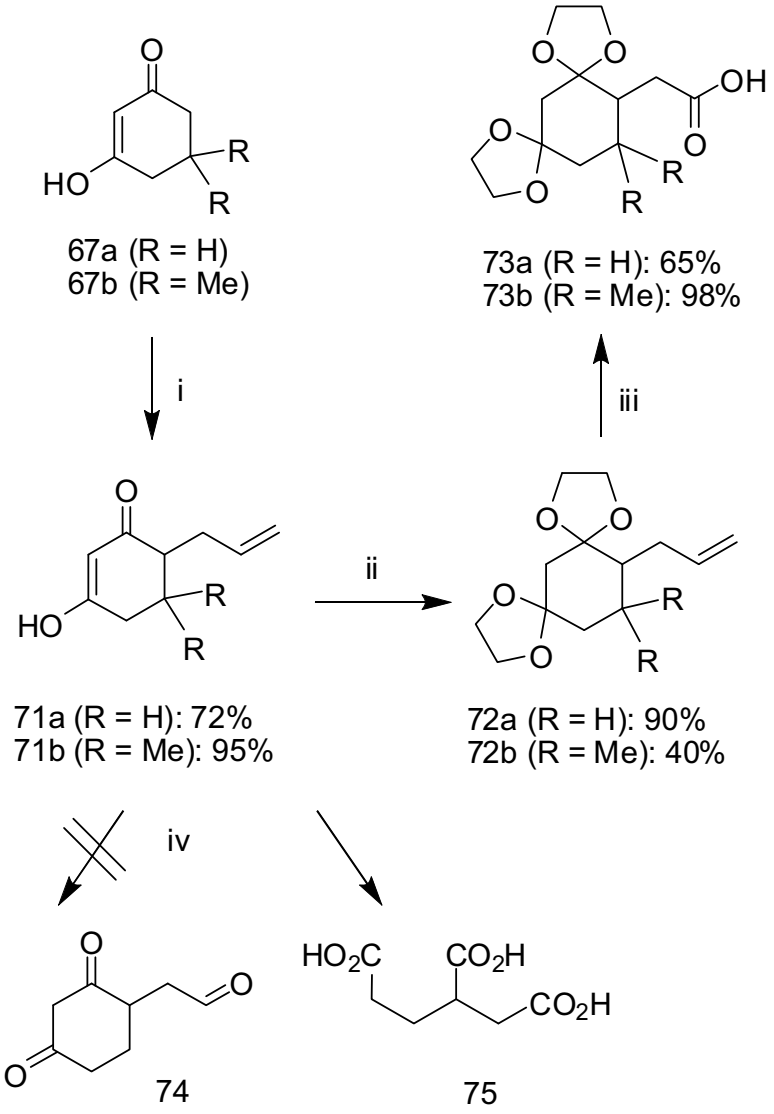
be explained by the β-oxygen effect. However, all attempts to prepare **70** by oxidation of **68** and **69** failed.

Deslongchamps and Guay reported the synthesis of 4-(3-oxopropyl)cyclopentane-1,3-dione by ozonolysis of 4-(homoallyl)cyclopentane-1,3-dione.[102] However, the ozonolysis of 4-allylcyclohexane-1,3-dione (**71a**), prepared by reaction of the dianion of **66a** with allylbromide,[103] afforded the triacid **75** rather than the desired aldehyde **74** (Scheme 40). The triacid **75** was also isolated when the oxidation was carried out using $KMnO_4$, $KMnO_4/NaIO_4$ in acetone, or $KMnO_4/CuSO_4{\cdot}5H_2O$ in CH_2Cl_2/tBuOH/H_2O. The formation of **75** can be explained by oxidative cleavage of the enolic double bond. The problem was solved by protection of the carbonyl groups of **71a** to give the bis(acetal) **72a**. The oxidation of **72a** by $KMnO_4/NaIO_4$ (in acetone) afforded the acid **63a**. Likewise, derivative **63b** was prepared in three steps from **67b**. The bis(acetal) **63a** can be deprotected to give the desired (2,4-dioxocyclohex-1-yl)acetic acid (**70**) which, however, proved to be unstable. Therefore, bis(acetals) **73a,b** were directly used for all further transformations.

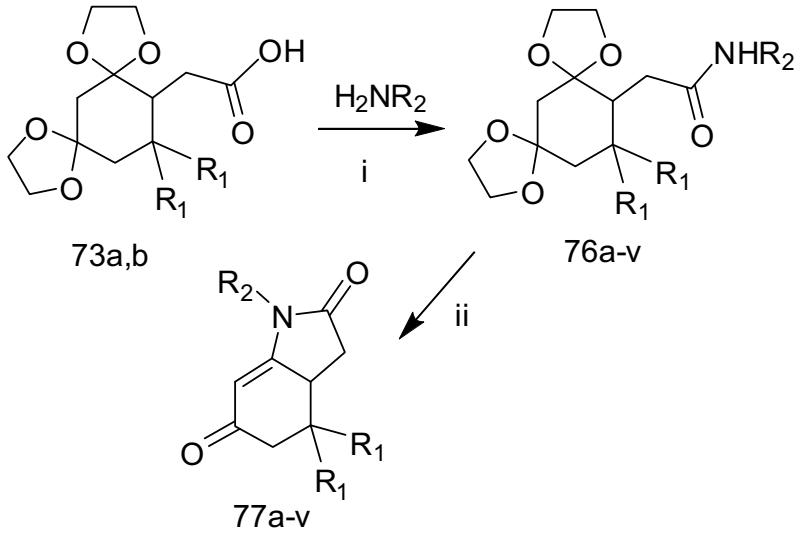


Scheme 39. Attempted synthesis of **70**; *i*, 1) 2.5 LDA, HMPTA, THF, −78 °C, 1 h, 2) electrophile, −40 → 20 °C, 12 h

The DCC-mediated reaction of **73a,b** with various amines afforded the amides **76a-v** (Table 1). Reflux of an acetone solution of **76a-v** in the presence of *para*-toluenesulfonic acid (PTSA) afforded the 2,6-dioxo-1,2,3,3a,4,5-tetrahydroindoles **77a-v**. The formation of an *erythrina*-type spiro-compound, such as **III** (see Scheme 38), was not observed. Products **77e,m,v** were prepared from the mono-acetals mono-**76e,m,v**. The latter were prepared from the mono-acetals mono-**73a,b** which are available by acetalization of **71a,b** using only one (rather than two) equivalents of glycol.

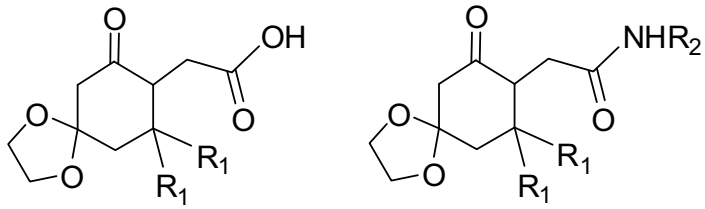


Scheme 40. Synthesis of **73a,b**; *i*, 1) 2.5 LDA, HMPTA, THF, –78 °C, 1 h, 2) allylbromide, –40 → 20 °C, 12 h; *ii*, $HO(CH_2)_2OH$, toluene, PTSA; *iii*, $NaIO_4$, $KMnO_4$, acetone; *iv*, 1) O_3, 2) Me_2S or other conditions (see text)



Conditions: i, 1) DCC, *N*-hydroxysuccinimide, CH_2Cl_2, 1 h, 0 °C, then 12 h, 20 °C, 2) R^2NH_2, 2 h, 20 °C; *ii*, PTSA, acetone, 6 h, reflux

Table 12: Synthesis of **77 a-v.**



76,**77**	R^1	R^2	**% (76)**[a]	**% (77)**[a]
a	H	H	62	90
b	H	*n*Hept	57	64
c	H	*i*Bu	76	81
d	H	*c*Pr	65	51
e	H	*c*Pent	86 [b]	91
f	H	*c*Hex	46	73
g	H	Allyl	65	93
h	H	$PhCH_2$	67	86
i	H	$(4\text{-}ClC_6H_4)CH_2$	79	71
j	H	Ph(Me)CH		49 [c]
k	H	$Ph(CH_2)_2$	64	85
l	H	$[2\text{-}(MeO)C_6H_4](CH_2)_2$		45 [c]
m	H	$[3\text{-}(MeO)C_6H_4](CH_2)_2$	89 [b]	53
n	H	$[4\text{-}(MeO)C_6H_4](CH_2)_2$	85	72
o	H	$[3,4\text{-}(MeO)_2C_6H_3](CH_2)_2$	64	65

p	H	$HO(CH_2)_2$	73	83
q	H	Ph	70	78
r	Me	$[3\text{-}(MeO)C_6H_4]CH_2$		43 [c]
s	Me	$[3,4\text{-}(MeO)_2C_6H_3]CH_2$		86 [c]
t	Me	$[2\text{-}(MeO)C_6H_4](CH_2)_2$		58 [c]
u	Me	$[4\text{-}(MeO)C_6H_4](CH_2)_2$	90	84
v	Me	$[3,4\text{-}(MeO)_2C_6H_3](CH_2)_2$	74 [b]	65

[a] Yields of isolated products;

[b] these products were prepared from mono-**76a,b** and were isolated in the form of mono-**76e,m,v** (structures see above);

[c] overall yield based on **73a,b**

The structures of all products were established by spectroscopic methods. The structures of **76o**, **77o**, and **77e** were independently confirmed by X-ray crystal structure analyses (Figures 22-24).[104]

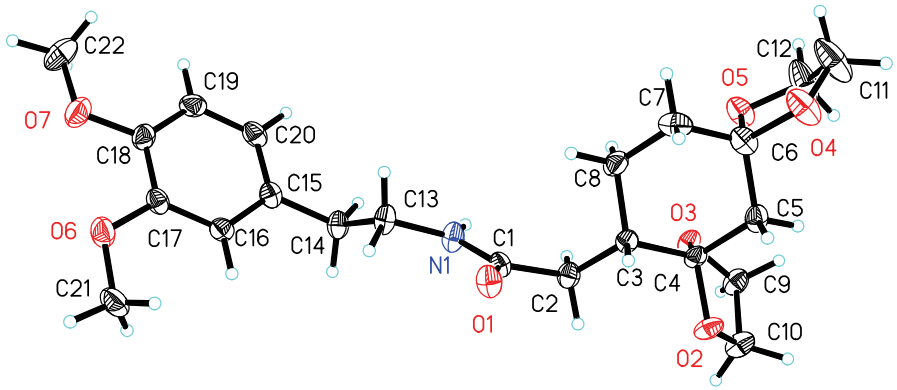


Figure 22. Ortep plot of **76o** (50% probability level)

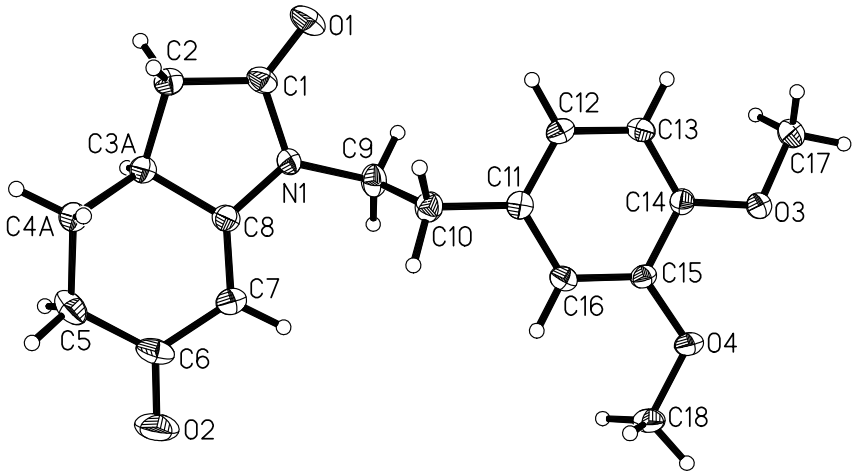


Figure 23. Ortep plot of **77o** (50% probability level)

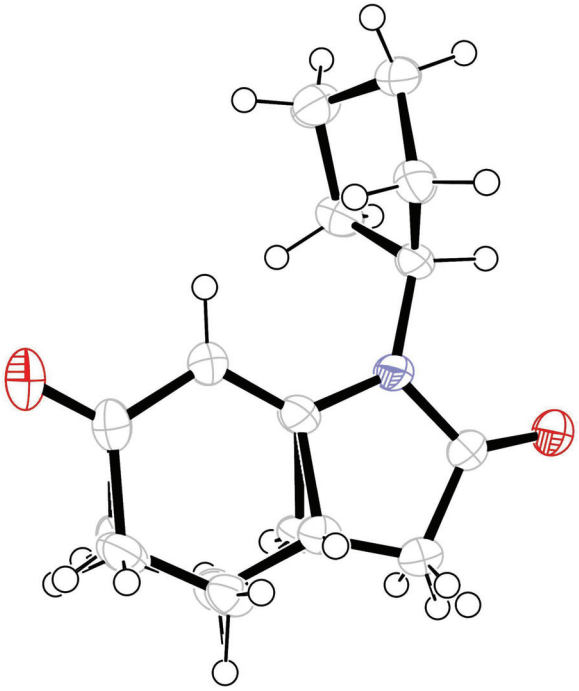
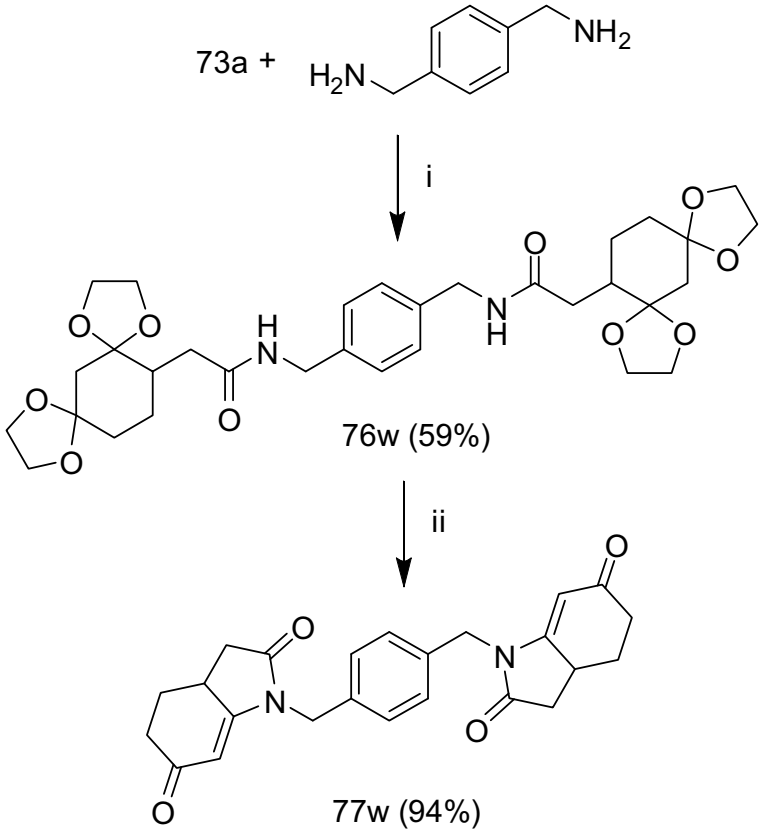


Figure 24. Ortep plot of **77e** (50% probability level)

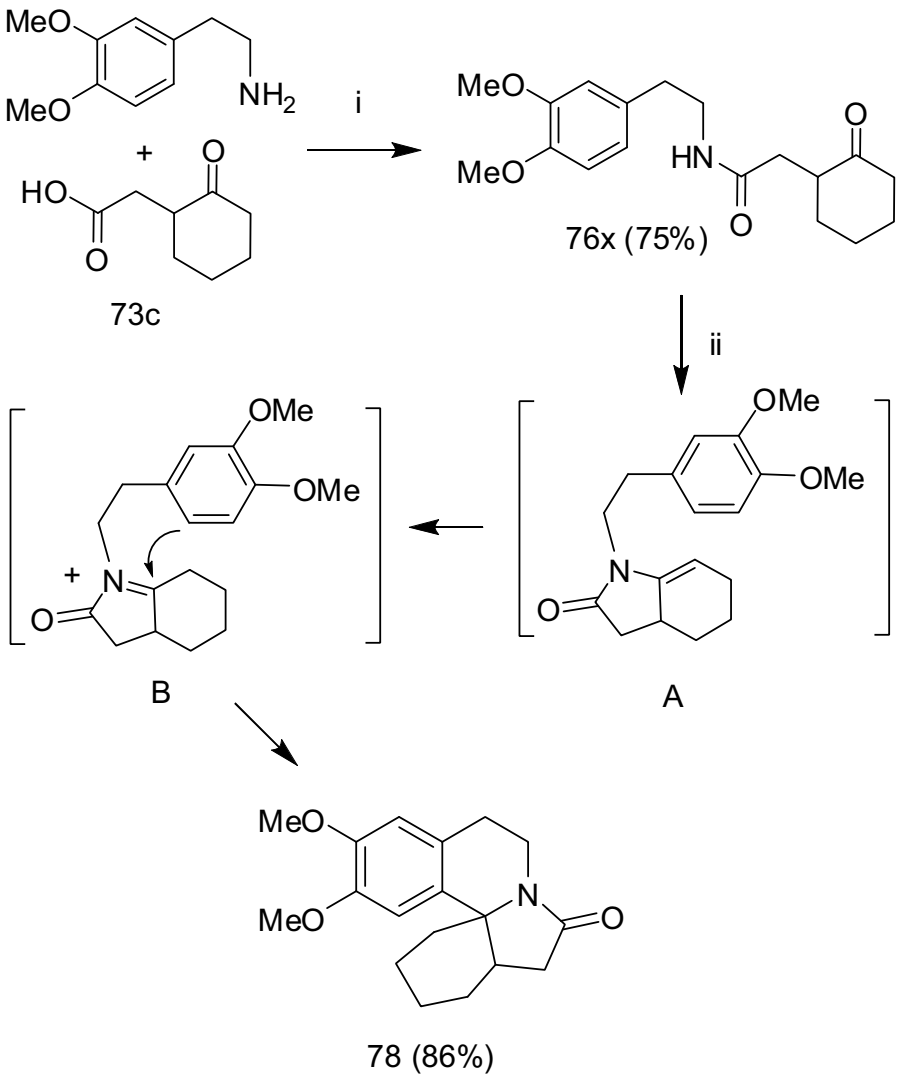
The reaction of **73a** with 1,4-bis(aminomethyl)benzene afforded the bis(amide) **77w** which was transformed into the bis(2,6-dioxo-1,2,3,3a,4,5-tetrahydroindole) **77v** (Scheme 41).



Scheme 41. Synthesis of **77w**: *i*, 1) DCC, *N*-hydroxysuccinimide, CH_2Cl_2, 1 h, 0 °C, then 12 h, 20 °C, 2) RNH_2, 2 h, 20 °C; *ii*, PTSA, acetone, 6 h, reflux.

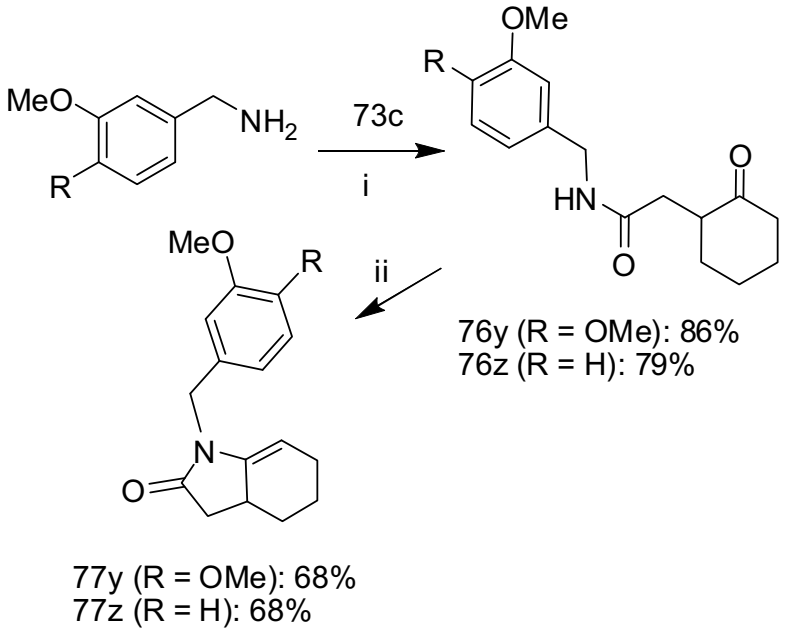
For comparison, we studied the reaction of PTSA with amide **76x** which contains one free carbonyl group (Scheme 42). The amide **76x** was prepared by DCC-mediated reaction of 2-(3,4-dimethoxyphenyl)ethylamine with the known acid **73c**.[105] The reaction of **76x** with PTSA afforded the *erythrina*-type spiro-compound **78** in excellent yield. Tietze and coworkers recently reported the synthesis of **78** by $AlMe_3$/$In(OTf)_3$-mediated reaction of 2-(3,4-dimethoxyphenyl)ethylamine with the ethyl ester of **73c**.[106] The formation of **78** can be explained, as outlined in the introduction, by acid-mediated reaction of the keto group with the electron-rich phenyl group to give intermediate **A**, protonation of the enamine moiety to give iminium salt **B**, and subsequent Pictet-

Spengler reaction. It is important to be noted that this reaction is not general: The reaction of PTSA with amides **76y,z**, again prepared from **73c** in good yields, afforded the 2-oxo-1,2,3,4,5,6-hexahydroindoles **77y,z** rather than the expected spirocyclic products (Scheme 42). This can be explained by the higher strain of a 5,5,6- compared to a 5,6,6-spirocyclic system.



Scheme 42. Synthesis of **78**: *i*, 1) DCC, *N*-hydroxysuccinimide, CH_2Cl_2, 1 h, 0 °C, then 12 h, 20 °C, 2) RNH_2, 2 h, 20 °C; *ii*, PTSA, acetone, 6 h, reflux

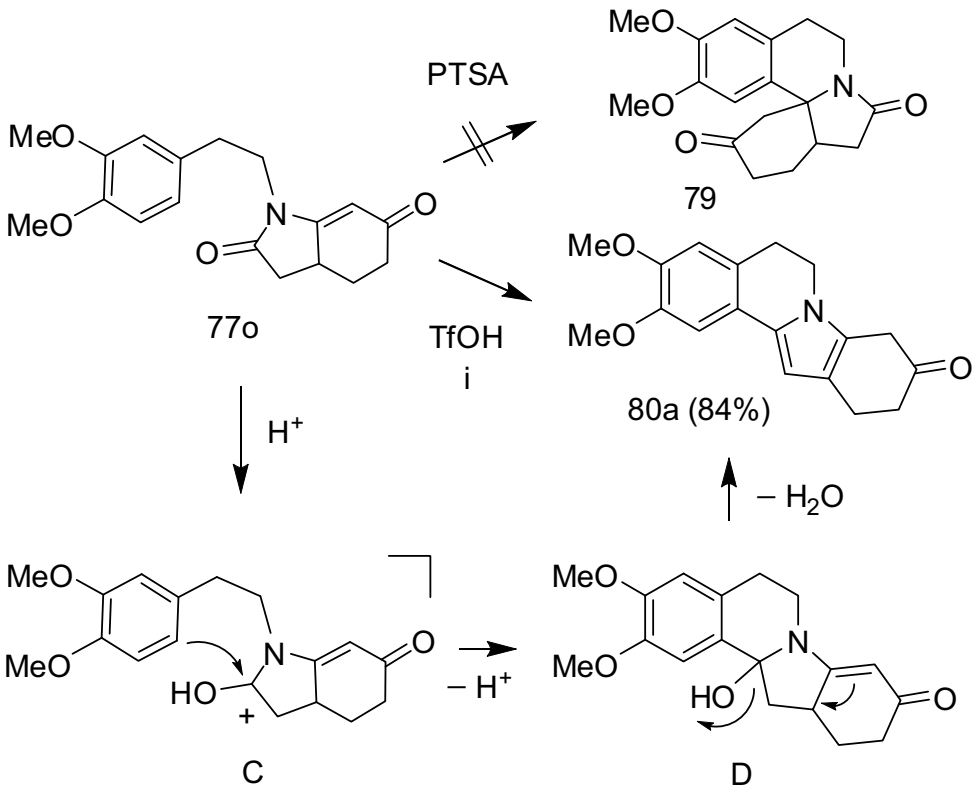
Our next plan was to study the transformation of 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles **77** into *erythrina*-type spirocycles, such as **III**, under more forcing conditions. 2,6-Dioxo-1,2,3,4,5,6-hexahydroindoles **77** represent poly-functionalized heterocycles containing an enone, enamine, and lactam moiety. In principle, a nucleophilic attack might occur at the enone moiety (1,2- or 1,4-addition) or at the amide group. Protonation of the enamine moiety might result in the formation of an iminium ion which might be subsequently attacked by a nucleophile.



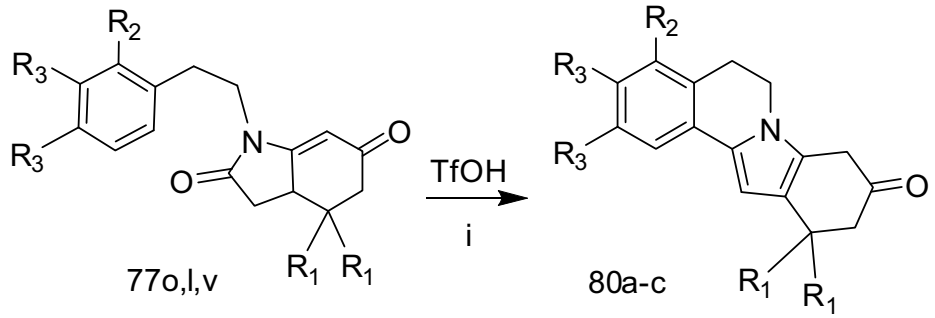
Scheme 43. Synthesis of **77y,z**: *i*, 1) DCC, *N*-hydroxysuccinimide, CH_2Cl_2, 1 h, 0 °C, then 12 h, 20 °C, 2) RNH_2, 2 h, 20 °C; *ii*, PTSA, acetone, 6 h, reflux

Heating of 2,6-dioxo-1,2,3,4,5,6-hexahydroindole **77o** in the presence of PTSA for an extended period of time (48 h) did not result in any conversion. Therefore, we have choosed triflic acid (TfOH) as a more reactive reagent. The reaction of **77o** with triflic acid (TfOH) afforded the 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-9-one **80a** (84% yield) rather than the *erythrina*-type spirocycle **79** (Scheme 44, Table 13). The formation of **80a** can be explained by protonation of the amide oxygen atom to give the

cationic intermediate **C**, cyclization via the electron-rich aryl group (intermediate **D**), and subsequent extrusion of water and double bond migration.



Scheme 44. Possible mechanism of the formation of **80a**: *i*, TfOH, CH_2Cl_2, reflux, 4 h



Conditions: *i*, TfOH, CH_2Cl_2, reflux, 4 h

Table 13. Synthesis of 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-9-ones **80a-c**

77	**80**	R^1	R^2	R^3	% (**80**)[a]
o	**a**	H	H	OMe	84
l	**b**	H	OMe	H	32
v	**c**	Me	H	OMe	57

[a] Yields of isolated products

The reaction of TfOH with 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles **77l** and **77v** afforded the 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-9-ones **80b** and **80c**, respectively (Table 13). In contrast, the reaction of TfOH with **77k** resulted in the formation of a complex mixture. This result suggests that the cyclization is only possible for substrates containing an electron-rich phenyl group. This can be explained by the high reactivity of activated, electron-rich arenes in electrophilic substitution reactions. The reaction of TfOH with **77s** also gave a complex mixture. This can be explained by the higher strain of 5,5,6- compared to 5,6,6-tricyclic products.

Padwa and Wang have recently reported the TfOH-mediated transformation of a 2,6-dioxo-1,2,3,4,5,6-hexahydroindole into a 5,6-dihydroindolo[2,1-*a*]isoquinolin-9-ol.[97,106] This reaction, which involves a cyclization, decarboxylation and an aromatization step, presumably proceeds by a mechanism similar to that suggested for the formation of 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-9-ones **80a-c**. The synthesis of 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-9-ones has, to the best of our knowledge, not been reported to date.[107]

7.3 Conclusion:

In conclusion, we have reported the synthesis of the first (2,4-dioxocyclohex-1-yl)acetic amides. Their reaction with PTSA provides a general method for the synthesis of 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles. The reaction of the latter with triflic acid afforded 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-9-ones rather than *erythrina*-type spirocycles.

8 Experimental Section:

8.1 General: Equipments, chemicals and work techniques

^{1}H NMR Spectroscopy: Bruker: AM 250, Avance 250, AC 250 (250 MHz); ARX 300, Avance 300 (300 MHz); Varian VXR 500 S, Avance 500 (500 MHz); δ = 0.00 ppm for Tetramethylsilane; δ = 2.04 ppm for Acetone d-6; δ = 7.26 ppm for Deuterochloroform (CDCl3); Characterization of the signal fragmentations: s = singlet, d = doublet, dd = double of doublet, ddd = doublet of a double doublet, t = triplet, q = quartet, quint = quintet; sext = Sextet, sept = Septet, m = multiplet, br = broadly. Spectra were evaluated according to first order rule. All coupling constants are indicated as (*J*).

^{13}C NMR Spectroscopy: Bruker: AM 250, Avance 250, AC 250 (62.9 MHz); ARX 300, Avance 300 (75 MHz); Varian VXR 500 S, Avance 500 (125 MHz); δ = 128.00 ppm for Acetone d-6; δ = 77.00ppm for CDCl3. The multiplicity of the carbon atoms was determined by the DEPT 135 and APT technique (APT = Attached Proton Test) and quoted as CH3, CH2, CH and C for primary, secondary, tertiary and quaternary carbon atoms. Characterization of the signal fragmentations: quart = quartet the multiplicity of the signals was determined by the DEPT recording technology and/or the APT recording technology.

Mass Spectroscopy: AMD MS40, AMD 402 (AMD Intectra), Varian MAT CH 7, MAT 731.

High Resolution mass spectroscopy: Finnigan MAT 95 or Varian MAT 311; Bruker FT CIR, AMD 402 (AMD Intectra).

Infrared spectroscopy (IR): Bruker IFS 66 (FT IR), Nicolet 205 FT IR; Nicolet Protege 460, Nicolet 360 Smart Orbit (ATR); KBr, KAP, Nujol, and ATR; Abbreviations for signal allocations: w = weak, m = medium, s = strong, br = broad.

Elementary analysis: LECO CHNS-932, Thermoquest Flash EA 1112.

X-ray crystal structure analysis: Bruker X8Apex Diffractometer with CCD-Kamera (Mo-K_a und Graphit Monochromator, λ = 0.71073 Å).56

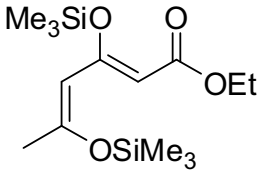
Melting points: Micro heating table HMK 67/1825 Kuestner (Büchi apparatus); Melting points are uncorrected.

Column chromatography: Chromatography was performed over Merck silica gel 60 (0,063 -0,200 mm, 70 - 230 mesh) as normal and/or over mesh silica gel 60 (0,040 - 0,063 mm, 200 -400 mesh) as Flash Chromatography. All solvent were distilled before use.

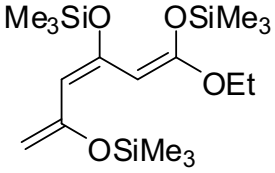
TLC: Merck DC finished foils silica gel 60 F_{254} on aluminum foil and Macherey finished foils Alugram® Sil G/UV_{254}. Detection under UV light with 254 nm and/or 366 nm without dipping reagent, as well as with anisaldehyde sulfuric acid reagent (1 mL anisaldehyde consisting in 100 mL stock solution of 85% methanol, 14% acetic acid and 1% sulfuric acid).

Chemicals and work technique: All solvents used, were distilled by standard methods. All reactions were carried out under an inert atmosphere, oxygen and humidity exclusion. All of the chemicals are standard, commercially available from Merck®, Aldrich®, Arcos® and others. The order of the characterized connections effected numerically, but does not correspond to the order in the main part of dissertation.

8.2 Procedures and spectroscopic data:



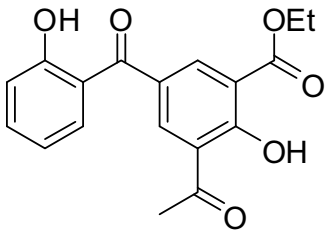
Ethyl 3,5-Bis(trimethylsiloxy)hexa-2,4-dienoate (2). To a stirred benzene solution (95 ml) of **1** (5.36 g, 31.16 mmol), was added triethylamine (13 ml, 93.6 mmol), After stirring for 2 h TMSCl (14.18 ml, 112.32 mmol) was added. After stirring for 72 h, the solvent was removed *in vacuo* and to the residue was added Hexane (50 ml) to give a suspension. The latter was filtered under Argon atmosphere. The filtrate was distilled *in vacuo* to give **2** as yellow oil (8.10 g, 82%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.14-0.21 (brs, 18H, CH_3), 1.16 (t, 3H, *J* = 7.1Hz, CH_3), 2.01 (s, 3H, CH_3), 4.01 (q, 2H, *J* = 6.8 Hz, OCH_2), 5.71 (s, 1H, CH), 6.67 (s, 1H, CH), ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 0.02-1.17 (6C, CH_3), 14.3 (CH_3), 21.57 (CH_3), 60.9 (OCH_2), 96.6, 103.5 (CH), 160.6, 165.0 (*C*OSi$(CH_3)_3$), 167.3 (C=O).



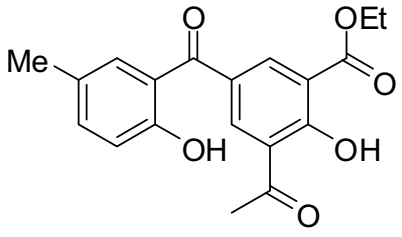
1,3,5-Tris (trimethylsiloxy)-1-ethoxyhexa-1,3,5-triene (3). Starting with LDA (38 mmol, 1.5 equiv.), **2** (8 g, 25.30 mmol), TMSCl (8.0 ml, 63.25 mmol) and THF (45ml), **3** was isolated as a yellow oil (7.80 g, 80%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.11-0.43 (brs, 27H, CH_3), 1.14 (t, 3H, *J* = 7.2 Hz, CH_3), 4.11 (q, 2H, *J* = 7.0 Hz, OCH_2), 4.20 (s, 1H, CH), 4.51 (d, 1H, *J* = 2 Hz, CH), 4.82 (s, 1H, CH), 5.57 (d, 1H, *J* = 2 Hz, CH), ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 0.05-1.23 (9C, CH_3), 14.0 (CH_3), 62.9 (OCH_2), 78.4 (CH), 92.1 (CH_2), 105.4 (CH), 153.0, 155.0, 158.7 (*C*OSi$(CH_3)_3$).

General procedure for the synthesis of 5: To 3-formylchromone **4** (1.0 equiv.) was added Me_3SiOTf (0.3 equiv.) at 20 °C. After stirring for 10 min CH_2Cl_2 (8 mL/m.mole) was added, the solution was cooled to 0 °C and the Ethyl 3,5-Bis(trimethylsiloxy)hexa-2,4-dienoate **2** (1.1 equiv.) was added. The mixture was stirred for 12 h at 20 °C and was subsequently poured into an aqueous solution of hydrochloric acid (10%). The organic and the aqueous layer were separated and the latter was extracted with CH2Cl2 (3 x 80 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and

the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*heptane/EtOAc = 10:1).

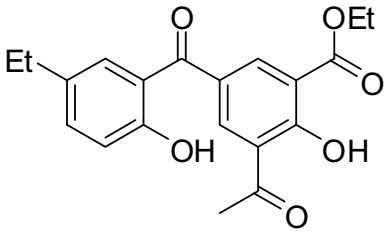


Ethyl 3-acetyl-2-hydroxy-5-(2-hydroxybenzoyl)benzoate (5a): Starting with 3-formylchromone **4a** (261 mg, 1.5 mmol), 3,5-bis(silyl enol ether) **2** (521 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **5a** was isolated as a yellowish crystalline solid (390 mg, 79%), mp. = 111-113°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (t, 3 H, *J* = 6.6 Hz, CH_3), 2.66 (s, 3H, CH_3), 4.35 (q, 2 H, *J* = 7.8 Hz, OCH_2), 6.80 (t, 1 H, *J* = 8.5 Hz, ArH), 6.98 (d, 1 H, *J* = 9.6 Hz, ArH), 7.42-7.48 (m, 2 H, ArH), 8.26 (d, 1 H, *J* = 2.8 Hz, ArH), 8.37 (d, 1 H, *J* = 3.4 Hz, ArH), 11.67 (s, 1 H, OH), 12.62 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1, 30.6 (CH_3), 62.3 (OCH_2), 115.6 (C), 118.6 (CH), 118.7 (C), 118.9 (CH), 125.3, 128.4 (C), 132.7, 136.5, 136.6, 137.3 (CH), 163.0 (C-OH), 164.2 (C=O), 168.3 (C-OH) 198.3, 199.0 (C=O); IR (neat): $\tilde{\nu}$ = 3066 (w), 2985 (w), 2850 (w), 1737 (w), 1677 (s), 1624 (s), 1586 (s), 1483 (m), 1454 (m), 1174 (s), 760 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 328 (M^+, 86), 282 (100), 254 (47), 239 (49), 211 (20), 121 (67); HRMS (EI) calcd for $C_{18}H_{16}O_6$ [M^+]: 328.09414, found 328.093983.

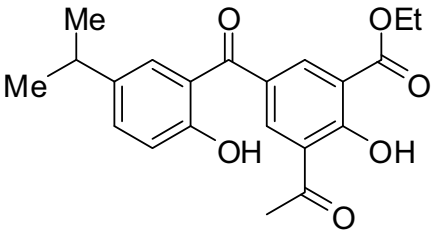


Ethyl 3-acetyl-2-hydroxy-5-(2-hydroxy-5-methyl-benzoyl)benzoate (5b): Starting with 6-methyl-3-formylchromone **4b** (282 mg, 1.5 mmol), 3,5-bis(silyl enol ether) **2** (521 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **5b** was isolated as a yellow crystalline solid (450 mg, 88%), mp. = 124-126°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (t, 3 H, *J* = 7.7 Hz, CH_3), 2.19 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 4.35 (q, 2 H, *J* = 9.0 Hz, CH_2), 6.89 (d, 1 H, *J* = 7.7 Hz, ArH), 7.19-7.28 (m, 2 H, ArH), 8.26 (d, 1 H, *J* = 2.2 Hz, ArH), 8.36 (d, 1 H, *J* = 2.3 Hz, ArH), 11.47 (s, 1 H, OH), 12.62 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1, 20.4, 30.6 (CH_3), 62.3 (OCH_2), 115.6 (C), 118.3 (CH), 118.4, 125.2, 128.1, 128.5 (C), 132.3, 136.9, 137.3, 137.6 (CH), 161.0 (C-OH), 164.2

(C=O), 168.3 (C-OH) 198.2, 199.1 (C=O); IR (neat): $\tilde{\nu}$ = 2983 (w), 2992 (w), 2855 (w), 1737 (w), 1682 (s), 1662 (s), 1628 (s), 1583 (s), 1480 (m), 1455 (m), 1170 (s), 784 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 342 (M^+, 77), 296 (100), 281 (18), 253 (41), 225 (17), 134 (48); HRMS (EI) calcd for $C_{19}H_{18}O_6$ [M^+]: 342.10979, found 342.109773.

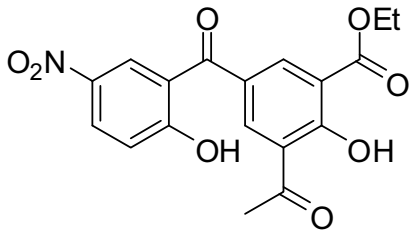


Ethyl 3-acetyl-5-(5-ethyl-2-hydroxybenzoyl)-2-hydroxy-benzoate (5c): Starting with 6-ethyl-3-formylchromone **4c** (303 mg, 1.5 mmol), 3,5-bis(silyl enol ether) **2** (521 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **5c** was isolated as yellowish oil (337 mg, 63%); ^1H NMR (250 MHz, $CDCl_3$): δ = 1.12 (t, 3H, J = 6.8 Hz, $3CH_3$), 1.35 (t, 3 H, *J* = 7.4 Hz, CH_3), 2.456 (q, 2 H, *J* = 8.1 Hz, CH_2), 2.66 (s, 3H, CH_3), 4.35 (q, 2 H, *J* = 7.4 Hz, OCH_2), 6.92 (d, 1 H, *J* = 7.4 Hz, ArH), 7.28-7.32 (m, 2 H, ArH), 8.30 (d, 1 H, *J* = 3.3 Hz, ArH), 8.39 (d, 1 H, *J* = 1.6 Hz, ArH), 11.48 (s, 1 H, OH), 12.64 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1, 15.7 (CH_3), 27.9 (CH_2), 30.5 (CH_3), 62.3 (OCH_2), 115.5 (C), 118.4 (CH), 125.3, 128.4, 128.5 (C), 131.2 (CH), 134.6 (C), 136.5, 136.8, 137.5 (CH), 161.1 (C-OH), 164.2 (C=O), 168.2 (C-OH) 198.1, 199.1 (C=O); IR (neat): $\tilde{\nu}$ = 2993 (w), 2966 (w), 2929 (w), 1737 (w), 1626 (m), 1584 (s), 1479 (m), 1322 (m), 1245 (s), 1169 (s), 1020 (s), 789 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 356 (M^+, 74), 310 (100), 282 (22), 267 (37), 239 (15), 148 (49); HRMS (EI) calcd for $C_{20}H_{20}O_6$ [M^+]: 356.12544, found 356.125099.

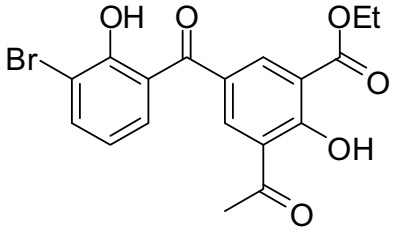


Ethyl 3-acetyl-2-hydroxy-5-(2-hydroxy-5-isopropyl-benzoyl)benzoate (5d): Starting with 6-isopropyl-3-formylchromone **4d** (324 mg, 1.5 mmol), 3,5-bis(silyl enol ether) **2** (521 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **5d** was isolated as a yellowish oil (329 mg, 59%); ^1H NMR (250 MHz, $CDCl_3$): δ = 1.11 (d, 6H, J = 7.0 Hz, $2CH_3$), 1.31 (t, 3 H, *J* = 7.2 Hz, CH_3), 2.66 (s, 3H, CH_3), 2.78 (m,1H, CH), 4.34 (q, 2 H, *J* = 7.6 Hz, OCH_2), 6.92 (d, 1 H, *J* = 8.6 Hz, ArH), 7.30-7.36 (m, 2 H, ArH), 8.32 (d, 1 H, *J* = 2.5 Hz, ArH), 8.40 (d, 1 H, *J* = 2.5 Hz, ArH), 11.47 (s, 1 H, OH),

12.65 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1 (CH_3), 23.9 (2C, CH_3), 30.4 (CH_3), 33.14 (CH), 62.3 (OCH_2), 115.6 (C), 118.3 (CH), 125.3, 128.3, 128.4 (C), 129.8, 135.2, 136.9, 137.6 (CH), 139.2 (C), 161.1 (C-OH), 164.3 (C=O), 168.2 (C-OH) 198.0, 199.1 (C=O); IR (neat): $\tilde{\nu}$ = 3067 (w), 2960 (w), 2928 (w), 2871 (w), 1731 (w), 1674 (s), 1628 (s), 1584 (s), 1480 (m), 1453 (m), 1176 (s), 788 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 370 (M^+, 81), 324 (100), 309 (90), 281 (26), 162 (26), 147 (93); HRMS (EI) calcd for $C_{21}H_{22}O_6$ [M^+]: 370.14109, found 370.140795.

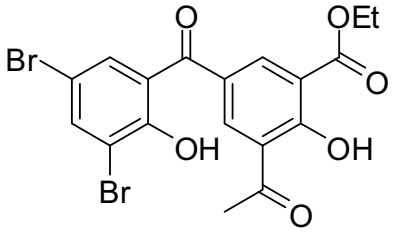


Ethyl 3-acetyl-5-(5-nitro-2-hydroxybenzoyl)-2-hydroxy-benzoate (5e): Starting with 6-nitro-3-formylchromone **4e** (138 mg, 0.63 mmol), 3,5-bis(silyl enol ether) **2** (218 mg, 0.69 mmol), and Me_3SiOTf (0.03 mL, 0.18 mmol), **5e** was isolated as a crystalline solid (100 mg, 43%), mp. = 107-109°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.36 (t, 3 H, *J* = 7.0 Hz, CH_3), 2.68 (s, 3H, CH_3), 4.40 (q, 2 H, *J* = 8.1 Hz, CH_2), 7.11 (d, 1 H, *J* = 8.9 Hz, ArH), 8.31-8.35 (m, 2 H, ArH), 8.40 (d, 1 H, *J* = 2.1 Hz, ArH), 8.45 (d, 1 H, *J* = 2.6 Hz, ArH), 12.28 (s, 1 H, OH), 12.70 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1, 30.7 (CH_3), 62.6 (OCH_2), 115.8, 117.6 (C), 119.7 (CH) 126.1, 126.9 (C), 128.7, 131.0, 136.4, 137.4 (CH), 139.58 (C), 164.9 (C-OH), 167.7 (C=O), 168.2 (C-OH) 197.2, 198.4 (C=O); IR (neat): $\tilde{\nu}$ = 3074 (w), 2990 (w), 2914 (m), 1731 (m), 1667 (s), 1620 (s), 1446 (s), 1331 (s), 1175 (s), 749 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 373 (M^+, 35), 327 (82), 312 (100), 299 (43), 189 (16), 166 (20), 135 (41); HRMS (EI) calcd for $C_{18}H_{15}NO_8$ [M^+]: 373.07922, found 373.078896.

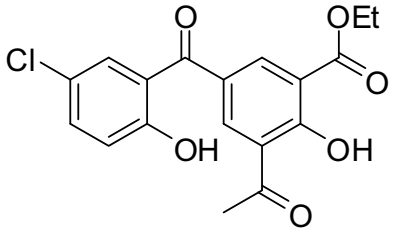


Ethyl 3-acetyl-5-(5-bromo-2-hydroxybenzoyl)-2-hydroxybenzoate (5f): Starting with 6-bromo-3-formylchromone **4f** (253 mg, 1.0 mmol), 3,5-bis(silyl enol ether) **2** (348 mg, 1.1 mmol), and Me_3SiOTf (0.05 mL, 0.3 mmol), **5f** was isolated as a crystalline solid (219 mg, 54%), mp. = 118-120°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.37 (t, 3 H, *J* = 7.1 Hz, CH_3), 2.68 (s, 3H, CH_3), 4.40 (q, 2 H, *J* = 7.1 Hz, OCH_2), 6.91 (d, 1 H, *J* = 8.4 Hz,

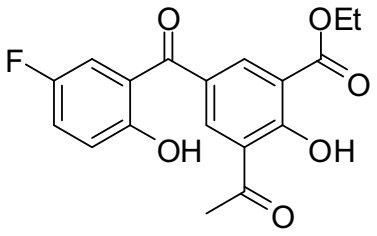
ArH), 7.51-7.57 (m, 2 H, ArH), 8.27 (d, 1 H, J = 2.6 Hz, ArH), 8.36 (d, 1 H, J = 3.6 Hz, ArH), 11.55 (s, 1 H, OH), 12.66 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1, 30.6 (CH_3), 62.4 (OCH_2), 110.5, 115.7, 120.0 (C), 120.7 (CH), 125.6, 127.7 (C), 134.6, 136.6, 137.3, 139.1 (CH), 161.9 (C-OH), 164.5 (C=O), 168.2 (C-OH) 197.2, 198.8 (C=O); IR (neat): $\tilde{\nu}$ = 3072 (w), 2942 (w), 2929 (w), 1731 (w), 1673 (s), 1627 (s), 1586 (s), 1462 (m), 1446 (s), 1407 (s), 1316 (s), 1174 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 408 (M^+,^{81}Br, 48), 406 (M^+,^{79}Br, 46), 362(98), 360 (100), 345 (22), 334 (28), 332 (24), 317 (30), 201 (43); HRMS (EI) calcd for $C_{18}H_{15}BrO_6$ [M^+, ^{79}Br]: 406.00465, found 406.003581.



Ethyl 3-acetyl-5-(3,5-dibromo-2-hydroxybenzoyl)-2-hydroxybenzoate (5g): Starting with 6,8-dibromo-3-formylchromone **4g** (331 mg, 1.0 mmol), 3,5-bis(silyl enol ether) **2** (348 mg, 1.1 mmol), and Me_3SiOTf (0.05 mL, 0.3 mmol), **5g** was isolated as a crystalline solid (219 mg, 56%), mp. = 139-141°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.37 (t, 3 H, J = 7.1 Hz, CH_3), 2.67 (s, 3H, CH_3), 4.40 (q, 2 H, J = 7.1 Hz, OCH_2), 7.55 (d, 1 H, J = 2 Hz, ArH), 7.83 (d, 1 H, J = 2.3 Hz, ArH), 8.27 (d, 1 H, J = 2.3 Hz, ArH), 8.36 (d, 1 H, J = 2 Hz, ArH), 12.10 (s, 1 H, OH), 12.68 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1, 30.6 (CH_3), 62.5 (OCH_2), 110.5, 113.5, 115.7, 120.5, 125.8, 127.2 (C), 133.8, 136.6, 137.4, 141.4 (CH), 158.4 (C-OH), 164.8 (C=O), 168.2 (C-OH) 196.8, 198.5 (C=O); IR (neat): $\tilde{\nu}$ = 3079 (w), 3062 (w), 2994 (w), 1731 (w), 1669 (s), 1622 (s), 1587 (s), 1434 (m), 1414 (s), 1247 (s), 1159 (s), 787 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 488 (M^+, [2 × ^{81}Br], 12), 486 (M^+, [^{81}Br^{79}Br], 25), 484 (M^+, [2 × ^{79}Br],12), 442 (48), 440 (100), 412 (23), 279 (18), 189 (36). HRMS (EI) calcd for $C_{18}H_{14}Br_2O_6$ [M^+, 2 X ^{79}Br]: 483.91516, found 483.915551.

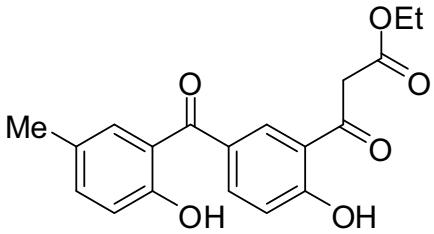


Ethyl 3-acetyl-5-(5-chloro-2-hydroxybenzoyl)-2-hydroxybenzoate (5h): Starting with 6-chloro-3-formylchromone **4h** (208 mg, 1.0 mmol), 3,5-bis(silyl enol ether) **2** (348 mg, 1.1 mmol), and Me_3SiOTf (0.05 mL, 0.3 mmol), **5h** was isolated as a crystalline solid (279 mg, 76%), mp. = 124-125°C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.37 (t, 3 H, *J* = 7.2 Hz, CH_3), 2.68 (s, 3H, CH_3), 4.40 (q, 2 H, *J* = 8.4 Hz, CH_2), 6.96 (d, 1 H, *J* = 9.8 Hz, ArH), 7.39-7.42 (m, 2 H, ArH), 8.27 (d, 1 H, *J* = 2.4 Hz, ArH), 8.36 (d, 1 H, *J* = 2.4 Hz, ArH), 11.54 (s, 1 H, OH), 12.65 (s, 1 H, OH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 14.1, 30.7 (CH_3), 62.5 (OCH_2), 115.3, 119.4 (C), 120.3 (CH) 123.7, 127.8, 127.9 (C), 131.5, 136.4, 136.5, 137.2 (CH), 161.5 (C-OH), 164.5 (C=O), 168.2 (C-OH) 197.3, 198.3 (C=O); IR (neat): $\tilde{\nu}$ = 3077 (w), 3005 (w), 2938 (w), 1738 (w), 1672 (s), 1622 (s), 1587 (s), 1455 (s), 1409 (s), 1318 (s), 1175 (s), 780 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 364 (M^+, ^{37}Cl, 17), 362 (M^+, ^{35}Cl, 54), 316 (100), 301 (26), 273 (28), 245 (13), 189 (16), 155 (31); HRMS (EI) calcd for $C_{18}H_{15}ClO_6$ [M^+, ^{35}Cl]: 362.05517, found 362.054803.

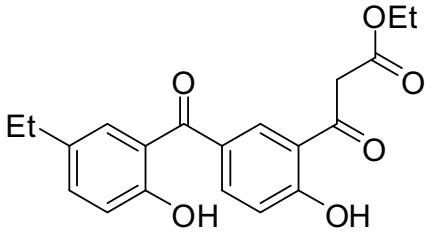


Ethyl 3-acetyl-5-(5-fluoro-2-hydroxybenzoyl)-2-hydroxybenzoate (5j): Starting with 6-fluoro-3-formylchromone **4j** (192 mg, 1.0 mmol), 3,5-bis(silyl enol ether) **2** (348 mg, 1.1 mmol), and Me_3SiOTf (0.05 mL, 0.3 mmol), **5j** was isolated as a crystalline solid (270 mg, 79%), mp. = 111-112°C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.36 (t, 3 H, *J* = 6.5 Hz, CH_3), 2.66 (s, 3H, CH_3), 4.36 (q, 2 H, *J* = 9.1 Hz, CH_2), 6.95-7.00 (m, 1 H, ArH), 7.10-7.24 (m, 2 H, ArH), 8.26 (d, 1 H, *J* = 2.5 Hz, ArH), 8.35 (d, 1 H, *J* = 2.5 Hz, ArH), 11.36 (s, 1 H, OH), 12.63 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.1, 30.7 (CH_3), 62.4 (OCH_2), 115.6 (C), 117.2, 119.9, 123.9 (CH), 125.6, 127.9 (C), 136.4, 137.2 (CH), 152.7, 156.5, (C) 159.1 (C-OH), 164.4 (C=O), 168.3 (C-OH) 197.3, 198.7 (C=O); IR (neat): $\tilde{\nu}$ = 3078 (w), 3008 (w), 2928 (w), 1737 (w), 1668 (s), 1591 (s), 1468 (s), 1420 (s), 1318 (s), 1241 (s), 783 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 346 (M^+, 56), 300 (100), 272 (32), 257 (37), 229 (16), 189 (13); HRMS (EI) calcd for $C_{18}H_{15}FO_6$ [M^+]: 346.08471, found 346.0084999.

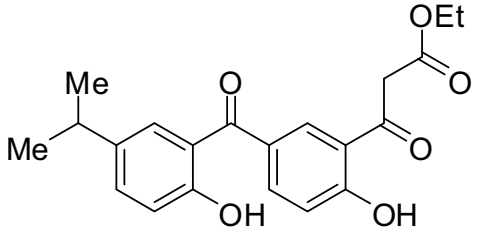
General procedure for the synthesis of 6: To 3-formylchromone **4** (1.0 equiv.) was added Me3SiOTf (0.3 equiv.) at 20 °C. After stirring for 10 min CH_2Cl_2 (8 mL/m.mole) was added, the solution was cooled to 0 °C and the 1,3,5-Tris (trimethylsiloxy)-1-ethoxyhexa-1,3,5-triene **3** (1.1 equiv.) was added. The mixture was stirred for 12 h at 20 °C and was subsequently poured into an aqueous solution of hydrochloric acid (10%). The organic and the aqueous layer were separated and the latter was extracted with CH2Cl2 (3 x 80 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*heptane/EtOAc = 10:1).



Ethyl 3-(2-hydroxy-5-(2-hydroxy-5-methylbenzoyl)-phenyl)-3-oxopropanoate (6b): Starting with 6-methyl-3-formylchromone **4b** (282 mg, 1.5 mmol), 1,3,5-tris(silyl enol ether) **3** (641 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **6b** was isolated as a yellow solid (186 mg, 36%), mp. = 81-84°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, 3 H, *J* = 7.1 Hz, CH_3), 2.32 (s, 3H, CH_3), 4.07 (s, 2H, CH_2), 4.25 (q, 2 H, *J* = 7.1 Hz, CH_2), 7.06 (d, 1 H, *J* = 9.0 Hz, ArH), 7.13 (d, 1 H, *J* = 9.0 Hz, ArH), 7.36 (m, 2 H, ArH), 7.89 (dd, 1H, *J* = 2.0 Hz, *J* = 8.7 Hz, ArH), 8.16 (d, 1H, *J* = 2.0 Hz, ArH), 11.60 (s, 1 H, OH), 12.29 (s, 1 H, OH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 14.0, 20.4 (CH_3), 45.7 (CH_2), 61.9 (OCH_2), 118.3 (CH), 118.4, 118.5 (C), 118.7 (CH), 128.0, 129.2 (C), 132.4, 132.9 (CH), 136.7, 137.8 (CH), 161.0, 165.6 (COH), 166.4, 198.3, 198.5 (C=O); IR (neat): $\tilde{\nu}$ = 2970 (w), 2930 (w), 2859 (w), 1726 (s), 1630 (s), 1587 (s), 1479 (s), 1324 (s), 1207 (s), 1170 (s), 785 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 342 (M^+, 86), 296 (100), 281 (23), 268 (31), 253 (48), 225 (19), 189 (12), 134 (45); HRMS (EI) calcd for $C_{19}H_{18}O_6$ [M^+]: 342.10979, found 342.109866.

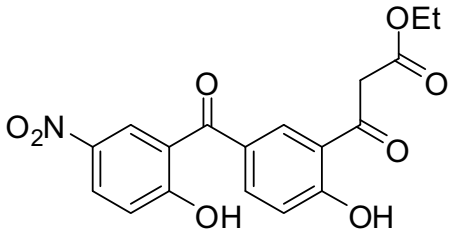


Ethyl 3-(5-(5-ethyl-2-hydroxybenzoyl)-2-hydroxy-phenyl)-3-oxopropanoate (6c): Starting with 6-ethyl-3-formylchromone **4c** (303 mg, 1.5 mmol), 1,3,5-tris(silyl enol ether) **3** (641 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **6c** was isolated as a yellowish brown solid (240 mg, 45%), mp. = 55-58°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22 (t, 3 H, *J* = 7.5 Hz CH_3), 1.30 (t, 3 H, *J* = 7.1 Hz CH_3), 2.456 (q, 2 H, *J* = 8.1 Hz, CH_2), 4.05 (s, 2H, CH_2), 4.12 (q, 2 H, *J* = 6.0 Hz, OCH_2), 7.03 (d, 1H, *J* = 8.3 Hz, ArH), 7.13 (d, 1H, *J* = 8.7 Hz, ArH), 7.39-7.7.43 (m, 2 H, ArH), 7.90 (dd, 1 H, *J* = 1.9 Hz, *J* = 8.7 Hz, ArH), 8.16 (d, 1H, *J* = 1.95 Hz, ArH), 11.60 (s, 1 H, OH), 12.30 (s, 1 H, OH); ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.0, 15.7 (CH_3), 27.9, 45.6 (CH_2), 61.9 (OCH_2), 118.4 (CH), 118.4, 118.5 (C), 118.7 (CH), 129.2 (C), 131.3, 132.9 (CH), 134.6 (C), 136.3, 137.8 (CH), 161.1, 165.6 (COH), 166.4, 198.1, 198.5 (C=O); IR (neat): $\tilde{\nu}$ = 2963 (m), 2930 (m), 1735 (m), 1680 (w), 1628 (s), 1583 (s), 1479 (s), 1352 (m), 1285 (s), 1201 (s), 832 (m) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 356 (M^+, 30), 310 (75), 267 (17), 241 (12), 148 (100), 133 (62), 84 (23); HRMS (EI) calcd for $C_{20}H_{20}O_6$ [M^+]: 356.12544, found 356.125284.

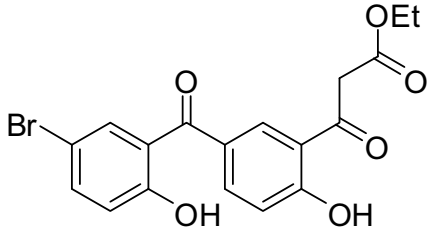


Ethyl 3-(2-hydroxy-5-(2-hydroxy-5 isopropylbenzoyl)-phenyl)-3-oxopropanoate (6d). Starting with 6-isopropyl-3-formylchromone **4d** (324 mg, 1.5 mmol), 1,3,5-tris(silyl enol ether) **3** (641 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **6d** was isolated as a yellow solid (260 mg, 47%), mp. = 60-63°C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22-1.32 (m, 9 H, $3CH_3$), 2.88 (m,1H, CH), 4.07 (s, 2H, CH_2), 4.25 (q, 2 H, *J* = 7.2 Hz, OCH_2), 7.04 (d, 1 H, *J* = 8.6 Hz, ArH), 7.14 (d, 1 H, *J* = 8.6 Hz, ArH), 7.40-7.48 (m, 2 H, ArH), 7.90 (dd, 1 H, *J* = 2.0 Hz, *J* = 8.8 Hz, ArH), 8.17 (d, 1H, *J* = 2.1 Hz, ArH), 11.59 (s, 1 H, OH), 12.30 (s, 1 H, OH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 14.1, 23.9, 24.0 (CH_3), 33.1 (CH), 45.7 (CH_2), 61.9 (OCH_2), 118.3 (C), 118.4 (CH), 118.5 (C), 118.7 (CH), 129.2 (C), 129.9, 132.9, 134.9, 137.8 (CH), 139.2 (C), 161.1, 165.6 (COH), 166.3, 198.5, 198.5 (C=O); IR (neat): $\tilde{\nu}$ =

3058 (w), 2956 (m), 2924 (m), 1744 (s), 1681 (w), 1653 (m), 1628 (s), 1583 (s), 1480 (s), 1343 (m), 1207 (s), 1181 (s), 832 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 370 (M^+, 77), 324 (53), 309 (78), 283 (17), 267 (23), 162 (46), 147 (100), 44 (37); HRMS (EI) calcd for $C_{21}H_{22}O_6$ [M^+]: 370.14109, found 370.140462.

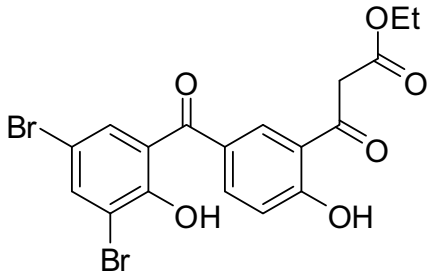


Ethyl 3-(2-hydroxy-5-(2-hydroxy-5-nitrobenzoyl)-phenyl)-3-oxopropanoate (6e): Starting with 6-nitro-3-formylchromone **4e** (328 mg, 1.5 mmol), 1,3,5-tris(silyl enol ether) **3** (641 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **6e** was isolated as a yellow solid (160 mg, 29%), mp. = 130-133°C; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, 3 H, *J* = 7.1 Hz, CH_3), 3.96 (s, 2H, CH_2), 4.25 (q, 2 H, *J* = 7.1 Hz, OCH_2), 7.10 (m, 2 H, ArH), 7.84 (dd, 1 H, *J* = 2.1 Hz, *J* = 8.7 Hz, ArH), 8.14 (d, 1 H, *J* = 2.0 Hz, ArH), 8.30 (m, 1 H, ArH), 8.55 (d, 1 H, *J* = 2.0 Hz, ArH), 12.30 (s, 2 H, OH); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.0 (CH_3), 45.9 (CH_2), 62.1 (OCH_2), 117.6, 118.7 (C), 119.5, 119.7, 128.8, 129.4, 130.8, 133.5 (CH), 137.5, 139.5 (C), 166.1, 166.5 (COH), 167.7, 197.3, 198.3 (C=O); IR (neat): $\tilde{\nu}$ = 3088 (w), 2969 (w), 2849 (w), 1726 (s), 1628 (s), 1593 (s), 1519 (m), 1470 (s), 1338 (s), 1209 (s), 742 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 373 (M^+, 37), 327 (100), 310 (23), 286 (64), 258 (40), 166 (40), 147 (25), 120 (60); HRMS (EI) calcd for $C_{18}H_{15}NO_8$ [M^+]: 373.07922, found 373.078728.

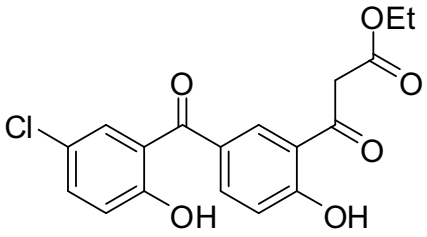


Ethyl 3-(5-(5-bromo-2-hydroxybenzoyl)-2-hydroxy-phenyl)-3-oxopropanoate (6f): Starting with 6-bromo-3-formylchromone **4f** (379 mg, 1.5 mmol), 1,3,5-tris(silyl enol ether) **3** (641 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **6f** was isolated as a yellow solid (190 mg, 31%), mp. = 117-120°C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.21 (t, 3 H, *J* = 6.9 Hz, CH_3), 2.68 (s, 2H, CH_2), 4.23 (q, 2 H, *J* = 7.1 Hz, OCH_2), 6.91 (d, 1 H, *J* = 8.85 ArH), 7.06 (d, 1 H, *J* = 8.75 ArH), 7.51 (m, 1 H, ArH), 7.79 (d, 1 H, *J* = 1.75 Hz, ArH), 7.83 (d, *J* = 1.75 Hz, 1 H, ArH), 8.06 (d, *J* = 1.8 Hz, 1 H, ArH), 11.56 (s, 1 H, OH), 12.24 (s, 1 H, OH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ =

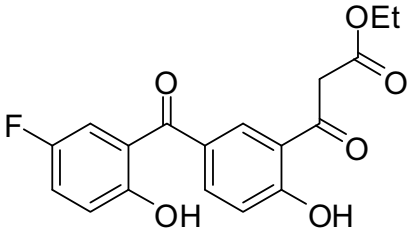
14.0 (CH_3), 45.7 (CH_2), 62.0 (OCH_2), 110.4, 118.6 (C), 119.1 (CH), 120.1 (C), 120.6 (CH), 128.3 (C), 133.0, 134.5, 137.3, 138.9 (CH), 161.8, 166.0 (COH), 166.3, 197.2, 198.5 (C=O); IR (neat): $\tilde{\nu}$ = 3073 (w), 3002 (w), 2966 (m), 1728 (s), 1680 (s), 1643 (s), 1626 (m), 1447 (s), 1462 (s), 1422 (s), 786 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 408 (M^+, ^{81}Br, 47), 406 (M^+,^{79}Br, 47), 362 (78), 360 (75), 291 (28), 200 (100), 147 (30), 120 (41), 92 (14); HRMS (EI) calcd for $C_{18}H_{15}BrO_6$ [M^+, ^{79}Br]: 406.00465, found 406.004404.



Ethyl 3-(5-(3,5-dibromo-2-hydroxybenzoyl)-2-hydroxyphenyl)-3-oxopropanoate (6g). Starting with 6,8-dibromo-3-formylchromone **4g** (331 mg, 1.0 mmol), 1,3,5-tris(silyl enol ether) **3** (427 mg, 1.1 mmol), and Me_3SiOTf (0.05 mL, 0.3 mmol), **6g** was isolated as a light brown solid (159 mg, 33%), mp. = 101-103°C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.21 (t, 3 H, *J* = 6.9 Hz, CH_3), 3.97 (s, 2H, CH_2), 4.14 (q, 2 H, *J* = 7.1 Hz, OCH_2), 7.06 (d, 1 H, *J* = 8.7 ArH), 7.58 (d, 1 H, *J* = 2.3 ArH), 7.78-7.84 (m, 2H, ArH), 8.07 (d, *J* = 2.0 Hz, 1 H, ArH), 12.13 (s, 1 H, OH), 12.27 (s, 1 H, OH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 14.0 (CH_3), 45.7 (CH_2), 62.1 (OCH_2), 110.4, 113.5, 118.7 (C), 119.2 (CH), 120.6, 128.3 (C), 133.3, 133.8, 137.6, 141.3 (CH), 158.4, 166.2 (COH), 166.3, 197.0, 198.4 (C=O); IR (neat): $\tilde{\nu}$ = 3067 (w), 3002 (w), 2974 (m), 2919 (m), 1735 (s), 1694 (w), 1651 (s), 1626 (s), 1583 (s), 1214 (s), 1159 (s), 771 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 488 (M^+, [2 × ^{81}Br], 13), 486 (M^+, [$^{81}Br^{79}Br$], 27), 484 (M^+, [2 × ^{79}Br],13), 442 (23), 440 (47), 399 (29), 371 (34), 278 (100), 147 (32), 120 (40). HRMS (EI) calcd for $C_{18}H_{14}Br_2O_6$ [M^+, 2 X ^{79}Br]: 483.91516, found 483.915113.



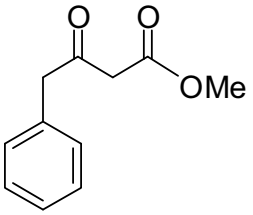
Ethyl 3-(5-(5-chloro-2-hydroxybenzoyl)-2-hydroxy-phenyl)-3-oxopropanoate (6h): Starting with 6,8-dibromo-3-formylchromone **4h** (312 mg, 1.5 mmol), 1,3,5-tris(silyl enol ether) **3** (641 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **6h** was isolated as a reddish brown solid (203 mg, 37%), mp. = 98-99°C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.30 (t, 3 H, J = 7.1 Hz CH_3), 4.07 (s, 2H, CH_2), 4.25 (q, 2 H, J = 7.1 Hz, OCH_2), 7.07 (d, 1H, J = 9.0 Hz, ArH), 7.16 (d, 1H, J = 8.7 Hz, ArH), 7.48-7.52 (m, 1 H, ArH), 7.56 (d, 1H, J = 2.5 Hz, ArH), 7.90 (dd, 1 H, J = 2.0 Hz, J = 8.7 Hz, ArH), 8.16 (d, 1H, J = 1.95 Hz, ArH), 11.63 (s, 1 H, OH), 12.33 (s, 1 H, OH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 14.1 (CH_3), 45.7 (CH_2), 62.0 (OCH_2), 118.6 (C), 119.1 (CH), 119.4, (C), 120.3 (CH), 123.6, 128.3 (C), 131.5, 133.0, 136.2, 137.6 (CH), 161.4, 164.5 (COH), 166.3, 197.5, 198.4 (C=O); IR (neat): $\tilde{\nu}$ = 3074 (w), 2978 (m), 2932 (w), 1728 (m), 1668 (s), 1626 (s), 1587 (s), 1459 (s), 1274 (s), 1173 (s), 1095 (s), 834 (m) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 364 (M^+, ^{37}Cl, 20), 362 (M^+, ^{35}Cl, 47), 316 (100), 301 (25), 273 (34), 245 (15), 207 (14), 155 (35), 44 (29); HRMS (EI) calcd for $C_{18}H_{15}O_6Cl$ [M^+, ^{35}Cl]: 362.05517, found 362.054802.



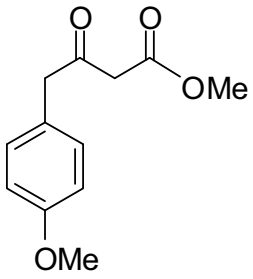
Ethyl 3-(5-(5-fluoro-2-hydroxybenzoyl)-2-hydroxy-phenyl)-3-oxopropanoate (6j): Starting with 6,8-dibromo-3-formylchromone **4j** (288 mg, 1.5 mmol), 1,3,5-tris(silyl enol ether) **3** (641 mg, 1.65 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **6j** was isolated as a light yellow solid (179 mg, 34%), mp. = 72-74°C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.22 (t, 3 H, J = 7.1 Hz, CH_3), 3.97 (s, 2H, CH_2), 4.22 (q, 2 H, J = 7.1 Hz, OCH_2), 6.96-6.99 (m, 1H, ArH), 7.08 (d, 1 H, J = 8.75, ArH), 7.20 (m, 1 H, ArH), 7.81 (d, 1 H, J = 2.0 Hz, ArH), 7.85 (d, 1 H, J = 2.1 Hz, ArH), 8.06 (d, 1 H, J = 2.0 Hz, ArH), 11.39 (s, 1 H, OH), 12.23 (s, 1 H, OH); ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 14.1 (CH_3), 45.7 (CH_2), 62.0 (OCH_2), 118.6 (C), 119.1 (CH), 119.4, (C), 120.3 (CH), 123.6, 128.3 (C), 131.5, 133.0, 136.2, 137.6 (CH), 161.4, 164.5 (COH), 166.3, 197.5, 198.4 (C=O); IR (neat): $\tilde{\nu}$ = 3069

(w), 2998 (w), 2974 (w), 1726 (s), 1655 (s), 1634 (s), 1622 (m), 1470 (s), 1598 (s), 1469 (s), 987 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 346 (M^+, 50), 326 (18), 300 (44), 259 (50), 231 (70), 139 (100), 120 (31), HRMS (EI) calcd for $C_{18}H_{15}FO_6$ [M^+]: 346.08472, found 346.084658.

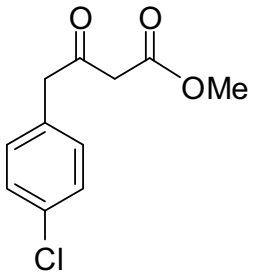
General procedure for the synthesis of methyl 3-arylacetoacetates 8a,b and d : A THF solution of LDA (2.3 equiv.) was prepared by addition of *n*BuLi (0.93 mL, 2.3 mmol, 2.5 M in hexane) to a THF solution (6 mL) of diisopropylamine (0.32 mL, 2.3 mmol) at 0 °C. After the solution was stirred for 30 min, methyl acetate (0.09 mL, 1.1 mmol) was added at 0 °C. After stirring for 45-60 min, to the solution was added a THF solution (4 mL) of the acid chloride (205 mg, 1.0 mmol) at –78 °C. The temperature was allowed to rise to ambient during 5-6 h and the solution was stirred at 20 °C for 10 h. To the solution was added a diluted aqueous solution of HCl and the mixture was extracted with EtOAc (3 x 200 mL). The combined organic layers were dried (Na_2SO_4) and filtered. The solvent of the filtrate was removed in vacuo and the residue was purified by chromatography (silica gel, EtOAc / *n*-heptane).



Methyl 4-phenylacetoacetate (8a): Starting with 2-phenylacetyl chloride (5.00 g, 32.3 mmol) and methyl acetate (2.83 mL, 35.6 mmol), **8a** was isolated as a yellowish oil (4.90 g, 60%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.35 (s, 2 H, CH_2), 3.58 (s, 2 H, CH_2), 3.70 (s, 3 H, OC*H*$_3$), 7.07 (m, 1 H, ArH), 7.11 (m, 2 H, ArH), 7.20 (m, 2 H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.9, 49.5 (CH_2), 52.2, (OCH_3), 126.9 (CH), 127.3 (2C, CH), 128.6 (2C, CH), 130.7 (C), 167.5, 200.7 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3087 (w), 3030 (w), 3006 (m), 2954 (m), 1713 (s), 1602 (w), 1496 (w), 1437 (m), 1316 (m), 1301 (m), 1203 (m), 1115 (m), 1012 (m), 848 (m), 799 (m), 698 (s). MS (EI, 70 eV): *m/z* (%): 192 (M^+, 35), 160 (6), 118 (47), 101 (37), 91 (100), 65(20), 59 (21). HRMS (EI, 70 eV): calcd for $C_{11}H_{12}O_3$ (M^+) 192.07810; found 192.07829.



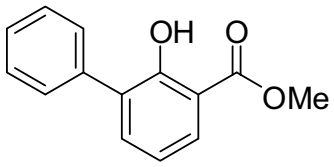
Methyl 4-(4-methoxyphenyl)acetoacetate (8b): Starting with 2-(4-methoxyphenyl)acetyl chloride (5.00 g, 27.1 mmol) and methyl acetate (2.21 mL, 29.9 mmol), **8b** was isolated as a yellowish oil (3.38 g, 56%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, OC*H*$_3$), 3.62 (s, 2 H, CH_2), 3.67 (s, 2 H, CH_2), 3.70 (s, 3 H, OC*H*$_3$), 6.77 (d, 2H, *J* = 8.6 Hz, ArH), 7.02 (d, 2 H, *J* = 8.8 Hz, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 47.7, 49.1 (CH_2), 52.2, 55.1 (OCH_3), 114.0 (2C, CH), 125.1 (C), 130.8 (2C, CH), 158.6 (C), 167.5, 200.7 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3000 (w), 2954 (m), 2837 (w), 1738 (s), 1713 (s), 1608 (m), 1510 (s), 1437 (m), 1317 (m), 1301 (m), 1244 (s), 1176 (s), 1028 (s), 829 (m), 773 (w). MS (EI, 70 eV): *m/z* (%): 222 (M^+, 55), 180 (15), 164 (9), 148 (25), 121 (100), 101(15), 91 (12). HRMS (EI, 70 eV): calcd for $C_{12}H_{14}O_4$ (M^+): 222.08866; found 222.08867.



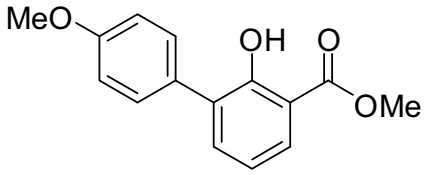
Methyl 4-(4-chlorophenyl)acetoacetate (8d): Starting with 2-(4-chlorophenyl)acetyl chloride (5.00 g, 26.4 mmol) and methyl acetate (2.31 mL, 29.1 mmol), **8d** was isolated as a brownish oil (2.22 g, 34%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.40 (s, 2 H, CH_2), 3.64 (s, 2 H, CH_2), 3.73 (s, 3 H, OC*H*$_3$), 7.04 (d, 2H, *J* = 8.6 Hz, ArH), 7.19 (d, 2 H, *J* = 8.6 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.1, 49.0 (CH_2), 52.4 (OCH_3), 129.9 (2C, CH), 130.9 (2C, CH), 134.2, 132.3 (C), 167.3, 199.7 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2999 (w), 2966 (m), 2932 (w), 2873 (w), 1721 (m), 1631 (m), 1491 (s), 1437 (m), 1370 (m), 1336 (m), 1205 (m), 1088 (s), 1014 (s), 805 (m), 756 (m), 593 (m). MS (EI, 70 eV): *m/z* (%): 228 (M^+, ^{37}Cl, 22), 226 (M^+, ^{35}Cl, 51), 210 (5), 128 (42), 99 (4), 86 (100), 43 (51). HRMS (EI, 70 eV): calcd for $C_{11}H_{11}O_3Cl$ [M^+, ^{35}Cl]: 226.03912; found 226.03935.

General procedure for the synthesis of biaryls 11a, b and d: To a dichloromethane solution (2 mL / mmol of **10**) of **10** (1.0 mmol) and of 1,1,3,3-tetramethoxypropane was added TMSOTf (0.1 mmol) at –78 °C. The solution was allowed to warm to 20 °C within 20 h. To the solution was added a diluted aqueous solution of HCl (15 mL). The organic and the aqueous layer were separated and the latter was extracted with dichloromethane

(3 x 15 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo and the residue was purified by chromatography.

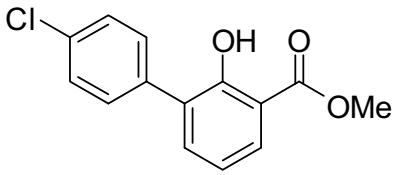


Methyl 3-phenylsalicylate (11a): Starting with 1,1,3,3-tetramethoxypropane (0.27 mL, 1.65 mmol) in CH_2Cl_2 (3.3 mL), 1,3-bis(silyl enol ether) **10a** (555 mg, 1.65 mmol), and TMSOTf (0.03 mL, 0.16 mmol), **11a** was isolated as a highly viscous colourless oil (156 mg, 44%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 3.86 (s, 3 H, CH_3), 6.84 (t, 1 H, *J* = 7.7 Hz, ArH), 7.29 (m, 1 H, ArH), 7.35 (m, 2 H, ArH), 7.45 (m, 1 H, ArH), 7.51 (m, 1 H, ArH), 7.76 (dd, 1 H, *J* = 6.1, 1.7 Hz, ArH), 11.21 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 51.4 (OCH_3), 111.5 (C), 118.0 (C, CH), 125.4 (CH), 126.3 (2C, CH), 128.3 (2C, CH), 129.8 (C), 135.5 (CH), 136.1 (C), 157.9 (C), 169.9 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3085 (w), 3059 (w), 3031 (w), 2953 (m), 1669 (s), 1636 (w), 1427 (s), 1325 (s), 1283 (m), 1244 (s), 1197 (m), 1146 (s), 1065 (m), 968 (m), 833 (m), 753 (s), 695 (s). GC-MS (EI, 70 eV): *m/z* (%): 228 (M^+, 67), 196 (100), 168 (95), 139 (55), 115 (13), 98 (7), 70 (7). HRMS (EI, 70 eV): calcd for $C_{14}H_{12}O_3$ (M^+): 228.07810; found 228.07832.



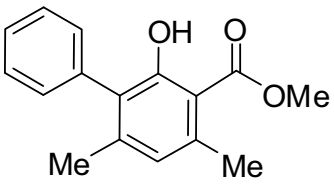
Methyl 3-(4-methoxyphenyl)salicylate (11b): Starting with 1,1,3,3-tetramethoxypropane (0.27 mL, 1.65 mmol) in CH_2Cl_2 (3.3 mL), 1,3-bis(silyl enol ether) **10b** (604 mg, 1.65 mmol), and TMSOTf (0.03 mL, 0.16 mmol), **11b** was isolated as a colourless solid (189 mg, 50%), mp. = 93 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.75 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 6.80 (d, 1 H, *J* = 7.7 Hz, ArH), 6.86 (d, 2 H, *J* = 8.8 Hz, ArH), 7.38 (d, 1 H, *J* = 1.7 Hz, ArH), 7.42 (d, 2H, *J* = 8.8, ArH), 7.71 (dd, 1H, *J* = 6.1, 1.7 Hz, ArH), 11.20 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 51.3, 54.2 (CH_3), 111.4 (C), 112.6 (2C, CH), 117.9 (CH), 127.7 (CH), 128.5 (C), 129.0 (C), 129.4 (2C, CH), 135.2 (C), 142.6, 157.8 (C), 170.0 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3188 (m), 3077 (w), 3004 (w), 2953 (m), 1668 (s), 1604 (m), 1512 (m), 1473 (w), 1434 (m), 1334 (s), 1286 (s), 1249 (s), 1149 (m), 1062 (s), 749 (s), 695 (m), 586 (m)

cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 258 (M^+, 58), 226 (100), 211 (6), 198 (16), 183 (40), 155 (11), 127 (12). HRMS (EI, 70 eV): calcd for $C_{15}H_{14}O_4$ (M^+): 258.08866; found 258.08877.

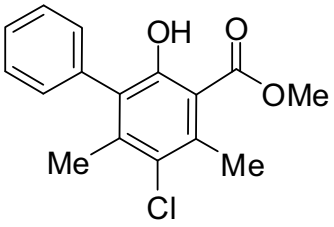


Methyl-3-(4-chlorophenyl)salicylate (11d): Starting with 1,1,3,3-tetramethoxypropane (0.27 mL, 1.65 mmol) in CH_2Cl_2 (3.3 mL), 1,3-bis(silyl enol ether) **10d** (612 mg, 1.65 mmol), and TMSOTf (0.03 mL, 0.16 mmol), **11d** was isolated as a colourless solid (170 mg, 43%), mp. = 113 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, OCH_3), 6.82 (t, 1 H, *J* = 7.7 Hz, ArH), 7.28 (d, 2 H, *J* = 8.6 Hz, ArH), 7.38 (d, 1 H, *J* = 1.7 Hz, ArH), 7.41 (d, 2H, *J* = 8.8, ArH), 7.75 (dd, 1H, *J* = 8.0, 1.7 Hz, ArH), 11.20 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 51.5 (OCH_3), 111.6 (C), 118.0 (CH), 127.2 (2C, CH), 128.0 (C), 128.5 (CH), 129.6 (2C, CH), 132.3, 134.5 (C), 135.3 (CH), 157.7 (C), 169.8 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3123 (m), 2962 (w), 2852 (w), 1677 (s), 1610 (m), 1594 (m), 1434 (s), 1344 (m), 1327 (m), 1245 (m), 1195 (m), 1051 (m), 1061 (m), 964 (m), 826 (s), 747 (s), 583 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 264 (M^+, ^{37}Cl, 29), 262 (M^+, ^{35}Cl, 89), 230 (100), 202 (34), 167 (13), 149 (9), 139 (98), 97 (57). Anal.: calcd (%) for $C_{14}H_{11}O_3Cl$: C 64.01, H 4.22; found: C 63.97, H 4.28.

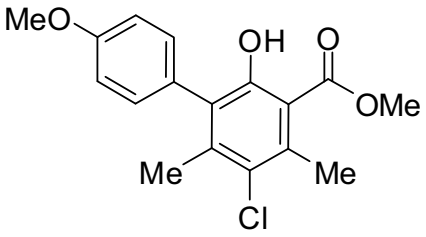
General procedure for the synthesis of biaryls 13a,b and e-i: To a dichloromethane solution (2 mL / mmol of **10**) of **10** (1.0 mmol) and of **12** (1.0 mmol) was added $TiCl_4$ (1.0 mmol) at –78 °C. The solution was allowed to warm to ambient temperature within 20 h. To the solution was added a saturated solution of $NaHCO_3$ (15 mL). The organic and the aqueous layers were separated and the latter was extracted with diethyl ether (3 x 20 mL). The filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, EtOAc / *n*-heptane = 1:4).



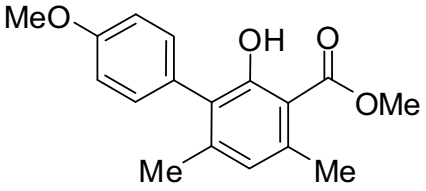
Methyl 4,6-dimethyl-3-phenylsalicylate (13a): Starting with 3-(siloxy)alk-2-en-1-one **12a** (284 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **10a** (555 mg, 1.65 mmol), and $TiCl_4$ (0.18 mL, 1.65 mmol), **13a** was isolated as colourless solid (172 mg, 41%), mp. = 123 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.46 (s, 3 H, CH_3), 3.86 (s, 3 H, OCH_3), 6.59 (s, 1 H, ArH), 7.13 (m, 1 H, ArH), 7.26 (m, 2 H, ArH), 7.33 (m, 2 H, ArH), 11.51 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 19.7, 22.7 (CH_3), 51.0 (OCH_3), 108.8 (C), 123.5, 126.0 (CH), 127.2 (2C, CH), 128.9 (2C, CH), 135.8, 138.7, 142.2, 159.3 (C), 171.4 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2930 (m), 2871 (w), 2835 (w), 1725 (w), 1652 (s), 1607 (m), 1556 (w), 1512 (m), 1430 (m), 1369 (s), 1297 (s), 1257 (s), 1240 (s), 1172 (m), 1203 (s), 1172 (s), 1070 (m), 1022 (s), 987 (m), 955 (m), 810 (s), 750 (m). GC-MS (EI, 70 eV): *m/z* (%): 256 (M^+, 73), 224 (100), 196 (46), 181 (64), 165 (37), 152 (25), 128 (16). HRMS (EI, 70 eV): calcd for $C_{16}H_{15}O_3$ (M^+): 256.10940; found 256.10992.



Methyl 4,6-dimethyl-5-chloro-3-phenylsalicylate (13b): Starting with 3-(siloxy)alk-2-en-1-one **12b** (455 mg, 2.2 mmol), 1,3-bis(silyl enol ether) **10b** (740 mg, 2.2 mmol), and $TiCl_4$ (0.24 mL, 2.2 mmol), **13b** was isolated as a yellow oil (252 mg, 40%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.08 (s, 3 H, CH_3), 2.57 (s, 3 H, CH_3), 3.89 (s, 3 H, OCH_3), 7.13 (m, 1 H, ArH), 7.29 (m, 2 H, ArH), 7.34 (m, 2 H, ArH), 10.62 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 18.7, 19.0 (CH_3), 51.4 (OCH_3), 111.4 (C), 112.9 (2C, CH), 125.4 (CH), 127.2 (2C, CH), 128.7 (2C, CH), 135.6, 140.5 (C), 170.4 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3081 (w), 3058 (m), 3025 (m), 3003 (w), 2959 (m), 2954 (s), 2929 (s), 1731 (m), 1660 (s), 1604 (s), 1550 (w), 1497 (w), 1441 (s), 1388 (s), 1354 (s), 1295 (s), 1253 (w), 1212 (s), 1093 (m), 1067 (m), 1009 (m), 807 (s), 704 (s), 604 (m). GC-MS (EI, 70 eV): *m/z* (%): 292 (M^+, ^{37}Cl, 19), 290 (M^+, ^{35}Cl, 58), 258 (100), 230 (24), 195 (79), 165 (41), 152 (25), 111 (16). HRMS (EI, 70 eV): calcd for $C_{16}H_{15}O_3Cl$ [M^+, ^{35}Cl]: 290.07127; found 290.070944.

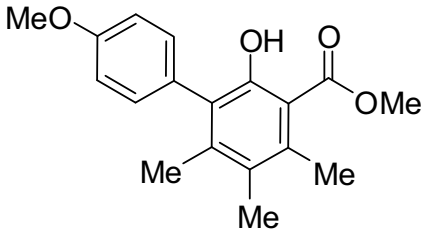


Methyl 4,6-dimethyl-5-chloro-3-(4-methoxyphenyl)salicylate (13e): Starting with 3-(siloxy)alk-2-en-1-one **12b** (450 mg, 2.2 mmol), 1,3-bis(silyl enol ether) **10b** (806 mg, 2.2 mmol), and $TiCl_4$ (0.241 mL, 2.2 mmol), **13e** was isolated as a colourless solid (241 mg, 38%), mp. = 94 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.10 (s, 3 H, CH_3), 2.56 (s, 3 H, CH_3), 3.77 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 6.89 (d, 2 H, *J* = 8.8 Hz, ArH), 7.03 (d, 2 H, *J* = 8.8 Hz, ArH), 10.54 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 19.0, 19.4 (CH_3), 51.4, 54.2 (OCH_3), 111.5 (C), 112.9 (2C, CH), 126.8, 127.6, 128.3 (C), 129.9 (2C, CH), 135.3, 140.8, 156.1, 157.8 (C), 170.5 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3430 (m), 3050 (w), 3002 (w), 2959 (m), 2931 (m), 2837 (m), 1653 (s), 1607 (m), 1572 (w), 1514 (s), 1444 (s), 1373 (m), 1361 (s), 1297 (s), 1253 (s), 1220 (s), 1176 (m), 1092 (m), 1036 (m) 810 (m), 686 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 322 (M^+, ^{37}Cl, 16), 320 (M^+, 47), 288 (100), 260 (11), 245 (27), 225 (29), 181 (7), 152 (12). HRMS (EI, 70 eV): calcd for $C_{17}H_{17}O_4Cl$ [M, ^{35}Cl]: 320.08099; found 320.08088.

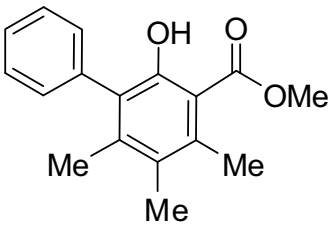


Methyl 4,6-dimethyl-3-(4-methoxyphenyl)salicylate (13f): Starting with 3-(siloxy)alk-2-en-1-one **12a** (284 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **10b** (604 mg, 1.65 mmol), and $TiCl_4$ (0.18 mL, 1.65 mmol), **13f** was isolated colourless solid (173 mg, 37%), mp. = 66 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, CH_3), 2.46 (s, 3 H, CH_3), 3.77 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 6.59 (s, 1 H, ArH), 6.89 (d, 2 H, *J* = 7.5 Hz, ArH), 7.06 (d, 2 H, *J* = 8.8 Hz, ArH), 11.51 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 19.7, 22.9 (CH_3), 51.0, 54.1 (OCH_3), 108.7 (C), 112.7 (2C, CH), 123.5 (CH), 126.9 (C), 127.8 (C), 129.9 (2C, CH), 138.5, 142.6, 157.5, 159.5 (C), 171.5 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3080 (w), 3061 (w), 3023 (w), 2957 (m), 1725 (w), 1650 (s), 1613 (m), 1558 (w), 1430 (m), 1392 (m), 1360 (m), 1295 (s), 1255 (s), 1197 (s), 1087 (m), 1066 (m), 955 (m), 807(s), 767 (s), 700 (s), 570 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 286 (M^+, 55), 254 (100),

226 (11), 211 (55), 153 (8), 127 (11). HRMS (EI, 70 eV): calcd for $C_{17}H_{18}O_4$ (M^+): 286.11996; found: 286.11977.

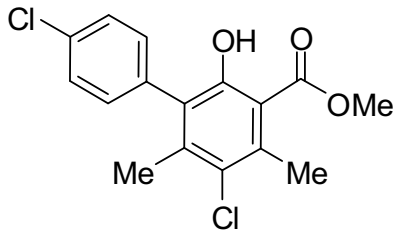


Methyl 4,5,6-trimethyl-3-(4-methoxyphenyl)salicylate (13g): Starting with 3-(siloxy)alk-2-en-1-one **12c** (184 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **10b** (604 mg, 1.65 mmol), and $TiCl_4$ (0.18 mL, 1.65 mmol), **13g** was isolated as a colourless solid (170 mg, 38%), mp. = 108 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, CH_3), 2.12 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 6.88 (d, 2 H, *J* = 8.8 Hz, ArH), 7.03 (d, 2 H, *J* = 8.8 Hz, ArH), 9.97 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 15.0, 17.8, 18.1 (CH_3), 51.0, 54.2 (OCH_3), 111.2 (C), 112.9 (2C, CH), 126.4, 126.8, 128.7 (C), 130.2 (2C, CH), 135.4, 140.7, 154.8, 157.6 (C), 171.1 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2996 (w), 2953 (w), 2939 (w), 2839 (w), 1650 (m), 1598 (m), 1514 (m), 1434 (m), 1393 (m), 1318 (m), 1215 (s), 1295 (s), 1175 (m), 1030 (m), 804 (s), 762 (m), 696 (m), 562 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 300 (M^+, 39), 268 (100), 240 (31), 225 (47), 197 (6), 134 (9) 69 (25). HRMS (EI, 70 eV): calcd for $C_{18}H_{20}O_4$ (M^+): 300.13561; found 300.13568.

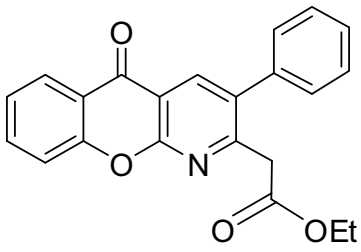


Methyl 4,5,6-trimethyl-3-phenylsalicylate (13h): Starting with 3-(siloxy)alk-2-en-1-one **12c** (308 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **10a** (555 mg, 1.65 mmol), and $TiCl_4$ (0.180 mL, 1.65 mmol), **13h** was isolated as a colourless solid (140 mg, 35%), mp. = 65°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.90 (s, 3 H, CH_3), 2.08 (s, 3 H, CH_3), 2.35 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 7.06–7.12 (m, 2 H, ArH), 7.22–7.32 (m, 3 H, ArH), 10.02 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 16.5, 19.3, 19.8 (CH_3), 52.6 (OCH_3), 112.6 (C), 127.5 (CH) 127.9 (C), 128.8 (2C, CH), 130.6 (2C, CH), 137.2, 138.2, 142.0, 156.2 (C), 172.6 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3022 (w), 2953 (w), 2922 (m), 2853 (w), 1727 (w), 1650 (m), 1604 (m), 1557 (w), 1427 (m), 1392 (m), 1316 (s), 1215 (s), 1068 (m), 961 (w), 807 (m), 773

(m), 722 (m), 699 (m). GC-MS (EI, 70 eV): *m/z* (%): 270 (M^+, 46), 238 (100), 210 (45), 195 (52), 165 (21), 97 (23), 83(34), 69 (34), 57 (49). Anal.: calcd (%) for $C_{17}H_{18}O_3$: C 75.53, H 6.71; found: C 73.84, H 7.03.

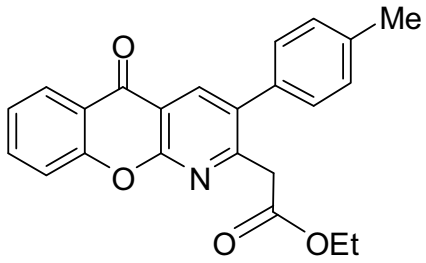


Methyl 4,6-dimethyl-5-chloro-3-(4-chlorophenyl)salicylate (13i): Starting with 3-(siloxy)alk-2-en-1-one **12b** (332 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **10d** (612 mg, 1.65 mmol), and $TiCl_4$ (0.18 mL, 1.65 mmol), **13i** was isolated as a colourless solid (190 mg, 40%), mp. = 96 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 2.56 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 7.03 (d, 2 H, *J* = 8.6 Hz, ArH), 7.31 (d, 2 H, *J* = 8.5 Hz, ArH), 10.85 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 18.7, 19.44 (CH_3), 51.52 (OCH_3), 111.2, 126.4, 127.5 (C), 127.6 (2C, CH), 130.3 (2C, CH), 132.4, 134.0, 136.1, 140.5, 156.2(C), 170.5 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3029 (w), 2950 (m), 2925 (w), 2849 (w), 1658 (s), 1591 (m), 1493 (m), 1434 (m), 1355 (s), 1288 (s), 1207 (s), 1082 (m), 1068 (m), 1008 (s), 980 (m), 956 (m), 824 (m), 802 (s), 727 (s), 607 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 326 (M^+, ^{37}Cl, ^{35}Cl, 29), 324 (M^+, 2 x ^{35}Cl, 44), 299 (100), 264 (10), 257 (28), 229 (45), 165 (45), 128 (10), 82 (22). Anal.: calcd (%) for $C_{16}H_{14}O_3Cl_2$: C 63.65, H 5.34; found: C 63.45, H 5.67.



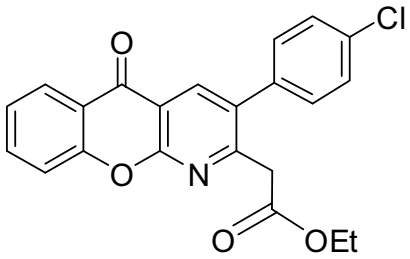
Ethyl 2-(5-oxo-3-phenyl-5*H*-chromeno[2,3-*b*]pyrid-2-yl)acetate (18a): Starting with 3-cynochromone **16** (256 mg, 1.5 mmol), **10a** (656 mg, 1.95 mmol), Me_3SiOTf (0.35 mL, 1.95 mmol), and Et_3N (0.45 mL, 3.0 mmol), **18a** was isolated as a colourless solid (320 mg, 62%), mp. = 152 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 3.85 (s, 3 H, CH_3), 4.65 (s, 2 H, CH_2), 7.11–7.27 (m, 5H, ArH), 7.38 (m, 2 H, ArH), 7.54 (m, 1 H, ArH), 7.72 (m, 1 H, 7-H), 8.21 (dd, ^3J = 7.9 Hz, ^4J = 1.5 Hz, 1 H, Ar-H), 9.13 (s, 1 H, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 42.5 (CH_3), 52.6 (CH_2), 114.3 (C), 118.6 (CH), 121.6, 123.2 (C), 125.1, 126.5, 126.8 (CH), 128.4, 129.2 (2C, CH), 135.9 (CH), 138.1 (C), 141.1 (CH), 155.5, 160.5, 165.1 (C), 167.7, 176.8 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3048 (w), 3061 (w), 3028 (w), 3007 (w), 2948 (w), 2929 (w), 1725 (s), 1669 (s), 1595 (s), 1547 (m), 1466 (s), 1413

(s), 1314 (m), 1270 (s), 1214 (s), 1069 (m), 968 (m), 765 (s), 742 (s), 690 (s). GC-MS (EI, 70 eV): *m/z* (%) = 345 (M^+, 100), 313 (56), 286 (28), 256 (8), 228 (12). HRMS (EI): calcd for $C_{21}H_{15}O_4N$ (M^+, ^{35}Cl): 345.09956, found 345.09971.

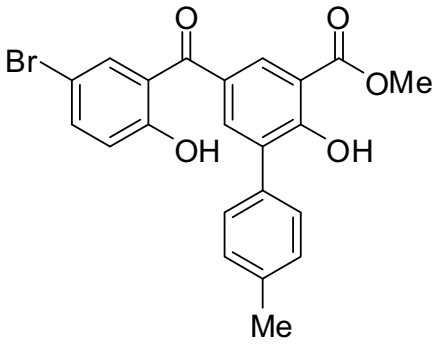


Synthesis of 3-aryl-1-azaxanthone (18b): To neat 3-cyanochromone **16** (256 mg, 1.5 mmol) was added Me_3SiOTf (433 mg, 0.35 mL, 1..95 mmol) and CH_2Cl_2 (13.5 mL) at 20 °C. After stirring for 1 h, CH_2Cl_2 and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **10e** (683 mg, 1.95 mmol) were added at 0 °C. The mixture was stirred for 12 h at 20 °C and subsequently poured into hydrochloric acid (10%). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were washed with water, dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was filtered through a pad of silica gel (EtOAc/hexane = 5:1) to give crude **17**. To an ethanol solution (15 mL) of **17** was added NEt_3 (326 mg, 0.44 mL, 3.0 mmol) and the solution was stirred for 12 h at 20 °C. To the solution were subsequently added an aqueous solution of hydrochloric acid (1 M) and ether (50 mL). The organic and the aqueous layer were separated and the latter was extracted with ether (3 x 100 mL). The combined organic layers were washed with water, dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc/hexane) to give **18b** as a yellow solid (333 mg, 63%), mp. = 173-174 °C. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.23(s, 3H, CH_3), 3.85 (s, 3 H, CH_3), 4.60 (s, 2 H, CH_2), 6.98(d, J = 7.8 Hz, 2 H, ArH), 7.15 (d, 2 H, ArH), 7.33-7.39 (m, 1 H, ArH), 7.53 (d, J = 7.87 Hz, 1H, ArH), 7.67-7.74 (m, 1H, ArH), 8.20 (m, 1H, ArH), 9.10 (s, 1H, ArH) ^{13}C-NMR (62 MHz, $CDCl_3$): δ = 21.0 (CH_3), 42.1 (CH_2), 52.5 (OCH_3), 114.3 (C), 118.6 (CH), 121.6, 123.2 (C), 125.1, 126.8 (CH), 129.0 (2C, CH), 129.1 (2C, CH), 135.0 (C), 135.8 (CH), 136.1 (C), 141.1(CH), 155.6, 160.5, 165.3 (C), 168.0, 176.8 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3084 (w), 3058 (w), 3009 (w), 2948 (w), 1720 (s), 1671 (s), 1613 (m), 1600 (s), 1597 (s), 1548 (m), 1467 (s), 1442 (m), 1412 (s), 1314 (m), 1271 (s), 1253 (s), 1216 (s), 1150 (s), 1069 (s), 793 (m), 755 (s), 615 (m).

GC-MS (EI, 70 eV): *m/z* (%): 359 (M^+, 100), 327 (M^+, 70), 298 (17), 285 (5), 256 (5), 228(4), 150 (7); HRMS (EI) calcd for $C_{22}H_{17}O_4N$ (M^+): 359.114605; found 359.11521.



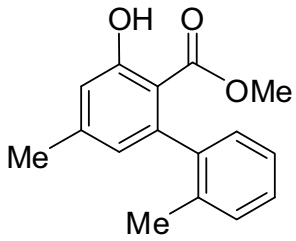
Ethyl 2-[3-(4-chlorophenyl)-5-oxo-5*H*-chromeno[2,3-*b*]pyrid-2-yl]acetate (18c): Starting with **16** (256 mg, 1.5 mmol), **10d** (723 mg, 1.95 mmol), Me_3SiOTf (0.36 mL, 1.95 mmol), and NEt_3 (0.45 mL, 3.0 mmol), **18c** was isolated as a colourless solid (284 mg, 50%), mp. = 182 °C. ^1H NMR ($CDCl_3$, 250 MHz): δ = 3.78 (s, 3 H, CH_3), 4.52 (s, 2 H, CH_2), 7.06–7.17 (m, 4H, ArH), 7.30 (m, 1 H, ArH), 7.45 (m, 1 H, ArH), 7.61 (m, 1 H, ArH), 8.13 (dd, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1 H, Ar-H), 9.06 (s, 1 H, ArH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 41.8 (*C*H_3), 52.6 (CH_2), 114.5 (C), 118.6 (CH), 121.6, 123.0 (C), 125.8, 126.8 (CH), 128.5, 130.6 (2C, CH), 132.4 (C), 135.9 (CH), 136.5 (C), 141.3 (CH), 155.5, 160.5, 165.1 (C), 167.2, 177.3 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 3048 (w), 2952 (w), 2918 (w), 1729 (s), 1664 (s), 1613 (m), 1600 (s), 1547 (m), 1492 (w), 1483 (s), 1414 (s), 1338 (w), 1310 (m), 1271 (s), 1247 (s), 1216 (s), 1139 (m), 1065 (m), 943 (m), 765 (s). GC-MS (EI, 70 eV): *m/z* (%) = 381 (M^+, ^{37}Cl, 34), 379 (M^+ ^{35}Cl, 100), 347 (46), 320 (15), 312 (59), 284 (13), 256 (14), 228 (9). HRMS (EI): calcd for $C_{21}H_{14}O_4NCl$ (M^+, ^{35}Cl): 379.06059, found 379.06052.



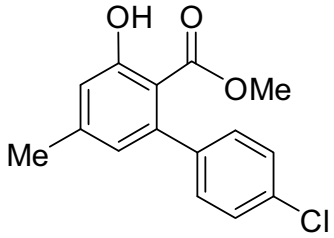
Synthesis of methyl 5-(2-hydroxy-3-bromobenzoyl)-3-(4-tolyl)salicylate (20): To 6-bromo-3-formylchromone **19** (379 mg, 1.5 mmol) was added Me_3SiOTf (0.355 mL, 1.95 mmol) at 20 °C. After stirring for 10 min, CH_2Cl_2 (13.5 mL) was added, the solution was cooled to 0 °C and 1,3-bis(silyl enol ether) **10e** (683 mg, 1.95 mmol) was added. The mixture was stirred at 20 °C for 12 h and was subsequently poured into an aqueous solution of HCl (10%). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were

washed with brine (25 mL) and dried over Na_2SO_4. The mixture was filtered and the solvent of the filtrate was removed under reduced pressure. The crude product was purified by chromatography (silica gel, EtOAc / *n*-heptane) to give **20** as a yellow solid (310 mg, 47%), mp. = 173–174 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 3.94 (s, 3 H, OCH_3), 6.90 (d, *J* = 8.9 Hz, 1 H, ArH), 7.18–7.22 (m, 2 H, ArH), 7.40–7.44 (m, 2 H, ArH), 7.49–7.54 (m, 1 H, ArH), 7.68 (d, *J* = 2.3 Hz, 1 H, ArH), 7.81 (d, *J* = 1.9 Hz, 1 H, ArH), 8.15 (d, *J* = 2.3 Hz, 1 H, ArH), 11.60 (s, 1 H, OH), 11.80 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 21.2 (CH_3), 52.9 (OCH_3), 110.3, 112.3, 120.3 (C), 120.5 (CH), 128.1 (C), 129.11 (2C, CH), 129.17 (2C, CH), 131.1(CH), 131.2, 132.8 (C), 134.9 (CH), 136.8 (CH), 137.9 (C), 138.7 (CH), 161.8, 162.4 (C), 170.4, 198.0 (C=O). IR (neat): $\tilde{\nu}$ = 3104 (w), 2961(m), 2920 (m), 2857 (w), 1783 (w), 1678 (s), 1629 (s), 1588 (s), 1565 (m), 1467 (m), 1437 (s), 1362 (s), 1332 (m), 1286 (s), 1255 (s), 1225 (m), 1198 (s), 1086 (s), 1022 (w), 958 (s), 889 (m), 814 (s), 683 (s), 646 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%): 440 (M^+, ^{79}Br, 90), 411 (24), 408 (93), 242 (19), 210 (65), 182 (30), 153 (34). Anal.: calcd (%) for $C_{22}H_{17}BrO_5$: C 59.88, H 3.88; found: C 59.48, H 4.11.

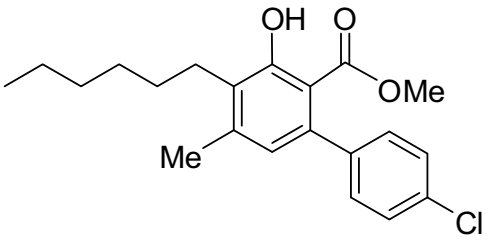
General procedure for the synthesis of salicylates 23: To a CH_2Cl_2 solution of 3-silyloxy-2-en-1-ones **21** (1.0 equiv.) and of 1,3-bis(silyl enol ethers) **22** (1.0 equiv.), $TiCl_4$ (1.0 equiv.) was added dropwise at –78 °C under argon atmosphere. The solution was stirred for 30 min at –78 °C and was then allowed to warm to 20 °C during 18 h. To the reaction mixture was added an aqueous solution of HCl (10%). The organic layer was separated and the aqueous layer was repeatedly extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by chromatography (silica gel, *n*-heptane/EtOAc) to gave salicylates **23**.



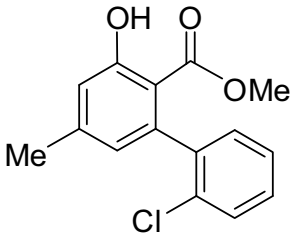
3-Hydroxy-5,2'-dimethyl-biphenyl-2-carboxylic acid methyl ester (23i): Starting with 1,3-bis(silyl enol ether) **21a** (0.287 g, 1.10 mmol), 4-*o*-tolyl-4-trimethylsilyloxy-but-3-en-2-one **22i** (0.273 g, 1.10 mmol) and $TiCl_4$ (0.1 mL, 1.10 mmol) in CH_2Cl_2 (2 mL), **23i** was isolated as a yellow oil (0.120 g, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.03 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.43 (s, 3H, OCH_3), 6.50 (s, 1H, CH), 6.82 (s, 1H, CH), 6.99-7.02 (m, 1H, CH), 7.15-7.20 (m, 3H, CH), 11.11 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 20.6 (CH_3), 50.6 (OCH_3), 108.3 (C), 115.8, 122.5, 123.9, 125.7, 128.4, 132.3 (CH), 133.7, 141.7, 143.2, 144.2 (C), 161.0 (COH), 170.3 (CO_2Me). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3069 (w) 3015 (w), 2954 (m), 2853 (w), 1661 (s), 1612 (m), 1572 (m), 1438 (m), 1353 (m), 1259 (s), 1215 (s), 1123 (m), 1013 (s). MS (EI, 70 eV): *m/z* (%) = 256 (M^+, 28), 225 (19), 224 (100), 181 (19), 153 (26). HRMS (EI): calcd for $C_{16}H_{16}O_3$ (M^+): 256.10940, found 256.110114.



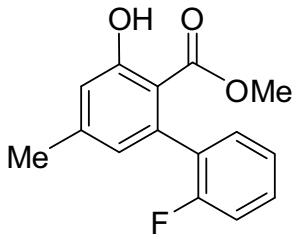
4'-Chloro-3-hydroxy-5-methyl-biphenyl-2-carboxylic acid methyl ester (23j): Starting with 1,3-bis(silyl enol ether) **21a** (0.573 g, 2.20 mmol), 4-(4-chlorophenyl)-4-trimethylsilyloxy-but-3-en-2-one **22i** (0.591 g, 2.20 mmol) and $TiCl_4$ (0.2 mL, 2.20 mmol) in CH_2Cl_2 (4 mL), **23j** was isolated as a colourless solid (0.242 g, 40%); mp 94-96 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 3.50 (s, 3H, OCH_3), 6.56 (br s, 1H, CH), 6.82 (br s, 1H, CH), 7.11-7.16 (m, 2H, CH), 7.29-7.34 (m, 2H, CH), 10.83 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6 (CH_3), 51.6 (OCH_3), 109.0 (C), 117.3, 123.9, 127.7, 129.4 (CH), 132.7, 141.4, 143.4, 145.0 (C), 161.9 (COH), 171.1 (CO_2Me). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3060 (w) 3020 (w), 2960 (m), 2848 (w), 1664 (s), 1612 (m), 1572 (m), 1438 (m), 1353 (m), 1259 (s), 1215 (s), 1123 (m), 1013 (s). MS (EI, 70 eV): *m/z* (%) = 278 (M^+, ^{37}Cl, 10), 276 (M^+, ^{35}Cl, 30), 246 (33), 244 (100), 216 (26), 152 (27). HRMS (EI): calcd for $C_{15}H_{13}ClO_3$ (M^+, ^{35}Cl): 276.05477, found 276.05567.



4'-Chloro-4-hexyl-3-hydroxy-5-methyl-biphenyl-2-carboxylic acid methyl ester (23k): Starting with 1,3-bis(silyl enol ether) **21c** (0.758 g, 2.20 mmol), 4-(4-chlorophenyl)-4-trimethylsilyloxy-but-3-en-2-one **22i** (0.591 g, 2.20 mmol) and $TiCl_4$ (0.2 mL, 2.20 mmol) in CH_2Cl_2 (4 mL), **23k** was isolated as a yellow oil (0.273 g, 34%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.76-0.82 (m, 3H, CH_3), 1.19 (m, 8H, $(CH_2)_4$), 2.04 (s, 3H, CH_3), 3.43 (m, 2H, CH_2), 3.63 (s, 3H, OCH_3), 6.72 (s, 1H, CH), 7.34 (d, 2H, *J* = 8.6 Hz, CH), 7.76 (d, 2H, *J* = 8.6 Hz, CH), 11.00 (s, 1H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0, 17.6 (CH_3), 19.2, 27.3, 28.8, 31.7, 48.1 (CH_2), 52.3 (OCH_3), 124.2, 128.7, 128.9 (CH), 137.2, 139.1, 154.5, 166.9, 189.6 (C), 200.8 (CO_2Me). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3074 (w) 3022 (w), 2955 (m), 2860 (w), 1665 (s), 1617 (m), 1568 (m), 1429 (m), 1353 (m), 1259 (s), 1215 (s), 1123 (m), 1013 (s). MS (EI, 70 eV): *m/z* (%) = 362 (M^+, ^{37}Cl, 16), 360 (M^+, ^{35}Cl, 49), 313 (67), 311 (28), 257 (68), 223 (100), 165 (46). HRMS (EI): calcd for $C_{21}H_{25}ClO_3$ (M^+, ^{35}Cl): 360.14867, found 360.147678.

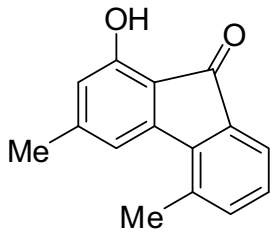


2'-Chloro-3-hydroxy-5-methyl-biphenyl-2-carboxylic acid methyl ester (23l): Starting with 1,3-bis(silyl enol ether) **21a** (0.537 g, 2.20 mmol), 4-(2-chlorophenyl)-4-trimethylsilyloxy-but-3-en-2-one **22j** (0.591 g, 2.20 mmol) and $TiCl_4$ (0.2 mL, 2.20 mmol) in CH_2Cl_2 (4 mL), **23l** was isolated as a colourless solid (0.226 g, 37%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3H, CH_3), 3.39 (s, 3H, OCH_3), 6.42 (s, 1H, CH), 6.77 (s, 1H, CH), 7.08-7.11 (m, 1H, CH), 7.14-7.20 (m, 2H, CH), 7.26-7.29 (m, 1H, CH), 11.05 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (CH_3), 50.8 (OCH_3), 108.4 (C), 116.7, 122.6, 125.8, 127.5, 128.9, 130.6 (CH), 134.5, 140.3, 140.7, 144.3 (C), 160.9 (COH), 169.9 (CO_2Me). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3070 (w) 3017 (w), 2952 (m), 2857 (w), 1660 (s), 1612 (m), 1572 (m), 1433 (m), 1353 (m), 1259 (s), 1215 (s), 1123 (m), 1013 (s). MS (EI, 70 eV): *m/z* (%) = 278 (M^+, ^{37}Cl, 10), 276 (M^+, ^{35}Cl, 30), 244 (29), 241 (100), 152 (21). HRMS (EI): calcd for $C_{15}H_{13}ClO_3$ (M^+, ^{35}Cl): 276.05477, found 276.054962.



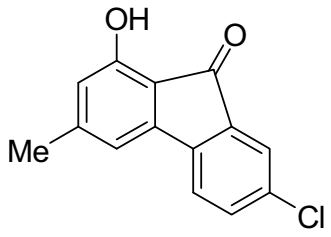
2'-Fluoro-3-hydroxy-5-methyl-biphenyl-2-carboxylic acid methyl ester (23o). Starting with 1,3-bis(silyl enol ether) **21a** (0.287 g, 1.10 mmol), 4-(2-fluorophenyl)-4-trimethylsilyloxy-but-3-en-2-one **22k** (0.278 g, 1.10 mmol) and $TiCl_4$ (0.1 mL, 1.10 mmol) in CH_2Cl_2 (2 mL), **23o** was isolated as a yellowish oil (0.127 g, 44%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 3.51 (s, 3H, OCH_3), 6.59 (s, 1H, CH), 6.85 (s, 1H, CH), 7.03 (t, J = 9.3 Hz, 1H, CH), 7.12-7.17 (m, 1H, CH), 7.20-7.23 (m, 1H, CH), 7.27-7.32 (m, 1H, CH), 11.02 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6 (CH_3), 51.7 (OCH_3), 109.7 (C), 114.4, 114.6, 117.8, 123.7, 124.3, 128.7, 128.8, 130.0 (CH), 130.4, 130.6, 137.7, 145.3, 157.7, 161.0, 161.9 (C), 171.0 (CO_2Me). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3060 (w) 3025 (w), 2960 (m), 2851 (w), 1653 (s), 1612 (m), 1572 (m), 1438 (m), 1353 (m), 1259 (s), 1215 (s), 1112 (m), 1013 (s). MS (EI, 70 eV): *m/z* (%) = 260 (M^+, 37), 229 (18), 228 (100), 200 (42), 171 (17). HRMS (EI): calcd for $C_{15}H_{13}FO_3$ (M^+) 260.08432, found 260.083875.

General procedure for the synthesis of fluorenones 24. Compound **23** was dissolved in concentrated H_2SO_4. After stirring for 1 h, the solution was poured into ice water and extracted (3x) with diethyl ether. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo to give **24**.

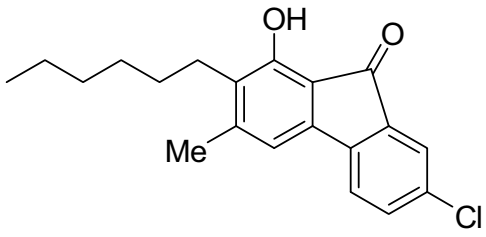


1-Hydroxy-3,5-dimethyl-fluoren-9-one (24y). Starting with **23i** (0.118 g, 0.46 mmol) and conc. H_2SO_4 (5.7 mL), **24y** was isolated as a yellow solid (0.070 mg, 68%), mp 140-145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 6.54 (s, 1H, CH), 6.89 (s, 1H, CH), 7.13-7.23 (m, 2H, CH), 7.46 (d, ^3J = 7.1 Hz, 1H, CH), 8.60 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.1, 22.6 (CH_3), 115.5 (C), 117.5, 121.5, 128.7 (CH), 134.1, 135.1 (C), 137.0 (CH), 141.6, 144.7, 149.1 (C), 157.5 (COH), 196.1 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3339 (s), 2355 (m), 2923 (m), 1675 (s), 1627 (s), 1602 (s), 1587 (m), 1457 (m), 1334 (m), 1295 (m), 1238 (m), 1207

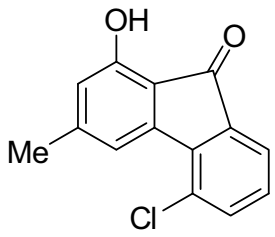
(m), 1172 (m). MS (EI, 70 eV): *m/z* (%) = 224 (M^+, 100), 195 (17), 181 (37), 165 (16), 152 (20). HRMS (EI): calcd for $C_{15}H_{12}O_2$ (M^+): 224.08318, found 224.083191.



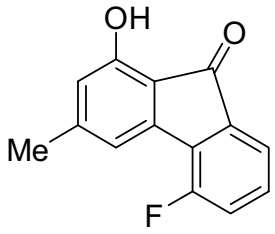
7-Chloro-1-hydroxy-3-methyl-fluoren-9-one (24z). Starting with **23j** (0.199 g, 0.72 mmol) and conc. H_2SO_4 (8.9 mL), **24z** was isolated as a yellow solid (0.146 g, 83%), mp 165-167 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3H, CH_3), 6.58 (br s, 1H, CH), 6.84 (br s, 1H, CH), 7.40-7.41 (m, 2H, CH), 7.56 (br s, 1H, CH), 8.22 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.4 (CH_3), 114.4 (CH), 115.3 (C), 118.2, 121.7, 124.2, 133.8 (CH), 135.0, 136.4, 142.0, 143.0, 149.8 (C), 157.4 (COH), 194.0 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3402 (s), 2917 (w), 1680 (s), 1624 (s), 1604 (s), 1445 (m), 1391 (w), 1309 (s), 1257 (m), 1217 (m), 1190 (s), 1160 (m), 1098 (m). MS (EI, 70 eV): *m/z* (%) = 246 (M^+, ^{37}Cl, 34), 244 (M^+, ^{35}Cl, 100), 181 (17), 152 (30). HRMS (EI): calcd for $C_{14}H_9ClO_2$ (M^+, ^{35}Cl): 244.02856, found 244.028552.



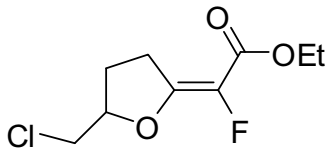
7-Chloro-2-hexyl-1-hydroxy-3-methyl-fluoren-9-one (24aa). Starting with **23k** (0.249 g, 0.69 mmol) and conc. H_2SO_4 (8.5 mL), **24aa** was isolated as a yellowish solid (0.147 g, 65%), mp 73-75 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.86-0.91 (m, 3H, CH_3), 1.24-1.33 (m, 8H, CH_2), 2.32 (s. 3H, CH_3), 2.56-2.62 (m, 2H, CH_2), 6.81 (s, 1H, CH), 7.35-7.41 (m, 2H, CH), 7.53 (dd, ^3J = 1.7 Hz, ^5J = 0.6 Hz, 1H, CH), 8.49 (s, 1H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.1, 20.5 (CH_3), 22.6, 25.4, 28.9, 29.5, 31.7 (CH_2), 115.4, 121.5, 124.2 (CH), 127.6, 131.1 (C), 133.7 (CH), 134.4, 136.4, 139.7, 142.4, 146.9 (C), 156.1 (COH), 194.8 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3349 (w), 2949 (m), 2918 (s), 2851 (m), 1676 (s), 1624 (m), 1596 (m), 1451 (m), 1384 (w), 1298 (m), 1258 (m), 1168 (s), 1115 (m), 1094 (m), 1031 (w). MS (EI, 70 eV): *m/z* (%) = 330 (M^+, ^{37}Cl, 7), 328 (M^+, ^{35}Cl, 21), 260 (18), 258 (55), 257 (100), 165 (19). HRMS (EI): calcd for $C_{20}H_{21}ClO_2$ (M^+, ^{35}Cl): 328.12246, found 328.122093.



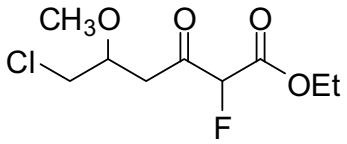
5-Chloro-1-hydroxy-3-methyl-fluoren-9-one (24ab). Starting with **23l** (0.219 g, 0.79 mmol) and conc. H_2SO_4 (9.7 mL), **24ab** was isolated as a colourless solid (0.145 g, 75%), mp 145-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 6.59 (s, 1H, CH), 7.19 (t, ^3J = 7.6 Hz, 1H, CH), 7.36-7.39 (m, 2H, CH), 7.50 (d, ^3J = 7.6 Hz, 1H, CH), 8.44 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7 (CH_3), 115.2 (C), 118.3 (CH), 118.4 (C), 118.5, 122.1, 129.8, 135.7 (CH), 137.1, 140.1, 142.2, 149.7 (C), 157.5 (COH), 194.2 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3345 (s), 2918 (m), 1694 (s), 1619 (s), 1592 (s), 1445 (m), 1412 (w), 1377 (w), 1316 (m), 1296 (s), 1239 (m), 1168 (s). MS (EI, 70 eV): *m/z* (%) = 246 (M^+, ^{37}Cl, 38), 244 (M^+, ^{35}Cl, 100), 216 (17), 181 (32), 152 (31). HRMS (EI): calcd for $C_{14}H_9ClO_2$ (M^+, ^{35}Cl): 244.02856, found 244.028810.



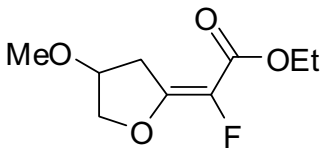
5-Fluoro-1-hydroxy-3-methyl-fluoren-9-one (24ae). Starting with **23o** (0.120 g, 0.46 mmol) and conc. H_2SO_4 (5.7 mL), **24ae** was isolated as a colourless solid (0.079 g, 75%), mp 113-118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 6.59 (s, 1H, CH), 7.03 (s, 1H, CH), 7.13-7.19 (m, 1H, CH), 7.23-7.29 (m, 1H, CH), 7.43 (d, ^3J = 7.2 Hz, 1H, CH), 8.30 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.9 (CH_3), 113.9 (C), 117.1, 118.8, 121.2 (CH), 128.3 (C), 129.7 (CH), 136.4, 139.7, 148.9, 155.2, 156.4, 158.5 (C), 193.3 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3341 (s), 2923 (s), 2853 (m), 1649 (s), 1620 (s), 1585 (s), 1455 (m), 1305 (m), 1240 (s), 1199 (s), 1144 (s), 1113 (m). MS (EI, 70 eV): *m/z* (%) = 228 (M^+, 100), 200 (15), 199 (41), 171 (12), 170 (22). HRMS (EI): calcd for $C_{14}H_9FO_2$ (M^+): 228.05811, found 228.0577962.



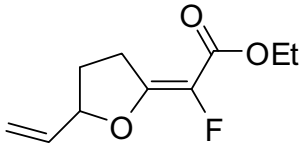
(Z)-ethyl 2-(5-(chloromethyl)dihydrofuran-2(3H)-ylidene)-2-fluoroacetate (28) : Starting with 1,3-Bis-silyl Enol Ether **27** (748mg, 2.5 mmoles), epichlorohydrin (277mg, 0.23 mL, 3 mmole), $TiCl_4$ (948mg, 1.09 mL, 5mmole) and molecular sieves (3g) in CH_2Cl_2 (19mL) **28** was obtained as yellow oil (320 mg, 48 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (t, 3 H, *J* = 7.5 Hz, CH_3), 2.02-2.16 (m, 1H, CH_2), 2.26-2.40 (m, 1H, CH_2), 2.96-3.28 (m, 2H, CH_2), 3.63-3.71 (m, 2H, CH_2), 4.24 (q, 2 H, *J* = 7.5 Hz, OCH_2), 4.71-4.81 (m, 1H, CH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.3 (CH_3), 27.1, 29.0, 45.1 (CH_2), 60.7 (OCH_2), 83.3 (CH), 132.8 (C), 155.4 (d, *J* = 10.59 Hz, CF), 169.0 (d, *J* = 31.80 Hz, C=O); ^{19}F NMR (235 MHz, CDCl3): δ = -160.61 (CF). IR (ATR): $\tilde{\nu}$ = 3430 (w), 2983 (w), 2942 (w), 1739 (m), 1693 (m), 1620 (s), 1372 (w), 1282 (s), 1189 (w), 1074 (s), 944 (m) cm^{-1}; MS (GC, 70 eV): *m/z* (%):224 (M^+, ^{37}Cl, 31), 222 (M^+, ^{35}Cl, 85), 194 (61), 179 (20), 176 (100), 159 (44), 141 (42), 132 (25), 104 (36); HRMS (EI) calcd for $C_9H_{12}O_3ClF$ [M^+, ^{35}Cl]: 222.04535 found 222.044988.



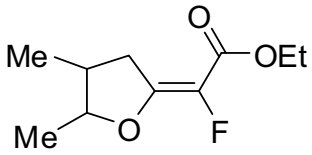
Ethyl 6-chloro-2-fluoro-5-methoxy-3-oxohexanoate (29): Starting with 1,3-Bis-silyl Enol Ether **27** (0.731g, 2.5 mmoles), 1-chloro-2,2-dimethoxyethane (0.311g, 0.28 mL, 2.5 mmole) and Me_3SiOTf (0.270g, 0.22 mL, 1.25 mmole) in CH_2Cl_2 (10ml), **29** was isolated as yellow oil (501 mg, 72%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23 (t, 3 H, *J*= 7.5 Hz, CH_3), 2.84-3.09 (m, 2H, CH_2), 3.35 (s, 3H, OCH_3), 3.57 (d, 2H, *J* = 5 Hz, CH_2), 3.88-3.98 (m, 1H, CH), 4.23 (q, 2H, *J* = 7.5 Hz, OCH_2), 5.12 (dd, 1H, $J_{F,H}$= 44.3 Hz, $J_{F,H}$= 5.62 Hz, CHF). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.8 (CH_3), 41.1 (d, *J* = 6.1 Hz, CH_2), 44.3 (d, *J* = 5.0 Hz, CH_2), 57.5 (d, *J* = 6.7 Hz, OCH_3), 62.6 (OCH_2), 75.5 (d, ^1J = 19.2 Hz, CH), 90.1 (d, *J* = 198 Hz, CF), 163.4 (d, *J* = 25.6 Hz, C=O), 198.4 (dd, *J* = 18.9 Hz, *J* = 4.1 Hz, C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -187.79 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2958 (w), 2938 (w), 2832 (w), 1758 (s), 1732 (s), 1462 (w), 1370 (m), 1263 (m), 1094 (s), 1014 (s). MS (GC, 70 eV): *m/z* (%): 240 (M^+, 2), 191 (53), 135 (41), 93 (100), 85 (69); HRMS (EI) calcd for $C_9H_{14}FClO_4$ [M^+]: 240.05592, found 240.056012.



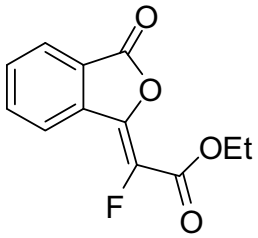
(Z)-ethyl 2-fluoro-2-(4-methoxydihydrofuran-2(3H)-ylidene)acetate (30): Starting with **29** (420 mg, 1.74 mmole) and DBU (530mg, 0.52 ml, 3.48 mmole) in 4 ml of THF, **30** was isolated as yellow oil (286 mg, 81%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29 (t, 3 H, *J*= 7.3 Hz, CH_3), 2.92-3.04 (m, 1H, CH_2), 3.29-3.36 (m, 1H, CH), 3.30 (s, 3H, OCH_3), 4.13-4.17 (m, 1H, CH_2), 4.19-4.27 (m, 1H, CH_2), 4.21-4.27 (m, 2H, OCH_2), 4.40 (m, 1H, CH_2). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.7 (CH_3), 35.1 (CH_2), 55.9 (OCH_3), 60.0 (CH_2), 75.9 (CH), 129.1 (C), 132.8 (C), 154.2 (d, *J* = 10.5 Hz, C), 161.5 (d, *J* = 31.5 Hz, C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -161.27 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3467 (w), 2922 (m), 2851 (w), 1732 (s), 1443 (w), 1371 (m), 1023 (s). MS (GC, 70 eV): *m/z* (%): 204 (M^+, 55), 172 (65), 159 (47), 145 (100), 127 (43), 99 (74), 74 (67); HRMS (EI) calcd for $C_9H_{13}FO_4$ [M^+]: 204.07924, found 204.079401.



(Z)-ethyl 2-fluoro-2-(5-vinyldihydrofuran-2(3H)-ylidene)acetate (31): Starting with LDA (12.5 mmoles), **25** (748mg, 0.62 mL, 5 mmole) and trans-1,2-dibromo butene (1.27g , 30 mmole) at -78°C, **31** was isolated as light yellow oil (441mg, 44%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, 3H, *J* = 7.7 Hz, CH_3), 1.76-1.91 (m, 1H, CH_2), 2.16-2.30 (m, 1H, CH_2), 2.84-3.15 (m, 2H, CH_2), 4.13 (q, 2 H, *J* = 7.0 Hz, OCH_2), 4.80 (q, 1H, *J* = 7.5 Hz, CH), 5.15-5.31 (m, 2H, C=CH_2), 5.74-5.90 (m, 1H, CH), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.2 (CH_3), 29.0, 29.9 (CH_2), 60.4 (OCH_2), 85.1 (CH), 117.7 (CH_2), 132.3 (C), 135.2 (CH), 155.7 (d, *J* = 8.66 Hz, CF), 162.2 (d, *J* = 27.0 Hz, C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -161.67 (CF). IR (ATR): $\tilde{\nu}$ = 3467 (w), 2983 (w), 2907 (w), 1747 (m), 1712 (s), 1665 (s), 1372 (m), 1320 (s), 1187 (s), 1135 (s), 1059 (s), 929 (s), 760 (m) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 200 (M^+, 44), 155 (M^+, 21), 134 (40), 105 (100), 87 (23), 67 (44); HRMS (EI) calcd for $C_{10}H_{13}O_3F$ [M^+]: 200.08432 found 216.084561.



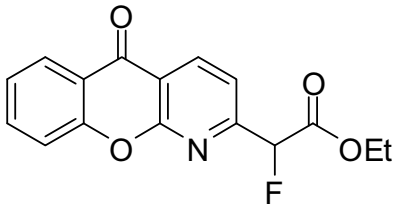
(Z)-ethyl 2-(4,5-dimethyldihydrofuran-2(3H)-ylidene)-2-fluoroacetate (32): Starting with 1,3-Bis-silyl Enol Ether **27** (890 mg, 3 mmole), 2,3-butenoxide (210mg, 0.260 mL, 3 mmole), $TiCl_4$ (1.13 g, 0.65 mL, 6mmole) and molecular sieves (3g) in CH_2Cl_2 (23mL) **32** was obtained as yellow oil (156 mg, 27 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.43 (d, 3 H, *J* = 6.47 Hz, CH_3), 1.65 (t, 3H, *J* = 7.12 Hz, CH_3), 1.72 (d, 3H, *J* = 6.17 Hz, CH_3), 2.28-2.38 (m, 1H, CH_2), 2.64-2.96 (m, 1H, CH_2), 3.64-3.74 (m, 1H, CH), 4.35-4.46 (m, 1H, CH), 4.57 (q, 2H, *J* = 7.3Hz, OCH_2). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.3, 15.9, 18.6 (CH_3), 37.7 (CH_2), 39.4 (CH), 60.4 (OCH_2), 87.3 (CH), 129.2 (C), 155.6 (d, *J* = 12.3 Hz, CF), 162.5 (d, *J* = 27.8 Hz, C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -163.01 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2972 (w), 2875 (w), 1739 (s), 1448 (w), 1372 (m), 1297 (s), 1012 (s), MS (GC, 70 eV): *m/z* (%): 202 (M^+, 98), 157 (59), 136 (48), 108 (100), 87 (30), 55 (97); HRMS (EI) calcd for $C_{10}H_{15}FO_3$ [M^+]: 202.09997, found 202.100294.



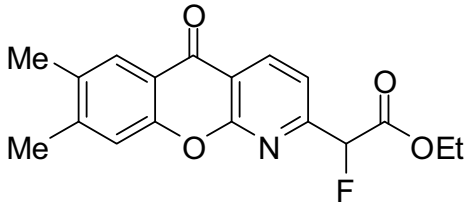
(E)-ethyl 2-fluoro-2-(3-oxoisobenzofuran-1(3H)-ylidene)acetate (33): Starting with phthalyl dichloride (500mg, 0.35ml, 2.5 mmole), 1,3-Bissilylenol Ether **27** (1.12 g, 3.75 mmole), $TiCl_4$ (270mg, 0.158ml, 2.5mmole), Molecular Sieves 4Å (2.5g) in CH_2Cl_2 (25ml) **33** was obtained ad crystalline solid (330mg, 57%) mp. = 96-98 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, 3 H, *J*= 7.4 Hz, CH_3), 4.40 (q, 2H, *J*= 7.1 Hz, OCH_2), 7.67-7.72 (m, 1H, ArH), 7.79-7.85 (m, 1H, ArH), 7.89-7.92 (m, 1H, ArH), 7.98-8.03 (m, 1H, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.1 (CH_3), 62.2 (OCH_2), 124.1 (C), 125.6, 126.1 (CH), 131.2 (C), 135.5, 136.0 (CH), 142.7 (C), 159.1 (d, *J* = 30.9 Hz, CF), 162.7, 165.0 (C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -153.78 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3098 (w), 2992 (m), 2931 (w), 1850 (m), 1788 (s), 1758 (s), 1673 (m), 1469 (m), 1285 (m), 1254 (s), 1108 (s), 1006 (s), 901 (s), 710 (s). MS (GC, 70 eV): *m/z* (%): 236 (M^+, 45), 208 (12), 191 (12), 164 (100), 135 (14), 107 (37), 76 (17); HRMS (EI) calcd for $C_{12}H_9FO_4$ [M^+]: 236.04794, found 236.047639.

General Procedure for the synthesis of Azaxanthones 35a-e.

General procedure for Azaxanthones **35a-e** is same as **18**.

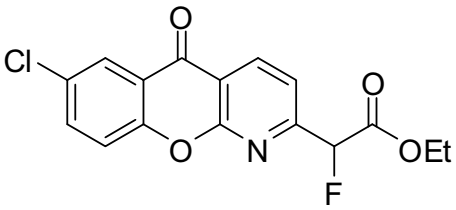


Ethyl 2-fluoro-2-(5-oxo-5H-chromeno[2,3-b]pyridin-2-yl)acetate (35a): Starting with 3-cyanochromone **33a** (256 mg, 1.5 mmol), Me_3SiOTf (433 mg, 0.35 mL, 1.95 mmol), **27** (602 mg, 1.95 mmol), CH_2Cl_2 (13.5 mL), EtOH (15 mL), and triethylamine (303 mg, 0.42 mL, 3 mmol), **35a** was isolated as a white solid (253 mg, 56 %), mp. = 147-148 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23 (t, 3 H, *J*= 7.2 Hz, CH_3), 4.18-4.31 (m, 2 H, OCH_2), 5.82 (d, 1H, $J_{F,H}$= 47.5 Hz, CH), 7.35-7.41 (m, 1H, ArH), 7.54-7.63 (m, 2H, ArH), 7.70-7.77 (m, 1H, ArH), 8.22 (dd, 1 H, *J* = 6.4 Hz, *J* = 1.6 Hz, ArH), 8.72 (d, 1H, *J* = 8.7 Hz, ArH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.0 (CH_3), 63.1 (OCH_2), 88.1-90.6 (d, *J* = 187 Hz, CF), 116.9 (C), 118.0 (d, $J_{F,C}$ = 5.28 Hz, CH), 118.5 (CH), 121.5 (C), 124.9, 126.7, 135.9, 138.9 (CH), 155.6 (C), 158.2 (d, $J_{F,C}$ = 25.0 Hz, C), 159.6 (C), 166.1 (d, $J_{F,C}$ = 25.6 Hz, C=O), 177.0 (C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -187.79 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3071 (w), 2980 (w), 2868 (w), 1757 (s), 1669 (s), 1600 (m), 1397 (s), 1205 (s), 1087 (s), 753 (s). MS (GC, 70 eV): *m/z* (%): 301 (M^+, 41), 229 (100), 200 (31), 146 (8); HRMS (EI) calcd for $C_{16}H_{12}FNO_4$ [M^+]: 301.07449, found 301.074205.

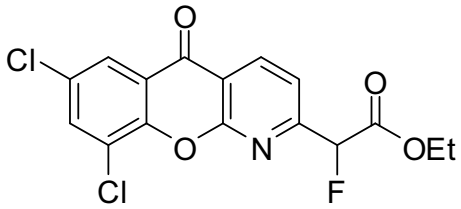


Ethyl 2-(7,8-dimethyl-5-oxo-5H-chromeno[2,3-b]pyridin-2-yl)-2-fluoroacetate (35b): Starting with 6,7-dimethyl-3-cyanochromone **33b** (298 mg, 1.5 mmol), Me_3SiOTf (433 mg, 0.35 mL, 1.95 mmol), **27** (602 mg, 1.95 mmol), CH_2Cl_2 (13.5 mL), EtOH (15 mL), and triethylamine (303 mg, 0.42 mL, 3 mmol), **35b** was isolated as a yellow solid (227 mg, 46 %), mp. = 134-136°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, 3 H, *J*= 7.3 Hz, CH_3), 2.34 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 4.19-4.38 (m, 2H, OCH_2), 5.87 (d, 1H, $J_{F,H}$= 46.9 Hz, CH), 7.32 (s, 1H, ArH), 7.63-7.60 (d, 1H, *J*= 7.8 Hz, ArH), 7.97 (s, 1H, ArH), 8.73 (d, 1H, *J* = 7.82 Hz, ArH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 13.9, 19.1, 20.6 (CH_3), 62.4 (OCH_2), 87.9-90.9 (d, *J* = 225.9 Hz, CF), 116.9 (C), 117.7, 118.5, 119.2

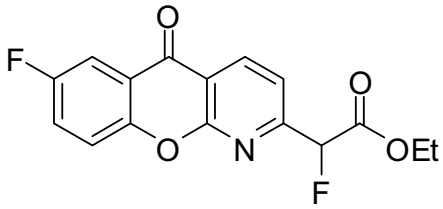
(CH), 126.2 (CH), 134.2 (C), 138.8 (CH), 146.8 (C), 154.1 (C), 157.7 (d, $J_{F,C}$ = 25.1 Hz, C), 159.5 (C), 166.2 (d, J = 30.12 Hz, C=O), 176.7 (C=O), ^{19}F NMR (235 MHz, CDCl3): δ = -187.93 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3067 (w), 2958 (w), 2920 (w), 1745 (s), 1658 (s), 1625 (s), 1602 (s), 1398 (s), 1207 (s), 1089 (s), 761 (m); MS (GC, 70 eV): *m/z* (%): 329 (M^+, 65), 257 (100), 228 (42), 213 (9); HRMS (EI) calcd for $C_{18}H_{16}NFO_4$ [M^+]: 329.10579, found 329.105736.



Ethyl 2-(7-chloro-5-oxo-5H-chromeno[2,3-b]pyridin-2-yl)-2-fluoroacetate (35c): Starting with 6-chloro-3-cyanochromone **33c** (205 mg, 1.0 mmol), Me_3SiOTf (288 mg, 0.23 mL, 1.30 mmol), **27** (380 mg, 1.30 mmol), CH_2Cl_2 (9.0 mL), EtOH (10 mL), and triethylamine (202 mg, 0.28 mL, 2 mmol), **35c** was isolated as a yellow solid (137 mg, 41 %), mp. = 135-137°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, 3 H, J= 7.2 Hz, CH_3), 4.23-4.35 (m, 2 H, OCH_2), 5.82 (d, 1H, $J_{F,\ H}$= 47.8 Hz, CH), 7.54 (d, 1H, J = 9.0 Hz, ArH), 7.67-7.74 (m, 2H, ArH), 8.23 (d, 1H, J = 2.7 Hz, ArH), 8.75 (d, 1H, J = 8.7 Hz, ArH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 14.0 (CH_3), 62.5 (OCH_2), 88.0-90.5 (d, J = 187.8 Hz, CF), 116.5 (C), 118.0 (d, $J_{F,C}$ = 5.23 Hz, CH), 120.2 (CH), 122.3 (C). 126.0 (CH), 130.8 (C), 135.6, 139.0 (CH), 153.9 (C), 158.2 (d, $J_{F,C}$ = 24.4 Hz, C), 159.4 (C), 166.1 (d, $J_{F,C}$ = 26.1 Hz, C=O), 176.0 (C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -187.93 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3081 (w), 2985 (w), 2941 (w), 1756 (s), 1667 (s), 1601 (s), 1470 (s), 1434 (s), 1392 (s), 1202 (s), 1086 (s), 825 (m). MS (GC, 70 eV): *m/z* (%): 337 (M^+, ^{37}Cl, 17), 335 (M^+, ^{35}Cl, 52), 263 (100), 234 (24), 180 (5); HRMS (EI) calcd for $C_{16}H_{11}ClNFO_4$ [M^+, ^{35}Cl]: 335.03552, found 335.035272.

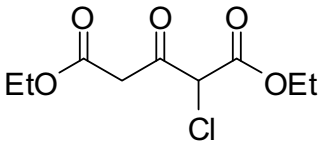


Ethyl 2-(7,9-dichloro-5-oxo-5H-chromeno[2,3-b]pyridin-2-yl)-2-fluoroacetate (35d): Starting with 6,8-dichloro-3-cyanochromone **33d** (240 mg, 1.0 mmol), Me_3SiOTf (288 mg, 0.23 mL, 1.30 mmol), **27** (380 mg, 1.30 mmol), CH_2Cl_2 (9.0 mL), EtOH (10 mL), and triethylamine (202 mg, 0.28 mL, 2 mmol), **35d** was isolated as a yellow solid (130 mg, 35 %), mp. = 164-166°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29 (t, 3 H, *J*= 7.2 Hz, CH_3), 4.20-4.39 (m, 2 H, OCH_2), 5.90 (d, 1H, $J_{F,\,H}$= 47.6 Hz, CH), 7.73 (d, 1H, *J* = 8.25 Hz, ArH), 7.81 (d, 1H, *J*= 3 Hz, ArH), 8.13 (d, 1H, *J*= 3 Hz, ArH), 8.74 (d, 1H, *J* = 8.25 Hz, ArH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 13.9 (CH_3), 62.6 (OCH_2), 88.0-90.5 (d, *J* = 188.5 Hz, CF), 116.2 (C), 118.8 (CH), 123.2 (C), 124.6 (CH), 130.5 (2C), 135.7, 139.0 (CH), 150.0 (C), 159.0 (d, $J_{F,C}$ = 10.2 Hz, C), 159.5 (C), 165.9 (d, *J* = 26.40 Hz, C=O), 175.4 (C=O), ^{19}F NMR (235 MHz, CDCl3): δ = -187.54 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3082 (w), 2987 (w), 2872 (w), 1745 (s), 1668 (s), 1608 (s), 1444 (s), 1238 (s), 1086 (s), 776 (s); MS (GC, 70 eV): *m/z* (%): 373 (M^+, 2 × ^{37}Cl, 4), 371 (M^+, ^{37}Cl, ^{35}Cl, 25), 369 (M^+, 2 × ^{35}Cl, 39), 297 (100), 268 (17); HRMS (EI) calcd for $C_{16}H_{10}O_4NCl_2F$ [M^+, 2 × ^{35}Cl]: 368.99654 found 368.995651.

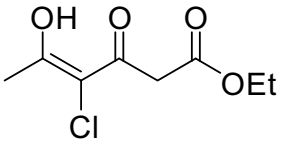


Ethyl 2-fluoro-2-(7-fluoro-5-oxo-5H-chromeno[2,3-b]pyridin-2-yl)acetate (35e): Starting with 6-flouro-3-cyanochromone **33e** (184 mg, 1.0 mmol), Me_3SiOTf (288 mg, 0.23 mL, 1.30 mmol), **27** (380 mg, 1.30 mmol), CH_2Cl_2 (9.0 mL), EtOH (10 mL), and triethylamine (202 mg, 0.28 mL, 2 mmol), **35e** was isolated as a crystalline solid (105 mg, 33 %), mp. = 134-136°C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, 3 H, *J*= 7.2 Hz, CH_3), 4.20-4.39 (m, 2 H, OCH_2), 5.87 (d, 1H, $J_{F,\,H}$= 47.1 Hz, CH), 7.47-7.54 (m, 1H, ArH), 7.59-7.69 (m, 2H, ArH), 7.89-7.94 (m, 1H, ArH), 8.76 (d, 1H, *J* = 8.0 Hz, ArH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 13.9 (CH_3), 62.5 (OCH_2), 88.0-90.5 (d, *J* = 189.3 Hz, CF), 111.4 (d, *J* = 24.1 Hz, CH), 116.5 (C), 118.1 (d, $J_{F,C}$ = 5.0 Hz, CH), 120.5 (d, $J_{F,C}$ = 5.0 Hz, CH), 122.4 (d, $J_{F,C}$ = 7.5 Hz, C), 123.7 (d, $J_{F,C}$ = 25.2 Hz, CH), 138.9 (CH), 151.7 (C), 157.5 (C), 158.5 (d, $J_{F,C}$ = 24.4 Hz, C), 159.3 (C), 160.7 (C=O), 165.0 (d, *J* = 27.9

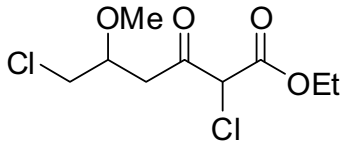
Hz, C=O). ^{19}F NMR (235 MHz, CDCl3): δ = -115.30, -187.93 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3072 (w), 2978 (w), 2926 (w), 1752 (s), 1672 (s), 1592 (s), 1566 (m), 1484 (s), 1447 (s), 1395 (s), 1243 (m), 1208 (s), 1140 (s), 888 (m) MS (GC, 70 eV): *m/z* (%): 319 (M^+, 42), 247 (52), 218 (26), 164 (7); HRMS (EI) calcd for $C_{16}H_{11}NF_2O_4$ [M^+]: 319.06507, found 319.065232.



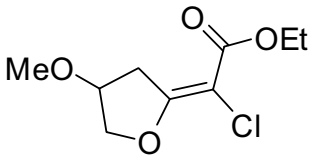
Diethyl 2-chloro-3-oxopentanedioate (40): Starting with LDA (22 mmole), **36** (1.64g, 0.91 mL, 10 mmoles) and ethylchloroformate (1.19g, 1.05 mL, 11 mmole) at -78°C, **40** was obtained as yellow oil (639 mg, 27%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20-1.34 (m, 6H, CH_3), 3.50-3.80 (m, 2H, CH_2), 4.12-4.29 (m, 4H, OCH_2), 4.98 (s, 1H, CH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.6 (2C, CH_3), 45.1 (CH_2), 60.4 (CH), 61.6 (OCH_2), 63.0 (OCH_2), 164.1, 165.7, 191.4 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2984 (m), 2940 (w), 2875 (w), 1727 (s), 1651 (w), 1446 (w), 1369 (m), 1245 (s), 1019 (s). MS (ESI-TOF/MS): (ESI+) $C_9H_{13}ClNaO_5$ $(M+Na)^+$ 259.03463. (ESI-) $C_9H_{12}ClO_5$ $(M-H)^-$ 235.03787.



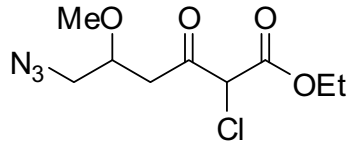
(E)-ethyl 4-chloro-5-hydroxy-3-oxohex-4-enoate (41): Starting with LDA (110 mmole), **39** (6.72g, 5.56 mL, 50 mmoles) and ethylchloroformate (2.7g, 2.40 mL, 25 mmole) at -78°C, **41** was obtained as yellow oil (3.82g, 37%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26 (t, 3H, *J* = 7.0 Hz, CH_3), 2.25 (s, 3H, CH_3), 3.59 (s, 2H, OCH_2), 4.12 (q, 1H, *J* = 7.4 Hz, OCH_2), 14.99 (s, 1H, OH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.0, 23.4 (CH_3), 43.4 (CH_2), 61.7 (OCH_2), 108.2 (C), 166.8 (CO), 184.5, 188.4 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2978 (m), 2936 (w), 2874 (w), 1739 (s), 1687 (m), 1590 (m), 1367 (m), 1253 (s), 1146 (s), 1029 (s), 903 (M). MS (GC, 70 eV): *m/z* (%): 208 (M^+, ^{37}Cl, 5), 206 (M^+, ^{35}Cl, 11), 164 (28), 160 (49), 132 (72), 119 (62), 43 (100); HRMS (EI) calcd for $C_8H_{11}ClO_4$ [M^+, ^{35}Cl]: 206.03404, found 256.034290.



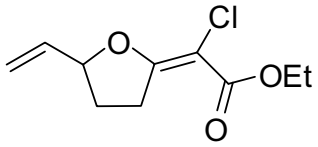
Ethyl 2,6-dichloro-5-methoxy-3-oxohexanoate (42): Starting with 1,3-Bis-silyl Enol Ether **38** (0.772 g, 2.5 mmoles), 1-chloro-2,2-dimethoxyethane (0.28 mL, 2.5 mmole) and Me_3SiOTf (0.22 mL, 1.25 mmole) in CH_2Cl_2 (10ml), **42** was isolated as yellow oil (460 mg, 72%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, 3 H, J = 7.2 Hz, CH_3), 2.94-3.04 (m, 2H, CH_2), 3.34 (s, 3H, OCH_3), 3.55-3.57 (m, 2H, CH_2), 3.84-3.92 (m, 1H, CH), 4.21 (q, 1H, J = 7.2 Hz, OCH_2), 4.80 (d, 1H, J = 2.2 Hz, CH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 13.7 (CH_3), 41.4, 44.4 (CH_2), 57.5 (OCH_3), 61.3 (CH), 63.0 (OCH_2), 75.9 (CH), 164.4, 196.5 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2984 (w), 2938 (w), 2831 (w), 1727 (s), 1446 (s), 1369 (m), 1117 (m), 1095 (s), 1017 (s), 748 (m). MS (GC, 70 eV): *m/z* (%): 258 (M^+, ^{37}Cl, 5), 256 (M^+, ^{35}Cl, 4), 207 (21), 135 (50), 93 (100), 85 (43), 71 (16); HRMS (EI) calcd for $C_9H_{14}Cl_2O_4$ [M^+, ^{35}Cl]: 256.02637, found 256.026928.



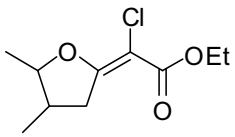
(Z)-ethyl 2-chloro-2-(4-methoxydihydrofuran-2(3H)-ylidene)acetate (43): Starting with **42** (300 mg, 1.16 mmole) and DBU (0.35 ml, 2.32 mmole) in 4 ml of THF, **43** was isolated as yellow oil (188 mg, 73%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (t, 3 H, J= 7.0 Hz, CH_3), 3.02-3.12 (m, 1H, CH_2), 3.32 (s, 3H, OCH_3), 3.49-3.56 (m, 1H, CH_2), 4.19 (q, 2 H, J = 7.0 Hz, OCH_2), 4.25-4.33 (m, 2H, CH_2), 4.48-4.52 (m, 1H, CH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.1 (CH_3), 38.1 (CH_2), 56.2 (OCH_3), 60.9 (OCH_2), 76.6 (CH_2), 78.2 (CH), 96.2, 164.0 (C), 168.0 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2922 (m), 2852 (w), 1737 (w), 1697 (m), 1623 (s), 1461 (m), 1367 (m), 1280 (s), 1214 (s), 1077 (s), 950 (m). MS (GC, 70 eV): *m/z* (%): 222 (M^+, ^{37}Cl, 16), 220 (M^+, ^{35}Cl, 46), 188 (84), 175 (52), 161 (100), 143 (62), 125 (40); HRMS (EI) calcd for $C_9H_{13}ClO_4$ [M^+, ^{35}Cl]: 220.04969, found 220.050278.



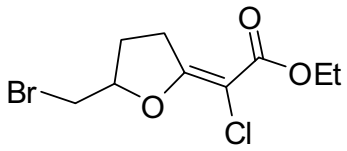
Ethyl 6-azido-2-chloro-5-methoxy-3-oxohexanoate (44): Starting with 1,3-Bis-silyl Enol Ether **38** (0.772 g, 2.5 mmoles), 1-azido-2,2-dimethoxyethane (420mg, 3.25 mmole) and Me_3SiOTf (0.14 mL, 0.38 mmole) in CH_2Cl_2 (25ml), **44** was isolated as yellow oil (690 mg, 82%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, 3 H, *J* = 7.2 Hz, CH_3), 2.73-2.84 (m, 1H, CH_2), 2.92-3.08 (m, 1H, CH_2), 3.16-3.24 (m, 1H, CH_2), 3.34 (s, 3H, OCH_3), 3.37-3.44 (m, 1H, CH_2), 3.76-3.85 (m, 1H, CH), 4.21 (q, 2H, *J* = 7.2 Hz, OCH_2), 4.81 (d, 1H, *J* = 2.2 Hz, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.7 (CH_3), 41.0, 52.5 (CH_2), 57.5 (OCH_3), 61.2 (CH), 63.0 (OCH_2), 75.7 (CH), 164.4, 196.2 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2983 (w), 2932 (w), 2833 (w), 2098 (s), 1726 (s), 1643 (w), 1607 (w), 1369 (w), 1250 (s), 1019 (s). MS (EI, 70 eV): *m/z* (%): 265 (M^+, ^{37}Cl, 2), 263 (M^+, ^{35}Cl, 4), 207 (33), 85 (100). HRMS (EI) calcd for $C_9H_{14}ClN_3O_4$ [M^+, ^{35}Cl]: 263.06674, found 263.066749.



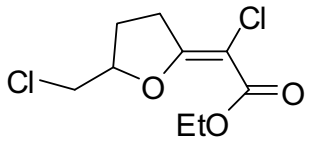
(Z)-ethyl 2-chloro-2-(5-vinyldihydrofuran-2(3H)-ylidene)acetate (45): Starting with LDA (62.5 mmoles), **36** (3.51 mL, 25 mmole) and trans-1,2-dibromo butene (6.41g , 30 mmole) at -78°C **45** was isolated as light yellow oil (3.5g, 65%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.21 (t, 3H, *J* = 7.5 Hz, CH_3), 1.77-1.92 (m, 1H, CH_2), 2.18-2.32 (m, 1H, CH_2), 2.92-3.06 (m, 1H, CH_2), 3.12-3.25 (m, 1H, CH_2), 4.34 (q, 2 H, *J* = 7.5 Hz, OCH_2), 4.84 (q, 1H, *J* = 7.5 Hz, CH), 5.13-5.29 (m, 2 H, C=CH_2), 5.72-5.85 (m, 1H, CH), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.1 (CH_3), 30.1, 31.6 (CH_2), 60.8 (CH_2), 85.2 (CH), 95.4 (C), 117.9 (CH_2), 135.0 (CH), 164.15 (C), 169.4 (C=O); IR (ATR): $\tilde{\nu}$ = 3087 (w), 2982 (w), 2905 (w), 1744 (w), 1695 (s), 1614 (s), 1367 (m), 1275 (s), 1225 (s), 1059 (s), 936 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 218 (M^+, ^{37}Cl, 16), 216 (M^+, ^{35}Cl, 49), 171 (31), 149 (35), 135 (69), 121 (100), 103 (34); HRMS (EI) calcd for $C_{10}H_{13}O_3Cl$ [M^+]: 216.05477 found 216.054810.



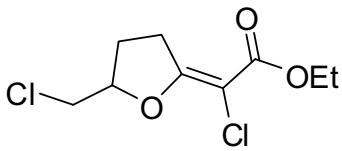
(Z)-ethyl 2-chloro-2-(4,5-dimethyldihydrofuran-2(3H)-ylidene)acetate (46): Starting with 1,3-Bis-silyl Enol Ether **38** (926 mg, 3 mmoles), 2,3-butenoxide (210mg, 0.260 mL, 3 mmole), $TiCl_4$ (1.13 g, 0.65 mL, 6mmole) and molecular sieves (3g) in CH_2Cl_2 (23mL) **46** was obtained as yellow oil (237mg, 37 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.03 (d, 3H, *J* = 7.5 Hz, CH_3), 1.23 (t, 3H, *J* = 7.5 Hz, CH_3), 1.34 (d, 3H, *J* = 7.5 Hz, CH_3), 1.93-2.06 (m, 1H, CH_2), 2.52-2.63 (m, 1H, CH), 3.42-3.52 (m, 1H, CH_2), 4.03-4.11 (m, 1H, CH), 4.12 (q, 2 H, *J* = 7.5 Hz, OCH_2), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.2, 16.0, 18.6 (CH_3), 39.8 (CH), 40.55 (CH_2), 60.9 (OCH_2), 87.3 (CH), 94.9, 164.5 (C), 169.2 (C=O); IR (ATR): $\tilde{\nu}$ = 2974 (w), 2933 (w), 1743 (w), 1695 (m), 1615 (s), 1386 (m), 1277 (s), 1232 (s), 1061 (s), 958 (m) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%): 220 (M^+, ^{37}Cl, 31), 218 (M^+, ^{35}Cl, 97), 203 (30), 173 (62), 157 (37), 137 (55), 55 (100); HRMS (EI) calcd for $C_{10}H_{15}O_3Cl$ [M^+]: 218.07042 found 218.070647.



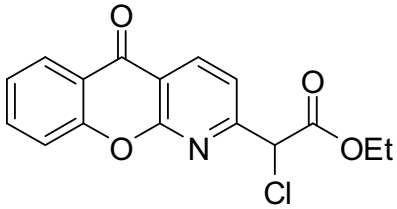
(Z)-ethyl 2-(5-(bromomethyl)dihydrofuran-2(3H)-ylidene)-2-chloroacetate (47): Starting with 1,3-Bis-silyl Enol Ether **38** (772 mg, 2.5 mmoles), epibromohydrin (342mg, 0.200 mL, 2.5 mmole), $TiCl_4$ (948 mg, 0.54 mL, 5mmole) and molecular sieves (3g) in CH_2Cl_2 (38mL) **47** was obtained as yellow oil (335mg, 47 %).^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.97-2.12 (m, 1H, CH_2), 2.29-2.42 (m, 1H, CH_2), 3.01-3.15 (m, 1H, CH_2), 3.24-3.35 (m, 1H, CH_2), 3.47-3.52 (m, 1H, CH_2), 3.24-3.35 (m, 1H, CH_2), 3.83-3.94 (m, 1H, CH), 4.14 (q, 2 H, *J* = 7.5 Hz, OCH_2), 4.70-4.80 (m, 1H, CH_2); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.4 (CH_3), 28.8, 32.0, 33.2 (CH_2), 61.5 (OCH_2), 83.1 (CH), 96.3, 164.4 (C), 169.4 (C=O); IR (ATR): $\tilde{\nu}$ = 3435 (w), 2979 (w), 2936 (w), 1737 (m), 1618 (m), 1279 (m), 1282 (s), 1067 (s), 1232 (s), 1067 (s), 940 (m) cm^{-1}; GC-MS (GC, 70 eV): *m/z* (%): 286 (M^+, ^{37}Cl, ^{81}Br, 18), 284 (M^+, ^{35}Cl, ^{81}Br, 71), 282 (M^+, ^{35}Cl, ^{79}Br, 51), 218 (M^+, ^{35}Cl, 97), 238 (100), 203 (22), 175 (45), 157 (55), 121 (58), 103(48); HRMS (EI) calcd for $C_9H_{12}O_3BrCl$ [M^+, ^{35}Cl, ^{81}Br]: 283.96324 found 283.963505.



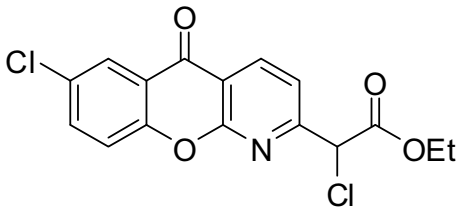
(E)-ethyl2-chloro-2-(5-(chloromethyl)dihydrofuran-2(3H)-ylidene)acetate (48): Starting with 1,3-Bis-silyl Enol Ether **38** (1.54 g, 5 mmoles), epichlorohydrin (550mg, 0.47 mL, 6 mmole), $TiCl_4$ (1.89 g, 1.09 mL, 10mmole) and molecular sieves (5g) in CH_2Cl_2 (38mL) **48** was obtained as yellow oil (72 mg, 17 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.91-2.06 (m, 1H, CH_2), 2.16-2.30 (m, 1H, CH_2), 3.18-3.03 (m, 2H, CH_2), 3.59-3.72 (m, 2H, CH_2), 4.17 (q, 2 H, *J* = 7.5 Hz, OCH_2), 4.82-4.93 (m, 1H, CH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.6 (CH_3), 25.9, 32.9, 45.5 (CH_2), 61.4 (OCH_2), 86.1 (CH), 98.2, 162.6 (C), 168.4 (C=O); IR (ATR): $\tilde{\nu}$ = 2981 (w), 2938 (w), 1740 (m), 1698 (m), 1618 (m), 1369 (w), 1280 (s), 1183 (s), 1068 (s), 940 (m) cm^{-1}; MS (GC, 70 eV): *m/z* (%): 242 (M^+, 2 × ^{37}Cl, 5), 240 (M^+, ^{37}Cl, ^{35}Cl, 28), 238 (M^+, 2 × ^{35}Cl, 46), 210 (10), 194 (68), 192 (100), 175 (15), 157 (35), 147 (19), 103 (35); HRMS (EI) calcd for $C_9H_{12}O_3Cl_2$ [M^+, 2 × ^{35}Cl]: 238.01580 found 238.015571.



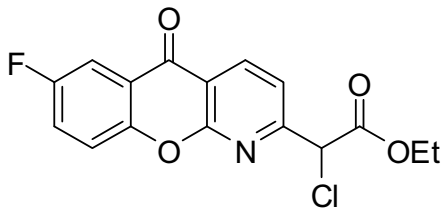
(Z)-ethyl 2-chloro-2-(5-(chloromethyl)dihydrofuran-2(3H)-ylidene)acetate (48): Starting with 1,3-Bis-silyl Enol Ether **38** (1.54 g, 5 mmoles), epichlorohydrin (550mg, 0.47 mL, 6 mmole), $TiCl_4$ (1.89 g, 1.09 mL, 10mmole) and molecular sieves (5g) in CH_2Cl_2 (38mL) **48** was obtained as yellow oil (136 mg, 32 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.00-2.15 (m, 1H, CH_2), 2.25-2.39 (m, 1H, CH_2), 3.02-3.30 (m, 2H, CH_2), 3.65-3.67 (m, 2H, CH_2), 4.14 (q, 2 H, *J* = 7.5 Hz, OCH_2), 4.72-4.82 (m, 1H, CH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.3 (CH_3), 27.4, 31.8, 45.2 (CH_2), 61.1 (OCH_2), 82.9 (CH), 95.8, 164.3 (C), 169.0 (C=O); IR (ATR): $\tilde{\nu}$ = 3434 (w), 2981 (w), 2939 (w), 1742 (m), 1697 (m), 1618 (s), 1368 (w), 1279 (s), 1185 (w), 1067 (s), 940 (m) cm^{-1}; MS (GC, 70 eV): *m/z* (%): 242 (M^+, 2 × ^{37}Cl, 5), 240 (M^+, ^{37}Cl, ^{35}Cl, 29), 238 (M^+, 2 × ^{35}Cl, 45), 210 (12), 194 (69), 192 (100), 175 (13), 157 (33), 147 (18), 103 (31); HRMS (EI) calcd for $C_9H_{12}O_3Cl_2$ [M^+, 2 × ^{35}Cl]: 238.01580 found 238.016442.



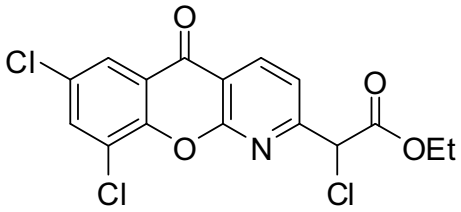
Ethyl 2-chloro-2-(9-oxo-9H-xanthen-3-yl)acetate (51a): Starting with 3-cyanochromone **49a** (256 mg, 1.5 mmol), Me_3SiOTf (433 mg, 0.35 mL, 1.95 mmol), **38** (602 mg, 1.95 mmol), CH_2Cl_2 (13.5 mL), EtOH (15 mL), and triethylamine (303 mg, 0.42 mL, 3 mmol), **51a** was isolated as a yellow solid (276 mg, 58 %), mp. = 91-93 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29 (t, 3 H, *J*= 7.2 Hz, CH_3), 4.25 (q, 2 H, *J* = 6.8 Hz, OCH_2), 5.56 (s, 1H, CH), 7.41 (t, 1H, *J* = 7.9 Hz, ArH), 7.59 (d, 1 H, ArH), 7.73-7.82 (m, 2 H, ArH), 8.34 (dd, 1 H, *J* = 6.4 Hz, *J* = 1.6 Hz, ArH), 8.76 (d, 1H, *J* = 8.8 Hz, ArH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 13.9 (CH_3), 58.9 (CH), 63.1 (OCH_2), 116.5 (C), 118.5, 119.8 (CH), 121.5 (C), 124.9, 126.7 135.8, 138.9 (CH), 155.6, 159.3, 159.8 (C), 166.6, 176.9 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2962 (w), 2925 (w), 2853 (w), 1747 (m), 1664 (s), 1598 (s), 1462 (m), 1403 (s), 1317 (m), 1182 (s), 1022 (s), 805 (m), 750 (s). MS (GC, 70 eV): *m/z* (%): 319 (M^+, ^{37}Cl, 11), 317 (M^+, ^{35}Cl, 32), 283 (11), 245 (100), 211 (27), 182 (11), 126 (8); HRMS (EI) calcd for $C_{16}H_{12}ClNO_4$ [M^+, ^{35}Cl]: 317.04494, found 317.045352.



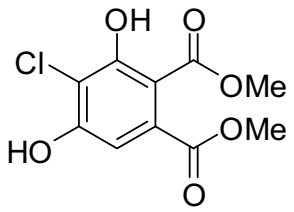
Ethyl 2-chloro-2-(7-chloro-9-oxo-9H-xanthen-3-yl)acetate (51b): Starting with 6-chloro-3-cyanochromone **51b** (205 mg, 1 mmol), Me_3SiOTf (288 mg, 0.23 mL, 1.3 mmol), **38** (400 mg, 1.3 mmol), CH_2Cl_2 (9 mL), EtOH (10 mL), and triethylamine (202 mg, 0.28 mL, 2 mmol), **51b** was isolated as a yellow solid (210 mg, 60%), mp. = 89-92 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, 3 H, *J*= 7.2 Hz, CH_3), 4.21 (q, 2 H, *J* = 7.1 Hz, OCH_2), 5.53 (s, 1H, CH), 7.53 (d, 1H, *J* = 8.8 Hz, ArH), 7.68-7.76 (m, 2H, ArH), 8.22 (d, 1 H, *J* = 2.6 Hz, ArH), 8.72 (d, 1H, *J* = 8.2 Hz, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.0 (CH_3), 58.8 (CH), 63.1 (OCH_2), 116.1 (C), 120.1 (CH), 122.5 (C), 126.1 (CH), 130.8 (C), 135.8, 138.9 (CH), 154.0, 159.2, 160.2 (C), 166.6, 175.9 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 2982 (w), 2929 (w), 1728 (s), 1662 (s), 1600 (s), 1466 (m), 1432 (s), 1392 (s), 1186 (s), 1019 (m), 752 (s). MS (EI, 70 eV): *m/z* (%): 353 (M^+, ^{37}Cl, ^{35}Cl, 7), 351 (M^+, 2 × ^{35}Cl, 32), 317 (33), 279 (47), 245 (100), 216 (20), 69 (16); HRMS (EI) calcd for $C_{16}H_{11}Cl_2NO_4$ [M^+, ^{35}Cl]: 351.00596, found 351.006048.



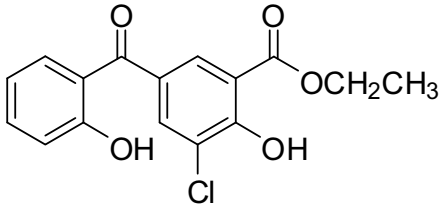
Ethyl 2-chloro-2-(7-fluoro-9-oxo-9H-xanthen-3-yl)acetate (51c): Starting with 6-fluoro-3-cyanochromone **49c** (189 mg, 1 mmol), Me_3SiOTf (288 mg, 0.23 mL, 1.3 mmol), **38** (400 mg, 1.3 mmol), CH_2Cl_2 (9 mL), EtOH (10 mL), and triethylamine (202 mg, 0.28 mL, 2 mmol), **51c** was isolated as a yellow solid (200 mg, 60%), mp. = 113-116 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, 3 H, *J*= 7.2 Hz, CH_3), 4.23 (q, 2 H, *J* = 7.0 Hz, OCH_2), 5.54 (s, 1H, CH), 7.46-7.63 (m, 2H, ArH), 7.74 (d, 1 H, *J* = 7.6 Hz, ArH), 8.34 (dd, 1 H, *J* = 6.9 Hz, *J* = 1.8 Hz, ArH), 8.72 (d, 1H, *J* = 7.5 Hz, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.9 (CH_3), 58.9 (CH), 63.2 (OCH_2), 111.4 (CH), 115.6 (C), 119.9, 120.5 (CH) 122.5 (C), 123.7, 138.8 (CH), 151.7, 157.4, 159.1, 160.0 (C), 166.4, 176.3 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3053 (w), 2982 (w), 2943 (w), 1729 (s), 1663 (s), 1604 (m), 1486 (s), 1448 (s), 1299 (s), 1190 (s), 1021 (m), 832 (s). MS (EI, 70 eV): *m/z* (%): 337 (M^+, ^{37}Cl, 7), 335 (M^+, ^{35}Cl, 11), 301 (34), 263 (40), 229 (100), 200 (21), 69 (36); HRMS (EI) calcd for $C_{16}H_{11}ClNFO_4$ [M^+, ^{35}Cl]: 335.03552, found 335.035168.



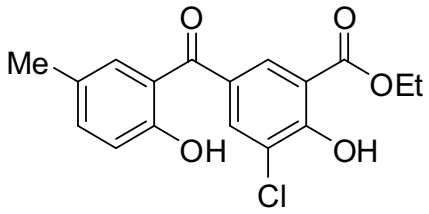
Ethyl 2-chloro-2-(5,7-dichloro-9-oxo-9H-xanthen-3-yl)acetate (51d): Starting with 6,8-dichloro-3-cyanochromone (**49d**) (240 mg, 1 mmol), Me_3SiOTf (288 mg, 0.23 mL, 1.3 mmol), **38** (400 mg, 1.3 mmol), CH_2Cl_2 (9 mL), EtOH (10 mL), and triethylamine (202 mg, 0.28 mL, 2 mmol), **51d** was isolated as a yellow solid (149 mg, 39%), mp. = 103-106 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, 3 H, *J*= 7.2 Hz, CH_3), 4.23 (q, 2 H, *J* = 7.1 Hz, OCH_2), 5.57 (s, 1H, CH), 7.79-7.82 (m, 2H, ArH), 8.12 (d, 1 H, *J* = 1.8 Hz, ArH), 8.71 (d, 1H, *J* = 7.5 Hz, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.9 (CH_3), 58.7 (CH), 63.2 (OCH_2), 115.7 (C), 120.7 (CH) 123.5 (C), 124.7 (CH), 130.5 (C), 135.7, 138.9 (CH), 150.1, 158.7, 160.7, (C), 166.6, 175.5 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 2979 (w), 2914 (w), 1722 (s), 1662 (s), 1607 (s), 1558 (m), 1386 (s), 1301 (m), 1180 (s), 1019 (m), 727 (s). MS (EI, 70 eV): *m/z* (%): 387 (M^+, ^{37}Cl, 5), 385 (M^+, ^{35}Cl, 5), 353 (21), 313 (20), 279 (100), 250 (12), 97 (18); HRMS (EI) calcd for $C_{16}H_{10}Cl_3NO_4$ [M^+, ^{35}Cl]: 384.96699, found 384.966901.



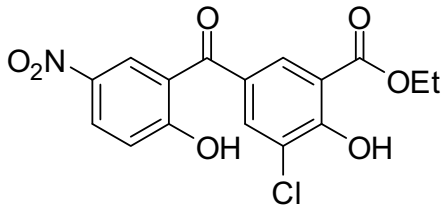
Dimethyl 4-chloro-3,5-dihydroxyphthalate (52): Starting with **38** (463mg, 1.5 mmol and DMAD (319mg, 0.27 mL, 2.25 mmol) **52** was isolated as crystalline solid (460, 54 %), mp. = 127-129 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 6.57 (s, 1H, OH), 6.57 (s, 1H, ArH), 11.55 (s, 1H, OH). ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 52.8 (OCH_3), 53.0 (OCH_3), 103.5 (C), 107.5 (CH), 109.3, 135.0 (C), 156.6, 158.7 (C-OH), 168.6, 169.0 (C=O). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2984 (w), 2954 (w), 2905 (w), 2847 (w), 1792 (w), 1722 (s), 1668 (m), 1435 (m), 1328 (m), 1243 (s), 1067 (s), 844 (m). MS (EI, 70 eV): *m/z* (%): 262 (M^+, ^{37}Cl, 9), 260 (M^+, ^{35}Cl, 15), 228 (53), 198 (23), 170 (100), 153 (23), 89 (25); Anal.: calcd (%) for $C_{10}H_9ClO_6$: C 46.08, H 3.48; found: C 46.21, H 3.31.



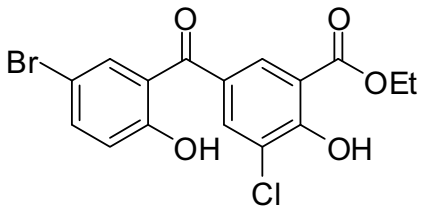
Ethyl-3-chloro-2-hydroxy-5-(2-hydroxybenzoyl)benzoate (57a): Starting with 3-formylchromone **56a** (261 mg, 1.5 mmol), 1,3-bis(silyl enol ether) **55b** (602 mg, 1.95 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **57a** was isolated as a colourless crystalline solid (200 mg, 42%), mp. = 117-118 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, *J* = 7.1 Hz, 3 H, CH_3), 4.36 (q, 2 H, *J* = 7.0 Hz, 14.2 Hz, OCH_2), 6.83 (m, 1 H, ArH), 6.96 (d, 1 H, *J* = 8.3 Hz, ArH), 7.40-7.47 (m, 2 H, ArH), 7.82 (d, 1 H, *J* = 2.25 Hz, ArH), 7.68 (d, *J* = 2.3 Hz, 1 H, ArH), 8.08 (d, *J* = 2.43 Hz, 1 H, ArH), 11.60 (s, 1 H, OH), 11.80 (s, 1 H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.0 (CH_3), 62.6 (OCH_2), 113.4, 118.6 (C), 118.6, 118.9 (CH), 122.7, 129.0 (C), 130.2, 132.7, 136.2, 136.5(CH), 160.3, 163.0 (C-OH), 169.3, 197.8 (C=O); IR (neat): $\tilde{\nu}$ = 3086 (w), 2991(m), 2962 (w), 1720 (w), 1680 (s), 1622 (s), 1567 (m), 1444 (m), 1374 (m), 1337 (s), 1239 (s), 1014 (m) cm^{-1}; MS (GC, 70 eV): *m/z* (%): 322 (M^+, ^{37}Cl, 26), 320 (M^+, 75), 274 (34), 181 (21), 154 (39), 121 (100); HRMS (EI) calcd for $C_{16}H_{13}ClO_5$ [M^+, ^{35}Cl]: 320.04460, found 320.044647.



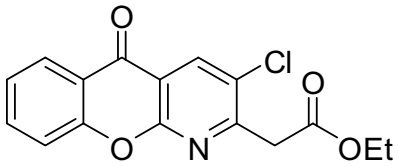
Ethyl-3-chloro-2-hydroxy-5-(2-hydroxy-5-methylbenzoyl)benzoate (57b): Starting with 6-methyl-3-formylchromone **56b** (282 mg, 1.5 mmol), 1,3-bis(silyl enol ether) **55b** (602 mg, 1.95 mmol), and Me_3SiOTf (0.08 mL, 0.45 mmol), **57b** was isolated as a colourless crystalline solid (201 mg, 40 %), mp. = 142-144 °C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 4.36 (q, 2 H, *J* = 7.0 Hz, 14.2 Hz, OCH_2), 6.89 (d, 1 H, *J* = 8.3 Hz, ArH), 6.96 (d, 1 H, *J* = 8.3 Hz, ArH), 7.24-7.29 (m, 2 H, ArH), 7.85 (d, 1 H, *J* = 2.1 Hz, ArH), 8.10 (d, *J* = 2.1 Hz, 1 H, ArH), 11.43 (s, 1 H, OH), 11.81 (s, 1 H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 (CH_3), 20.5 (CH_3), 62.6 (OCH_2), 113.4, 118.0 (C), 118.4 (CH), 122.7, 128.0, 129.2 (C), 130.2, 132.3, 136.1, 137.5 (CH), 160.2, 160.9 (C-OH), 169.3, 197.7 (C=O); IR (neat): $\tilde{\nu}$ = 3065 (w), 2993 (w), 2856 (w), 1679 (s), 1627 (s), 1581 (s), 1482 (m), 1375 (m), 1338 (s), 1288 (s), 1210 (s), 786 (s) cm^{-1}; MS (GC, 70 eV): *m/z* (%): 336 (M^+, ^{37}Cl, 13), 334 (M^+, 37), 288 (11), 181 (9), 134 (100), 77 (11); HRMS (EI) calcd for $C_{17}H_{15}ClO_5$ [M^+, ^{35}Cl]: 334.06025, found 334.060293.



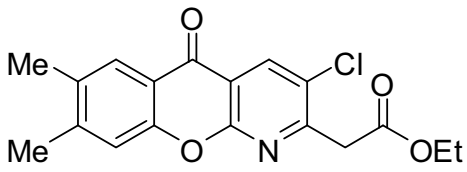
Ethyl-3-chloro-2-hydroxy-5-(2-hydroxy-5-nitrobenzoyl)benzoate (57c): Starting with 6-nitro-3-formylchromone **56c** (219 mg, 1 mmol), 1,3-bis(silyl enol ether) **55b** (401 mg, 1.3 mmol), and Me_3SiOTf (0.05 mL, 0.3 mmol), **57c** was isolated as a yellowish solid (141 mg, 39 %), mp. = 159-161 °C; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.34 (t, *J* = 7.1 Hz, 3 H, CH_3), 4.36 (q, 2 H, *J* = 7.2 Hz, 14.2 Hz, OCH_2), 7.12 (d, 1 H, *J* = 9.3 Hz, ArH), 7.93 (d, 1 H, *J* = 2.62 Hz, ArH), 8.14 (d, 1 H, *J* = 2.35 Hz, ArH), 8.32 (dd, 1 H, *J* = 3.0, 9.3 Hz, ArH), 8.50 (d, 1 H, *J* = 2.5 Hz, ArH), 11.99 (s, 1 H, OH), 12.29 (s, 1 H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 (CH_3), 62.9 (OCH_2), 113.6, 117.5 (C), 119.7 (CH), 123.8, 127.4 (C), 128.7, 130.5, 131.0, 136.0 (CH), 139.5 (C), 161.3, 167.7 (C-OH), 169.1, 196.6 (C=O); IR (neat, cm^{-1}): $\tilde{\nu}$ = 2919 (m), 2850 (w), 1682 (m), 1632 (m), 1460 (m), 1336 (s); MS (GC, 70 eV): *m/z* (%): 367 (M^+, ^{37}Cl, 21), 365 (M^+, 77), 329 (7), 319 (100), 283 (16), 154 (58); HRMS (EI) calcd for $C_{16}H_{12}NClO_7$ [M^+, ^{35}Cl]: 365.02919, found 365.029150.



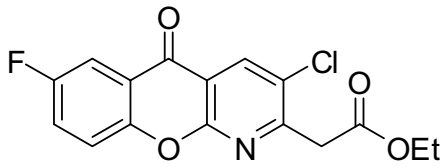
Ethyl-5-(5-bromo-2-hydroxybenzoyl)-3-chloro-2-hydroxybenzoate (57d): Starting with 6-bromo-3-formylchromone **56d** (253 mg, 1 mmol), 1,3-bis(silyl enol ether) **55b** (401 mg, 1.3 mmol), and Me_3SiOTf (0.05 mL, 0.3 mmol), **57d** was isolated as a yellowish solid (140 mg, 36 %), mp. = 133-135 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.2 Hz, 3 H, CH_3), 4.37 (q, 2 H, *J* = 7.2 Hz, 14.2 Hz, OCH_2), 6.90 (d, 1 H, *J* = 8.8 Hz, ArH), 7.51-7.60 (m, 2 H, ArH), 7.8 (d, 1 H, *J* = 2.1 Hz, ArH), 8.09 (d, 1 H, *J* = 2.1 Hz, ArH), 11.50 (s, 1 H, OH), 11.88 (s, 1 H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 (CH_3), 62.7 (OCH_2), 110.4, 113.5, 119.8, (C), 120.7 (CH), 123.2, 128.3 (C), 130.4, 134.5, 136.0, 139.1 (CH), 160.8, 161.9 (C-OH), 169.2, 196.6 (C=O); IR (neat, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2917 (w), 1686 (s), 1625 (s), 1595 (s), 1567 (s), 1343 (s), 1164 (s), 681 (s); MS (GC, 70 eV): *m/z* (%): 401 (M^+, ^{37}Cl, 12), 399 (M^+, 77), 354 (33), 200 (100), 198 (75), 154 (67); HRMS (EI) calcd for $C_{16}H_{12}BrClO_5$ [M^+, ^{35}Cl, ^{81}Br]: 399.95307, found 399.952332.



3-chloro-2-(2-oxobutyl)-5*H*-chromeno[2,3-*b*]pyridin-5-one (60a): Starting with 3-cyanochromone (**58a**) (256 mg, 1.5 mmol), Me_3SiOTf (433 mg, 0.35 mL, 1.95 mmol), **55b** (602 mg, 1.95 mmol), CH_2Cl_2 (13.5 mL), EtOH (15 mL), and triethylamine (303 mg, 0.42 mL, 3 mmol), **60a** was isolated as a yellow solid (276 mg, 58 %), mp. = 110-114 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 (t, 3 H, *J*= 7.0 Hz, CH_3), 4.40 (q, *J* = 7.6 Hz, 2 H, OCH_2), 5.14 (s, 2 H, CH_2), 7.38-7.45 (m, 1 H, ArH), 7.56-7.50 (m, 1 H, ArH), 8.34 (dd, 1 H, *J* = 7.6 Hz, *J* = 1.4 Hz, ArH), 9.22 (s, 1 H, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.2 (*C*H_3), 44.6 (CH_2), 62.2 (OCH_2), 115.7 (C), 118.6 (CH), 121.6, 123.0 (C), 125.4, 126.9, 141.6, (CH), 155.5, 162.4 (C), 164.0, 176.5 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2979 (w), 1715 (m), 1673 (m), 1596 (s), 1425 (m), 1308 (w), 1262 (s), 1213 (m), 1067 (m), 763 (m). MS (GC, 70 eV): *m/z* (%): 319 (M^+, ^{37}Cl, 34), 317 (M^+, 100), 289 (49), 283 (14), 274 (25), 272 (58), 254 (89); HRMS (EI) calcd for $C_{16}H_{12}ClNO_4$ [M^+, ^{35}Cl]: 317.04579, found 317.045442.

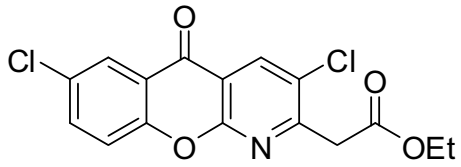


3-chloro-7,8-dimethyl-2-(2-oxobutyl)-5*H*-chromeno[2,3-*b*]pyridin-5-one (60b): Starting with 6,7-dimethyl-3-cyanochromone (**58b**) (290 mg, 1.5 mmol), Me_3SiOTf (433 mg, 0.350 mL, 1.95 mmol), **55b** (602 mg, 1.95 mmol), CH_2Cl_2 (13.5 mL), EtOH (15 mL), and triethylamine (303 mg, 0.42 mL, 3 mmol), **60b** was isolated as a yellow solid (170 mg, 34 %), mp. = 148 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20 (t, 3 H, *J*= 7.1 Hz, CH_3), 2.31 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 4.09 (s, 2 H, CH_2), 4.14 (q, 2 H, *J* = 7.1 Hz, OCH_2), 7.28 (s, 1 H, ArH), 7.94 (s, 1 H, ArH), 8.97 (s, 1 H, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.1 (*C*H_3), 19.2 (*C*H_3), 20.6 (*C*H_3), 42.2 (CH_2), 61.5 (OCH_2), 116.5, 117.5 (C), 117.5 (CH), 123.4, 125.3 (C), 126.3 (CH), 134.3 (C), 137.1 (CH), 146.9, 154.2, 157.5 (C), 168.5, 176.7 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2979 (w), 1715 (m), 1673 (m), 1596 (s), 1425 (m), 1308 (w), 1262 (s), 1213 (m), 1067 (m), 763 (m). MS (GC, 70 eV): *m/z* (%): 347 (M^+, ^{37}Cl, 25), 345 (M^+, 74), 311 (16), 301 (11), 273 (100), 244 (26); HRMS (EI) calcd for $C_{18}H_{16}ClNO_4$ [M^+, ^{35}Cl]: 345.07624, found 345.076341.

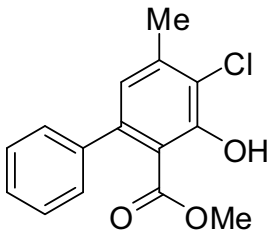


3-chloro-7-fluoro-2-(2-oxobutyl)-5*H*-chromeno[2,3-*b*]pyridin-5-one (60c): Starting with 6-floro-3-cyanochromone (**58c**) (280 mg, 1.5 mmol), Me_3SiOTf (433 mg, 0..35 mL, 1.95 mmol), **55b** (602 mg, 1.95 mmol), CH_2Cl_2 (13.5 mL), EtOH (15 mL), and triethylamine (303 mg, 0.42 mL, 3 mmol), **60c** was isolated as a yellow solid (.180 mg, 37 %), mp. = 126-130 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20 (t, 3 H, *J*= 7.4 Hz, CH_3), 4.06 (s, 2 H, CH_2), 4.14 (q, 2 H, *J* = 7.4 Hz, OCH_2), 7.41-7.49 (m, 1 H, ArH), 7.52-7.57 (m, 1 H, ArH), 7.83 (dd, 1 H, *J*= 7.8 Hz, *J*= 2.9 Hz, ArH), 8.57 (s, 1 H, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.1 (*C*H_3), 42.2 (CH_2), 61.6 (OCH_2), 111.4 (CH), 115.6 (C), 120.5 (CH), 122.1 (C), 123.8 (CH), 128.8 (C), 137.1, 141.6 (CH), 151.7, 157.2, 158.1 (C), 166.1, 175.9 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2981 (w), 2925 (w), 1727 (s), 1658 (s), 1593 (w), 1480 (s), 1397 (s), 1259 (s), 1193 (s), 791 (s). MS (GC, 70 eV): *m/z* (%): 337 (M^+, ^{37}Cl, 19), 335 (M^+, 68), 300 (27), 290 (14), 272 (18), 263

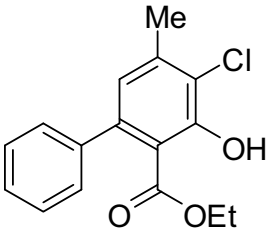
(100), 234 (17); HRMS (EI) calcd for $C_{16}H_{11}ClFNO_4$ [M^+, ^{35}Cl]: 335.03522, found 335.035008.



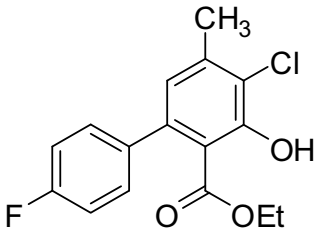
3,7-dichloro-2-(2-oxobutyl)-5*H*-chromeno[2,3-*b*]pyridin-5-one (60d): Starting with 6-chloro-3-cyanochromone (**60d**) (300 mg, 1.5 mmol), Me_3SiOTf (433 mg, 0.35 mL, 1.95 mmol), **55b** (602 mg, 1.95 mmol), CH_2Cl_2 (13.5 mL), EtOH (15 mL), and triethylamine (303 mg, 0.42 mL, 3 mmol), **60d** was isolated as a yellow solid (199 mg, 39 %), mp. = 154-157 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.21 (t, 3 H, *J*= 7.0 Hz, CH_3), 4.06 (s, 2 H, CH_2), 4.12 (q, 2 H, *J* = 7.0 Hz, OCH_2), 7.48 (d, 1 H, *J*= 8.4 Hz, ArH), 8.34 (dd, 1 H, *J* = 9.22 Hz, *J* = 2.3 Hz, ArH), 8.19 (d, 1 H, *J*= 2.3 Hz, ArH), 8.58 (s, 1 H, ArH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.1 (*C*H_3), 42.5 (CH_2), 61.6 (OCH_2), 116.1 (C), 120.2 (CH), 122.1 (C), 126.0 (CH), 128.9, 130.9 (C), 136.0, 137.2 (CH), 153.9, 157.5, 158.1 (C), 168.1, 175.5 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2979 (w), 1715 (m), 1673 (m), 1596 (s), 1425 (m), 1308 (w), 1262 (s), 1213 (m), 1067 (m), 763 (m). MS (GC, 70 eV): *m/z* (%): 353 (M^+, ^{37}Cl, 26), 351 (M^+, 41), 316 (28), 288 (21), 279 (100), 250 (17), 139 (11); HRMS (EI) calcd for $C_{16}H_{11}Cl_2NO_4$ [M^+, ^{35}Cl]: 351.00596, found 351.006388.



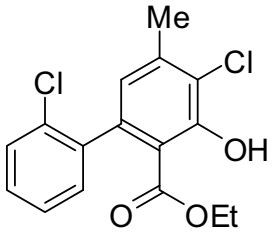
Methyl 4-chloro-3-hydroxy-5-methylbiphenyl-2-carboxylate (62a): Starting with monosilylenolether **60a** (234 mg, 1mmol), 1,3-bis(silyl enol ether) **55a** (324 mg, 1.1 mmol), and $TiCl_4$ (208mg, 0.12mL, 0.58 mmol), **62a** was isolated as a white solid (119 mg, 42 %), mp. = 94-96 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.43 (s, 3H, CH_3), 3.49 (s, 3H, OCH_3), 6.75 (s, 1H, ArH), 7.18-7.21 (m, 2H, ArH), 7.31-7.37 (m, 3H, ArH), 11.32 (s, 1 H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.7 (CH_3), 51.9 (OCH_3), 110.8, 121.4 (C), 124.2, 127.0 (CH), 127.4, 128.0 (2C, CH), 142.0, 142.38, 142.47, 157.0 (C), 171.1 (C=O). IR (neat): $\tilde{\nu}$ = 3369 (w), 2951 (w), 2918 (w), 1664 (s), 1596 (w), 1435 (s), 1347 (m), 1050 (m), 771 (s); MS (GC, 70 eV): *m/z* (%): 278 (M^+, ^{37}Cl, 7), 276 (M^+, 20), 244 (100), 216 (9), 181 (9), 152 (24); HRMS (EI) calcd for $C_{15}H_{13}ClO_3$ [M^+, ^{35}Cl]: 276.05477, found 276.054965 .



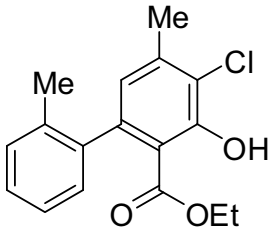
Ethyl 4-chloro-3-hydroxy-5-methylbiphenyl-2-carboxylate (62b): Starting with monosilylenolether **61b** (234 mg, 1mmol), 1,3-bis(silyl enol ether) **55b** (330 mg, 1.1 mmol), and $TiCl_4$ (208mg, 0.12mL, 0.58 mmol), **62b** was isolated as a crystalline solid (112 mg, 41%), mp. = 94-96 °C.^{1}H NMR (300MHz, $CDCl_3$): δ = 0.74 (t, 3H, *J* = 7.4 Hz, CH_3), 2.42 (s, 3H, CH_3), 3.95 (q, 2 H, *J* = 7.4 Hz, OCH_2), 6.71 (s, 1H, ArH), 7.17-7.20 (m, 2H, ArH), 7.31-7.36 (m, 3H, ArH), 11.53 (s, 1 H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 12.9 (CH_3), 20.7 (CH_3), 61.3 (OCH_2), 110.8, 121.4 (C), 124.1, 126.8 (CH), 127.6, 128.0 (2C, CH), 142.32, 142.36, 142.5, 157.2 (C), 170.7 (C=O). IR (neat): $\tilde{\nu}$ = 3063 (s), 2988 (m), 2921 (m), 2881 (w), 1651 (m), 1599 (m), 1440 (m), 1375 (s), 1266 (s), 1216 (s); MS (GC, 70 eV): *m/z* (%): 292 (M^+, ^{37}Cl, 7), 290 (M^+, ^{37}Cl, 18), 244 (100), 216 (7), 181 (9), 152 (21); HRMS (EI) calcd for $C_{16}H_{15}ClO_3$ [M^+, ^{35}Cl]: 290.07042, found 290.070573.



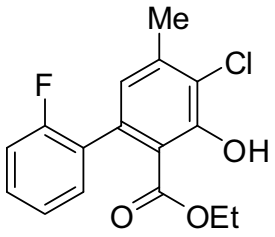
Ethyl 4-chloro-4'-fluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (62c): Starting with monosilylenolether **61c** (101 mg, 0.4 mmol), 1,3-bis(silyl enol ether) **55b** (135 mg, 0.44 mmol), and $TiCl_4$ (0.05 mL, 0.44 mmol), **62c** was isolated as a crystalline solid (59 mg, 48 %), mp. = 140-142 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.75 (t, 3H, *J* = 7.1 Hz, CH_3), 2.35 (s, 3H, CH_3), 3.94 (q, 2 H, *J* = 7.0 Hz, OCH_2), 6.60 (s, 1H, ArH), 6.94-7.01 (m, 2H, ArH), 7.06-7.12 (m, 2H, ArH), 11.53 (s, 1 H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.06 (CH_3), 20.6 (CH_3), 61.4 (OCH_2), 110.7 (C), 114.2, 114.6 (CH), 121.7 (C), 124.2, 129.6, 129.7 (CH), 138.3, 141.3, 142.4, 157.4, 160.1 (C), 170.5 (C=O). IR (neat): $\tilde{\nu}$ = 3076 (w), 2917 (s), 2837 (m), 1656 (m), 1602 (s), 1504 (m), 1453 (m), 1375 (s), 1221 (m), 1155 (s), 777 (m); MS (GC, 70 eV): *m/z* (%): 310 (M^+, ^{37}Cl, 6), 308 (M^+, 19), 262 (100), 234 (9), 199 (9), 170 (22); HRMS (EI) calcd for $C_{16}H_{14}ClFO_3$ [M^+, ^{35}Cl]: 308.06100, found 308.060716.



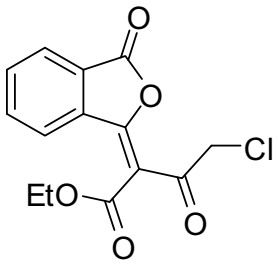
Ethyl 2',4-dichloro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (62d): Starting with monosilylenolether **61d** (140 mg, 0.53 mmol), 1,3-bis(silyl enol ether) **55b** (179 mg, 0.58 mmol), and $TiCl_4$ (0.06 mL, 0.58 mmol), **62d** was isolated as a crystalline solid (85 mg, 49 %), mp. = 85-88 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.69 (t, 3H, *J* = 7.4 Hz, CH_3), 2.35 (s, 3H, CH_3), 3.92 (q, 2 H, *J* = 7.4 Hz, OCH_2), 6.54 (s, 1H, ArH), 7.07-7.11 (m, 1H, ArH), 7.18-7.20 (m, 2H, ArH), 7.21-7.32 (m, 1H, ArH), 11.90 (s, 1 H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 12.8 (CH_3), 20.7 (CH_3), 61.5 (OCH_2), 110.8, 112.2 (C), 123.8, 126.2,128.3, 128.6, 129.6 (CH), 132.3, 139.1, 141.3, 142.9, 157.7 (C), 170.3 (C=O). IR (neat): $\tilde{\nu}$ = 3305 (br), 2986 (m), 2855 (w), 1731 (w), 1651 (s), 1435 (w), 1374 (s), 1214 (s), 1011 (m), 753 (s); MS (GC, 70 eV): *m/z* (%): 326 (M^+, ^{37}Cl, 2), 324 (M^+, 4), 289 (98), 280 (65), 278 (100), 261 (67); HRMS (EI) calcd for $C_{16}H_{14}Cl_2O_3$ [M^+, ^{35}Cl]: 324.03145, found 324.030996.



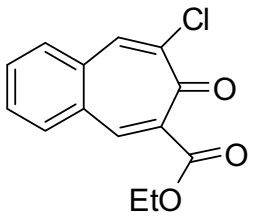
Ethyl 4-chloro-3-hydroxy-2',5-dimethyl[1,1'-biphenyl]-2-carboxylate (62e): Starting with monosilylenolether **61e** (248 mg, 1 mmol), 1,3-bis(silyl enol ether) **55b** (339 mg, 1.1 mmol), and $TiCl_4$ (0.12 mL, 1.1 mmol), **62e** was isolated as a crystalline solid (120 mg, 40 %), mp. = 77-79 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.69 (t, 3H, *J* = 7.4 Hz, CH_3), 1.95 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.87 (q, 2 H, *J* = 7.4 Hz, OCH_2), 6.53 (s, 1H, ArH), 6.90-6.94 (m, 1H, ArH), 7.07-7.10 (m, 2H, ArH), 7.15-7.21 (m, 1H, ArH), 11.85 (s, 1 H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 12.8 (CH_3), 19.9 (CH_3), 20.7 (CH_3), 61.3 (OCH_2), 110.7, 121.3 (C), 123.7, 125.0, 127.0, 128.4, 129.1 (CH), 134.9, 141.9, 142.2, 142.8, 157.7 (C), 170.7 (C=O). IR (neat): $\tilde{\nu}$ = 2985 (w), 2922 (m), 2853 (w), 1650 (s), 1600 (m), 1373 (s), 1294 (s), 1213 (m), 727 (s); MS (GC, 70 eV): *m/z* (%): 306 (M^+, ^{37}Cl, 4), 304 (M^+, 13), 260 (35), 258 (100), 195 (21), 165 (24); HRMS (EI) calcd for $C_{17}H_{17}ClO_3$ [M^+, ^{35}Cl]: 304.08607, found 304.0086736.



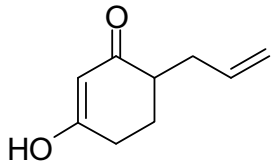
Ethyl 4-chloro-2'-fluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (62f): Starting with monosilylenolether **61f** (720 mg, 2.85 mmol), 1,3-bis(silyl enol ether) **55b** (970 mg, 3.14 mmol), and $TiCl_4$ (0.34 mL, 3.14 mmol), **61f** was isolated as a crystalline solid (390 mg, 45 %), mp. = 76-79 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.75 (t, 3H, *J* = 6.5 Hz, CH_3), 2.34 (s, 3H, CH_3), 3.96 (q, 2 H, *J* = 7.0 Hz, OCH_2), 6.60 (s, 1H, ArH), 6.91-6.98 (m, 1H, ArH), 7.06-7.11 (m, 2H, ArH), 7.22 (m, 1H, ArH), 11.53 (s, 1 H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.0 (CH_3), 20.7 (CH_3), 61.5 (OCH_2), 111.0 (C), 114.4, 114.8 (CH), 122.3 (C), 123.7, 124.4, 129.0 (CH), 135.4, 142.9, 142.4, 157.7, 161.0 (C), 170.5 (C=O). IR (neat): $\tilde{\nu}$ = 3040 (w), 2979 (m), 1657 (m), 1604 (m), 1495 (m), 1440 (m), 1374 (s), 1260 (s), 1215 (s), 759 (s); MS (GC, 70 eV): *m/z* (%): 310 (M^+, ^{37}Cl, 8), 308 (M^+, 24), 262 (100), 234 (12), 199 (11), 170 (24); HRMS (EI) calcd for $C_{16}H_{14}ClFO_3$ [M^+, ^{35}Cl]: 308.06100, found 308.060555.



4-Chloro-3-oxo-2-[3-oxo-3*H*-isobenzofuran-(1E)-ylidene]-butyric acid ethyl ester (64): A CH_2Cl_2 solution (10ml) of the 1,3-bis(silyl enol ether) **55b** (1.85g, 6mmol) was added phthaloyl dichloride **63** (0.81g, 4mmol) at -78 °C under argon atmosphere. The solution was allowed to warm to 20 °C within 6 h and was stirred at this temperature for 6-8 hrs. To the solution was added a sat. aq solution of $NaHCO_3$ (50ml), the organic and aqueous layers were separated and the latter was extracted with CH_2Cl_2 (3 × 50ml). The combined organic layers were purified by chromatography (silica gel, heptane/EtOAc 9: 1) to give the **64** as crystaline solid (360 mg, 36 %), m.p = 111-113 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (t, 3 H, *J* = 7.1 Hz, CH_3), 4.32(q, 2 H, *J* = 7.1 Hz, 14.3 Hz, OCH_2), 4.56 (s, 2 H, CH_2), 7.67-7.80 (m, 2 H, ArH), 7.94 (d, 1 H, *J* = 7.3 Hz, ArH), 7.97 (d, 1 H, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 (CH_3), 49.2 (CH_2), 62.5 (OCH_2), 113.4, 125.4 (C), 126.2, 127.0, 133.4, 135.7 (CH), 137.3, 154.3 (C), 163.1, 163.4, 189.9 (C=O); IR (neat, cm^{-1}): $\tilde{\nu}$ = 2919 (m), 2850 (w), 1682 (m), 1632 (m), 1460 (m), 1336 (s); MS (GC, 70 eV): *m/z* (%): 296 (M^+, ^{37}Cl, 1), 294 (M^+, 1), 245 (88), 173 (100), 104 (14), 76 (19); HRMS (EI) calcd for $C_{14}H_{11}ClO_5$ [M^+, ^{35}Cl]: 294.02895, found 294.028548.

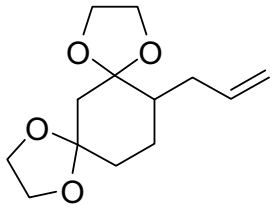


Ethyl 8-chloro-7-oxo-7*H*-benzo[*a*]cycloheptene-6-carboxylate (66): A CH_2Cl_2 solution (140 mL) of phthalic dialdehyde **65** (2.0 m.mol, 268 mg) and molecular sieves (4 Å, 1.0 g) was stirred for 15 min at -78 °C. A CH_2Cl_2 solution (5ml) each of 1,3-bis(silyl enol ether) **55b** (1.1 m.mol, 339 mg) and of $TiCl_4$ (2.2 m.mol, 0.417 g, 0.24 ml) was added at -78 °C. The temperature of reaction mixture was allowed to rise to 20 C during 12 h. After the mixture was stirred for 2h at 20 °C, an aqueous solution of hydrochloric acid (100ml, 10%) was added. The organic layer was separated, and aqueous layer was extracted three times with dichloromethane (100ml). The combined organic layers were extracted with brine, dried with (Na_2SO_4), and filtered. The filtrate was removed in vacuo. The residue was purified by column chromatography (silica gel, Heptane/EtOAc 9:1) to give **66** as crystalline solid (257 mg, 51%) m.p. = 102-106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, 3 H, *J* = 7.0 Hz, CH_3), 4.32(q, 2 H, *J* = 7.2 Hz, 14.3 Hz, OCH_2), 7.58-7.64 (brs, 3 H, ArH), 7.69 (m, 1 H, ArH), 7.88 (s, 1H, C=CH), 8.01 (s, 1H, C=CH); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.2 (CH_3), 62.2 (OCH_2), 130.8, 132.1 (C), 133.1, 133.4 (C), 133.6, 134.9 (CH), 135.2 (C), 139.4 (CH), 139.9 (C), 141.4 (CH), 167.4, 177.5 (C=O); IR (neat, cm^{-1}): $\tilde{\nu}$ = 2919 (m), 2850 (w), 1682 (m), 1632 (m), 1460 (m), 1336 (s); MS (GC, 70 eV): *m/z* (%): 264 (M^+, ^{37}Cl, 6), 262 (M^+, 17), 234 (45), 219 (12), 217 (24), 189 (100), 161 (36), 126 (64); HRMS (EI) calcd for $C_{14}H_{11}ClO_3$ [M^+, ^{35}Cl]: 262.03912, found 262.038666.

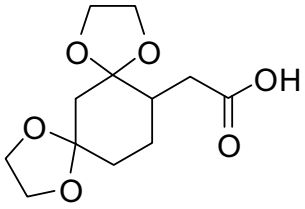


4-Allylcyclohexane-1,3-dione (71a). To a THF solution (98 ml) of 1,3-cyclohexanedione **67a** (5.0 g, 44.6 mmol) and of anhydrous HMPA (20 ml) was added a THF solution of LDA which was prepared from *n*BuLi (2.5 M solution in hexane, 40 ml, 98.2 mmol) and diisopropylamine at –78 °C. After stirring for 1 h, the reaction mixture was allowed to warm to -40 °C and 2-methylallyl bromide (4.1 ml, 44.6 mmol) was added rapidly. The mixture was slowly warmed to room temperature and stirred for additional 10 h at 20 °C. The reaction mixture was concentrated, diluted with hydrochloric acid (5%), and extracted with diethyl ether (3 x 100 ml). The organic layer was washed with hydrochloric acid (3%) and with brine, dried ($MgSO_4$), filtered and

concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica gel, heptanes/EtOAc = 1:1) to give **71a** as a pale yellow oil (5.90 g, 87%). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.77 (m, 1H, C=CH), 5.45 (s, 1H, CH), 5.03 (m, 2H, $C=CH_2$), 2.67 (m, 3H, CH, CH_2), 2.43 (m, 2H, CH_2), 2.23 (m, 2H, CH_2), 1.7 (m, 1H, CH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 196.7 (C=O), 189.5 (C=COH), 136.2 (C=CH), 117.9 ($C=CH_2$), 104.3 (CH), 41.9 (CH), 34.8 (CH_2), 30.2 (CH_2), 25.7 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3076 (m), 2934 (w), 2664 (w), 1598 (s, br), 1413 (m). MS (GC, 70 eV): *m/z* (%) 152 $[M]^+$ (13), 124 (16), 123 (27), 110 (46), 109 (24), 96 (26), 95 (52), 92 (10), 83 (42), 82 (62), 81 (33), 79 (15), 69 (22), 68 (56), 67 (100). HRMS (EI, 70 eV): calcd. for $C_9H_{12}O_2$ $[M^+]$: *m/z* = 152.083669; found: 152.08318.

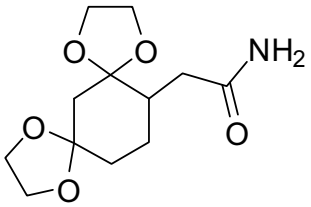


12-Allyl-1,4,8,11-tetraoxadispiro[4.1.4.3]tetradecane (72a). A mixture of **71a** (6.08 g, 40.0 mmol), ethylene glycol (5.0 ml, 85.0 mmol) and *p*-toluenesulfonic acid monohydrate (50 mg, 2.6 mmol) in toluene (300 ml) was stirred under reflux for 4 h using Dean-Stark conditions. Approximately 1.6 ml of water was collected in the Dean-Stark trap. The toluene solution was washed with a saturated aqueous solution of $NaHCO_3$ (40 ml) and with brine (60 ml). The solution was dried ($MgSO_4$), filtered and the solvent of the filtrate was removed *in vacuo*. The residue was purified by chromatography (silica gel) to give **6a** (3.65 g, 18.6 mmol, 90%) as a colourless oil. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 5.92 (m, 1H, CH), 5.15 (m, 2H, CH_2), 4.06 (m, 8H, OCH_2), 2.58 (m, 1H, CH), 2.18 - 1.86 (m, 6H, CH_2), 1.69 (m, 2H, CH_2). ^{13}C-NMR: ($CDCl_3$, 75.4 MHz): δ_C = 137.8 (C=CH), 116.1 ($C=CH_2$), 110.5 (C), 109.3 (C), 65.6 (OCH_2), 65.0 (OCH_2), 64.9 (OCH_2), 64.2 (OCH_2), 43.8 (CH), 43.1 (CH_2), 33.5 (CH_2), 32.7 (CH_2), 24.9 (CH_2). MS (GC, 70 eV): *m/z* (%) = 240 ($[M+1]^+$, 1), 157 (35), 154 (22), 139 (15), 138 (10), 126 (26), 125 (14), 113 (5), 99 (35), 87 (12), 86 (100), 55 (11), 42 (10). HRMS (EI, 70 eV): calcd. for $C_{13}H_{20}O_4$ $[M+1]^+$: *m/z* = 240.13561; found: 240.13589.

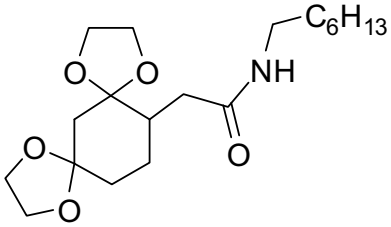


2-(1,4,8,11-Tetraoxadispiro[4.1.4.3]tetradec-12-yl)acetic acid (73a). To a stirred water solution (250 ml) of $NaIO_4$ (15.00 g, 196.0 mmol) and $KMnO_4$ (0.63 g, 3.9 mmol) was added an acetone solution (39 ml) of **72a** (2.30 g, 11.7 mmol). The solution was stirred at room temperature until a colour change from violet to red was observed. The solution was then extracted with EtOAc (3 x 100 ml) and the combined organic layers were dried ($MgSO_4$). The solution was filtered and the filtrate was concentrated *in vacuo* to give **72a** (1.61 g, 65%) as a light brown gummy substance which required no further purification. ^{1}H-NMR (300 MHz, $CDCl_3$): 10.09 (brs, 1H, COOH), 3.86 (m, 8H, OCH_2), 2.51 (dd, J = 15.0, 4.5 Hz, 1H), 2.21 (m, 1H), 2.05 (dd, J = 14.7, 8.1 Hz, 1H), 1.90 (dd, J = 12.5, 1.8 Hz, 2H), 1.69 (m, 2H), 1.50 (brd, d, J = 8.7, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): 178.7 (C=O), 109.7 (C), 109.0 (C), 65.5 (OCH_2), 65.4 (OCH_2), 64.9 (OCH_2), 64.1 (OCH_2), 42.6 (CH_2), 40.9 (CH), 33.8 (CH_2), 33.5 (CH_2), 26.0 (CH_2). MS (EI, 70 eV): *m/z* (%) 258 $[M]^+$ (2), 215 (8), 172 (18), 157 (87), 152 (6), 144 (32), 128 (8), 113 (32), 100 (9), 99 (93), 87 (20), 86 (100), 85 (15), 83 (22). HRMS (EI, 70 eV): calcd. for $C_{12}H_{18}O_6$ $[M]^+$: *m/z* = 258.10979; found: 258.109219.

Typical procedure for the synthesis of amides 76: To a CH_2Cl_2 solution (20 mL) of **73a** (1 equiv.) was added *N*-hydroxysuccinimide (1.1 equiv.) and dicyclohexylcarbodiimide (1.1 equiv.) at 0 °C and the mixture was stirred for 1 h at the same temperature. After stirring for 12 h, the mixture was filtered, amine (1equiv.) was added to the filtrate and the mixture was stirred for 2 h. The mixture was filtered and washed for several times with water (50 mL for each washing). The organic layer was dried ($NaSO_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, heptanes/EtOAc) to give **77.**

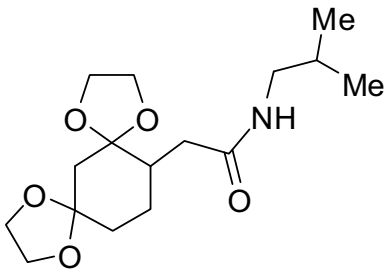


2-(1,4,8,11-Tetraoxadispiro[4.1.4.3]tetradec-12-yl)acetamide (76a). Starting with CH_2Cl_2 (40 mL), **73a** (340 mg, 1.3 mmol), *N*-hydroxysuccinimide (178.4 mg, 1.6 mmol), dicyclohexylcarbodiimide (328.8 mg, 1.6 mmol) and ammonia (25% aqueous solution, 0.12 ml, 1.6 mmol), **76a** (210 mg, 62%) was isolated as a white solid, mp. = 149 - 152 °C. ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 5.81 (brs, 1H, NH), 5.69 (brs, 1H, NH), 3.89 (m, 8H, OCH_2), 2.46 (dd, *J* = 14.5, 4.5 Hz, 1H, CH_2), 2.16 (m, 1H, CH), 1.98 (dd, *J* = 8.5, 2.5 Hz, 1H, CH_2), 1.92 (dd, *J* = 7.5, 5.3 Hz, 1H, CH_2), 1.77 (m, 2H, CH_2), 1.70 (br, *J* = 13.8 Hz, 1H, CH_2), 1.53, (dd, *J* = 11.0, 2.0 Hz, 1H, CH_2), 1.49 (dd, *J* = 11.2, 2.7 Hz, 1H, CH_2). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ_C = 175.4 (NC=O), 109.7 (C), 108.6 (C), 65.0 (OCH_2), 64.7 (OCH_2), 64.6 (OCH_2), 63.9 (OCH_2), 42.3 (CH_2), 40.6 (CH), 35.0 (CH_2), 33.2 (CH_2), 25.8 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3411 (w), 3175 (w), 2946 (w), 2966 (w), 2946 (w), 2880 (w), 1669 (s, br), 1625 (m). MS (GC, 70 eV): *m/z* (%) 257 ($[M]^+$, 2), 214 (5), 212 (5), 199 (9), 171 (19), 157 (69), 143 (16), 127 (6), 113 (13), 99 (67), 87 (14), 86 (100). HRMS (EI, 70 eV): calcd. for $C_{12}H_{19}O_5$ $[M]^+$: *m/z* = 257.125885; found: 257.12577.

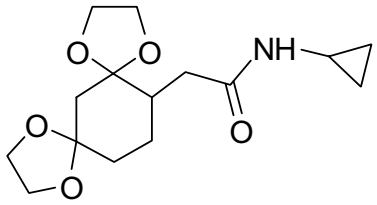


***N*-Heptyl-2-(1,4,8,11-tetraoxadispiro [4.1.4.3]tetradec-12-yl)acetamide (76b).** Starting with CH_2Cl_2 (20 mL), **73a** (200 mg, 0.8 mmol), *N*-hydroxysuccinimide (97 mg, 0.9 mmol), dicyclohexylcarbodiimide (175 mg, 0.9 mmol) and *n*-heptylamine (0.1 ml, 0.8 mmol), **76b** (153 mg, 57%) was isolated as a white solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 5.68 (s, 1H, NH), 3.80-3.96 (m, 8H, CH_2), 3.11 (q, 2H, *J* = 1.9, *J* = 5.6 Hz, CH_2), 2.38 (dd, 1H, *J* = 4.4, *J* = 14.3 Hz, CH_2), 2.13-2.23 (m, 1H, CH_2), 1.67-1.97 (m, 6H, CH_2), 1.38-1.97 (m, 1H, CH_2), 1.20 (br, 10H, CH_2), 0.80 (t, *J* = 6.9 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 172.2 (C=O), 109.8 (C-O), 108.7 (C-O), 65.0 (CH_2), 64.6 (2C, CH_2), 63.8 (CH_2), 42.3 (CH_2), 40.7 (CH), 39.5 (CH_2), 35.8 (CH_2), 31.6 (CH_2), 29.6 (CH_2), 28.8 (CH_2), 26.8 (CH_2), 25.6 (CH_2), 24.9 (CH_2), 22.5 (CH_2), 14.0 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3268 (m), 2924 (s), 1626 (br), 1549 (br) 947 (s). MS (GC, 70 eV): *m/z* (%) = 355 (M^+, 3), 310 (17), 296 (9), 199 (10), 157 (100), 113 (19), 99 (58), 86

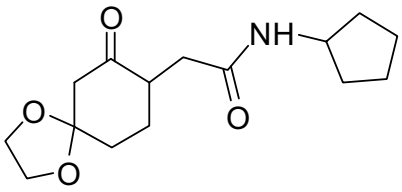
(116), 55 (21). HRMS (EI, 70 eV): calcd. for $C_{19}H_{33}O_5N$ [M^+]: *m/z* = 355.23532; found: 355.23558.



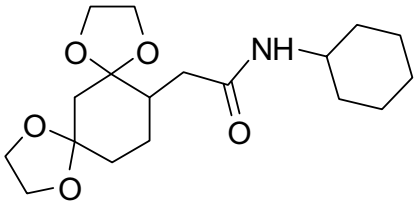
***N*-Isobutyl-2-(1,4,8,11-tetraoxadispiro[4.1.4.3]tetradec-12-yl)acetamide (76c)**. Starting with CH_2Cl_2 (20 mL), **73a** (200 mg, 0.8 mmol), *N*-hydroxysuccinimide (97.0 mg, 0.9 mmol), dicyclohexylcarbodiimide (175.0 mg, 0.9 mmol) and isopropylamine (0.08 ml, 0.8 mmol), **76c** (170 mg, 76%) was isolated as a white solid. Although a small amount of impurity could not be removed, the product was used for the next reaction.



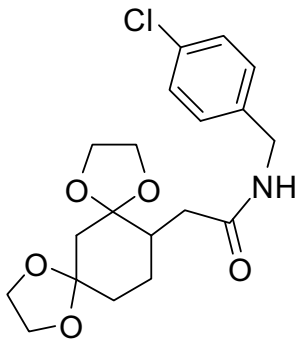
***N*-Cyclopropyl-2-(1,4,8,11-tetraoxadispiro [4.1.4.3]tetradec-12-yl)acetamide (76d).** Starting with CH_2Cl_2 (20 mL), **73a** (200 mg, 0.8 mmol), *N*-hydroxysuccinimide (106 mg, 0.9 mmol), dicyclohexylcarbodiimide (195 mg, 0.9 mmol) and cyclopropylamine (0.1 ml, 0.9 mmol), **76d** (150 mg, 65%) was isolated as a white solid. ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 6.08 (br, 1H, NH), 3.92 (m, 8H, OCH_2), 3.64 (br, 2H, CH_2), 2.63 (m, 1H, CH), 2.39 (dd, *J* = 14.3, 4.8 Hz, 1H, CH_2), 2.13 (m, 1H, CH), 1.95 (dd, *J* = 14.0, 2.0 Hz, 1H, CH_2), 1.83 (dd, *J* = 14.5, 8.8, 1H, CH_2), 1.70 (m, 1H, CH_2), 1.66 (d, *J* = 14.0, 1H, CH_2), 1.50 (m, 2H, CH_2), 0.67 (ddd, *J* = 12.3, 5.1, 1.9, 2H, CH_2), 0.40 (m, 1H, CH_2). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ_C = 174.2 (C=O), 109.7 (C), 108.6 (C), 64.9 (OCH_2), 64.6 (OCH_2), 63.8 (OCH_2), 63.7 (OCH_2), 42.2 (NCH_2), 40.6 (CH), 35.4 (CH_2), 33.0 (CH_2), 25.6 (CH_2), 25.3 (CH_2), 22.5 (CH), 6.51 (CH_2), 6.44 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3338 (w), 2944 (w), 2925 (w), 2892 (w), 1720 (s), 1640 (s, br), 11517 (s, br). MS (EI, 70 eV): *m/z* (%) 297 (M+, 5), 252 (14), 241 (35), 213 (54), 211 (14), 199 (9), 195 (11), 157 (85), 151 (17) 127 (9), 113 (99), 99 (100), 97 (11), 87 (28), 86 (91), 83 (15). HRMS (EI, 70 eV): calcd. for $C_{15}H_{23}NO_5$ [M^+]: *m/z* = 297.157256; found: 297.15707.



***N*-Cyclopentyl-2-(7-oxo-1,4-dioxaspiro[4.5]dec-8-yl) acetamide (mono-76e).** Starting with CH_2Cl_2 (20 mL), mono-**73a** (monoacetal, 200 mg, 0.8 mmol), *N*-hydroxysuccinimide (97 mg, 0.9 mmol), dicyclohexylcarbodiimide (175 mg, 0.9 mmol) and cyclopentylamine (0.1 ml, 0.8 mmol), mono-**76e** (180 mg, 86%) was isolated as a white solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 5.52 (d, 1H, J = 5.8 Hz, NH), 4.13 (q, 1H, J = 6.9, J = 13.7 Hz, CH), 3.83-3.97 (m, 4H, CH_2), 2.43-2.60 (m, 2H, CH_2), 2.28-2.34 (m, 1H, CH), 1.83-2.00 (m, 6H, CH_2), 1.52-1.63 (m, 6H, CH_2), 1.18-1.35 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 207.1 (C=O), 171.2 (C=O), 110.6 (C), 65.2 (CH_2), 64.7 (CH_2), 51.2 (C), 50.6 (CH_2), 40.6 (CH), 39.7 (CH_2), 35.4 (CH_2), 33.1 (2C, CH_2), 26.0 (CH_2), 23.6 (2C, CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3260 (m), 2930 (s), 1620 (br), 1552 (br) 942 (s). MS (GC, 70 eV): *m/z* (%) = 281 (M^+, 3), 236 (19), 224 (16), 169 (18), 128 (100), 113 (24), 99 (16), 86 (35), 55 (31). HRMS (EI, 70 eV): calcd. for $C_{15}H_{23}O_4N$ [M^+]: *m/z* = 281.16216; found: 281.162100.

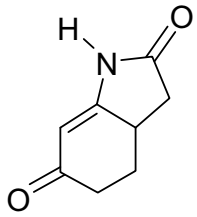


***N*-Cyclohexyl-2-(1,4,8,11-tetraoxadispiro[4.1.4.3] tetradec-12-yl)acetamide (76f).** Starting with CH_2Cl_2 (20 mL), **73a** (200 mg, 0.8 mmol), *N*-hydroxysuccinimide (106 mg, 0.9 mmol), dicyclohexylcarbodiimide (195 mg, 0.9 mmol) and cyclohexylamine (0.1 ml, 0.9 mmol), **76f** (120 mg, 46%) was isolated as a white solid. ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 5.45 (d, J = 5.5 Hz, 1H, NH), 3.92 (m, 8H, OCH_2), 3.87 (m, 1H, NCH), 3.71 (dd, J = 14.3, 4.5 Hz, 1H, CH_2), 2.38 (m, 1H, CH), 2.18 (dd, J = 14.0, 2.5, 1H, CH_2), 1.88 - 1.05 (m, 16H, CH_2). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ_C = 171.3 (C=O), 109.8 (C), 108.7 (C), 65.0 (OCH_2), 64.6 (OCH_2), 64.6 (OCH_2), 63.9 (OCH_2), 48.0 (NCH), 42.3 (CH_2), 40.7 (CH), 36.0 (CH_2), 33.2 (CH_2), 33.1 (CH_2), 25.7 (CH_2), 25.5 (CH_2), 24.8 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3325 (w), 2930 (w), 2861 (w), 1731 (w), 1636 (s, br), 1531 (s). MS (EI, 70 eV): *m/z* (%) = 339 (M^+, 9), 294 (44), 256 (12), 253 (14), 213 (21), 199 (16), 195 (14), 158 (11), 157 (100) 153 (10), 141 (25), 128 (10), 127 (14), 125 (10), 113 (52), 112 (10), 111 (14), 102 (11), 99 (87), 86 (97). HRMS (EI, 70 eV): calcd. for $C_{18}H_{29}NO_5$ [M^+]: *m/z* = 339.204629; found: 339.20402.

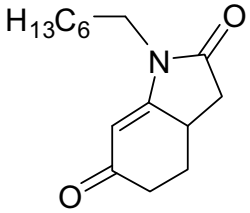


***N*-(4-Chlorobenzyl)-2-(1,4,8,11-tetraoxadispiro[4.1.4.3]tetradec-12-yl)acetamide (76i).** Starting with CH_2Cl_2 (20 mL), **73a** (200 mg, 0.8 mmol), *N*-hydroxysuccinimide (97 mg, 0.9 mmol), dicyclohexylcarbodiimide (175 mg, 0.9 mmol) and 4-chlorobenzylamine (0.1 ml, 0.8 mmol), **76i** (170 mg, 79%) was isolated as a white solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.20 (d, 2H, *J* = 8.5 Hz, ArH), 8.67 (d, 2H, *J* = 8.6 Hz, ArH), 6.03 (s, 1H, NH), 4.31 (q, 2H, *J* = 1.9, *J* = 5.6 Hz, CH_2), 3.70-3.90 (m, 8H, CH_2), 3.66 (s, 2H, CH_2), 2.44-2.62 (m, 2H, CH_2), 2.10-2.27 (m, 1H, CH_2), 1.89-2.01 (m, 4H, CH_2), 1.67-1.76 (m, 2H, CH_2), 1.42-1.55 (m, 2H, CH_2), 1.21 (t, *J* = 7.2 Hz, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 172.6 (C=O), 133.2 (C), 129.1 (2CH), 128.7 (2CH), 109.7 (C), 108.69 (C), 65.0 (CH_2), 64.6 (CH_2), 64.5 (CH_2), 64.5 (CH_2), 63.9 (CH_2), 42.9 (CH_2), 42.2 (CH_2), 40.6 (CH), 35.8 (CH_2), 33.1 (CH_2), 25.9 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3268 (m), 2924 (s), 1626 (br), 1549 (br) 947 (s). MS (EI, 70 eV): *m/z* (%) = 383 (M^+, ^{37}Cl, 15) 381 (M^+, ^{35}Cl, 51), 336 (25), 295 (13), 267 (15), 213 (45), 157 (100), 125 (72), 86 (99). HRMS (EI, 70 eV): calcd. for $C_{19}H_{34}O_5NCl$ [M^+]: *m/z* = 381.13460; found: 381.134472.

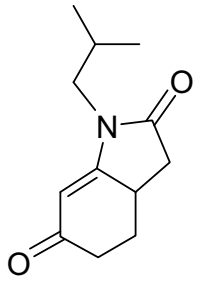
General procedure for the synthesis of 77: An acetone solution of amide **76** and of a catalytic amount of *p*-toluenesulfonic acid (PTSA) was heated under reflux for 6 h. The solution was cooled to 20 °C and concentrated in vacuo to give a solid residue which was purified by column chromatography (silica gel, heptanes/EtOAc).



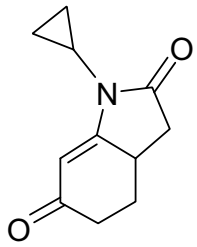
3,3a,4,5-Tetrahydro-1*H*-indole-2,6-dione (77a). Starting with **76a** (70 mg, 0.27 mmol), PTSA (5 mg, 0.02 mmol) and dry acetone (40 mL), **77a** was isolated (31 mg, 90%) as a white solid. ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 9.05 (br, 1H, NH), 5.51 (d, *J* = 2.0 Hz, 1H, CH), 3.14 (m, 1H, CH), 2.66 (dd, *J* = 17.3, 8.8 Hz, 1H, CH_2), 2.49 (ddd, *J* = 17.3, 6.8, 2.3 Hz, 1H, CH_2), 2.38 (dd, *J* = 13.3, 4.8 Hz, 1H, CH_2), 2.26 (dd, *J* = 17.3, 8.8 Hz, 1H, CH_2), 2.24 (m, 1H, CH_2), 1.77 (ddd, *J* = 27.3, 14.8, 6.3 Hz, 1H, CH_2). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ_C = 197.8 (C=O), 177.0 (NC=O), 165.3 (NC=C), 103.1 (CH), 37.4 (CH_2), 36.2 (CH), 35.4 (CH_2), 27.9 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3098 (w), 2991 (w), 2950 (w), 2799 (w), 1746 (s, br), 1574 (a, br). MS (GC, 70 eV): *m/z* (%) = 151 ($[M]^+$, 51), 124 (7), 123 (100), 122 (7), 95 (35), 68 (16), 67 (21). HRMS (EI, 70 eV): calcd. for $C_8H_9O_2$ $[M]^+$: *m/z* = 151.063012; found: 151.06278.



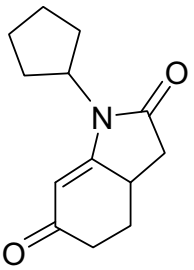
1-Heptyl-3,3a,4,5-tetrahydro-1*H*-indole-2,6-dione (77b). Starting with **76b** (150 mg, 0.4 mmol), PTSA (5 mg, 0.02 mmol) and dry acetone (40 mL), **77b** was isolated (67 mg, 64%) as a white solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 5.41 (d, 1H, *J* = 1.7 Hz, C=CH), 3.25-3.63 (m, 2H, CH_2), 2.94-3.09 (m, 1H, CH), 2.10-2.76 (m, 6H, CH_2), 1.21 (m, 10H, CH_2), 0.80 (t, *J* = 6.9 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 197.0 (C=O), 175.3 (C=O), 166.2 (C), 101.9 (CH), 40.4 (CH_2), 37.5 (CH_2), 34.9(CH_2), 34.7 (CH), 31.6 (CH_2), 28.7 (CH_2), 28.0 (CH_2), 26.7 ($2CH_2$), 22.4 (CH_2), 14.0 (CH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2926 (m), 1739 (m), 1608 (br). MS (GC, 70 eV): *m/z* (%) = 249 (M^+, 72), 220 (43), 206 (18), 192 (79), 178 (32), 165 (100), 150 (56), 137 (53), 108 (36). HRMS (EI, 70 eV): calcd. for $C_{15}H_{23}O_2N$ $[M^+]$: *m/z* = 249.17233; found: 249.172014.



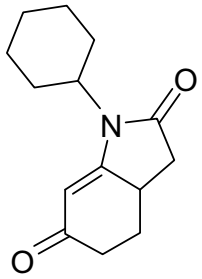
1-Isobutyl-3,3a,4,5-tetrahydro-1*H*-indole-2,6-dione (77c). Starting with **76c** (150 mg, 0.5 mmol), PTSA (5 mg, 0.02 mmol) and dry acetone (40 mL), **77c** was isolated (80 mg, 81%) as a highly viscous yellow oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 5.43 (d, 1H, *J* = 1.7 Hz, C=CH), 3.34-3.43 (dd, 1H, *J* = 8.3, 13.7 Hz, CH_2), 2.96-3.17 (m, 2H, CH_2), 2.68 (dd, 1H, *J* = 8.5, *J* = 13.8 Hz, CH_2), 2.34-2.43 (m, 2H, CH_2), 2.18-2.29 (m, 2H, CH_2), 1.89-2.02 (m, 2H, CH_2), 0.83 (t, *J* = 6.6 Hz, 6H, CH_3). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 197.2 (C=O), 175.6 (C=O), 166.6 (C), 102.2 (CH), 47.6 (CH_2), 37.4 (CH_2), 34.9 (CH2), 34.7 (CH), 28.0 (CH_2), 26.4 (CH) 20.1 ($2CH_3$). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2957 (m), 1735 (m), 1597 (br). MS (GC, 70 eV): *m/z* (%) = 207 (M^+, 37), 179 (22), 152 (100), 136 (47), 123 (30), 108 (35). HRMS (EI, 70 eV): calcd. for $C_{12}H_{17}O_2N$ [M^+]: *m/z* = 207.12538; found: 207.125713.



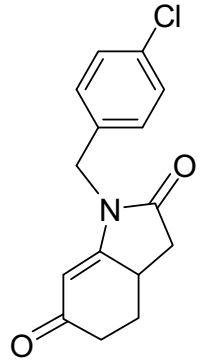
1-Cyclopropyl-3,3a,4,5-tetrahydro-1*H*-indole-2,6-dione (77d). Starting with **76d** (120 mg, 0.3 mmol), PTSA (5 mg, 0.02 mmol) and dry acetone (40 mL), **77d** was isolated (40 mg, 51%) as a white solid. ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 5.72 (d, 1H), 2.95 (m, 1H), 2.74 (dd, 1H), 2.57 (ddd, 1H), 2.39 (dd, 1H), 2.35 (dd, 1H), 2.23 (dd, 1H), 2.20 (m, 1H), 1.75 (ddd, 1H), 1.02 (m, 1H), 0.86 (m, 2H), 0.59 (m, 1H). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ_C = 198.2 (C=O), 175 9 (NC=O), 168.1 (NC=C), 103.2 (CH), 37.2 (CH_2), 35.5 (CH_2), 34.1 (CH), 28.1 (CH_2), 22.5 (NCH), 6.9 (CH_2), 5.1 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2945 (m), 2862 (s), 1702 (br), 1589 (br), 1413 (m), 1196 (br). MS (GC, 70 eV): *m/z* (%) 191 (M^+, 78), 163 (28), 162 (7), 149 (12), 136 (10), 135 (100), 134 (74), 121 (31), 120 (40), 108 (23), 107 (84), 106 (65), 81 (11), 80 (19). HRMS (EI, 70 eV): calcd. for $C_{11}H_{13}NO_2$ [M^+]: *m/z* = 191.093697; found: 191.09408.



Synthesis of 1-cyclopentyl-3,3a,4,5-tetrahydro-1*H*-indole-2,6-dione (77e). Starting with mono-**76e** (150 mg, 0.5 mmol), PTSA (5 mg, 0.02 mmol) and dry acetone (40 mL), **77e** was isolated (100 mg, 91%) as white crystals. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 5.47 (d, 1H, *J* = 1.7 Hz, C=CH), 4.46 (q, 1H, *J* = 8.3 Hz, CH_2), 2.89-3.03 (m, 1H, CH), 2.63 (d, 1H, *J* = 8.82, 17.2 Hz, CH_2), 2.48-2.57 (m, 1H, CH_2), 2.31-2.39 (m, 1H, CH_2), 2.15-2.26 (m, 2H, CH_2), 2.01 (s, 1H, CH_2), 1.70-1.89 (m, 6H, CH_2), 1.54-1.59 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 197.3 (C=O), 175.5 (C), 165.3 (C=O), 103.4 (CH), 53.0 (CH), 37.1 (CH_2), 35.3 (CH_2), 34.6 (CH), 27.9 (CH_2), 27.7 (CH_2), 27.1 (CH_2), 25.1 (CH_2), 25.0 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (m), 1731 (m), 1638 (m), 1595 (br). MS (GC, 70 eV): *m/z* (%)= 219 (M^+, 20), 191 (6), 152 (100), 123 (5). HRMS (EI, 70 eV): calcd. for $C_{13}H_{17}O_2N$ [M^+]: *m/z* = 219.12538; found: 219.125710.



1-Cyclohexyl-3,3a,4,5-tetrahydro-1*H*-indole-2,6-dione (77f). Starting with **76f** (100 mg, 0.3 mmol), PTSA (5 mg, 0.02 mmol) and dry acetone (40 mL), **77f** was isolated (50 mg, 73%) as a white solid. ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 5.59 (d, *J* = 1.8 Hz, 1H, CH), 3.83 (tt, *J* = 12.5, 4.0 Hz, 1H, NCH), 2.94 (m, 1H, CH), 2.68 (dd, *J* = 17.0, 8.8 Hz, 1H, CH_2), 2.52 (ddd, *J* = 17.3, 6.5, 2.0 Hz, 1H, CH_2), 2.33 (dd, *J* = 13.5, 5.0 Hz, 1H, CH_2), 2.21 (dd, *J* = 17.0, 8.8 Hz, 1H, CH_2), 2.19 (m, 1H, CH_2), 1.99 (m, 2H, CH_2), 1.80 (m, 2H, CH_2), 1.59 (m, 3H, CH_2), 1.28 - 1.17 (m, 4H, CH_2). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ_C = 197.3 (C=O), 175 3 (NC=O), 165.8 (NC=C), 103.5 (CH), 53.4 (CH), 37.1 (CH_2), 35.4 (CH_2), 34.8 (CH), 29.0 (CH_2), 27.9 (CH_2), 25.9 (CH_2), 25.7 (CH_2), 25.0 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2921 (w), 2850 (w), 1730 (s), 1586 (s, br), 1387 (m). MS (GC, 70 eV): *m/z* (%) = 233 (M^+, 19), 205 (9), 177 (12), 176 (17), 152 (100), 123 (41), 98 (9), 95 (8). HRMS (EI, 70 eV): calcd. for $C_{14}H_{19}NO_2$ [M^+]: *m/z* = 233.140814; found: 233.14103.



1-(4-Chlorobenzyl)-3,3a,4,5-tetrahydro-1*H*-indole-2,6-dione (77i). Starting with **76i** (200 mg, 0.5 mmol), PTSA (5 mg, 0.02 mmol) and dry acetone (40 mL), **77i** was isolated (102 mg, 71%) as highly viscous brownish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.19 (d, 2H, *J* = 8.5 Hz, ArH), 7.08 (d, 2H, *J* = 8.6 Hz, ArH), 5.43 (d, 1H, *J* = 1.7 Hz, C=CH), 4.42-4.7 (m, 2H, CH_2), 2.96-3.10 (m, 1H, CH), 2.46-2.82 (m, 2H, CH_2), 2.17-2.36 (m, 2H, CH_2), 1.65-1.98 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 197.0 (C=O), 175.3 (C=O), 165.4 (C), 133.9 (C), 133.6 (C), 129.1 (4CH), 102.7 (CH), 43.3(CH_2), 37.5 (CH_2), 34.8 (CH2), 34.8 (CH), 27.9 (CH_2). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2934 (m), 2908 (m), 1731 (m), 1606 (br). MS (GC, 70 eV): *m/z* (%) = 277 (M^+, ^{37}Cl, 17), 275 (M^+, ^{35}Cl, 50), 247 (37), 218 (11), 125 (100), 89 (16). HRMS (EI, 70 eV): calcd. for $C_{15}H_{14}O_2NCl$ [M^+, ^{35}Cl]: *m/z* = 275.07076; found: 275.070624.

References:

(1) Review: For a review of 1,3-bis(silyloxy)-1,3-butadienes, see: Langer, P. *Synthesis* **2002**, 441.

(2) Review: Langer, P. *Synlett* **2006**, 3369.

(3) Review: Feist, H.; Langer, P. *Synthesis* **2007**, 327.

(4) Review: Bellur, E.; Feist, H.; Langer, P. *Tetrahedron* **2007**, *63*, 10865.

(5) Review: Langer, P. *Eur. J. Org. Chem.* **2007**, 2233.

(6) Review: Langer, P. *Synlett* **2007**, 1016.

(7) (a) Chan, T.-H.; Stössel, D. *J. Org. Chem.* **1988**, *53*, 4901. (b) Chan, T.-H.; Stössel, D. *J. Org. Chem.* **1986**, *51*, 2423.

(8) Freifeld, I.; Bose, G.; Eckardt, T.; Langer, P. *Eur. J. Org. Chem.* **2007**, 351.

(9) Appel, B.; Rotzoll, S.; Reinke, H.; Langer, P. *Eur. J. Org. Chem.* **2006**, 3638.

(10) CCDC-xxx contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk.

(11) Cynandiones A-C : (a) Lin, Y.-L.; Wu, Y.-M.; Kuo, Y.-H. *Phytochemistry* **1997**, *45*, 1057. (b) Huang, P.-L.; Won, S.-J.; Day, S.-H.; Lin, C.-N. *Helv. Chim. Acta* **1999**, *82*, 1716. (c) Lin, Y.-L.; Lin, T.-C.; Kuo, Y.-H. *J. Nat. Prod.* **1997**, *60*, 368. (d) Buchanan, M. S.; Gill, M.; Yu, J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 919.

(12) Knipholone: (a) van Staden, L. F.; Drewes, S. E. *Phytochemistry* **1994**, *35*, 685. 6'-*O*-Methylknipholone: (b) Bezabih, M.; Motlhagodi, S.; Abegaz, B. M. *Phytochemistry* **1997**, *46*, 1063. (+)-Asphodelin: (c) Adinolfi, M.; Lanzetta, R.; Marciano, C. E.; Parrilli, M.; De Giulio, A. *Tetrahedron* **1991**, *47*, 4435.

(13) Secalonic acid A: (a) Pettit, G. R.; Meng, Y.; Herald, D. L.; Graham, K. A. N.; Pettit, R. K.; Doubek, D. L. *J. Nat. Prod.* **2003**, *66*, 1065. Globulixanthone E: (b) Nkengfack, A. E.; Mkounga, P.; Meyer, M.; Fomum, Z. T.; Bodo, B. *Phytochemistry* **2002**, *61*, 181.

(14) 2,3-Dihydroamentoflavone: (a) Das, B.; Mahender, G.; Rao, Y. K.; Prabhakar, A.; Jagadeesh, B. *Chem. Pharm. Bull.* **2005**, *53*, 135. Bartramiaflavone: (b) Basile, A.; Sorbo, S.; Lopez-Saez, J. A.; Cobianchi, R. C. *Phytochemistry* **2003**, *62*, 1145. Robustaflavone: (c) Chen, J.-J.; Duh, C.-Y.; Chen, J.-F. *Planta Med.* **2005**, *71*, 659. Dichamanetin: (d) Anam, E. M.; Ekpa, O. D.; Gariboldi, P. V.; Morah, F. N. I.; Dosunmu, M. I. *Indian J. Chem. Sect. B* **1993**, *32*, 1051. (e) Dasgupta, Binayak; Burke, Basil A.; Stuart, Kenneth L. *Phytochemistry* **1981**, *20*, 153. (f) Zeng, G.-Z.; Tan, N.-H.; Hao, X.-J.; Mu, Q.-Z.; Li, R.-T. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 6178. (g) Zeng, G.-Z.; Pan, X.-L.; Tan, N.-H.; Xiong, J.; Zhang, Y.-M. *Eur. J. Med. Chem. Chim. Ther.* **2006**, *41*, 1247.

(15) Anastatin A.; Yoshikawa, M.; Xu, F.; Morikawa, T.; Ninomiya, K.; Matsuda, H. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1045.

(16) *Metal-Catalyzed Cross-Coupling Reactions* (eds: de Meijere, A.; Diederich, F.), Wiley-VCH, Weinheim **2004**.

(17) (a) Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534. (b) Brownbridge, P.; Chan, T.-H.; Brook, M. A.; Kang, G. J. *Can. J. Chem.* **1983**, *61*, 688.

(18) Review of [3+3] cyclizations: Feist, H.; Langer, P. *Synthesis* **2007**, 327.

(19) Review of 1,3-bis(trimethylsilyloxy)-1,3-dienes: Langer, P. *Synthesis* **2002**, 441.

(20) Sher, M.; Ahmed, Z.; Rashid, M. A.; Fischer, C.; Langer, P. *J. Org. Chem.* **2007**, *72*, 6284.

(21) CCDC-xxx (**5b**) and CCDC-665870 (**5c**) contain all crystallographic details of this publication which are available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk.

(22) Bose, G.; Nguyen, V. T. H.; Ullah, E.; Lahiri, S.; Görls, H.; Langer, P. *J. Org. Chem.* **2004**, *69*, 9128.

(23) Langer, P.; Appel, B. *Tetrahedron Lett.* **2003**, 5133.

(24) Appel, B.; Rotzoll, S.; Reinke, H.; Langer, P. *Eur. J. Org. Chem.* **2006**, 3638.

(25) a) Talapatra, S. K.; Bose, S.; Mallik, Asok K.; Talapatra, B. *Tetrahedron* **1985**, *41*, 2765; b) Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2553; c) Fan, C.; Wang, W.; Wang, Y.; Qin, G.; Zhao, W. *Phytochemistry* **2001**, *57*, 1255; d) Wu, X. Y.; Qin, G. W.; Fan, D. J.; Xu, R. S. *Phytochemistry* **1994**, *36*, 477.

(26) Campo, M. A.; Larock, R. C. *J. Org. Chem*. **2002**, 67, 5616, and references cited therein.

(27) Tierney, M. T.; Grinstaff, M. W. *J. Org. Chem*. **2000**, 65, 5355.

(28) Perry, P. J.; Read, M. A.; Davies, R. T.; Gowan, S. M.; Reszka, A. P.; Wood, A. A.; Kelland, L. R.; Neidle, S. *J. Med. Chem.* **1999**, *42*, 2679.

(29) Gould, S. J.; Melville, C. R.; Cone, M. C.; Chen, J.; Carney, J. R. *J. Org. Chem.* **1997**, *62*, 320.

(30) Tilly, D.; Samanta, S. S.; Faigl, F.; Mortier, J. *Tetrahedron Lett.* **2002**, *43*, 8347.

(31) Underwood, H. W.; Kochmann, E. L. *J. Am. Chem. Soc.* **1924**, *46*, 2073; b) Lemal, D. M.; Gosselink, E. P.; McGregor, S. D. *J. Am. Chem. Soc.* **1966**, *88*, 582; c) Bandyopadhyay, T. K.; Bhattacharya, A. *J. Indian J. Chem. Sect. B* **1980**, *19*, 439; d) Kym, P. R.; Hummert, K. L.; Nilsson, A. G.; Lubin, M.; Katzenellenbogen, J. A. *J. Med. Chem.* **1996**, *39*, 4897; e) Gruber, J.; Li, R. W. C.; Aguiar, L. H.; Benvenho, J. M. C.; Adriano R. V.; Lessmann, R.; Huemmelgen, I. A. *J. Mater. Chem.* **2005**, *15*, 517; F) Olah, G. A.; Mathew, T.; Farnia, M.; Prakash, S. *Synlett* **1999**, 1067.

(32) Danheiser, L. R.; Gould, E. A.; Pradilla, F. R.; Helgason, L. A. *J. Org. Chem.* **1994**, *59*, 5514.

(33) a) Murahashi, S.-I.; Komiya, N.; Oda, Y.; Kuwabara, T.; Naota, T. *J. Org. Chem.* **2000**, *65*, 9186; b) Lippert, E.; Walter, H. *Angew. Chem.* **1959**, *71*, 429.

(34) Fu, J.-m.; Zhao, B.-p.; Sharp, M. J.; Snieckus, V. *J. Org. Chem.* **1991**, *56*, 1683.

(35) Yu, Z.; Velasco, D. *Tetrahedron Lett.* **1999**, *40*, 3229.

(36) Ciske, F. L.; Jones Jr., W. D. *Synthesis* **1998**, 1195.

(37) Schmidt, J. M.; Tremblay, G. B.; Page, M.; Mercure, J.; Feher, M.; Dunn-Dufault, R.; Peter, M. G.; Redden, P. R. *J. Med. Chem.* **2003**, *46*, 1289.

(38) a) Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534; b) Brownbridge, P.; Chan, T.-H.; Brook, M. A.; Kang, G. J. *Can. J. Chem.* **1983**, *61*, 688.

(39) For a review of 1,3-bis(silyl enol ethers), see: Langer, P. *Synthesis* **2002**, 441.

(40) For a review of [3+3] cyclizations, see: Feist, H.; Langer, P. *Synthesis* **2007**, 327.

(41) Reim, S.; Lau, M.; Langer, P. *Tetrahedron Lett.* **2006**, *47*, 6903.

(42) An isolated example of this method has been previously reported by Chan: see ref. 14a. During the synthesis of chlorinated and fluorinated arenes, we have recently reported the synthesis of fluorenones: a) Hussain, I.; Yawer, M. A.; Lau, M.; Pundt, T.; Fischer, C.; Reinke, H.; Görls, H.; Langer, P. *Eur. J. Org. Chem.* **2008**, 503; b) Yawer, M. A.; Hussain, I.; Reim, S.; Ahmed, Z.; Ullah, E.; Iqbal, I.; Fischer, C.; Reinke, H.; Görls, H.; Langer, P. *Tetrahedron* **2007**, *63*, 12562.

(43) (a) *Fluorine in Bioorganic Chemistry*, Filler, R.; Kobayasi, Y.; Yagupolskii, L. M., eds., Elsevier: Amsterdam, **1993**. (b) Filler, R. *Fluorine Containing Drugs in Organofluorine Chemicals and their Industrial Application*; Pergamon: New York, **1979**, chapter 6. (c) Hudlicky, M. *Chemistry of Organic Compounds*; Ellis Horwood: Chichester, **1992**. (d) Kirsch, P. *Modern Fluoroorganic Chemistry*, VCH, Weinheim, **2004**. (e) Chambers, R. D. *Fluorine in Organic Chemistry*, Blackwell Publishing CRC Press, **2004**. See also: (f) Ryckmanns, T.; Balancon, L.; Berton, O.; Genicot, C.; Lamberty, Y.; Lallemand, B.; Passau, P.; Pirlot, N.; Quéré, L.; Talaga, P. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 261. (e) Malamas, M. S.; Sredy, J.; Moxham, C.; Katz, A.; Xu, W.; McDevitt, R.; Adebayo, F. O.; Sawicki, D. R.; Seestaller, L.; Sullivan, D.; Taylor, J. R. *J. Med. Chem*. **2000**, *43*, 1293. (f) Ciha, A. J.; Ruminski, P. G. *J. Agric. Food Chem.* **1991**, *39*, 2072. (g) Albrecht, H. A.; Beskid, G.; Georgopapadakou, N. H.; Keith, D. D.; Konzelmann, F. M.; Pruess, D. L.; Rossman, P. L.; Wei, C. C.; Christenson, J. G. *J. Med. Chem.* **1991**, *34*, 2857. (h) Albrecht, H. A.; Beskid, G.; Christenson, J. G.; Deitcher, K. H.; Georgopapadakou, N. H.; Keith, D. D.; Konzelmann, F. M.; Pruess, D. L.; Wie, C. C. *J. Med. Chem.* **1994**, *37*, 400. (i) Song, C. W.; Lee, K. Y.; Kim, C. D.; Chang, T-M.; Chey, W. Y. *J. Pharmacol. Exp. Ther.* **1997**, *281*, 1312. (j) De Voss, J. J.; Sui, Z.; DeCamp, D. L.; Salto, R.; Babe, L. M.; Craik, C.

S.; Ortiz de Montellano, P. R. *J. Med. Chem.* **1994**, *37*, 665. (k) Anjaiah, S.; Chandrasekhar, S.; Gree, R. *Adv. Synth. Catal.* **2004**, *346*, 1329. (l) Iorio, M. A.; Paszkowska, R. T.; Frigeni, V. *J. Med. Chem.* **1987**, *30*, 1906. (m) Popp, J. L.; Musza, L. L.; Barrow, C. J.; Rudewicz, P. J.; Houck, D. R. *J. Antibiot.* **1994**, *47*, 411. (n) Chen, T. S.; Petuch, B.; MacConnell, J.; White, R.; Dezeny, G. *J. Antibiot.* **1994**, *47*, 1290. (o) Lam, K. S.; Schroeder, D. R.; Veitch, J. M. J. M.; Colson, K. L.; Matson, J. A.; Rose, W. C.; Doyle, T. W.; Forenza, S. *J. Antibiot.* **2001**, *54*, 1.

(44) (a) Schmidbaur, H.; Kumberger, O. *Chem. Ber*. **1993**, *126*, 3. (b) Dinger, M. B.; Henderson, W. *J. Organomet. Chem.* **1998**, *560*, 233. (c) Liedtke, J.; Loss, S.; Widauer, C.; Grützmacher, H. *Tetrahedron* **2000**, *56*, 143.

(45) See for example: (a) Schneider, S.; Tzschucke, C. C.; Bannwarth, W. *Multiphase Homogeneous Catalysis* (Cornils, B.; Herrmann, W. A.; Horvath, I. T.; Leitner, W.; Mecking, S.; Olivier-Booubigou, H.; Vogt, D., ed.), Wiley VCH, **2005**, Chapter 4, p. 346. (b) Clarke, D.; Ali, M. A.; Clifford, A. A.; Parratt, A.; Rose, P.; Schwinn, D.; Bannwarth, W.; Rayner, C. M. *Current Topics in Medicinal Chemistry* **2004**, *7*, 729.

(46) Reviews: (a) Wittkopp, A.; Schreiner, P. R. *The chemistry of diens and polyenes,* Vol. 2; John Wiley & Sons Ltd, **2000**. (b) Schreiner, P. R. *Chem. Soc. Rev.* **2003**, 32, 289. See also: (c) Wittkopp, A.; Schreiner, P. R. *Chem. Eur. J.* **2003**, 9, 407. (d) Kleiner, C. M.; Schreiner, P. R. *Chem. Commun.* **2006**, 4315. (e) Kotke, M.; Schreiner, P. R. *Synthesis* **2007**, 5, 779. Review: Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, 1701.

(47) *Metal-Catalyzed Cross-Coupling Reactions* (eds: de Meijere, A.; Diederich, F.), Wiley-VCH, Weinheim **2004**.

(48) (a) Shi, G.-q.; Cottens, S.; Shiba, S. A.; Schlosser, M. A. *Tetrahedron* **1992**, *48*, 10569. (b) Shi, G.-q.; Schlosser, M. *Tetrahedron* **1993**, *49*, 1445. (c) Patrick, T. B.; Rogers, J.; Gorrell, K. *Org. Lett.* **2002**, *4*, 3155.

(49) Lefebvre, O.; Brigaud, T.; Portella, C. *Tetrahedron* **1998**, *54*, 5939.

(50) For a review of 1,3-bis(silyl enol ethers), see: Langer, P. *Synthesis* **2002**, 441.

(51) Chan, T.-H.; Brownbridge, P. *J. Chem. Soc., Chem. Commun.* **1979**, 578.

(52) For a review of [3+3] cyclizations, see: Feist, H.; Langer, P. *Synthesis* **2007**, 327.

(53) For [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-dienes with 2-fluoro-3-silyloxy-2-en-1 ones, see: Hussain, I.; Yawer, M. A.; Lau, M.; Pundt, T.; Fischer, C.; Reinke, H.; Görls, H.; Langer, P. *Eur. J. Org. Chem.* **2008**, 503.

(54) Langer, P.; Stoll, M.; Schneider, S. *Chem. Eur. J.* 2000, *6*, 3204.

(55) (a) Bellur, E.; Görls, H.; Langer, P. *Eur. J. Org. Chem.* **2005**, 2074. See also: (b) Langer, P.; Krummel, T. *Chem. Eur. J.* **2001**, *7*, 1720.

(56) Bellur, E., Langer, P. *J. Org. Chem.* **2005**, *70*, 10017.

(57) Langer, P.; Ambrust, H, Eckardt, T, Magull, J. *Chem. Eur. J.* 2002, *6*, 1446.

(58) Albrecht, U.; Nguyen, V. T. H.; Langer, P. *Synthesis* **2006**, 1111.

(59) For pharmacologically active chlorinated natural products and drugs: Griseofulvin: (a) Osborne, C. S.; Leitner, I.; Hofbauer, B.; Fielding, C. A.; Favre, B.; Ryder, N. S. *Antimicrob. Agents Chemother* **2006**, *50*, 2234. (b) Takano, R.; Sugano, K.; Higashida, A.; Hayashi, Y.; Machida, M.; Aso, Y.; Yamashita, S. *Pharm. Res.* **2006**, *23*, 1144. (c) Xue, C.; Li, T.; Deng, Z.; Fu, H.; Lin, W. *Pharmazie* **2006**, *61*, 1041. (d) Phelps, J. B.; Hoffman, W. P.; Lee, C.; Murphy, G. P.; Garriott, M. L. *Mutat. Res.* **2004**, *561*, 153. (e) Rosefort, C.; Fauth, E.; Zankl, H. *Mutagenesis* **2004**, *19*, 277. (f) Kinobe, R. T.; Dercho, R. A.; Vlahakis, J. Z.; Brien, J. F.; Szarek, W. A.; Nakatsu, K. *J. Pharmacol. Exp. Ther.* **2006**, *319*, 277. (g) Albaugh, D.; Albert, G.; Bradford, P.; Cotter, V.; Froyd, J. *J. Antibiot.* **1998**, *51*, 317. Dihydronidulin: Finlay-Jones, P. F.; Sala, T.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1981**, 874.

(60) For an example from our laboratory, see: (a) Albrecht, U.; Lalk, M.; Langer, P. *Bioorg. Med. Chem.* **2005**, *13*, 1531. (b) Nguyen, V. D.; Wolf, C.; Mäder, U.; Lalk, M.; Langer, P.; Lindequist, U.; Hecker, M.; Antelmann, H. *Proteomics* **2007**, *7*, 1391.

(61) *Metal-Catalyzed Cross-Coupling Reactions* (eds: de Meijere, A.; Diederich, F.), Wiley-VCH, Weinheim **2004**.

(62) Corral, C.; Lissavetzky, J.; Manzanares, I. *Synthesis* **1997**, 29.

(63) For a review of 1,3-bis(silyl enol ethers), see: Langer, P. *Synthesis* **2002**, 441.

(64) Chan, T.-H.; Brownbridge, P. *J. Chem. Soc., Chem. Commun.* **1979**, 578.

(65) For a review of [3+3] cyclizations, see: Feist, H.; Langer, P. *Synthesis* **2007**, 327.

(66) For the synthesis and reactions of 4-chloro-1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene, see: (a) Reim, S.; Langer, P. *Tetrahedron Lett.* **2008**, *49*, 2329. For an isolated example of a 2-chloro-1,3-bis(trimethylsilyloxy)-1,3-butadiene, see: (b) Savard, J.; Brassard, P. *Tetrahedron Lett.* **1979**, *20*, 4911. For [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-dienes with 2-chloro-3-silyloxy-2-en-1-ones, see: (c) Yawer, M. A.; Hussain, I.; Reim, S.; Ahmed, Z.; Ullah, E.; Iqbal, I.; Fischer, C.; Reinke, H.; Görls, H.; Langer, P. *Tetrahedron* **2007**, *63*, 12562.

(67) Anthony G.; Barret M.; Robin A.E. Carr. *J. Org. Chem.* **1986**, 51, 4258.

(68) Bellur, E.; Görls, H.; Langer, P. *J. Org. Chem.* **2005**, 70, 4753.

(69) Römpp Lexikon Naturstoffe (Steglich, W.; Fugmann, B.; Lang-Fugmann, S., eds.), Thieme, Stuttgart: 1997.

(70) *Metal-Catalyzed Cross-Coupling Reactions* (eds: de Meijere, A.; Diederich, F.), Wiley-VCH, Weinheim **2004**.

(71) Dihydronidulin: Finlay-Jones, P. F.; Sala, T.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1981**, 874.

(72) Griseofulvin: (a) Osborne, C. S.; Leitner, I.; Hofbauer, B.; Fielding, C. A.; Favre, B.; Ryder, N. S. *Antimicrob. Agents Chemother* **2006**, *50*, 2234. (b) Takano, R.; Sugano, K.; Higashida, A.; Hayashi, Y.; Machida, M.; Aso, Y.; Yamashita, S. *Pharm. Res.* **2006**, *23*, 1144. (c) Xue, C.; Li, T.; Deng, Z.; Fu, H.; Lin, W. *Pharmazie* **2006**, *61*, 1041. (d) Phelps, J. B.; Hoffman, W. P.; Lee, C.; Murphy, G. P.; Garriott, M. L. *Mutat. Res.* **2004**, *561*, 153. (e) Rosefort, C.; Fauth, E.; Zankl, H. *Mutagenesis* **2004**, *19*, 277. (f) Kinobe, R. T.; Dercho, R. A.; Vlahakis, J. Z.; Brien, J. F.; Szarek, W. A.; Nakatsu, K. *J. Pharmacol. Exp. Ther.* **2006**, *319*, 277. (g) Albaugh, D.; Albert, G.; Bradford, P.; Cotter, V.; Froyd, J. *J. Antibiot.* **1998**, *51*, 317.

(73) Epigriseofulvin: Namikoshi, M.; Kobayashi, H.; Yoshimoto, T.; Meguro, S.; Akano, K. *Chem. Pharm. Bull.* **2000**, *48*, 1452.

(74) Belofsky, G. N.; Gloer, K. B.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *J. Nat. Prod.* **1998**, *61*, 1115.

(75) Geodin: (a) Katoh, T.; Ohmori, O. *Tetrahedron Lett.* **2000**, 41, 465. (b) Fujii, I.; Iijima, H.; Ebizuka, Y.; Sankawa, U. *Chem. Pharm. Bull.* **1983**, *31*, 337. (c) Katoh, T.; Ohmori, O.; Iwasaki, K; Inoue, M. *Tetrahedron* **2002**, *58*, 1289.

(76) Geodinhydrate methyl ester: (a) Hargreaves, J.; Park, J.-o.; Ghisalberti, E. L.; Sivasithamparam, K.; Skelton, B. W.; White, A. H. *J. Nat. Prod.* **2002**, *65*, 7.

(77) 7-Chloro-1-*O*-methylemodin: (a) Cohen, P. A.; Towers, G. H. N. Phytochemistry 1996, 42, 1325. (b) Shu, Y.-Z.; Arcuri, M.; Kozlowski, M. R.; Wang, R. R.; Lam, K. S. J. Antibiot. 1994, 47, 1328. (c) Cohen, P. A.; Hudson, J. B.; Towers, G. H. N. *Experientia* **1996**, *52*, 180.

(78) (a) Ahad, A. M.; Goto, Y.; Kiuchi, F.; Tsuda, Y.; Kondo, K.; Sato, T. *Chem. Pharm. Bull.* **1991**, *39*, 1043. (b) Kim, Y.-J.; Nishida, H.; Pang, C.-H.; Saito, T.; Shinichi, S.; Tonai-Kachi, H.; Yoshikawa, N.; Vanvolkenburg, M. A.; Parkerf, J. C.; Kojima, Y. *J. Antibiot.* **2002**, 55, 121. Longissiminone B: (c) Choudhary, M. I.; Azizuddin, M.; Jalil, S.; Atta-ur-Rahman *Phytochemistry* **2005**, *66*, 2346. Chloroisosulochrin: (d) Shimada, A.; Takahashi, I.; Kawano, T.; Kimura, Y. *Z. Naturforsch. B* **2001**, *56*, 797. Pestalone: (e) Cueto, M.; Jensen, P. R.; Kauffman, C.; Fenical, W.; Lobkovsky, E.; Clardy, J. *J. Nat. Prod.* **2001**, *64*, 1444. (f) Iijima, D.; Tanaka, D.; Hamada, M.; Ogamino, T.; Ishikawa, Y.; Nishiyama, S.; *Tetrahedron Lett.* **2004**, *45*, 5469. Methyl chloroasterrate: (g) Hargreaves, J.; Park, J.-o.; Ghisalberti, E. L.; Sivasithamparam, K.; Skelton, B. W.; White, A. H. *J. Nat. Prod.* **2002**, *65*, 7. (h) Lee, H. J.; Lee, J. H.; Hwang, B. Y.; Kim, H. S.; Lee, J. J. *J. Antibiot.* **2002**, *55*, 552.

(79) Falconensin B: Itabashi, T.; Nozawa, K.; Miyaji, M.; Udagawa, S.-i.; Nakajima, S.; Kawai, K.-i. *Chem. Pharm. Bull.* **1992**, *40*, 3142.

(80) Chromones: Kawamura, N.; Sawa, R.; Takahashi, Y.; Issiki, K.; Sawa, T. *J. Antibiot.* **1995**, *48*, 435.

(81) Hoeller, U.; Koening, G.; Wright, A. D. *J. Nat. Prod.* **1999**, *62*, 114.

(82) (a) Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534. (b) Brownbridge, P.; Chan, T.-H.; Brook, M. A.; Kang, G. J. *Can. J. Chem.* **1983**, *61*, 688.

(83) For a review of 1,3-bis(trimethylsilyloxy)-1,3-dienes in general, see: Langer, P. *Synthesis* **2002**, 441.

(84) For a review of [3+3] cyclizations, see: Feist, H.; Langer, P. *Synthesis* **2007**, 327.

(85) M. A. Yawer, I. Hussain, S. Reim, Z. Ahmed, E. Ullah, I. Iqbal, C. Fischer, H. Reinke, H. Görls, P. Langer, *Tetrahedron* **2007**, *63*, 12562.

(86) S. Reim, I. Hussain, M. Adeel, M. A. Yawer, A. Villinger, P. Langer, *Tetrahedron Lett.* **2008**, *49*, 4901.

(87) S. Reim, P. Langer, *Tetrahedron Lett.* **2008**, *49*, 2329.

(88) Appel, B.; Rotzoll, S.; Reinke, H.; Langer, P. *Eur. J. Org. Chem.* **2006**, 3638.

(89) (a) Ruegg, R.; Lindlar, H.; Montavon, M.; Savey, G.; Schaeren, S. T.; Schwieter, U.; Isler, O. *Helv. Chim. Acta* **1959**, *42*, 844. (b) Ruegg, R.; Lindlar, H.; Montavon, M.; Savey, G.; Schaeren, S. T.; Schwieter, U.; Isler, O. *Helv. Chim. Acta* **1959**, *42*, 859.

(90) Albrecht, U.; Nguyen, V. T. H.; Langer, P. *Synthesis* **2006**, 1111.

(91) Albrecht, U.; Nguyen, V. T. H.; Langer, P. *J. Org. Chem.* **2004**, 69, 3417.

(92) B. A. Krukoff, R. C. Barneby, *Mem. New York Bot. Gard.* 1970, **20**, 1.

(93) a) A. S. Chawla, V. K. Kapor, in *Handbook of Plant andFungal Toxicants*, J. F. D'Mello (ed.), CRC Press: New York, 1997, 37; b) D. S. Bhakuni, *J. Indian Chem. Soc.* 2002, 203; c) A. J. Lehman, *J. Pharmacol.* 1937, 69; d) M. Williams, J. L. Robinson, *J. Neurosci.* 1984, 2906; e) M. W. Decker, D. J. Anderson, J. D. Brioni, D. L. Donnelly-Roberts, C. H. Kang, A. B. O'Neil, M. Piattoni-Kaplan, S. Swanson, J. P. Sullivan, *Eur. J. Pharmacol.* 1995, 79.

(94) For reviews, see: a) V. Boekelheide, in *The Alkaloids*, **Vol. 7**, R. H. F. Manske (ed.), Academic Press: New York, 1960, 201; b) R. K. Hill, in *The Alkaloids*, **Vol. 9**, R. H. F. Manske (ed.), Academic Press: New York, 1967, 483; c) S. F. Dyke, S. N. Quessy, in *The Alkaloids*, **Vol. 18**, R. G. A. Rodrigo (ed.), Academic Press: New York, 1981, 1; d) A. H. Jackson, in *Chemistry and Biology of Isoquinoline Alkaloids*, J. D. Phillipson, M. F. Margaret, M. H. Zenk (eds.), Springer: Berlin, 1985, 62; e) A. S. Chawla, A. H. Jackson, *Nat. Prod. Rep.* 1984, **1**, 371; for early original reports, see: f) K. Wiesner, Z. Valenta, A. J. Manson, F. W. Stonner, *J. Am. Chem. Soc.* **1955**, *77*, 675; g) V. Prelog, *Angew. Chem.* 1957, **69**, 33; h) V.

Prelog, A. Langemann, O. Rodig, M. Ternbah, *Helv. Chim. Acta* 1959, **42**, 1301; i) A. Mondon, H. J. Nestler, *Angew. Chem.* 1964, **76**, 651; j) R. V. Stevens, M. P. Wentland, *J. Chem. Soc., Chem. Commun.* 1968, 1104.

(95) a) P. C. Stanislawski, A. C. Willis, M. G. Banwell, *Org. Lett.* 2006, **8**, 2143; b) A. Padwa, Q. Wang, *J. Org. Chem.* 2006, **71**, 7391; c) A. K. Ganguly, C. H. Wang, D. Biswas, J. Misiaszek, A. Micula, *Tetrahedron Lett.* 2006, **47**, 5539; d) S. Gao, Y. Q. Tu, X. Hu, S. Wang, R. Hua, Y. Jiang, Y. Zhao, X. Fan, S. Zhang, *Org. Lett.* 2006, **8**, 2373; e) H. Fukumoto, K. Takahashi, J. Ishihara, S. Hatakeyama, *Angew. Chem. Int. Ed.* 2006, **45**, 2731; f) J. H. Rigby, J. H.; Cavezza, A.; Heeg, M. J. *J. Am. Chem. Soc.* 1998, **120**, 3664.

(96) L. F. Tietze, N. Tölle, C. Noll *Synlett* 2008, 525.

(97) A. Padwa, Q. Wang, *J. Org. Chem.* 2006, **71**, 7391.

(98) B. Juma, M. Adeel, A. Villinger, P. Langer, *Tetrahedron Lett.* 2008, **49**, 2272.

(99) For other syntheses of 2,6-dioxo-1,2,3,4,5,6-hexahydroindoles, see: a) Birch reaction: K. Ito, M. Haruna, H. Furukawa, *J. Chem. Soc., Chem. Commun.* 1975, 681; b) aza-Claisen rearrangement of isoquinuclidines: Y. Chen, P. L. Huesmann, P. S. Mariano, *Tetrahedron Lett.* 1983, **24**, 1021; Diels-Alder reaction of 2-imidofurans: c) A. Padwa, J. D. Ginn, *J. Org. Chem.* 2005, **70**, 5197; d) A. Padwa, S. K. Bur, H. Zhang, *J. Org. Chem.* 2005, **70**, 6833.

(100) (a) N. M. Berry, M. C. P. Darey, L. M. Harwood, *Synthesis* 1986, 476; see also: b) G. Vassilikogiannakis, I. Margaros, M. Tofi, *Org. Lett.* 2004, **6**, 205.

(101) For a recent review of dianions, see: P. Langer, W. Freiberg, *Chem. Rev.* 2004, **104**, 4125, and references cited therein.

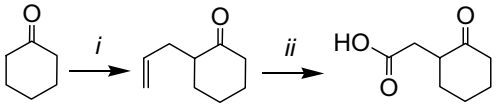
(102) B. Guay, P. Deslongchamps, *J. Org. Chem.* 2003, **68**, 6140.

(103) W. Zhang, G. Pugh, *Tetrahedron* 2003, **59**, 4237.

(104) CCDC 716534, CCDC 670738, and CCDC 716346 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(105) We have prepared **7c** by oxidation of 2-allylcyclohexanone (**5c**) which is readily available from cyclohexanone (see below). This approach to **7c** has, to the best of

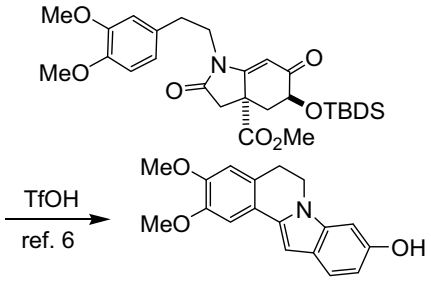
our knowledge, not yet been reported. For a different synthesis of **7c**, see for example: S. M. Allin, S. L. James, M. R. Elsegood, W. P. Martin, *J. Org. Chem.* 2002, **67**, 9464.



5c (79%) **7c** (75%)

Conditions: *i*, 1) LDA, HMPTA, THF, −78 °C, 1 h, 2) allylbromide, –40 → 20 °C, 12 h; *ii*, $NaIO_4$, $KMnO_4$, acetone

(106) The following reaction has been reported by Padwa and Wang (ref. 6):



(107) For related heterocycles, such as 5,8,9,10-tetrahydro-6*H*-indolo[2,1-*a*]isoquinolin-11-ones, see: a) H. Meyer, *Liebigs Ann. Chem.* 1981, 1534; b) Z. Vincze, P. Nemes, ´B. Balazs, G. Toth, P. Scheiber, *Synlett* 2004, 1023; c) M. Menes-Arzate, R. Martinez, R. Cruz-Almanza, J. M. Muchowski, Y. M. Osornio, L. D. Miranda, *J. Org. Chem.* 2004, **69**, 4001.

Data of Crystals from X-ray Measurements:

Crystal data and structure refinement for 5e (Fig 1).

Identification code	av_ma242	
Empirical formula	C_{18} H_{15} N O_8	
Formula weight	373.31	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.1158(14)Å	α= 81.23(3)°.
	b = 9.5538(19)Å	β= 80.71(3)°.
	c = 12.574(3)Å	γ = 82.26(3)°.
Volume	828.4(3) $Å^3$	
Z	2	
Density (calculated)	1.497 Mg/m^3	
Absorption coefficient	0.120 mm^{-1}	
F(000)	388	
Crystal size	0.38 x 0.13 x 0.11 mm^3	
Θ range for data collection	4.72° to 30.00°.	
Index ranges	-10≤h≤9, -13≤k≤12, -17≤l≤17	
Reflections collected	16899	
Independent reflections	3964 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	97.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9869 and 0.9559	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4791 / 0 / 254	
Goodness-of-fit on F^2	1.026	
Final R indices [I>2σ(I)]	R1 = 0.0515, wR2 = 0.1246	
R indices (all data)	R1 = 0.0407, wR2 = 0.1183	
Largest diff. peak and hole	0.408 and -0.255e.$Å^{-3}$	

Crystal data and structure refinement for 5h (Fig 2)

Identification code	ma248	
Empirical formula	$C_{18}\ H_{15}\ Cl\ O_6$	
Formula weight	362.75	
Temperature	98(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 5.6086(5) Å	α= 79.276(6)°.
	b = 11.6290(9) Å	β= 86.269(6)°.
	c = 12.5307(10) Å	γ = 82.285(6)°.
Volume	795.07(11) $Å^3$	
Z	2	
Density (calculated)	1.515 Mg/m^3	
Absorption coefficient	0.274 mm^{-1}	
F(000)	376	
Crystal size	0.60 x 0.30 x 0.02 mm^3	
Θ range for data collection	2.21 to 29.82°.	
Index ranges	-7≤h≤7, -16≤k≤16, -17≤l≤17	
Reflections collected	15882	
Independent reflections	4405 [R(int) = 0.0908]	
Completeness to Θ = 29.82°	96.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9945 and 0.8528	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4405 / 0 / 230	
Goodness-of-fit on F^2	1.005	
Final R indices [I>2σ(I)]	R1 = 0.0771, wR2 = 0.1802	
R indices (all data)	R1 = 0.1786, wR2 = 0.2482	
Largest diff. peak and hole	1.084 and -1.697 $e.Å^{-3}$	

Crystal data and structure refinement for 5j (Fig 3)

Identification code	ma239	
Empirical formula	C_{18} H_{15} F O6	
Formula weight	346.30	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P-1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 5.5132(6) Å	α= 77.479(6)°.
	b = 11.6841(14) Å	β= 87.431(6)°.
	c = 12.5530(16) Å	γ = 79.203(6)°.
Volume	775.41(16) $Å^3$	
Z	2	
Density (calculated)	1.483 Mg/m^3	
Absorption coefficient	0.119 mm^{-1}	
F(000)	360	
Crystal size	0.45 x 0.08 x 0.03 mm^3	
Θ range for data collection	2.71 to 26.70°.	
Index ranges	-6≤h≤6, -14≤k≤14, -15≤l≤15	
Reflections collected	14035	
Independent reflections	3223 [R(int) = 0.0405]	
Completeness to Θ = 26.70°	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9964 and 0.9482	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3223 / 0 / 233	
Goodness-of-fit on F^2	1.043	
Final R indices [I>2σ(I)]	R1 = 0.0528, wR2 = 0.0968	
R indices (all data)	R1 = 0.0890, wR2 = 0.1112	
Largest diff. peak and hole	0.257 and -0.240 $e.Å^{-3}$	

Crystal data and structure refinement for 11b (Fig. 4):

Identification code	av_ma89	
Empirical formula	C15 H14 O4'	
Formula weight	258.26	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group (H.-M.)	'P n a 21'	
Space group (Hall)	'P 2c -2n'	
Unit cell dimensions	a = 26.312(5)Å	α= 90.00°.
	b = 3.8740(8)Å	β= 90.00°.
	c = 11.824(2)Å	γ = 90.00°.
Volume	1205.3(4) $Å^3$	
Z	4	
Density (calculated)	1.423 Mg/m^3	
Absorption coefficient	0.103 mm^{-1}	
F(000)	544	
Crystal size	0.52 x 0.51 x 0.05 mm^3	
Θ range for data collection	3.10 to 29.99°.	
Index ranges	-37≤h≤37, -4≤k≤5, -14≤l≤14	
Reflections collected	14947	
Independent reflections	3964 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	97.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9949 and 0.9482	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2943 / 1 / 178	
Goodness-of-fit on F^2	1.026	
Final R indices [I>2σ(I)]	R1 = 0.0426, wR2 = 0.0870	
R indices (all data)	R1 = 0.0346, wR2 = 0.0839	
Largest diff. peak and hole	0.251 and -0.178e.$Å^{-3}$	

Crystal data and structure refinement for 13e (Fig 5).

Identification code	av_ma75	
Empirical formula	$C_{17}H_{17}ClO_4$	
Formula weight	320.76	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 6.534(4) Å	α= 97.420(15)°.
	b = 9.574(6) Å	β= 100.56(2)°.
	c = 12.694(8) Å	γ = 96.042(14)°.
Volume	767.3(8) $Å^3$	
Z	2	
Density (calculated)	1.388 Mg/m^3	
Absorption coefficient	0.264 mm^{-1}	
F(000)	336	
Crystal size	0.55 x 0.27 x 0.01 mm^3	
Θ range for data collection	4.40 to 29.00°.	
Index ranges	-8≤h≤8, -13≤k≤13, -17≤l≤17	
Reflections collected	14947	
Independent reflections	3964 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	97.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8683 and 0.9974	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3091 / 0 / 207	
Goodness-of-fit on F^2	1.093	
Final R indices [I>2σ(I)]	R1 = 0.0403, wR2 = 0.1170	
R indices (all data)	R1 = 0.0563, wR2 = 0.1247	
Largest diff. peak and hole	0.308 and -0.230 $e.Å^{-3}$	

Crystal data and structure refinement for 13i (Fig 8).

Identification code	ma93	
Empirical formula	$C_{16}\ H_{14}\ Cl_2\ O3$	
Formula weight	325.17	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1$	
Space group (Hall)	P 2yb	
Unit cell dimensions	a = 4.0956(5) Å	α= 90°.
	b = 13.3066(17) Å	β= 92.711(7)°.
	c = 13.3656(16) Å	γ = 90°.
Volume	727.59(16) $Å^3$	
Z	2	
Density (calculated)	1.484 Mg/m^3	
Absorption coefficient	0.453 mm^{-1}	
F(000)	336	
Crystal size	0.65 x 0.50 x 0.06 mm^3	
Θ range for data collection	3.05 to 29.88°.	
Index ranges	-5≤h≤5, -18≤k≤15, -17≤l≤18	
Reflections collected	9311	
Independent reflections	3754 [R(int) = 0.0217]	
Completeness to Θ = 29.88°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9734 and 0.7575	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3754 / 1 / 197	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2σ(I)]	R1 = 0.0302, wR2 = 0.0700	
R indices (all data)	R1 = 0.0385, wR2 = 0.0742	
Absolute structure parameter	0.05(5)	
Largest diff. peak and hole	0.324 and -0.179 $e.Å^{-3}$	

Crystal data and structure refinement for 23j (Fig 9).

Identification code	ma10	
Empirical formula	$C_{15}H_{13}ClO_3$	
Formula weight	276.70	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	$Pna2_1$	
Space group (Hall)	P 2c -2n	
Unit cell dimensions	a = 15.1424(4) Å	α= 90°.
	b = 8.2046(3) Å	β= 90°.
	c = 21.5336(6) Å	γ = 90°.
Volume	2675.28(14) $Å^3$	
Z	8	
Density (calculated)	1.374 Mg/m^3	
Absorption coefficient	0.286 mm^{-1}	
F(000)	1152	
Crystal size	0.90 x 0.56 x 0.12 mm^3	
Θ range for data collection	2.66 to 30.00°.	
Index ranges	-21≤h≤19, -11≤k≤11, -30≤l≤30	
Reflections collected	33153	
Independent reflections	7807 [R(int) = 0.0296]	
Completeness to Θ = 30.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9665 and 0.7829	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7807 / 1 / 355	
Goodness-of-fit on F^2	1.013	
Final R indices [I>2σ(I)]	R1 = 0.0381, wR2 = 0.0952	
R indices (all data)	R1 = 0.0462, wR2 = 0.1011	
Absolute structure parameter	0.06(4)	
Largest diff. peak and hole	0.320 and -0.219 $e.Å^{-3}$	

Crystal data and structure refinement for 24ab (Fig 10).

Identification code	ma32	
Empirical formula	$C_{14}H_9ClO_2$	
Formula weight	244.66	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1$	
Space group (Hall)	P 2yb	
Unit cell dimensions	a = 9.7610(2) Å	α= 90°.
	b = 5.02930(10) Å	β= 96.0950(10)°.
	c = 11.3448(2) Å	γ = 90°.
Volume	553.779(19) $Å^3$	
Z	2	
Density (calculated)	1.467 Mg/m^3	
Absorption coefficient	0.329 mm^{-1}	
F(000)	252	
Crystal size	0.67 x 0.10 x 0.08 mm^3	
Θ range for data collection	2.62 to 29.99°.	
Index ranges	$-13\leq h\leq 13$, $-7\leq k\leq 7$, $-13\leq l\leq 15$	
Reflections collected	8643	
Independent reflections	3164 [R(int) = 0.0346]	
Completeness to Θ = 29.99°	98.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9742 and 0.8099	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3164 / 1 / 158	
Goodness-of-fit on F^2	1.026	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0398, wR2 = 0.0840	
R indices (all data)	R1 = 0.0558, wR2 = 0.0911	
Absolute structure parameter	0.02(6)	
Largest diff. peak and hole	0.320 and -0.208 $e.Å^{-3}$	

Crystal data and structure refinement for 35e (Fig 12).

Identification code	ma233	
Empirical formula	C_{16} H_{11} F_2 N O_4	
Formula weight	319.26	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	$P2_12_12_1$	
Space group (Hall)	P 2ac 2ab	
Unit cell dimensions	a = 4.7205(3) Å	α= 90°.
	b = 11.9607(7) Å	β= 90°.
	c = 24.1144(12) Å	γ= 90°.
Volume	1361.51(14) $Å^3$	
Z	4	
Density (calculated)	1.558 Mg/m^3	
Absorption coefficient	0.130 mm^{-1}	
F(000)	656	
Crystal size	0.58 x 0.18 x 0.06 mm^3	
Θ range for data collection	2.40 to 30.00°.	
Index ranges	-6≤h≤6, -16≤k≤15, -33≤l≤30	
Reflections collected	13914	
Independent reflections	2302 [R(int) = 0.0941]	
Completeness to Θ = 30.00°	98.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9922 and 0.9283	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2302 / 0 / 209	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2σ(I)]	R1 = 0.0654, wR2 = 0.1044	
R indices (all data)	R1 = 0.1035, wR2 = 0.1132	
Absolute structure parameter	0(10)	
Largest diff. peak and hole	0.341 and -0.330 $e.Å^{-3}$	

Crystal data and structure refinement for 52 (Fig 13).

Identification code	av_ma254	
Empirical formula	'C10 H9 Cl O6'	
Formula weight	260.62	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	'P b c a'	
Space group (Hall)	'-P 2ac 2ab'	
Unit cell dimensions	a = 8.326(3) Å	α= 90°.
	b = 14.430(6) Å	β= 90°.
	c = 17.680(7)Å	γ = 90°.
Volume	2124.1(15) $Å^3$	
Z	8	
Density (calculated)	1.630 Mg/m^3	
Absorption coefficient	0.374 mm^{-1}	
F(000)	1072	
Crystal size	0.63 x 0.38 x 0.33 mm^3	
Θ range for data collection	4.47 to 30.00°.	
Index ranges	-7≤h≤11, -19≤k≤20, -24≤l≤24	
Reflections collected	13973	
Independent reflections	2741 [R(int) = 0.0941]	
Completeness to Θ = 30.00°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8865 and 0.7984	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3079 / 0 / 164	
Goodness-of-fit on F^2	1.079	
Final R indices [I>2σ(I)]	R1 = 0.0324, wR2 = 0.0823	
R indices (all data)	R1 = 0.0282, wR2 = 0.0795	
Largest diff. peak and hole	0.458 and -0.274 $e.Å^{-3}$	

Crystal data and structure refinement for 57a (Fig 14).

Identification code	av_ma208	
Empirical formula	$C_{16}\ H_{13}\ Cl\ O_5$	
Formula weight	320.71	
Temperature	100(2)K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21/n	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 10.977(8)Å	α= 90.00°.
	b = 10.528(8)Å	β= 100.081(15)°.
	c = 12.486(10)Å	γ = 90.00°.
Volume	1420.6(19)Å^3	
Z	4	
Density (calculated)	1.499 Mg/m^3	
Absorption coefficient	0.291 mm^{-1}	
F(000)	664	
Crystal size	0.31 x 0.29 x 0.21 mm^3	
Θ range for data collection	4.30° to 32.50°.	
Index ranges	-16≤h≤16, -15≤k≤13, -18≤l≤14	
Reflections collected	22084	
Independent reflections	4510 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	99.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9153 and 0.9415	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5106 / 0 / 208	
Goodness-of-fit on F^2	1.074	
Final R indices [I>2σ(I)]	R1 = 0.0367, wR2 = 0.0949	
R indices (all data)	R1 = 0.0313, wR2 = 0.0919	
Largest diff. peak and hole	0.505 and -0.238e.Å^{-3}	

Crystal data and structure refinement for 60c (Fig 15).

Identification code	av_ma211	
Empirical formula	C_{16} H_{11} Cl F N O_4	
Formula weight	335.71	
Temperature	173(2)K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 4.833(3)Å	α= 97.74(4)°.
	b = 10.824(6)Å	β= 91.31(4)°.
	c = 14.809(9)Å	γ = 92.29(3)°.
Volume	766.6(7)Å^3	
Z	2	
Density (calculated)	1.454 Mg/m^3	
Absorption coefficient	0.279 mm^{-1}	
F(000)	344	
Crystal size	0.83 x 0.14 x 0.05 mm^3	
Θ range for data collection	4.17° to 27.50°.	
Index ranges	-3≤h≤6, -14≤k≤14, -19≤l≤19	
Reflections collected	9597	
Independent reflections	1845 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	92.7%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9862 and 0.8014	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3275 / 0 / 238	
Goodness-of-fit on F^2	1.074	
Final R indices [I>2σ(I)]	R1 = 0.1195, wR2 = 0.1569	
R indices (all data)	R1 = 0.0539, wR2 = 0.1371	
Largest diff. peak and hole	0.560 and -0.355e.Å^{-3}	

Crystal data and structure refinement for 62b (Fig 16).

Identification code	av_ma258B	
Empirical formula	$C_{16}\ H_{15}\ Cl\ O_3$	
Formula weight	290.73	
Temperature	173(2)K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.243(2)Å	α= 75.67(2)°.
	b = 9.084(3)Å	β= 68.683(16)°.
	c = 10.418(3)Å	γ = 86.17(2)°.
Volume	703.9(4)Å^3	
Z	2	
Density (calculated)	1.372 Mg/m^3	
Absorption coefficient	0.275 mm^{-1}	
F(000)	304	
Crystal size	0.19 x 0.16 x 0.10 mm^3	
Θ range for data collection	4.30° to 27.50°.	
Index ranges	-10≤h≤10, -11≤k≤11, -13≤l≤13	
Reflections collected	11010	
Independent reflections	2339 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	98.5%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9730 and 0.9496	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3187 / 0 / 187	
Goodness-of-fit on F^2	1.054	
Final R indices [I>2σ(I)]	R1 = 0.0616, wR2 = 0.1206	
R indices (all data)	R1 = 0.0407, wR2 = 0.1119	
Largest diff. peak and hole	0.393 and -0.258e.Å^{-3}	

Crystal data and structure refinement for 62c (Fig 17).

Identification code	ma223	
Empirical formula	$C_{16}H_{14}ClFO_3$	
Formula weight	308.72	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/m$	
Space group (Hall)	-P 2yb	
Unit cell dimensions	a = 8.1793(2) Å	α= 90°.
	b = 6.9958(2) Å	β= 105.7850(10)°.
	c = 13.4427(3) Å	γ = 90°.
Volume	740.19(3) $Å^3$	
Z	2	
Density (calculated)	1.385 Mg/m^3	
Absorption coefficient	0.276 mm^{-1}	
F(000)	320	
Crystal size	0.53 x 0.21 x 0.12 mm^3	
Θ range for data collection	2.59 to 28.62°.	
Index ranges	$-11\leq h\leq 11$, $-9\leq k\leq 9$, $-18\leq l\leq 16$	
Reflections collected	15329	
Independent reflections	2029 [R(int) = 0.0273]	
Completeness to Θ = 28.62°	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9677 and 0.8677	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2029 / 0 / 127	
Goodness-of-fit on F^2	1.018	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0381, wR2 = 0.1068	
R indices (all data)	R1 = 0.0533, wR2 = 0.1184	
Extinction coefficient	0.018(4)	
Largest diff. peak and hole	0.157 and -0.226 $e.Å^{-3}$	

Crystal data and structure refinement for 62d (Fig 18).

Identification code	ma221	
Empirical formula	$C_{16}\ H_{14}\ Cl_2\ O_3$	
Formula weight	325.17	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.237(2) Å	α= 78.700(16)°.
	b = 14.226(5) Å	β= 85.993(18)°.
	c = 19.964(6) Å	γ = 80.558(18)°.
Volume	2261.3(12) $Å^3$	
Z	6	
Density (calculated)	1.433 Mg/m^3	
Absorption coefficient	0.437 mm^{-1}	
F(000)	1008	
Crystal size	0.52 x 0.12 x 0.04 mm^3	
Θ range for data collection	2.51 to 29.96°.	
Index ranges	-10≤h≤10, -19≤k≤18, -27≤l≤27	
Reflections collected	22611	
Independent reflections	9718 [R(int) = 0.0608]	
Completeness to Θ = 29.96°	73.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9827 and 0.8047	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9718 / 0 / 577	
Goodness-of-fit on F^2	0.961	
Final R indices [I>2σ(I)]	R1 = 0.0588, wR2 = 0.0909	
R indices (all data)	R1 = 0.1763, wR2 = 0.1286	
Largest diff. peak and hole	0.354 and -0.353 $e.Å^{-3}$	

Crystal data and structure refinement for 62f.(Fig 19).

Identification code	av_ma210	
Empirical formula	C_{16} H_{14} Cl F O_3	
Formula weight	308.72	
Temperature	173(2)K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.212(4)Å	α= 71.18(3)°.
	b = 9.780(3)Å	β= 76.41(2)°.
	c = 10.156(3)Å	γ = 71.34(2)°.
Volume	723.5(5)Å^3	
Z	2	
Density (calculated)	1.417 Mg/m^3	
Absorption coefficient	0.282 mm^{-1}	
F(000)	320	
Crystal size	0.31 x 0.18 x 0.08 mm^3	
Θ range for data collection	4.57° to 29.00°.	
Index ranges	-11≤h≤11, -10≤k≤13, -13≤l≤13	
Reflections collected	12813	
Independent reflections	2902 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	98.2%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9177 and 0.9778	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3773 / 0 / 195	
Goodness-of-fit on F^2	1.067	
Final R indices [I>2σ(I)]	R1 = 0.0647, wR2 = 0.1393	
R indices (all data)	R1 = 0.0472, wR2 = 0.1318	
Largest diff. peak and hole	0.869 and -0.243e.Å^{-3}	

Crystal data and structure refinement for ma64 (Fig 20).

Identification code	ma192	
Empirical formula	$C_{14}H_{11}ClO_5$	
Formula weight	294.68	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.3207(3) Å	α= 69.638(2)°.
	b = 8.3976(3) Å	β= 79.963(2)°.
	c = 11.2648(4) Å	γ = 61.383(2)°.
Volume	647.76(4) $Å^3$	
Z	2	
Density (calculated)	1.511 Mg/m^3	
Absorption coefficient	0.311 mm^{-1}	
F(000)	304	
Crystal size	0.81 x 0.57 x 0.22 mm^3	
Θ range for data collection	2.79 to 30.00°.	
Index ranges	-11≤h≤11, -11≤k≤11, -15≤l≤15	
Reflections collected	15827	
Independent reflections	3732 [R(int) = 0.0428]	
Completeness to Θ= 30.00°	99.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9347 and 0.7866	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3732 / 0 / 182	
Goodness-of-fit on F^2	1.054	
Final R indices [I>2σ(I)]	R1 = 0.0339, wR2 = 0.0912	
R indices (all data)	R1 = 0.0383, wR2 = 0.0949	
Largest diff. peak and hole	0.379 and -0.637 $e.Å^{-3}$	

Crystal data and structure refinement for 66 (Fig 21).

Identification code	av_ma194	
Empirical formula	C_{14} H_{11} Cl O_3	
Formula weight	262.68	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group (H.-M.)	P -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.964(5)Å	α= 102.460(10)°.
	b = 9.959(6)Å	β= 94.583(16)°.
	c = 15.587(9)Å	γ = 96.925(14)°.
Volume	1191.2(13)Å^3	
Z	4	
Density (calculated)	1.465 Mg/m^3	
Absorption coefficient	0.317 mm^{-1}	
F(000)	544	
Crystal size	0.39 x 0.18 x 0.14 mm^3	
Θ range for data collection	2.23° to 32.57°.	
Index ranges	-11≤h≤12, -15≤k≤15, -23≤l≤23	
Reflections collected	29864	
Independent reflections	7110 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	96.9%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9974 and 0.8683	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8388 / 0 / 327	
Goodness-of-fit on F^2	1.031	
Final R indices [I>2σ(I)]	R1 = 0.0420, wR2 = 0.0910	
R indices (all data)	R1 = 0.0330, wR2 = 0.0855	
Largest diff. peak and hole	0.518 and -0.230e.Å^{-3}	

Crystal data and structure refinement for 77e (Fig 24).

Identification code	av_ma139	
Empirical formula	C_{13} H_{17} N O_2	
Formula weight	219.28	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group (H.-M.)	P 21/c	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 8.6600(17)Å	α= 90.00°.
	b = 9.800(2)Å	β= 116.74(2)°.
	c = 14.801(5) Å	γ = 90.00°.
Volume	1121.8(5)$Å^3$	
Z	4	
Density (calculated)	1.388 Mg/m^3	
Absorption coefficient	0.264 mm^{-1}	
F(000)	336	
Crystal size	0.55 x 0.27 x 0.01 mm^3	
Θ range for data collection	4.40 to 29.00°.	
Index ranges	-8≤h≤8, -13≤k≤13, -17≤l≤17	
Reflections collected	12323	
Independent reflections	3964 [R(int) = 0.0239]	
Completeness to Θ = 29.82°	97.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9726 and 0.9931	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2517 / 0 / 176	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2σ(I)]	R1 = 0.0567, wR2 = 0.1081	
R indices (all data)	R1 = 0.0413, wR2 = 0.1026	
Largest diff. peak and hole	0.219 and -0.174e.$Å^{-3}$	

Curriculum Vitae

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Language Skills	English (TOEFL 220/300), Graduate Degree in English Literature, Deutsch (Basic Knowledge), Urdu.

Education:

2007-2009 Ph.D. (Dr. rer. Nat) *Synthetic Organic Chemistry* (Group of Prof Dr. Peter Langer). Institute of Chemistry. University of Rostock.

2004-2006 M.phil leading to Ph.D. *Supramolecular Chemistry.* H.E.J Research Institute of Chemistry University of Karachi Pakistan.

2001-2004 M.Sc. in *Organic Chemistry* Gomal University Dera Ismail Khan (N.W.F.P) Pakistan

1998-2000 B.Sc. in *Chemistry* Gomal University Dera Ismail Khan (N.W.F.P) Pakistan.

Research Experience:

- 2007-2009. Scientific Co-worker (Wissenschaftlicher Mitarbeiter) at Institute of Chemistry University of Rostock.
- 2004-2006. Junior Reserch Fellow at H.E.J Research Institute of Chemistry University of Karachi, Karachi Pakistan.
- 2003-2004. M.Sc. thesis titled "Phyto-chemical Studies on Biologically Active Diterpenes of *Euphorbia Peplus"* at Department of Chemistry Gomal University, Dera Ismail Khan (N.W.F.P) Pakistan.

Technical Skills:

- Excellent handling in Vacuum and Schlenck techniques for oxygen and moisture sensitive reactions.
- Working experience with 1D and 2D NMR technique.
- Working experience in MS Office, Chem. Office, Sci-finder, Crossfire and other computer utilities.

Conferences and Poster Presentations:

- Poster titled "Octacyclodextrin-*p*-octiphenyls into Hydrophilic, Hydrophobic Barrel Stave Pores Having Practical Applications in Drug Designing" 10th International Symposium on Natural Product Chemistry. January 6-9, 2006, Karachi, Pakistan at International Center for Chemical Sciences University of Karachi.

- Poster titled "*Octacyclodextrin-p-octiphenyls into Hydrophilic, Hydrophobic* Barrel Stave *Pores Having Practical Applications in Drug Designing*" Presented at 6th International and 16th National Chemistry Conference Multan Pakistan**.**
  (*Awarded by* ***IUPAC Best Poster Prize***)

List of Publications:

1. Verena Wolf, **Muhammad Adeel,** Stefanie Reim, Alexander Villinger, Helmut Reinke, and Peter Langer. *Synthesis* Submitted "Synthesis of 3-Chlorosalicylates by Formal [3+3] Cyclocondensations of 4-Chloro-1,3-bis(trimethylsilyloxy)-1,3-butadienes".

2. Muhammad Nawaz, **Muhammad Adeel,** Muhammad Farooq Ibad, Peter Langer. *Synlett* **2009** Accepted "Synthesis of functionalized 2′,4-diarylbenzophenones based on site-selective Suzuki cross-coupling reactions".

3. **Muhammad Adeel,** Stefanie Reim, Verena Wolf, Alexander Villinger, Christine Fischer, Peter Langer. *Mnauscript in Preparation* "The first 4-chloro-1.3-bis(trimethylsiloxy)-1,3-diene and its applications to the regioselective synthesis of chlorinated arenes".

4. **Muhammad Adeel,** Muhammad Nawaz, Alexander Villinger, Helmut Reinke, Christine Fischer, Peter Langer. *Tetrahedron* 65, **2009,** 4099–4105. Synthesis of Polyketide-Type Phenols by Domino ′Michael / Retro-Michael / Aldol Reactions of 3-Formylchromones with Silyl Enol Ethers derived from Ethyl 3,5-Dioxohexanoate.

5. Benard Juma, **Muhammad Adeel,** Alexander Villinger, Anke Spannenberg, Christine Fischer, Peter Langer* *Advanced Synthesis & Catalysis* **2009** *In print* "Synthesis of 2,6-Dioxo-1,2,3,4,5,6-hexahydroindoles by Acid-Catalyzed Cyclization of Acetal-Protected (2,4-Dioxocyclohex-1-yl) acetamides and their Transformation into 5,8,9,10-Tetrahydro-6H-indolo[2,1-a]isoquinolin-9-ones".

6. Stefanie Reim, Matthias Lau, **Muhammad Adeel,** Ibrar Hussain, Mirza A. Yawer, Abdolmajid Riahi, Christine Fischer, Helmut Reinke, and Peter Langer* *Synthesis* **2009,** No. 3, pp 0445–0463 "Synthesis of Functionalized Fluorenones based on the Combination of Formal [3+3] Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes with Intramolecular Friedel-Crafts-Acylations".

7. **Muhammad Adeel,** Muhammad A. Rashid, Nasir Rasool, Rasheed Ahmad, Helmut Reinke, Christine Fischer and Peter Langer* *Synthesis* **2009**, No. 2, 243–250, "Regioselective Synthesis of Functionalized Biaryls based on Cyclizations of 4-Aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes".

8. **Muhammad Adeel,** Stefanie Reim, Verena Wolf, Mirza A. Yawer, Ibrar Hussain, Alexander Villinger, Peter Langer* , *Synlett* **2008**, 2629-2632. "Synthesis and Reactions of the First Fluorine-Containing 1,3-Bis(trimethylsilyloxy)-1,3-butadienes".

9. Stefanie Reim, **Muhammad Adeel,** Ibrar Hussain, Mirza A. Yawer, Alexander Villinger, Peter Langer*, *Tetrahedron Lett.* **2008**, 49, 4901-4904. "Synthesis and Reactions of the First 2-Chloro-1,3-bis(trimethylsilyloxy)-1,3-butadienes".

10. Muhammad A. Rashid, Nasir Rasool, **Muhammad Adeel**, Christine Fischer, Helmut Reinke, Peter Langer* *Tetrahedron* **2008**, 64, 529-535. "Regioselective Synthesis of Diaryl Ethers based on One-Pot Cyclizations of 4-Aryloxy-1,3-bis(trimethylsilyloxy)-1,3-dienes".

11. Mirza A. Yawer, Abdolmajid Riahi, **Muhammad Adeel,** Ibrar Hussain, Christine Fischer Peter Langer*, *Synthesis* **2008**, 1276-1282. "One-pot synthesis of 6-(pyridyl)salicylates by formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 3-pyridyl-3-silyloxy-2-en-1-ones".

12. Benard Juma, **Muhammad Adeel,** Alexander Villinger and Peter Langer*, *Tetrahedron Lett.* **2008**, 49, 2272–2274. "Efficient synthesis of 2,6-dioxo-1,2,3,4,5,6-hexahydro-indoles based on the synthesis and reactions of (2,4-dioxocyclohex-1-yl)acetic acid derivatives".

13. Nasir Rasool, Muhammad A. Rashid, **Muhammad Adeel,** Helmut Reinke and Peter Langer*, *Tetrahedron Lett.* **2008,** 49, 2254–2257. "Synthesis and Reactions of Hydroxyspiro[5.2]cyclo-octenones based on the Cyclization of the Dianions of Acetone and Diethyl 2-Oxopropylphosphonate with 1,1-Diacylcyclopropanes".

14. Muhammad A. Rashid, Nasir Rasool, **Muhammad Adeel,** Helmut Reinke, Christine Fischer and Peter Langer* *Tetrahedron,* **2008**, 64, 3782-3793. "Synthesis of Functionalized Diarylsulfides based on Regioselective One-Pot Cyclizations of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes".

15. Muhammad A. Rashid, Nasir Rasool, Bettina Appel, **Muhammad Adeel,** Vahuni Karapetyan, Satenik Mkrtchyan, Helmut Reinke, Christine Fischer, and Peter Langer* *Tetrahedron* **2008,** *64, 5416-5425* **"**Synthesis of 1-Azaxanthones by Condensation of 1,3-

Bis(trimethylsilyloxy)-1,3-butadienes with 3-(Cyano)-benzopyrylium Triflates and Subsequent Domino ′Retro-Michael / Nitrile-Addition / Heterocyclization′ Reaction”.

Declaration/Erklärung

Here by I declare that this work has so for neither submitted to the Faculty of Mathematics and Natural Sciences at the University of Rostock nor to any other scientific Institution for the purpose of doctorate. Further more, I declare that I have written this work by myself and that I have not used any other sources, other than mentioned earlier in this work.

Hiermit erkläre ich, daß diese Arbeit bisher von mir weder an der Mathematisch-Naturwissenschaftlichen Fakultät der Universität Rostock noch einer anderen wissenschaftlichen Einrichtung zum Zwecke der Promotion Eingereicht wurde.

Ferner erkläre ich, dass ich diese Arbeit selbständig verfasst und keine anderen als die darin angegebenen Hilfsmittel benutzt habe

I hereby apply irrevocably to take oral examination if the form of a private viva voce and a public presentation.

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Muhammad Adeel