Synthesis of Functionalized Triarylmethanes based on Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes, One-Pot Synthesis of Functionalized Pyranones and Synthesis of Functionalized Indoles and Pyrroles based on Pd(0)-Catalyzed Reactions

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Tag der Promotion:

Affectionately Dedicated to
My dearest friend Ajaz Ahmad
For his memorable company
during start of PhD

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Synthesis of Functionalized Triarylmethanes Based on Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes, One pot Sythesis of Functionalized Pyranones and Synthesis of Functionalized Indoles and Pyrroles Based on Pd(0)-Catalyzed Reactions

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Rasheed Ahmad

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Abbreviations

Ar	Aromatic
APT	Attached Proton Test
ATCC	American Type Culture Collection
*n*BuLi	*n*-Butyllithium
DEPT	Distortionless Enhancement by Polarisation Transfer
EI	Electronic Impact
ESI	Electrospray Ionization
EtOAc	Ethyl acetate
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
$FeCl_3$	Ferric(III) chloride
Me_3SiCl	Trimethylsilyl chloride
mp.	Melting Point
RCM	Ring Closing Metathesis
TOF	Time of flight
TFA	Trifluoroacetic Acid
Tf_2O	Trifluoromethanesulfonic Anhydride
THF	Tetrahydrofurane
TLC	Thin Layer Chromatography
TMS	Trimethylsilane
UV	Ultraviolet Spectroscopy

General introduction

One of the main goal of modern organic chemistry is to develop efficient methods for the synthesis of complex molecules with high chemo-, regio- and stereoselectivity. In addition, the development of new drugs is a great challenge for organic chemists[1]. For example, it is important to develop new antibiotics, due to the increasing problem of resistance of many bacteria against various antibiotics.

In search of new active ingredients, natural substances are often important lead structures for drug discovery. So, it is impartant to construct synthetic compounds or substances which are derived from nature, following the example of nature. Usual procedure for the synthesis of organic compounds is stepwise formation of individual bonds. However, it would be much more efficient if one could form several bonds in one step without isolating the intermediates, changing the reaction conditions and adding reagents.[1] It is obvious that this type of reaction would allow to reduce wastes compared to sequential reactions. In addition, consumed amounts of solvents, reagents, adsorbents and energy would be dramatically decreased. Furthermore the amount of labour would also go down. Thus, these reactions would allow an ecologically and economically favourable synthesis. This sort of transformation is called as a domino reaction[1].

The value of domino and cyclization reactions using free and masked dianions lies in the heart of organic synthesis and has immense applications. Reactions are often carried out as a one-pot method and can provide an easy access to a large number of natural product analogues. The pharmacological efficiency of these analogues may be better than that of the natural products themselves.

My studies are focussed on the development of new and reliable synthetic strategies and their application for the preparation of natural product analogues and of pharmacologically active carba- and heterocycles. The target structures include triarylmethanes, pyranones, *N*-methylpyrroles and *N*-methylindoles.

Summary

Major part of this dissertation has been recently published (see list of publications at the end). Work described in this dissertation is concerned with synthesis of functionalized triarylmethanes based on [3+3] cyclocondesations of 1,3-bis(silyloxy)-1,3-butadienes, synthesis of pyranones and synthesis of new derivatives of *N*-methylpyrroles and *N*-methylindoles with Suzuki and Heck couplings. Title of thesis is given below.

Synthesis of Functionalized Triarylmethanes Based on Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes, One pot Sythesis of Functionalized Pyranones and Synthesis of Functionalized Indoles and Pyrroles Based on Pd(0)-Catalyzed Reactions

The first chapter deals with the synthesis of functionalized and sterically encumbered triarylmethanes prepared by combination of $FeCl_3$-catalyzed benzylations of 1,3-diketones and formal [3+3] cyclocondensation reactions of 1,3-bis(silyl enol ethers). In the first step, penta-2,4-dione (**5**) was benzylated with respective benzylalcoholes **6a-f** in the presence of $FeCl_3$. In the second step, the strategy of formal [3+3] cyclocondensation reactions of 1,3-bis(silyl enol ethers) was sucessfully applied to afford triarylmethanes **9a-q.**

The second chapter includes the synthesis of functionalized pyranones based on the one-pot reaction of substituted benzaldehydes with dianions. A new methodology was developed to produce functionalized pyranones including trifluoromethyl-substituted pyranones with high yields.

In the third chapter, I have described the synthesis of di- and tri-alkenylindoles by palladium(0)-catalyzed Heck cross-coupling reactions of di- and tribromo-*N*-methylindoles **19, 20,** and **22.** In the second part, regioselective reactions of brominated *N*-methylpyrrole are described which provide a new strategy for the synthesis of 5-aryl-2,3,4-tribromopyrroles, 2,5-diaryl-3,4-dibromopyrroles **26, 28** and tetraarylpyrroles **29** based on regioselective Suzuki cross-coupling reactions.

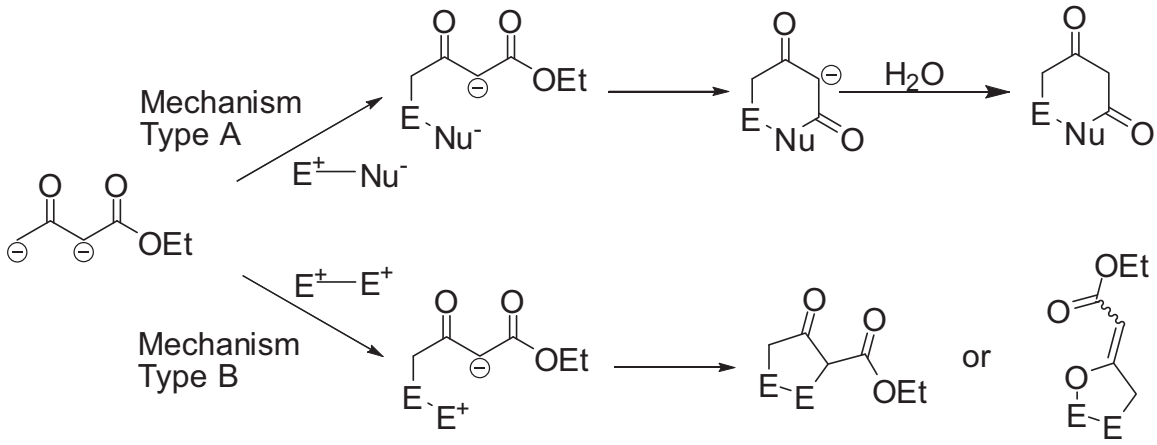
The fifth chapter contains the experimental, spectroscopic data and complete characterization of all new products.

1. Synthesis of triarylmethanes based on [3+3] cyclocondensations of 1,3-bis(silyl enol ethers)

1.1 Synthesis of 4-alkyl-1,3-bis(trimethylsiloxy)buta-1,3-dienes

1.1.1 Introduction

Dianions represent important building blocks for the regioselective formation of carbon-carbon bonds. Ambident dianions are organic substrates containing two delocalized negative charges. Dianions can be generated by reaction of 1,3-dicarbonyl compounds in the presence of strong base, such as LDA or *n*-BuLi[1]. The functionalization of the terminal carbon atom of 1,3-dicarbonyl compounds by reaction of the corresponding dianions with electrophiles represents an important synthetic method which has been used in the synthesis of natural products. The terminal carbon atom of the dianion can be regioselectively coupled with one equivalent of an electrophile E^+ to give a monoanion which can be subsequently trapped by addition of a second electrophile. Two general mechanistic pathways for cyclization reactions of dianions can be discussed as follows[1] (Scheme 1-1).



Scheme 1-1: Possible mechanistic pathways for cyclization reactions of 1,3-dicarbonyl dianions. Nu = nucleophile center, E = electrophile center.

Mechanism type A: the dianion can react with monofunctional electrophiles with transposition of a negative charge from the dianion to the electrophile. This carbanion attacks an E^+ centre of the former dianion moiety (e.g. the ester group) to give a cyclic monoanion which is subsequently quenched with water.

Mechanism type B: the dianion can react as a dinucleophile with a dielectrophile. A monoanion is formed, followed by attack of the latter onto a second E^+ center.

Cyclization reactions of dianions with dielectrophiles are synthetically useful. However, problems can arise since both starting materials are highly reactive compounds which have low reactivity matching. In addition, 1,2-dielectrophiles are often rather labile, and reactions with nucleophiles can result in polymerization, decomposition, formation of open-chained products, elimination or SET-process. These intrinsic limitations can be overcome by two ways: a) a proper tuning of the reactivity of dianion and dieletrophile and b) the use of eletroneutral dianion equivalents (masked dianions) in Lewis acid catalyzed reactions.[1]

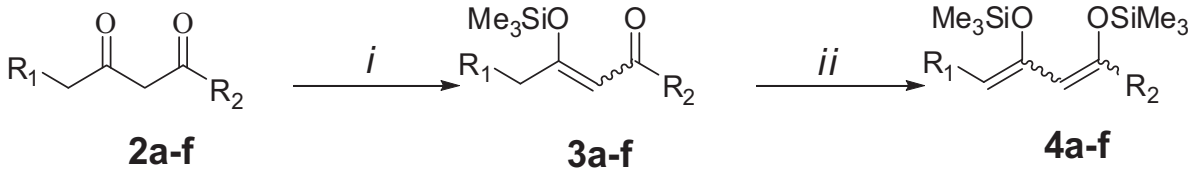
Many studies proved that 1,3-bis(enol silyl ethers) can be considered as equivalents of the corresponding 1,3-dicarbonyl dianions.[2] The chemistry of bis(silyl enol ethers) has been developed during the last two decades.[2d] It is, for example, known that silyl enol ethers can condense with various carbonyl compounds in the presence of Lewis acids.[3] These Lewis-acid-mediated reactions[4] (e. g. alkylation and aldol condensation) provide useful alternatives to classical enolate chemistry. In cyclization reactions, 1,3-bis(silyl enol ethers) can react as 1,3-dinucleophiles or, similar to the well-known Danishefsky diene[5], as functionalized butadienes. 1,3-Bis(silyl enol ethers) undergo reactions with electrophiles at the terminal carbon atom followed by reaction of the central carbon or the oxygen atom. Silyl enol ethers can be cleaved with nucleophiles such as MeLi, $LiNH_2$ or $R_4N^+F^-$ to give enolates. These can be reacted with halides (Br_2, Cl_2, I_2) or pseudohalides (PhSCl, PhSeCl, Cl-N=O).[6] Whereas enolates can be alkylated only by primary or secondary halides, silyl enol ethers can be alkylated by tertiary halides.[7]

Preparation of silyl enol ethers mainly follows the procedures reported by Chan and Molander. This procedure relies on the preparation of mono(silyl enol ethers), which are subsequently transformed into bis(silyl enol ethers) by deprotonation with LDA and subsequent silylation.[8,9]

In this chapter, I present the synthesis of 4-alkyl-1,3-bis(trimethylsilyoxy)-1,3-butadiens following the procedure of Chan.

1.1.2 Results and discussion

Following the procedures of Chan and Molander, 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4a-f** can be prepared from the respective 1,3-dicarbonyl compounds **2a-f** in two steps. Treatment of the *β*-ketoesters with NEt_3, Me_3SiCl afforded silyl enol ethers **3a-f.** Deprotonation of the latter with LDA and subsequent addition of Me_3SiCl afforded the dienes **4a-f**.

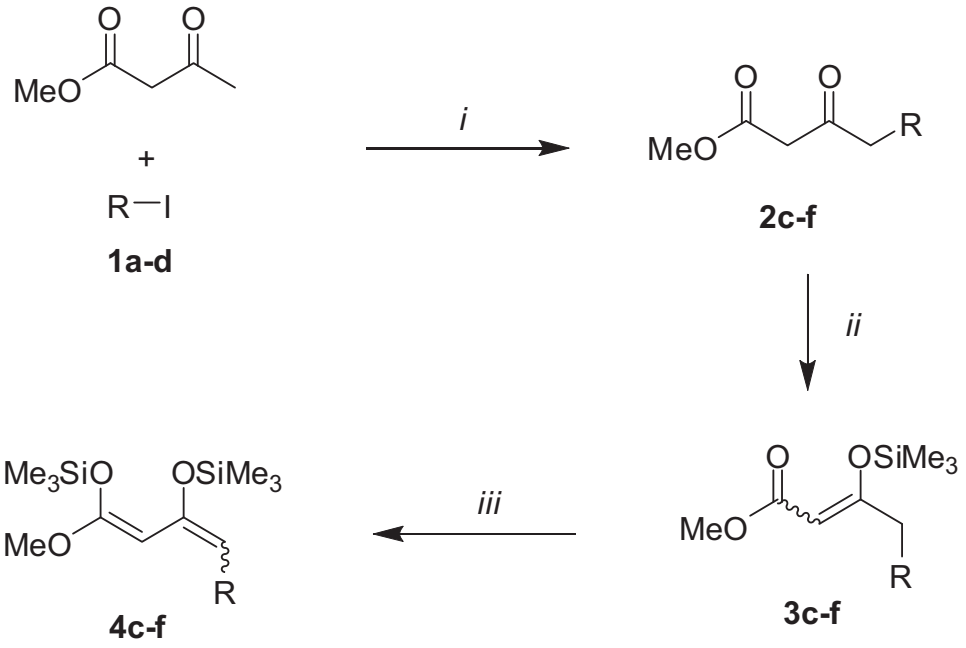


2a-f **3a-f** **4a-f**

Scheme 1-2: Synthesis of 1,3-bis(silyl enol ethers) **4a-f**; *i*: 1) NEt3 (1.5 equiv.); 2) Me3SiCl (1.5 equiv.), C6H6, 20 °C, 12 – 48 h; *ii*: 1) LDA (1.5 equiv.), THF, 0 °C, 2 h; 2) Me3SiCl (1.5 equiv.), –78 → 20 °C, 6 – 12 h.

The synthesis of alkyl-substituted 1,3-bis(silyl enol ether) derivatives require the synthesis of the respective β-ketoesters **2c-f** which was carried out in collaboration with R. Khera and M. Riahi. It is known that the regioselectivities of the reactions of monoanions and dianions generally differ greatly. 1,3-Dicarbonyl monoanions are generally alkylated at the central carbon or at the oxygen atom, whereas the formation of dianions allows the functionalization of the terminal carbon atom. Based on this, the 4-alkyl-3-oxobutanoates **2c-f** were prepared by reactions of the dianion of methyl

acetoacetate with the respective alkyl halides **1a-d** (RI). These compounds were transformed, according to a known procedure,[2] into the desired 1,3-bis(silyl enol ethers) **4c-f** via the respective mono(silyl enol ethers) **3c-f** (Scheme 1-3, Table 1-1).



Scheme1-3: Synthesis of alkyl-substituted 1,3-bis(silyl enol ether) derivatives; *i*: 1) 2.5 LDA, THF, 0 °C, 1 h; 2) methyl acetoacetate, **1a-d**, –78 → 20 °C; *ii*: Me_3SiCl (1.5 equiv.), NEt_3 (1.5 equiv.), C_6H_6, 20 °C, 48 h; *iii*: 1) LDA (1.5 equiv.), THF, –78 °C, 1 h; 2) Me_3SiCl (1.5 equiv.), 20 °C, –78 → 20 °C.

All 4-alkyl-1,3-bis(silyl enol ethers) prepared could be stored at suitable conditions (-20 ^{o}C, dry, inert gas atmosphere) for several months without decomposition. The 1,3-bis(silyl enol ethers) **4** of ß-ketoesters used in this synthesis are listed in the following table.

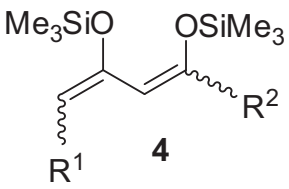


Table 1-1: 1,3-bis(silyl enol ethers) **4** used in this work

4	R^1	R^2
a	H	OMe
b	H	OEt
c	Me	OMe
d	Et	OEt
e	*n*-Bu	OMe
f	*n*-Pent	OMe

1.1.3 Conclusions

The application of a the known procedure allows the synthesis of 4-alkyl-1,3-bis(silyl enol ethers). These masked dianions are used in the cyclization reactions for the synthesis of aromatic rings - important building blocks for the assembly of natural product analogues.

1.2 Synthesis of Functionalized Triarylmethanes

1.2.1 Introduction

Triarylmethanes are of considerable pharmacological relevance and occur in a number of natural products. Pharmacological activities include estrogen receptor binding affinity,[10a] inhibition of hepatic cholesterol,[10b] inhibition of aldose reductase[2,10c] antiproliferative activity,[10d] antiviral and cytotoxic activity,[10e] antifungal activity,[10f] anti-HIV activity,[10g,h] and CNS activity.[10i] Naturally occuring triarylmethanes, containing a

(1,1-diphenylmethyl)phenol substructure, include mohsenone and a number of related molecules.[11] (1,1-Diphenylmethyl)salicylates and related structures have been reported to possess anti-HIV activity,[12a,10g] and antibacterial activity.[12b]

Triarylmethanes are of considerable pharmacological relevance and occur in a variety of natural products.[10] Bis(4-hydroxyphenyl)-[2-(phenoxysulfonyl)-phenylmethane and bis(4-hydroxyphenyl)-[2-(benzensulfonamidyl)-phenylmethane (Figures 1.1-1.2) were isolated from commercial preparations of phenol red, a pH indicator dye mostly used in cell culture media. [10] Isolation of some substituted triphenylmethanes (Figures 1.3-1.4) was also reported from the leaves of the *cajeput* tree *Melaleuca quinqueneruia (Myrtaceae)*.[11]

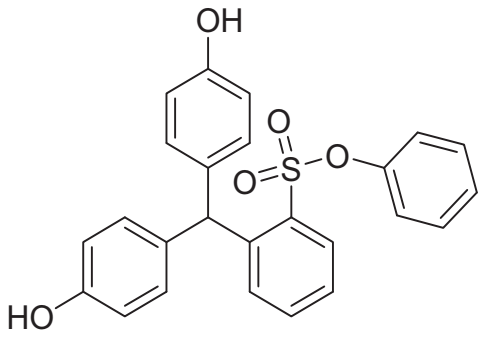


Figure 1.1

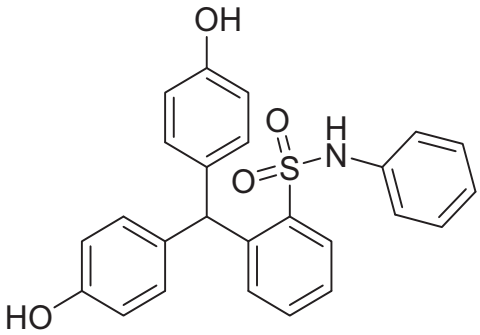


Figure 1.2

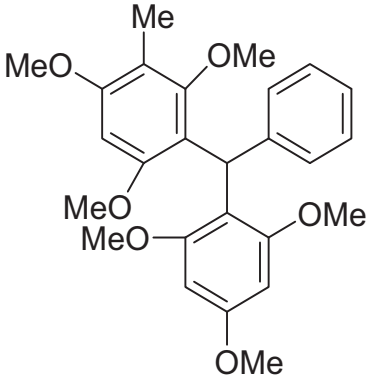


Figure 1.3

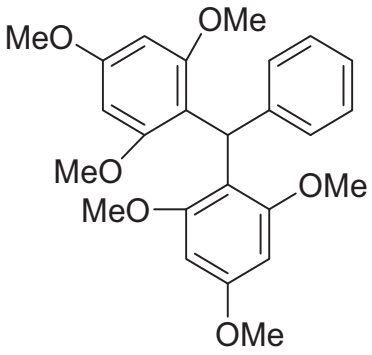


Figure 1.4

Well known C-C coupling reactions, such as Friedel-Crafts alkylations, are used for the functionalization of arenes. In spite of the great synthetic utility of these methods, they have several drawbacks, such as drastic reaction conditions and the formation of regioisomeric mixtures or isomerization products. To address these problems, Beller and coworkers developed novel $FeCl_3 \cdot 6H_2O$-catalyzed Friedel-Crafts type benzylations of arenes using simple benzylic alcohols under mild conditions and with high functional group tolerance.[13] Christoffers et al. studied $FeCl_3$-catalyzed conjugate additions of 1,3-dicarbonyl compounds to enones.[14] Beller and coworkers have recently reported the $FeCl_3$-catalyzed condensation of 1,3-dicarbonyl compounds with simple benzylic alcohols.[15] A number of related transformations have been studied in recent years.[7]

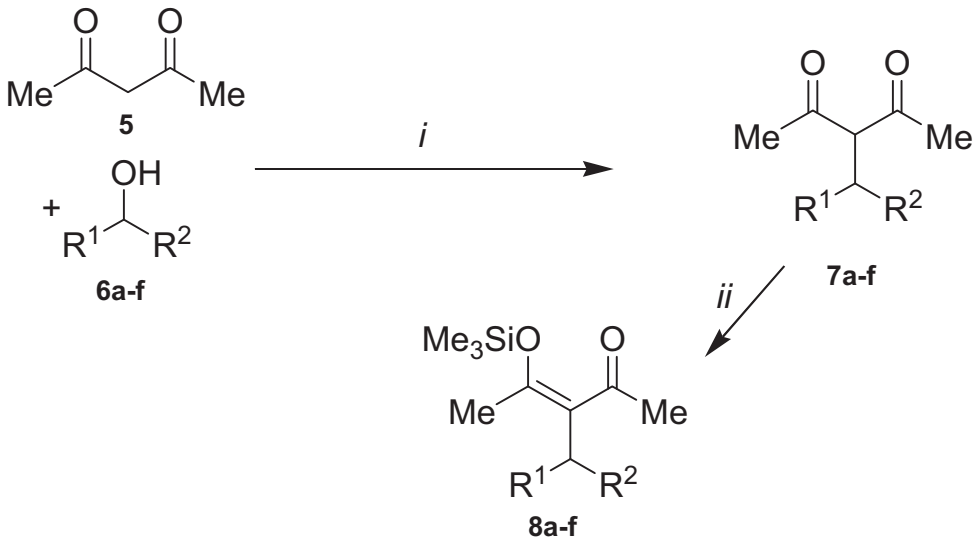
Despite the preparative utility of these reactions, the direct synthesis of sterically encumbered triarylmethanes and diarylmethanes by Fe-catalyzed benzylation of 1,3-dicarbonyl compounds is problematic. In addition, the synthesis of highly substituted and functionalized products depends on the availability of the starting materials, functionalized and highly substituted arenes. Their regioselective synthesis by electrophilic aromatic substitution reactions can be a very difficult task. An alternative strategy for the synthesis of sterically encumbered and highly functionalized arenes relies on the application of suitable dienes in cyclization reactions (building block approach). 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.

Herein, I report, for the first time, the synthesis of sterically encumbered and functionalized triarylmethanes by a combined $FeCl_3$-catalyzed benzylation / [3+3] cyclocondensation approach. The products reported herein are not readily available by other methods and have, to the best of our knowledge, not yet been prepared.

1.2.2 Results and discussion

The $FeCl_3$-catalyzed benzylation of acetylacetone (**5**) with benzylalcohols **6a-f**, following conditions reported by Beller *et al.*,[15] afforded products **7a-f** in very good

yields (Scheme 1-4, Table 1-2). The silylation of **7a-f** afforded the 3-silyloxy-2-en-1-ones **8a-f**.

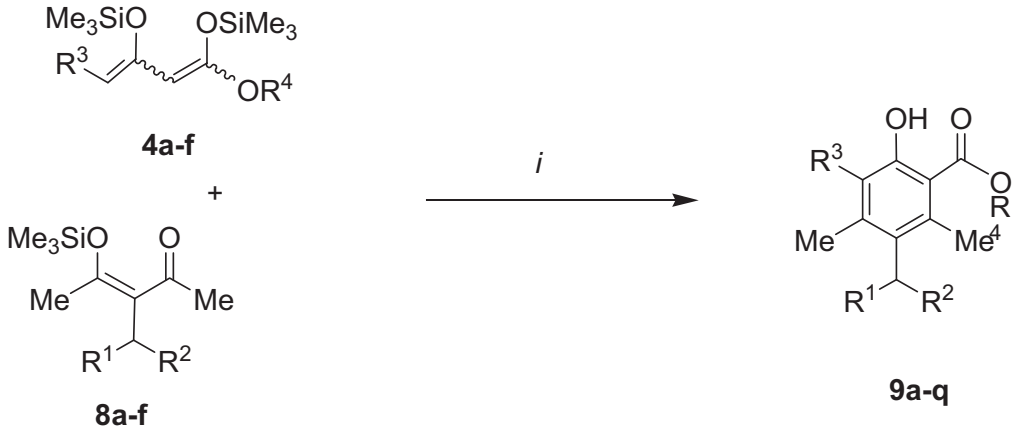


Scheme 1-4. Synthesis of **8a-f**, *i*: $FeCl_3$, NO_2CH_3, 50 °C, 4 h; *ii*: Me_3SiCl, NEt_3, C_6H_6, 20 °C, 72 h

Table 1-2. Synthesis of **7a-f** and **8a-f**

7,8	R^1	R^2	% (**7**)[a]	% (**8**)[a]
a	Ph	Ph	91	90
b	4-(MeO)C_6H_4	4-(MeO)C_6H_4	88	91
c	4-FC_6H_4	4-FC_6H_4	87	89
d	4-ClC_6H_4	4-ClC_6H_4	85	92
e	Me	Ph	94	81
f	Me	4-(MeO)C_6H_4	87	86

[a] Isolated yields



Scheme1-5. Synthesis of **9a-q**, *i*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 20 h

The $TiCl_4$-mediated formal [3+3] cyclocondensation of **8a-f** with 1,3-bis(silyloxy)-1,3-dienes **5a-f**, available from the corresponding 1,3-dicarbonyl compounds in one or two steps,[17] afforded the triarylmethanes **9a-q** (Scheme 1-5, Table 1-3). During the optimization, it proved to be important to carry out the reactions in a highly concentrated solution.[20] The yield of diarylmethane **9m** was higher than the yields of triarylmethanes **9a-q**. The best yields of the triarylmethanes were obtained for derivatives **9i,j** which are derived from the chloro-substituted benzylalcohol **6d**. The yields of triarylmethanes **9a,b** and **9i,j**, derived from the unsubstituted dienes **4a,b**, were higher than those of products **9c,d** and **9k,l** which are derived from dienes **4c,d** (containing a substituent located at the terminal carbon atom).

1.2.3 Possible mechanism for synthsis of 9a-q

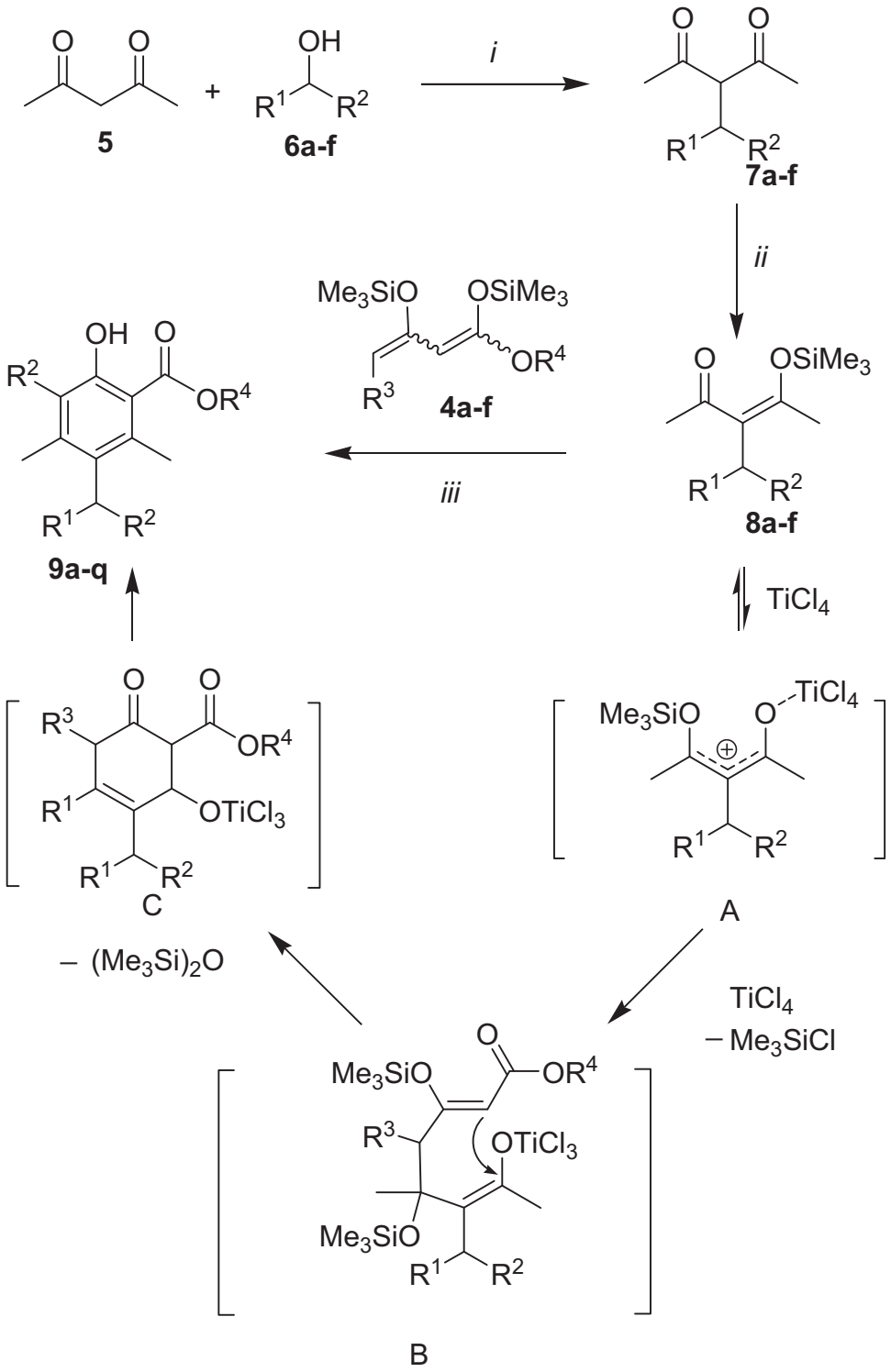


Table 1-3. Synthesis of Triarylmethane and diarylmethanes **9a-q**

4	**8**	**9**	R^1	R^2	R^3	R^4	% (**9**)[a]
a	**a**	**a**	Ph	Ph	H	Me	42
b	**a**	**b**	Ph	Ph	H	Et	45
c	**a**	**c**	Ph	Ph	Me	Me	31[b]
d	**a**	**d**	Ph	Ph	Et	Me	42[b]
a	**b**	**e**	4-(MeO)C_6H_4	4-(MeO)C_6H_4	H	Me	32
b	**b**	**f**	4-(MeO)C_6H_4	4-(MeO)C_6H_4	H	Et	37
a	**c**	**g**	4-FC_6H_4	4-FC_6H_4	H	Me	33
b	**c**	**h**	4-FC_6H_4	4-FC_6H_4	H	Et	37
a	**d**	**i**	4-ClC_6H_4	4-ClC_6H_4	H	Me	50
b	**d**	**j**	4-ClC_6H_4	4-ClC_6H_4	H	Et	53
c	**d**	**k**	4-ClC_6H_4	4-ClC_6H_4	Me	Me	40[b]
d	**d**	**l**	4-ClC_6H_4	4-ClC_6H_4	Et	Me	42[b]
a	**e**	**m**	Me	Ph	H	Me	55
e	**a**	**n**	Ph	Ph	n-C_4H_9	Me	43[c]
f	**a**	**o**	Ph	Ph	n-C_5H_{11}	Me	41[c]
f	**d**	**p**	4-ClC_6H_4	4-ClC_6H_4	n-C_5H_{11}	Me	45[c]
a	**f**	**q**	Me	4-(MeO)C_6H_4	H	Me	48[c]

[a]Isolated yields, [b]contributed by Majeed Riahi, [c]contributed by Hung

1.2.4 Conclusions

In conclusion, a variety of functionalized and sterically encumbered triarylmethanes were prepared by combination of $FeCl_3$-catalyzed benzylations of 1,3-diketones and formal [3+3] cyclocondensation reactions. The products are not readily available by other methods.

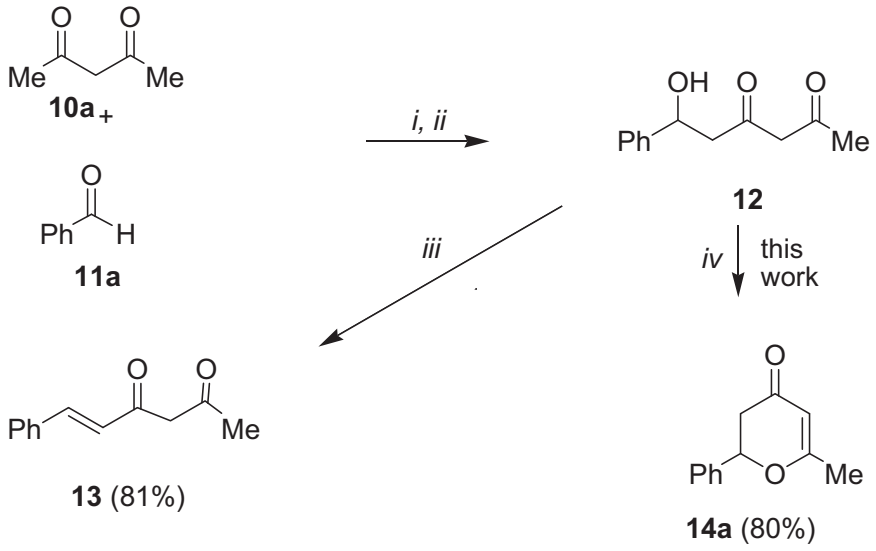
2. One pot synthesis of functionalized pyranones

2.1 Introduction

2,3-Dihydro-4*H*-pyran-4-ones are present in many natural products and in a great variety of pharmacologically relevant synthetic molecules.[20] 2,3-Dihydro-4*H*-pyran-4-ones are available by hetero-Diels–Alder reaction of aldehydes with Danishefsky's diene[21] or related electron-rich dienes.[22, 23] The use of these dienes requires, due to their unstable nature and rapid hydrolysis, a special handling. The synthesis of the dienes requires two or three steps, depending on the substitution pattern. In addition, they cannot be stored for a long period of time (not even at –20 °C). Other syntheses of 2,3-dihydro-4*H*-pyran-4-ones include, for example, palladium(II)-catalyzed oxidative cyclizations of β-hydroxyenones[24] and reactions of β-ethoxy-α,β-unsaturated lactones.[25] Despite their great utility, these methods have some limitations related to the preparative scope.

Feng and coworkers have reported the synthesis of 2,3-dihydro-4*H*-pyran-4-ones by LDA-mediated reaction of 3-methoxy-2-en-1-ones with aldehydes and subsequent acid-mediated cyclization.[26] This method requires the synthesis of the enone starting materials which is sometimes not straightforward. Xian *et al.* reported the synthesis of 2,3-dihydro-4*H*-pyran-4-ones by reaction of lithiated dithianes with epoxides and subsequent deprotection, oxidation and cyclization.[27] Light and Hauser were the first to study the reaction of 1,3-dicarbonyl dianions with aldehydes to give 5-hydroxy-1,3-dicarbonyl compounds and their HCl/MeOH-mediated dehydration or transformation into 2,3-dihydro-4*H*-pyran-4-ones.[28,29] Hassner *et al.* reported the application of this method to the synthesis of the natural product stegobinone.[30] Miller and coworkers reported the transformation of 5-hydroxy-1,3-diketones into 6-alkyl-2,3-dihydro-4*H*-pyran-4-ones using *para*-toluenesulfonic acid (*p*-TsOH, CH_2Cl_2, 24 h, reflux, Dean-Stark trap, 3Å MS).[31] It is important to note that the preparative scope of this method is limited to the synthesis of 6-*alkyl*-2,3-dihydro-4*H*-pyran-4-ones (derived from *aliphatic* aldehydes) because of the competing dehydration in case of aromatic substrates. It is important to note that the reaction of *p*-TsOH with 6-hydroxy-6-phenyl-hexane-2,4-dione (**13**), prepared by condensation of the dianion of acetylacetone (**10a**) with benzaldehyde (**11a**),

has been reported[31] to give 6-phenyl-hex-5-ene-2,4-dione (**13**) rather than the desired pyran-4-one **14a** (Scheme 2-1). The facile formation of **13** is a result of the conjugation of the double bond with the aryl group.

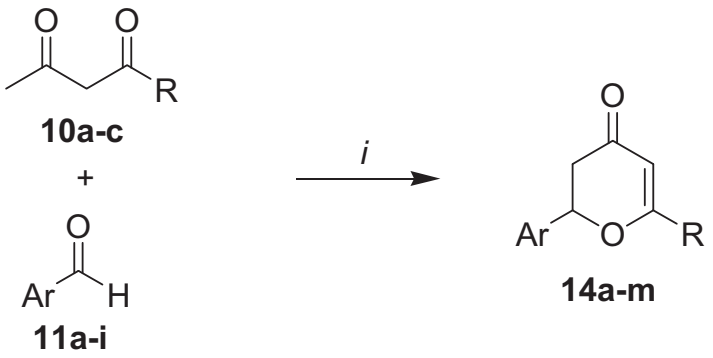


Scheme 2-1. Dehydration and cyclization of **12**, *i*: 1) NaH, THF, 0 °C, 15 min, 2) nBuLi, 20 min, 0 °C, 3) 2a, 15 min, 0 °C; *ii*: NH_4Cl (sat.); *iii*: *p*-TsOH, CH_2Cl_2, 24 h, reflux, Dean-Stark trap, 3Å MS; *iv*: variant A: $FeCl_3 \cdot 6H_2O$, NO_2CH_3, 50 °C, 4 h; variant B: HCl (10%), THF, 15 min, 20 °C, then extraction (EtOAc)

I was interested in a direct and convenient method for the synthesis of 6-*aryl*-2,3-dihydro-4*H*-pyran-4-ones which are, as discussed above, not directly available so far. Therefore, we have reinvestigated the reaction of 1,3-diketone dianions with aldehydes and preliminary results of our efforts are reported. I have found that a variety of 6-aryl-2,3-dihydro-4*H*-pyran-4-ones can be successfully prepared in good yields and in only one step by reaction of 1,3-diketone dianions with aromatic aldehydes. Interestingly, it proved to be very important to use hydrochloric acid (10%) for the aqueous work-up.

2.2 Results and discussion

My starting point was to find suitable conditions for the transformation of **12** into **14a**. The reaction of a nitromethane solution of **12** with catalytic amounts of $FeCl_3 \cdot 6H_2O$ (10 mol-%) afforded the desired 6-phenyl-2,3-dihydro-4*H*-pyran-4-one **14a** in high yield (Scheme 2-2). The same transformation could be induced in high yield by employment of hydrochloric acid (10%). This result suggests that $FeCl_3 \cdot 6H_2O$ reacted as a Lewis or Brønstedt acid. Based on these observations, we developed a one-pot protocol for the synthesis of **14a**. We were pleased to find that the reaction of the dianion of acetylacetone **10a** (generated by means of 2.5 equiv. of LDA) with benzaldehyde **11a** (–78 → 20 °C, 12 h), addition of hydrochloric acid (10%) and, after 15 min, extraction of the mixture with EtOAc afforded the desired pyran-4-one **14a** in 86% yield (Scheme2-2).



Scheme 2-2. Synthesis of **14a-m**, *i*: 1) LDA (2.5 equiv), THF, 0 °C, 1 h; 2) –78 °C, **10a-c**, 1 h; 3) **11a-i** , –78 → 20 °C, 12 h; *ii*: addition of HCl (10%), 15 min, 20 °C, then extraction (EtOAc)

The formation of **14a** (rather than **13**) can be explained by acid-mediated attack of the hydroxyl group onto the carbonyl group and subsequent elimination of water. The use of an aqueous solution of NH_4Cl, as reported by Miller *et al.* for the synthesis of **12**,[31] did not result in formation of **14a**, presumably due to the low acidity of NH_4Cl. On the other hand, the reaction of **12** with *p*-TsOH gave **13** which can be explained by the dehydrating effect of a strong acid in the absence of water. The elevated temperature (CH_2Cl_2, reflux) presumably also plays a role to induce a rapid elimination. The clean transformation of **12** into **14a** by application of hydrochloric acid (10%) can be explained by the fact that the latter is, on the one hand, sufficiently acidic and concentrated to induce the cyclization, but not concentrated enough to induce a direct dehydration. The silica gel chromatography of the products may also play a role to induce a complete transformation of **12** into **14a**.

The reaction of the dianions of acetylacetone **10a** and 1,1,1-trifluoropentane-2,4-dione **10b** with aldehydes **11a-h** afforded the 6-aryl-2,3-dihydro-4*H*-pyran-4-ones **14a-l** in very good yields (Scheme 3, Table 1). The best yields were obtained for reactions of **10a** with more electron-rich aldehydes. This might be explained by a slightly increased nucleophilicity of the hydroxy group. In case of 3-nitrobenzaldehyde **11i**, only the open-chained 5-hydroxy-1,3-diketone (rather than **14m**) was isolated. This can be explained by the decreased nucleophilicity of the hydroxy group of the open-chained product. The reaction of the dianion of benzoylacetone **10c** with **11a** resulted in the formation of **14n** which, however, could not be isolated in pure form. The novel trifluoromethyl-substituted pyran-4-ones **14i-l** are of special interest, due to the great importance of fluorinated heterocycles in medicinal chemistry.[32]

The structures of all products were established by spectroscopic methods. The structure of **14a** was independently confirmed by X-ray crystal structure analysis (Figure 2-1).

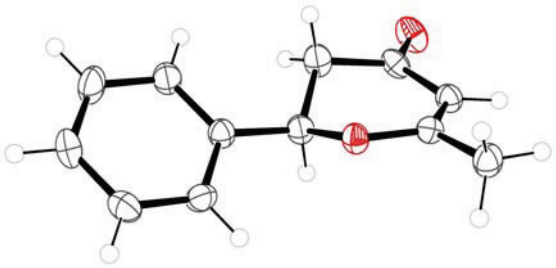
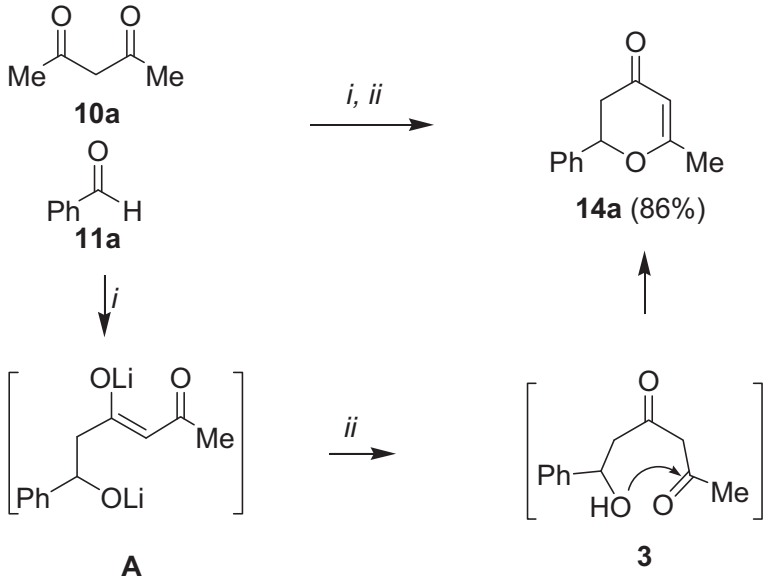


Figure 2-1. Ortep plot of **14a** (50% probability level)



Scheme 2-3. Possible mechanism of the formation of **14a**, *i*: 1) LDA (2.5 Equiv), THF, 0 °C, 1 h; 2) –78 °C, 1 h; 3) **11a** , –78 → 20 °C, 12 h; *ii*: addition of HCl (10%), 15 min, 20 °C, then extraction (EtOAc)

Table 2-1. Synthesis of **14a-m**

10	11	14	R	Ar	% (**5**)[a]
a	**a**	**a**	Me	Ph	86
a	**b**	**b**	Me	4-MeC_6H_4	89
a	**c**	**c**	Me	4-$(MeO)C_6H_4$	84
a	**d**	**d**	Me	3-BrC_6H_4	67
a	**e**	**e**	Me	2,4-$(MeO)_2C_6H_3$	76
a	**f**	**f**	Me	4-$(HO)C_6H_4$	78
a	**g**	**g**	Me	4-PhC_6H_4	80
a	**h**	**h**	Me	2-Furyl	87
b	**a**	**i**	CF_3	4-MeC_6H_4	78[c]
c	**b**	**j**	Ph	4-MeC_6H_4	75[c]
c	**c**	**k**	Ph	4-$(MeO)C_6H_4$	74[c]
c	**h**	**l**	Ph	4-PhC_6H_4	80[c]
a	**i**	**m**	Me	3-$(NO_2)C_6H_4$	0[b]

[a] Isolated yields [b]Presence of the product as an open chain mixture

[c]contributed by Rasheed Khera

2.3. Conclusions

In conclusion, a variety of 6-aryl-2,3-dihydro-4*H*-pyran-4-ones were prepared in one step by cyclocondensation of 1,3-diketone dianions with aldehydes and subsequent work-up using hydrochloric acid (10%). Currently, R. Khera synthesizes more derivatives to extend the scope of this methodology.

3. Synthesis of functionalized indoles and pyrroles based on palladium(0)-catalyzed reactions

3.1 . Synthesis of functionalized indoles based on palladium(0)-catalyzed reactions

3.1.1. Introduction

Carbazoles (derivatives of indoles) are of considerable pharmacological relevance (antifungal, antibiotic, and antitumor activity) and occur in a variety of natural products.[33,34] Knölker and coworkers reported elegant syntheses of carbazoles based on (stoichiometric) iron-mediated cyclizations[33d] and on Buchwald-Hartwig reaction of aryl halides with anilines and subsequent oxidative cyclization.[35] Ackermann an coworkers have recently reported an efficient synthesis of indoles and carbazoles by a new palladium-catalyzed domino ′N-H/C-H activation′ reaction of anilines with 1,2-dihaloalkenes.[36,37] Carbazoles have been prepared also by Diels-Alder reactions of 2- or 3-vinylindoles.[37] Kano and coworkers were the first to report the synthesis of carbazoles by 6π-electrocyclization of 2,3-di(alkenyl)indoles.[38] Later, this approach has been also studied by Pindur and Adam.[39] However, the synthesis of the starting materials was not straightforward and required many steps which is a severe drawback of this method. 2,3-Di(alkenyl)indoles were prepared by Pd(II)-catalyzed reaction of carbon atom C-3 of 2-formylindoles with alkenes to give 2-formyl-3-vinylindoles which were transformed into the desired products by Wittig reaction. However, this approach is not general. The alternative strategy, based on the double Wittig reaction of (unstable) 2,3-diformyl-*N*-methylindole, has been reported to proceed in low yield.

In recent years, it has been shown that polyhalogenated heterocycles can undergo site-selective palladium(0)-catalyzed cross-coupling reactions by selective activation of a single halogen atom. The site-selectivity is controlled by electronic and steric parameters.[40] Recently, we have reported the synthesis of aryl-substituted thiophenes,[41] pyrroles,[42] and selenophenes,[43] by site-selective Suzuki reactions of tetrabromothiophene, tetrabromo-*N*-methylpyrrole, and tetrabromoselenophene, respectively. Gribble and Liu reported the synthesis of 2,3-diarylindoles by twofold Suzuki reactions of 2,3-dihalo-*N*-

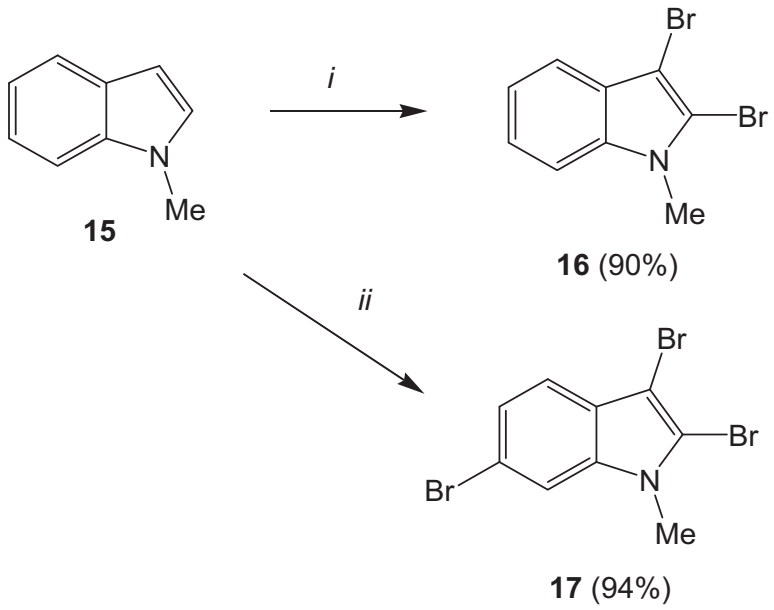
(phenylsulfonyl)indoles.[44] Other palladium(0)-catalyzed cross-coupling reactions of 2,3-dihaloindoles have, to the best of our knowledge, not been reported to date. De Meijere and coworkers reported twofold Heck reactions of 1,2-dibromocycloalk-1-enes and related substrates and subsequent 6π-electrocyclization.[45] It occurred to us that domino ′twofold Heck / 6π-electrocyclization′ might provide a useful method for the direct and convenient synthesis of dihydrocarbazoles and carbazoles. Mainly this project was handled Than Dang Tung, herein, I report preliminary results of my contribution to these studies.

3.1.2. Results and discussion

2,3-Dibromo-*N*-methylindole **16** has been recently prepared in 90% yield by reaction of *N*-methylindole **15** with copper(II) bromide.[46] It was found that the reaction of *N*-methylindole **15** with NBS (2.1 equiv.) in THF (–78 °C, 4 h) resulted in selective formation of 2,3-dibromo-*N*-methylindole **16** in 90% yield (Scheme 1).[47] In addition, 2,3,6-tribromo-*N*-methylindole **17** was prepared in 94% yield by reaction of **15** with NBS (3.1equiv.) in THF (–78°C, 4h).

The Heck reaction of **16** with acrylates **18a** afforded the 2,3-di(alkenyl)indoles **19a** in good yields (Scheme 2, Table 1). The best yields were obtained when the reactions were carried out using $Pd(OAc)_2$ (5 mol-%) and the biaryl monophosphine ligand **L** (10 mol-%) which has been recently developed by Buchwald and coworkers.[48] The reactions were carried out in DMF at 90 ˚C for 36 h. The employment of $Pd(PPh_3)_4$ was less successful in terms of yield.

The $Pd(OAc)_2$/**L**-catalyzed reaction of **16** with acrylates **18a,b** carried out at 120 °C rather than 90 °C, afforded the 1,2-dihydrocarbazoles **20a,b** in good yields. The formation of these products can be explained by a domino ′twofold Heck / 6π-electrocyclization′ cyclization and subsequent double bond migration. The initially formed 2,3-dihydrocarbazoles undergo a rearrangement into the more stable 1,2-dihydrocarbazoles. For the electrocyclization, a thermally-induced process appears to be more likely as the product distribution (formation of **19** or **20**) depends on the temperature.

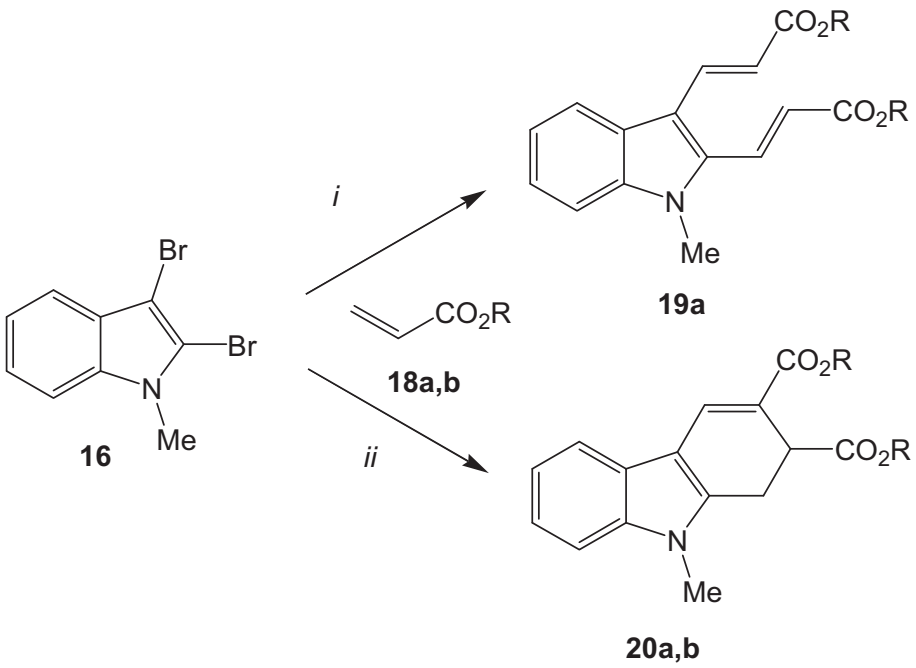


Scheme 3-1. Bromination of *N*-methylindole (**25**); *conditions*: *i*, NBS (2.1 equiv.), THF, −78 °C, 4 h; *ii*, NBS (3.1 equiv.), THF, −78 °C, 4 h, then 20 °C, 14 h

Table 3-1. Synthesis of **19a** and **20a,b**

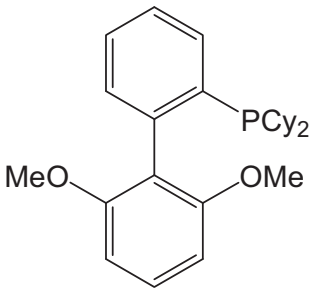
19,20	R	% (**19**) [a]	% (**20**) [a]
a	Me	66	77
b	*i*Bu	- [b]	69

[a]Yields of isolated products based on **2a**; [b]experiment was not carried out



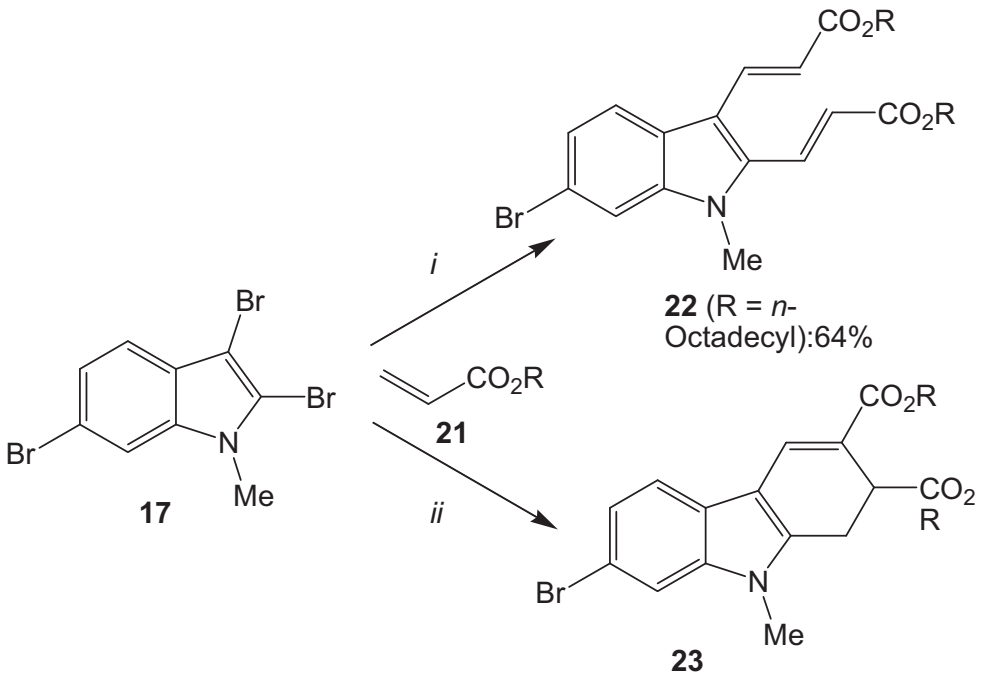
Scheme 3-2. Synthesis of **19a** and **20a,b**. Conditions: *i*, **16**, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 90 ˚C, 36 h; *ii*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3 (8.0 equiv.), DMF, 120 ˚C, 48 h

L =



Cy = Cyclohexyl

The $Pd(OAc)_2$/**L**-catalyzed reaction of **17** with an excess of acrylates **21** (90 °C, 36 h) afforded the 2,3,6-tris(alkenyl)indoles **22** in good yields (Scheme 3-3). The cross-coupling reactions of **17** with **21** with variety of R groups carried out at 120 rather than 90 °C, gave the 7-alkenyl-1,2-dihydrocarbazoles **23** by Munawar Hussain.



Scheme 3-3. Synthesis of **22,** Conditions: *i*, $Pd(OAc)_2$ (5 mol-%), **L** (10 mol-%), NEt_3, DMF, 90 ˚C, 36

3.1.3. Conclusion

In conclusion, I have reported the synthesis of di- and tri-alkenylindoles by palladium(0)-catalyzed Heck cross-coupling reactions of di- and tribromo-*N*-methylindoles. The reactions were carried out at 90 °C using a novel biaryl monophosphine ligand developed by Buchwald and coworkers. 1,2-Dihydrocarbazoles were formed by a domino ′twofold Heck / 6π-electrocyclization′ when the reaction was carried out at 120 rather than 90 °C.

3.2. Synthesis of functionalized pyrroles based on palladium(0)-catalyzed reactions

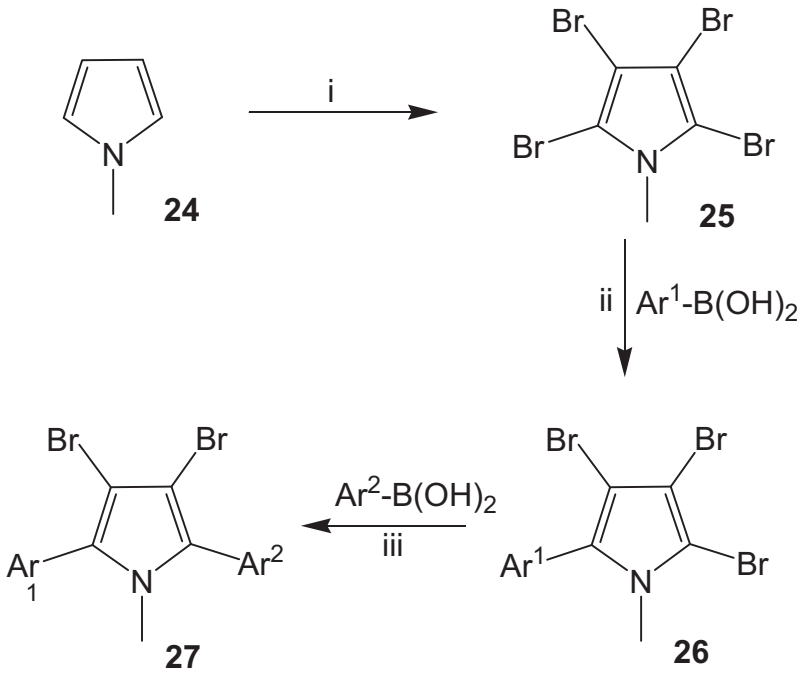
3.2.1. Introduction

Pyrroles are of considerable pharmacological relevance. They occur in a number of synthetic drugs (e.g., zomepirac and atorvastatin) and natural products (e.g., in the tetrapyrrole pigments porphobilinogen and bilirubin).[49–51] Oligopyrroles proved to be important as organic materials (e.g., as synthetic metals).[52] Heterocycles have been widely functionalized by palladium(0)-catalyzed cross-coupling reactions.[53] In recent years, it has been shown that polyhalogenated heterocycles may be regioselectively functionalized in such reactions by selective activation of a single halogen atom—a process which is controlled by electronic and steric parameters.[54] Recently, my coleagues reported the synthesis of tetraarylthiophenes based on regioselective Suzuki reactions of tetrabromothiophene.[55] Despite their potential synthetic utility, regioselective functionalization reactions of polyhalogenated pyrroles have only scarcely been reported to date. Bach and Schroter recently reported regioselective Suzuki reactions of ethyl 2,3,4-tribromopyrrole-5-carboxylate and of 2,3-dibromo-5-nitropyrrole.[56] Herein, I describe my preliminary work related to Suzuki crosscoupling reactions of 2,3,4,5-tetrabromo-1-methylpyrrole. Palladium(0)-catalyzed cross-coupling reactions of tetrahalopyrroles have, to the best of our knowledge, not been reported. In general, reactions of tetrahalogenated pyrroles are rather rare, which can be explained by the unstable nature of these compounds.[57]

3.2.2. Results and discussion

2,3,4,5-Tetrabromo-1-methylpyrrole **25** was prepared by NBS-mediated bromination of N-methylpyrrole. The published procedure[55] for the synthesis of **25** was modified, [54] as I was not able to isolate the pure product by the original protocol. The reaction was carried out at 78 °C for 8 h. It proved to be helpful for the separation of succinimide to add heptane to the reaction mixture, which results in the precipitation of succinimide and of side-products. The yellowish crude product was purified by repeated washing with old ethyl acetate to give the pure material in the form of colourless crystals. Noteworthy,

impure product fails to undergo the desired Suzuki reactions and also more rapidly decomposes. The solid can be stored under argon at 18 °C for a few weeks. After a few weeks, the compound starts to become slightly yellow and the quality is not sufficient anymore for Suzuki reactions. The Suzuki reaction of **25** with various boronic acids (1.1 equiv) afforded 5-aryl-2,3,4-tribromopyrroles **26** in good yields and with very good regioselectivity (Scheme 3-4).



27 (45%) Ar^1 = 4-MeC6H4; Ar^2 = 3-ClC6H4

Scheme 3-4. Synthesis of 5-aryl-2,3,4-tribromopyrroles **26** and of 2,5-diaryl-3,4-dibromopyrroles **27**. Reagents and conditions: (i) N-methyle Pyrrole, NBS (4equiv), THF, -78 °C, 8h; (ii) **25** (1.0 equiv), $Ar^1B(OH)_2$ (1.1 equiv), $Pd(PPh_3)_4$ (6 mol %), K_3PO_4 (4.0 equiv), solvent , 90 °C, 12 h; (ii) **26** (1.0 equiv), $Ar^2B(OH)_2$ (1.1 equiv), $Pd(PPh_3)_4$ (10 mol %), K_3PO_4 (4.0 equiv), DMF/ toluene/EtOH/H_2O (4:1:1:1), reflux, 48 h.

During the optimization, it proved to be important to suppress the formation of 2,5-diaryl-3,4-dibromopyrroles, as their separation from the desired products proved to be difficult and tedious. The stoichiometry, temperature, solvent and the presence of water

proved to play an important role in terms of yield. Noteworthy, the employment of benzyl-, carbamate- and sulfonyl-protected pyrroles was unsuccessful (decomposition). The reaction of **26** with 1.1 equiv of (3-chlorophenyl)-boronic acid resulted in regioselective formation of 2,5-diaryl-3,4-dibromopyrroles **27**, respectively (Scheme 3-4). The Suzuki reaction of **25** with 2.5 equiv of various arylboronic acids afforded 2,5-diaryl-3,4-dibromopyrroles **28** in good yields and with very good regioselectivity (Scheme 3-5, Table 3-2).

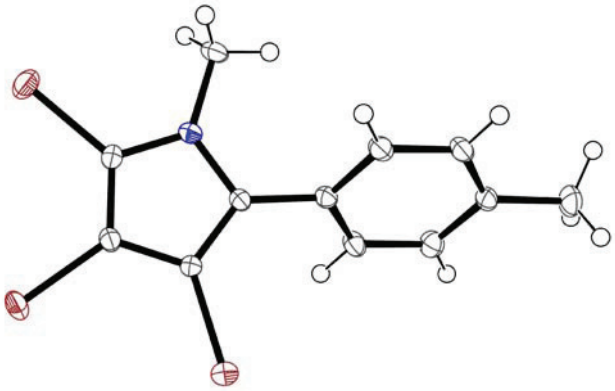
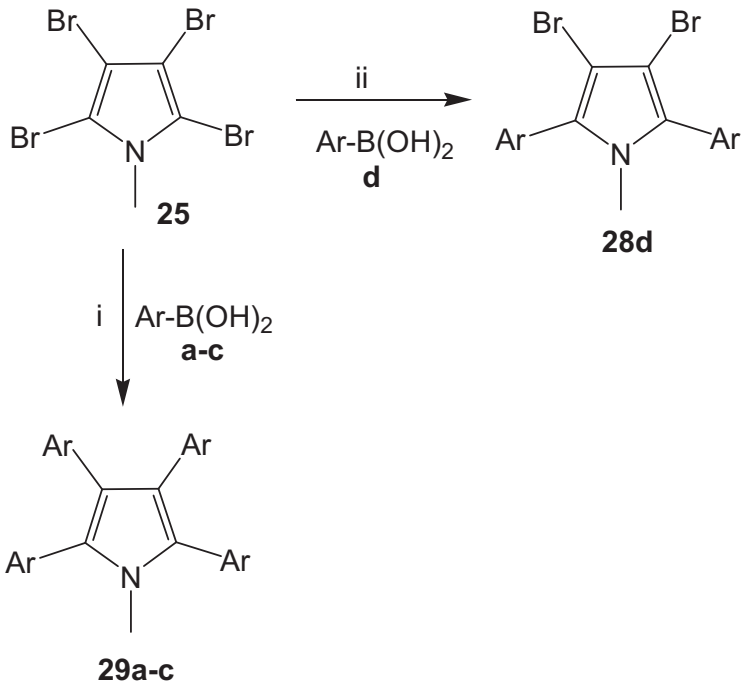


Fig. 3-1 Ortep Plot of **26**



Scheme 3-5. Synthesis of 2,5-diaryl-3,4-dibromopyrroles **28** and of tetraarylpyrroles **29a-c** (i) **25** (1.0 equiv), $ArB(OH)_2$ (2.5 equiv), $Pd(PPh_3)_4$ (6–10 mol %), K_3PO_4 (4.0 equiv), solvent, 90 °C, 12 h; (ii) **25** (1.0 equiv), $ArB(OH)_2$ (5.0 equiv), $Pd(PPh_3)_4$ (20 mol %), K_3PO_4 (5.0 equiv), DMF/toluene/ $EtOH/H_2O$ (4:1:1:1), reflux, 96 h.

The solvent proved again to be a very important parameter during the optimization of the yield. Tetraarylpyrroles **29a-c**, containing four identical aryl groups, were prepared by reaction of **25** with (4-ethylphenyl)-, (2,4-dimethyl)- and (3-chlorophenyl)boronic acid (5.0 equiv). The best yields of **29a-c** and were obtained when the reactions were carried out using a quaternary solvent mixture (DMF/toluene/EtOH/H2O = 4:1:1:1) and an increased amount of catalyst and reagents and when the reaction time was extended. Considerable amounts of 2,3,5-triaryl-4-bromopyrroles were formed when the amounts of reagents and catalyst were too low. Noteworthy, the bromide groups of 2,5-diaryl-3,4-dibromopyrroles 4a–f proved to be considerably less reactive than those of 2,5-diaryl-3,4-dibromothiophenes.[55] This must be explained by electronic reasons, as the steric hindrance is similar for both types of substrates. The conditions developed for the

synthesis of **29a-c** could be successfully applied to the synthesis of related tetraarylpyrroles. All products were characterized by spectroscopic methods. The structure of **26** was independently confirmed by X-ray crystal structure analysis (Fig. 3-1).

Table 3-2

28, 29	Ar	solvents	% (**28**)[a]	% (**29**)[a]
a	4-EtC_6H_4	DMF/toluene/EtOH/H_2O = 4:1:1:1	78	-
b	3-ClC_6H_4	2,4-Dioxane/H_2O (5:1)	57	-
c	3,5-$Me_2C_6H_4$	DMF/toluene/EtOH/H_2O = 4:1:1:1	76	-
d	4-MeC_6H_4	Toluene/H_2O (5:1)	-	67

[a]Isolated yields

3.2.3. Conclusion

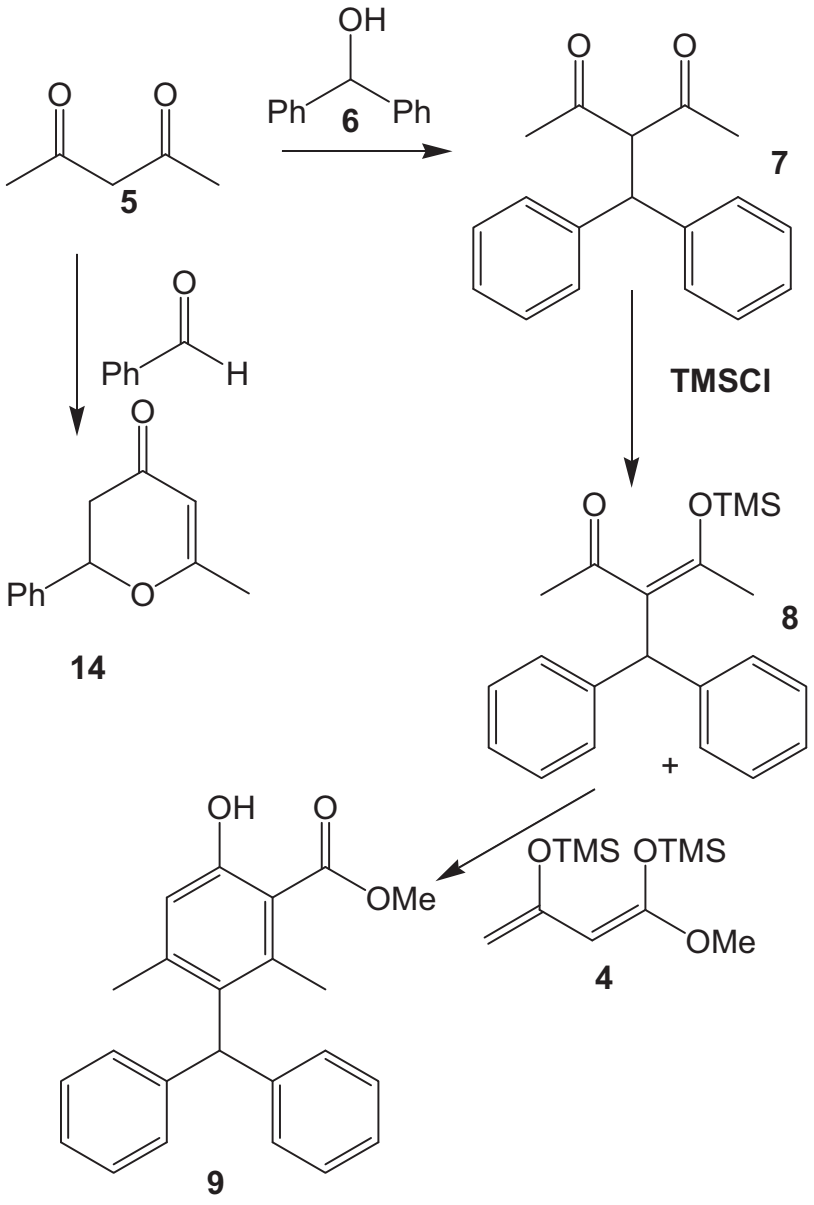
In conclusion, I have described a new strategy for the synthesis of 5-aryl-2,3,4-tribromopyrroles, 2,5-diaryl-3,4-dibromopyrroles and tetraarylpyrroles based on regioselective Suzuki cross-coupling reactions of *N*-methyltetrabromopyrrole.

4. Abstract

Dianions and masked dianions represent important building blocks for the regioselective formation of carbon-carbon bonds. Cyclocondensation reactions of 1,3-bis(silyl enol ethers) with different mono(silyl enol ethers) provide an elegant approach for the synthesis of various complex carba- and heterocycles from simple starting materials. A variety of functionalized and sterically encumbered triarylmethanes are prepared by combination of $FeCl_3$-catalyzed benzylations of 1,3-diketones and formal [3+3] cyclocondensation reactions of 1,3-bis(silyl enol ethers) and 3-benzyl-1-silyloxy-1-en-3-ones. In this context, 4-methoxy-, 4-chloro and 4-fluoro-substituted triarylmethanes are prepared. These products are not readily available by other methods. In addition, functionalized diarylmethanes have been also prepared by cyclocondensation of 1,3-bis(silyl enol ethers) with the respective 3-benzyl-1-silyloxy-1-en-3-ones. Furthermore, dianions were converted to pyranones by reaction with functionalized benzaldehydes. Various pyranones were synthesized containing 3-bromo-, 4-methyl-, 4-phenyl-, 4-methoxy- and 4-hydoxy-substituted phenyl groups.

Dianionen und maskierte Dianionen sind wichtige Bausteine für die regioselektive Bildung von Kohlenstoff-Kohlenstoff-Bindungen. Cyclocondensationsreaktionen der 1,3-Bis(silylenolether) mit verschiedenen Mono(silylenolethern) stellen ein elegantes Konzept für die Synthese von komplexen Carba- und Heterocyclen aus einfachen Ausgangsmaterialien dar. Eine Vielzahl von funktionalisierten und sterisch gehinderten Triarylmethanen wurde durch die Kombination von $FeCl_3$-katalysierten Benzylierungen von 1,3-Diketonen mit formalen [3+3] Cyclocondensationsreaktionen von 1,3-Bis(silylenolethern) mit 3-Benzyl-1-silyloxy-1-en-3-onen dargestellt. In diesem Zusammenhang wurden 4-methoxy-, 4-chlor- und 4-fluor-substituierte Triarylmethane synthetisiert. Produkte diesen Typs sind nur unter großem Aufwand durch andere Methoden erhältlich. Darüber hinaus wurden funktionalisierte Diarylmethane auch durch Cyclokondensationen von 1,3-Bis(silylenolethern) mit den jeweiligen 3-Benzyl-1-silyloxy-1-en-3-onen dargestellt. Weiterhin wurden die Dianionen durch einen neuen Syntheseansatz mit funktionalisierten Benzaldehyden in wertvolle cyclische Pyranon-

Strukturen überführt. Es wurden verschiedene Pyranone mit 3-Brom-, 4-Methyl-, 4-Phenyl-, 4-Methoxy und 4-Hydroxyphenyl-Gruppen synthetisiert.



General Scheme: Most part of this thesis carried out using 1,3-dicarbonyl compounds (only one substitution pattern is shown for clarity).

5. Experimental Section:

5.1 General: Equipment, chemicals and work technique

^{1}H NMR Spectroscopy: Bruker: AM 250, Bruker ARX 300, Bruker ARX 500; δ = 0.00 ppm for Tetramethylsilane; δ = 2.04 ppm for Acetone d-6; δ = 7.26 ppm for (CDCl3); 2.50 ppm for DMSO-d_6; 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, (62.9 MHz); Bruker: ARX 300, (75 MHz), Bruker: ARX 500, (125 MHz) Ref: 29.84 ± 0.01 ppm and 206.26 ± 0.13 ppm for $(CD_3)_2CO$. δ = 128.00 ppm for Acetone d-6; δ = 77.00 ppm 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, $\lambda = 0.71073$ Å).

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.

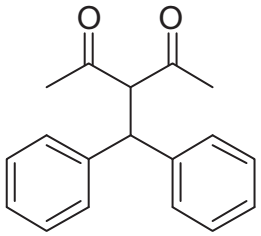
TLC: Merck DC finished foils silica gel 60 F_{254} on aluminum foil and Macherey finished foils Alugram® Sil G/UV_{254}. Detection under UV light with 254 nm and/or 366 nm without dipping reagent, as well as with anisaldehyde sulfuric acid reagent (1 mL anisaldehyde consisting in 100 mL stock solution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

Chemicals and work technique: All solvents for using 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.

5.2. Procedures and Spectroscopic Data

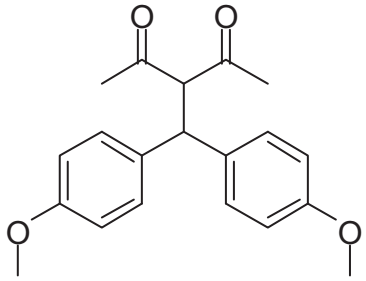
General procedure for the synthesis of 3-substituted pentane-2,4-diones: In a pressure tube, $FeCl_3$ $6H_2O$ (5 mol %), **6a-f** (5.0 mmol), and acetylacetone (20.0 mmol) were dissolved in 10 mL of nitromethane. After stirring for 4 h at 50 °C, the reaction was quenched with water followed by extraction with dichloromethane. The combined organic layers were dried over MgSO4 and the solvents were distilled off. Then, products **7a-f** were purified by column chromatography (heptanes/ethyl acetate = 1:1).

3-Benzhydrylpentane-2,4-dione (7a):



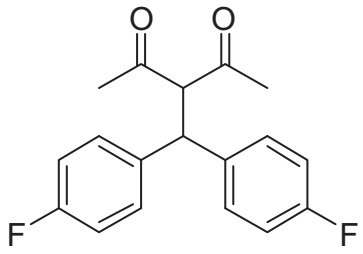
Starting with $FeCl_3 \cdot 6H_2O$ (0.043 g, 5 mol %), **6a** (0.921 g, 5.0 mmol), acetylacetone (2 g, 20.0 mmol) and 10 mL of nitromethane, the reaction was quenched with water followed by extraction with dichloromethane and purification by column chromatography (heptanes/ethyl acetate = 1:1) to give **7a** as white crystalline solid (1.21, 91 %) mp 132-134 °C: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.92 (s, 6H, $2CH_3$), 4.65, 4.74 (d, 1H, CH), 7.18 (m, 10H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 29.6 (CH_3), 51.2, 74.5 (CH), 127.0, 127.7, 128.9 (CH_{Ar}), 141.2, 202.9 (C), (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1603 (s), 1507 (s), 1297(m), 1246 (s), 1159 (m), 1095 (m), 1014 (w), 849 (s), 786 (s), 506 (w). MS (EI, 70 eV): *m/z* (%) = 266 ($[M]^+$, 64), 251 (45), 165 (43), 148 (34), 143 (100), 129 (6), 95 (48), 85 (15), 75 (26), 69 (54), 50 (45), 43 (26). HRMS (EI): Calcd. for $C_{18}H_{18}O_2$ ($[M]^+$): 266.13068; found: 266.130655.

3-(Bis(4-methoxyphenyl)methyl)pentane-2,4-dione (7b):



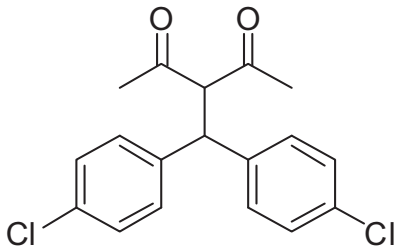
Starting with $FeCl_3 \cdot 6H_2O$ (0.043 g, 5 mol %), **6b** (1.22 g, 5.0 mmol), acetylacetone (2 g, 20.0 mmol) and 10 mL of nitromethane, the reaction was quenched with water followed by extraction with dichloromethane and purification by column chromatography (heptanes/ethyl acetate = 1:1) to give **7b** as white crystalline solid (1.43, 88 %) mp 125-127 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.92 (s, 3H, CH_3), 3.67 (s, 6H, $2CH_3$), 4.54, 4.63 (d, 1H, CH), 6.70-7.09 (m, 10H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 29.6 (CH_3), 49.7 (CH), 55.1 (OCH_3), 74.9(CH), 114.2, 128.6 (CH_{Ar}), 133.7, 158.3, 203.2 (C), (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1608 (s), 1547 (m), 1287(m), 1246 (s), 1159, 1145 (m), 1095 (s), 1014 (w), 849 (s), 743 (m), 506 (w). MS (EI, 70 eV): *m/z* (%) = 326 ($[M]^+$, 64), 283 (34) 265 (66), 238 (100), 183 (32), 108 (63), 95 (48), 85 (13), 75 (24), 69 (53), 50 (25), 43 (53). HRMS (EI): Calcd. for $C_{20}H_{22}O_4$ ($[M]^+$): 326.15181; found: 326.151265.

3-(Bis(4-fluorophenyl)methyl)pentane-2,4-dione (7c):



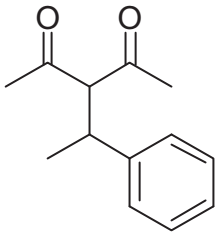
Starting with $FeCl_3 \cdot 6H_2O$ (0.043 g, 5 mol %), **6c** (1.10 g, 5.0 mmol), acetylacetone (2 g, 20.0 mmol) and 10 mL of nitromethane, the reaction was quenched with water followed by extraction with dichloromethane and purification by column chromatography (heptanes/ethyl acetate = 1:1) to give **7c** as white crystalline solid (1.31, 87 %) mp 102-104 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.93 (s, 3H, CH_3), 4.56, 4.73 (d, 1H, CH), 6.86-7.15 (m, 10H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 29.6 (CH_3), 49.4, 74.8 (CH), 115.7/116.0, 129.1/129.2 (CH_{Ar}), 136.8, 160.0/163.3, 202.4 (C), (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1612 (s), 1527 (m), 1297, 1245 (m), 1212 (s), 1134 (m), 1023 (w), 1014 (m), 848 (s), 788 (s), 545 (w). MS (EI, 70 eV): *m/z* (%) = 302 ($[M]^+$, 64), 287 (66), 259 (6), 183 (100), 109 (16), 95 (48), 85 (14), 75 (50), 69 (54), 50 (45), 43 (53). HRMS (EI): Calcd. for $C_{18}H_{16}F_2O_2$ ($[M]^+$): 302.11184; found: 302.111765.

3-(Bis(4-chlorophenyl)methyl)pentane-2,4-dione (7d):



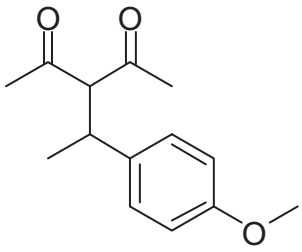
Starting with $FeCl_3 \cdot 6H_2O$ (0.043 g, 5 mol %), **6d** (1.26 g, 5.0 mmol), acetylacetone (2 g, 20.0 mmol) and 10 mL of nitromethane, the reaction was quenched with water followed by extraction with dichloromethane and purification by column chromatography (heptanes/ethyl acetate = 1:1) to give **7d** as white crystalline solid (1.41, 85 %) mp 142-144 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.98 (s, 6H, $2CH_3$), 3.67 (s, 6H, $2CH_3$), 4.78, 4.85 (d, 1H, CH), 7.15-7.25 (m, 10H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 29.6 (CH_3), 49.7 (CH), 55.1 (CH_3), 74.9(CH), 114.2, 128.6 (CH_{Ar}), 133.7, 158.3, 203.2 (C), (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1609 (s), 1407, 1324, 1309 (m), 1297(s), 1254, 1243 (m), 1158 (m), 1088 (m), 1022 (w), 846 (s), 754 (s), 554 (w). MS (EI, 70 eV): *m/z* (%) = 334 ($[M]^+$, 84), 319 (34), 291 (65), 165 (54), 135 (6), 123 (43), 109 (100), 96 (48), 87 (11), 75 (67), 69 (26), 50 (5), 43 (23). HRMS (EI): Calcd. for $C_{18}H_{16}Cl_2O_2$ ($[M]^+$): 334.05274; found: 334.052365.

3-(1-Phenylethyl)pentane-2,4-dione (7e):



Starting with $FeCl_3 \cdot 6H_2O$ (0.043 g, 5 mol %), **6e** (0.61 g, 5.0 mmol), acetylacetone (2 g, 20.0 mmol) and 10 mL of nitromethane, the reaction was quenched with water followed by extraction with dichloromethane and purification by column chromatography (heptanes/ethyl acetate = 1:1) to give **7e** as white crystalline solid (0.96, 94 %) mp 112-114 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (d, 3H, CH_3), 1.80, 2.23 (s, 6H, $2CH_3$), 3.55 (m, 1H, CH), 4.02 (d, 1H, CH) 7.13-7.23 (m, 5H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 20.8, 29.6, 40.3 ($3CH_3$), 40.3, 76.6 (CH), 126.9, 127.2, 128.7 (CH_{Ar}), 143.0, 203.3 (C), (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1605 (s), 1534, 1434, 1389 (m), 1283(m), 1254 (w), 1146 (m), 1097 (s), 1033 (w), 845 (s), 785 (s), 576 (w). MS (EI, 70 eV): *m/z* (%) = 204 ($[M]^+$,44), 189 (34), 175 (36), 138 (46), 125 (100), 109 (65), 95 (48), 85 (11), 75 (20), 69 (50), 50 (5), 43 (23). HRMS (EI): Calcd. for $C_{10}H_9FO_2$ ($[M]^+$): 204.11503; found: 204.115651.

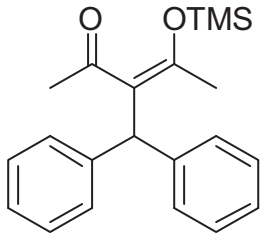
3-(1-(4-Methoxyphenyl)ethyl)pentane-2,4-dione (7f):



Starting with $FeCl_3 \cdot 6H_2O$ (0.043 g, 5 mol %), **6f** (0.76 g, 5.0 mmol), acetylacetone (2 g, 20.0 mmol) and 10 mL of nitromethane, the reaction was quenched with water followed by extraction with dichloromethane and purification by column chromatography (heptanes/ethyl acetate = 1:1) to give **7f** as white crystalline solid (1.01, 87 %) mp 138-140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (d, 3H, CH_3), 1.76, 2.18 (s, 6H, $2CH_3$), 3.48 (m, 1H, CH), 3.57 (s, 3H, OCH_3), 3.90 (d, 1H, CH) 6.73-7.04 (m, 5H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9, 29.6/29.8, 38.7 ($3CH_3$), 55.2 (OCH_3), 76.9 (CH), 114.5, 128.2 (CH_{Ar}), 134.9, 158.4, 203.5/203.6 (C), (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1712 (s), 1554, 1529, 1456, 1324 (m), 1277(s), 1246 (s), 1157 (m), 1095 (s), 1056 (w), 847 (s), 773 (s), 645(w). MS (EI, 70 eV): *m/z* (%) = 234 ($[M]^+$, 64), 165 (66), 138 (6), 123 (100), 109 (6), 95 (48), 85 (11), 75 (20), 69 (50), 50 (5), 43 (23). HRMS (EI): Calcd. for $C_{14}H_{18}O_2$ ($[M]^+$): 234.12559; found: 234.125855.

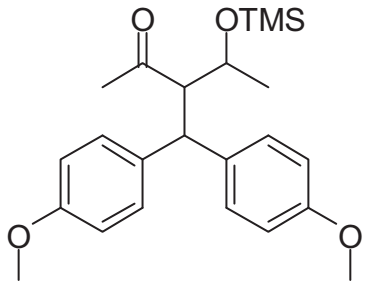
General procedure for the synthesis of silyl enol ethers 8a-f: To a stirred benzene solution (2.5 mL/1.0 mmol of **7a-f**) of **17** (10.0 mmol) was added triethylamine (16.0 mmol). After stirring of the solution for 2 h, trimethylchlorosilane (18.0 mmol) was added. After stirring of the solution for 72 h, the solvent was removed in *vacuo* and hexane (25 mL) was added to the residue to give a suspension. The latter was filtered under argon atmosphere. The filtrate was concentrated in *vacuo* to give silyl enol ethers **8a-f**. Due to the unstable nature of the silyl enol ethers, they were characterized only by NMR spectroscopy. The double bond configuration of the products has not been unambigiously confirmed as it is irrelevant for the cyclization reaction.

3-Benzhydryl-4-(trimethylsilyloxy)pent-3-en-2-one (8a):



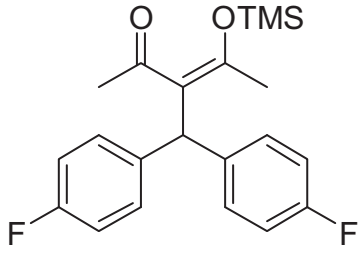
Starting with benzene (25 mL), **6a** (2.66 g, 10 mmol), triethylamine (2.10 mL, 15 mmol) and trimethylchlorosilane (2.26 mL, 18 mmol), **7a** was isolated as a reddish oil (3.04 g, 90%) ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00-0.24 (m, 9 H, $3CH_3$), 1.91, 1.99, 2.17 (s, 3H, $3CH_3$), 5.48, 5.53(s, 1H, CH), 7.17-7.27 (m, 10H, CH_{Ar}). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 0.5, 0.6, 0.7, 0.8, 0.9, 2.3 (CH_3), 111.5, 111.8, 120.6, 129.9, 130.6 (CH), 132.0, 132.4, 150.1, 153.2 (C), 191.8 (C=O)..

3-(Bis(4-methoxyphenyl)methyl)-4-(trimethylsilyloxy)pent-3-en-2-one (8b):



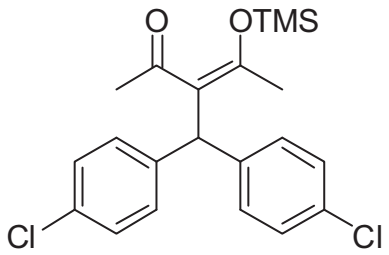
Starting with benzene (25 mL), **6b** (3.26 g, 10 mmol), triethylamine (2.10 mL, 15 mmol) and trimethylchlorosilane (2.26 mL, 18 mmol), **7b** was isolated as a reddish oil (3.62 g, 91%) ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.16 (s, 9 H, $3CH_3$), 0.35 (s, 9 H, $3CH_3$), 3.79 (s, 3 H, OCH_3), 4.60 (d, *J*=1.7 Hz, 1 H, CH_2), 5.14 (s, 1 H, CH_2), 5.39 (d, *J*=1.7 Hz, 1 H, CH_2), 6.96-7.00 (m, 1 H, Ar), 7.02-7.06 (m, 1 H, Ar), 7.35-7.39 (m, 1 H, Ar), 7.42-7.45 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 0.6, 0.7, 0.8, 0.9, 2.3 (CH_3), 55.6 (OCH_3), 95.6 (CH_2), 111.5, 111.8, 120.6, 129.9, 130.6 (CH), 131.4, 132.4, 149.8, 153.0 (C), 190.9 (C=O)..

3-(Bis(4-fluorophenyl)methyl)-4-(trimethylsilyloxy)pent-3-en-2-one (8c):



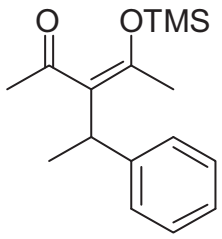
Starting with benzene (25 mL), **6c** (3.02 g, 10 mmol), triethylamine (2.10 mL, 15 mmol) and trimethylchlorosilane (2.26 mL, 18 mmol), **7c** was isolated as a reddish oil (3.33 g, 89%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.19-0.20 (s, 9 H, $3CH_3$), 0.34-0.37 (s, 9 H, $3CH_3$), 4.61-4.63 (m, 1 H, CH_2), 5.10-5.11 (m, 1 H, CH_2), 5.54-5.55 (s, 1 H, CH), 7.01-7.17 (m, 1 H, Ar), 7.19-7.22 (m, 1 H, Ar), 7.31-7.38 (m, 1 H, Ar), 7.51-7.56 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3, ($3CH_3$), 0.6 ($3CH_3$), 96.4 (CH_2), 113.0, 116.2, 123.8, 127.4, 130.0 (CH), 146.1, 152.6, 157.9 161.1 (C), 188.8 (C=O).

3-(Bis(4-chlorophenyl)methyl)-4-(trimethylsilyloxy)pent-3-en-2-one (8d):



Starting with benzene (25 mL), **6d** (3.34 g, 10 mmol), triethylamine (2.10 mL, 15 mmol) and trimethylchlorosilane (2.26 mL, 18 mmol), **7d** was isolated as a reddish oil (3.73 g, 92%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.28 (s, 9 H, $3CH_3$), 0.66 (s, 9 H, $3CH_3$), 4.94 (m, 1 H, CH_2), 5.51 (s, 1 H, CH_2), 5.68 (m, 1 H, CH_2), 7.85-7.86 (m, 2 H, Ar), 7.89-7.92 (m, 2 H, Ar), 8.19-8.23 (m, 2 H, Ar), 8.64-8.67 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4 ($3CH_3$), 0.6 ($3CH_3$), 95.3 (CH_2), 112.0, 126.0, 126.3, 126.6, 128.6, 129.0, 130.9, 131.6 (CH), 133.7, 134.0, 137.8, 152.1, 152.9 (C), 189.7 (C=O).

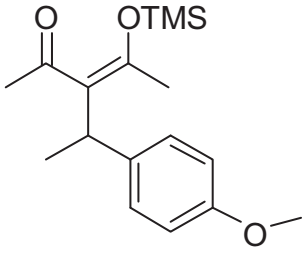
3-(1-Phenylethyl)-4-(trimethylsilyloxy)pent-3-en-2-one (8e):



Starting with benzene (25 mL), **6e** (2.04 g, 10 mmol), triethylamine (2.10 mL, 15 mmol) and trimethylchlorosilane (2.26 mL, 18 mmol), **7e** was isolated as a reddish oil (2.23 g, 81%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.00-0.05 (m, 9 H,

$3CH_3$), 1.28, 1.34, 1.43 (d, 3H, $3CH_3$), 1.66, 1.78, 1.94 (s, 6H, $2CH_3$), 3.89 (m, 1H, CH), 4.12 (q, 1H, CH) 7.07-7.11 (m, 5H, CH_{Ar}). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 0.5, 0.6, 0.7, 0.8, 0.9, 2.3 (CH_3) 111.5, 111.8, 120.6, 129.9, 130.6 (CH), 131.4, 132.4, 149.8, 153.0 (C), 188.8 (C=O)..

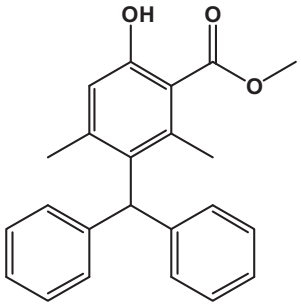
3-(1-(4-Methoxyphenyl)ethyl)-4-(trimethylsilyloxy)pent-3-en-2-one (8f):



Starting with benzene (25 mL), **6f** (2.34 g, 10 mmol), triethylamine (2.10 mL, 15 mmol) and trimethylchlorosilane (2.26 mL, 18 mmol), **7f** was isolated as a reddish oil (2.63 g, 86%). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.00-0.02 (m, 9 H, $3CH_3$), 0.98, 1.23, 1.29 (d, 3H, $3CH_3$), 1.64, 1.73, 2.06 (s, 6H, $3CH_3$), 3.89 (s, 3H, OCH_3), 4.12 (q, 1H, CH) 7.07-7.11 (m, 5H, CH_{Ar}). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 0.5, 0.6, 0.7, 0.8, 0.9, 2.3 (CH_3) 111.5, 111.8, 120.6, 129.9, 130.6 (CH), 131.4, 132.4, 149.8, 153.0 (C), 192.1 (C=O).

General procedure for the synthesis of substituted triarylmethanes 9a-q: A CH_2Cl_2 solution (5 mL) of **4a** (1.0 mmol) and **8a** (1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at –78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9a-q.**

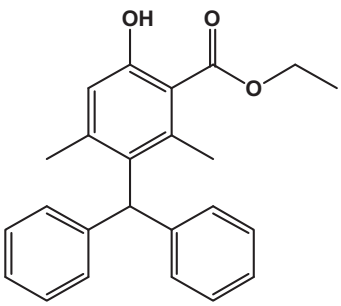
Methyl 3-benzhydryl-6-hydroxy-2,4-dimethylbenzoate (9a):



To a CH_2Cl_2 solution (5 mL) of **4a** (0.260 g, 1.0 mmol) and **8a** (0.372 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at –78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added.

The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9a** as a colourless solid (115 mg, 33%), mp. 153-155 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.07 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 5.92 (s, 1 H, CH), 6.65 (s, 1 H, ArH), 6.99-7.26 (m, 10 H, Ph), 10.51 (s, 1 H, OH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 20.3, 21.7 (CH_3), 49.6 (CH), 50.9 (OCH_3), 111.7 (C), 116.7, 124.9, 127.1, 128.0 (CH_{Ar}), 132.1, 139.3, 141.0, 144.3, 158.8, 170.9 (C). IR (KBr): $\tilde{\nu}$ = 2987 (w), 1663 (s), 1564 (m), 1435 (m), 1341 (m), 1210 (s), 1069 (s), 857 (m), 801 (s), 719 (s) 696 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 346 (M^+, 66), 314 (100), 299 (21), 237 (18), 165 (49). HRMS (EI): calcd. for $C_{23}H_{22}O_3$ $[M]^+$: 346.15635.; found: 346.156966.

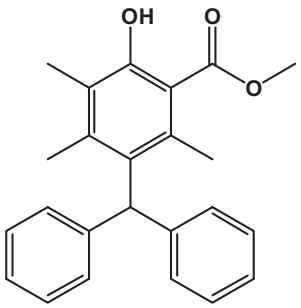
Ethyl 3-benzhydryl-6-hydroxy-2,4-dimethylbenzoate (9b):



To a CH_2Cl_2 solution (5 mL) of **4b** (0.274 g, 1.0 mmol) and **8a** (0.372 g, 1.1 mmol), $TiCl_4$ (0.12 mL, 1.1 mmol) was added dropwise at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9b** as a yellow oil (0.162 g, 45%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (t, 3 H, CH_3), 1.90 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 4.21 (s, 2 H, OCH_2), 5.85 (s, 1 H, CH), 6.57 (s, 1 H, ArH), 6.95-7.15 (m, 10 H, Ph), 10.52 (s, 1 H, OH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.1, 20.2, 21.7 (CH_3), 49.7 (CH), 60.4 (OCH_2), 111.8 (C), 116.8, 124.9, 127.1, 128.0, (CH_{Ar}), 132.1, 139.3, 141.1, 144.2, 158.9, 170.5 (C). IR (KBr): $\tilde{\nu}$ = 3082, 2961 (w), 1654, 1598, 1568, 1492, 1370 (w), 1258, 1008, 1013 (s), 860 (w), 799, 696 (s) cm^{-1}. MS (EI,

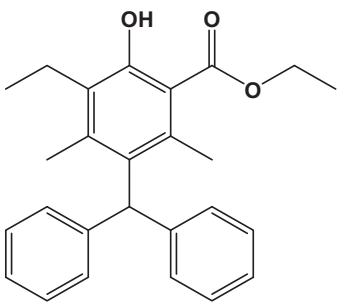
70 eV): *m/z* (%) = 360 (M^+, 88), 314 (100), 299 (26), 237 (32), 165 (50). HRMS (EI): calcd. for $C_{24}H_{24}O_3$ $[M]^+$: 360.17200; found: 360.171717.

Methyl 3-benzhydryl-6-hydroxy-2,4,5-trimethylbenzoate (9c):



To a CH_2Cl_2 solution (5 mL) of **4c** (0.274 g, 1.0 mmol) and **8a** (0.372 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9c** as a yellow oil (0.111 g , 31%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.80, 1.92, 2.10 (s, 3 H, CH_3), 3.82(s, 3H, OCH_3), 5.99 (s, 1 H, CH), 7.12-7.22 (m, 10 H, Ph), 10.77 (s, 1 H, OH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 11.2, 20.0, 24.0 (CH_3), 50.2 (CH), 51.0 (OCH_3), 111.2 (C), 124.9, 127.4, 128.0, (CH_{Ar}), 132.0, 140.3, 141.6, 142.7, 156.8, 171.7 (C). IR (KBr): $\tilde{\nu}$ = 2958, 2922 (w), 1697, 1657, 1598, 1450, 1354 (w), 1257, 1089, 1022 (s), 917 (w), 793, 746, 698 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 360 (M^+, 35), 314 (100), 299 (66), 237 (38), 165 (43). HRMS (EI): calcd. for $C_{24}H_{24}O_3$ $[M]^+$: 360.17200; found: 360.171620.

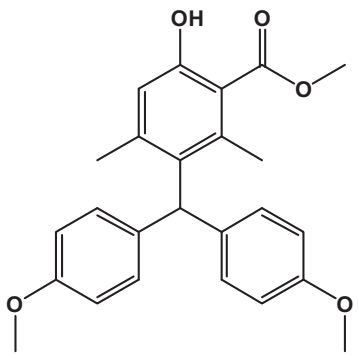
Methyl 3-(bis(4-chlorophenyl)methyl)-5-ethyl-6-hydroxy-2,4-dimethylbenzoate(9d):



To a CH_2Cl_2 solution (5 mL) of **4d** (0.288 g, 1.0 mmol) and **8a** (0.372 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added.

The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9d** as a yellow oil (0.191 g, 42%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.02 (q, 2 H, CH_3), 1.28 (t, 3 H, CH_3), 1.93, 2.05 (s, 3H, CH_3), 3.81 (s, 3 H, OCH_3), 5.88 (s, 1 H, CH), 6.93,7.18 (d, 4 H, Ph), 10.83 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 (CH_3), 17.0, 18.9 (CH_3), 19.3 (CH_2), 20.2 (CH_3), 49.1 (CH), 60.6 (OCH_3), 111.4 (C), 127.3, 127.3, (CH_{Ar}), 130.8, 135.7, 139.5 141.4, 157.1, 170.9 (C). IR (KBr): $\tilde{\nu}$ = 2962, 2903 (w), 1721, 1651, 1489, 1445 (w), 1257, 1089, 1012, 788 (s), 700, 660 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 388 (M^+, 77), 312 (94), 310 (100), 282 (45), 275 (13), 165 (32). HRMS (ESI-TOF): calcd. for $C_{26}H_{27}O_3$ [M-H]$^-$: 387.20384; found: 387.2032805.

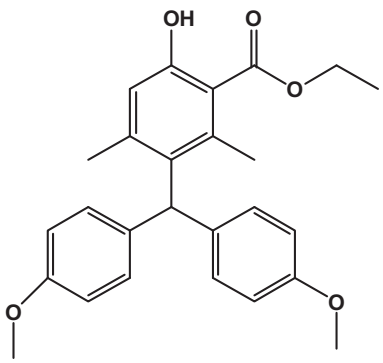
Methyl 3-(bis(4-methoxyphenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (9e):



To a CH_2Cl_2 solution (5 mL) of **4a** (0.260 g, 1.0 mmol) and **8b** (0.437 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9e** as a crystalline solid (0.130 g , 32%) mp = 124-125 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.07 (s, 3 H, CH_3), 3.72 (s, 6 H, OCH_3), 3.81 (s, 3 H, OCH_3), 5.81 (s, 1 H, CH), 6.64 (s, 1 H, ArH), 6.72 (d, 4 H, ArH), 6.90 (d, 4 H, ArH), 10.47 (s, 1 H, OH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.2, 22.7 (CH_3), 49.1 (CH), 51.0, 55.2 (OCH_3), 112.7 (C), 113.5 117.7, 129.9, (CH_{Ar}), 133.6, 134.4, 140.2, 145.3, 157.7, 159.7, 172.0 (C). IR (KBr): $\tilde{\nu}$ = 3027, 2951, 2929 (w), 1658 (m), 1506 (s), 1461, 1438 (m), 1240, 1170, 1029 (s), 857 (m), 802, 778 (m), 752, 700 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 407 (M^+, 66),

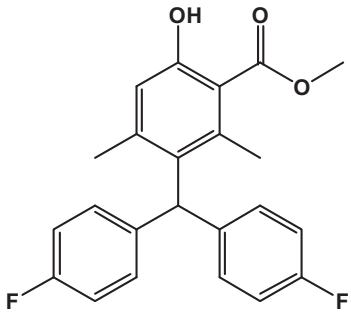
314 (100), 299 (21), 237 (18), 165 (49). HRMS (ESI-TOF): calcd. for $C_{25}H_{25}O_7$ $[M]^+$: 407.1853; found: 407.18548.

Ethyl 3-(bis(4-methoxyphenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (9f):



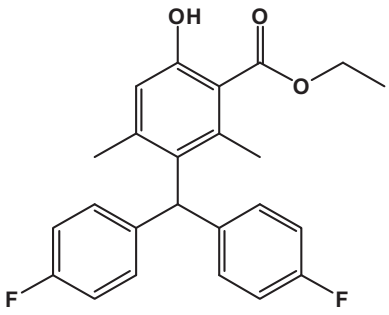
To a CH_2Cl_2 solution (5 mL) of **4b** (0.260 g, 1.0 mmol) and **8b** (0.437 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give as a **9f** was synthesized according to the *general procedure A* at 1 mmol scale as a crystalline solid (0.155 g, 37%) mp 95-97 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, 3 H, CH_3, J = 7.12 Hz), 1.97 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 3.72 (s, 6 H, OCH_3), 4.30 (q, 2 H, OCH_2, J = 7.12 Hz), 5.81 (s, 1 H, CH), 6.64 (s, 1 H, ArH), 6.73 (d, 4 H, ArH), 6.92 (d, 4 H, ArH), 10.56 (s, 1 H, OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.1, 21.1, 22.7 (CH_3), 49.1 (CH), 55.2 (OCH_3), 61.4 (OCH_2), 112.9 (C), 113.5 117.8, 129.9, (CH_{Ar}), 133.6, 134.4, 140.2, 145.2, 157.7, 159.7, 171.5 (C). IR (KBr): $\tilde{\nu}$ = 2952, 2930, 2833 (w), 1651, 1506, 1461 (s), 1572 (m), 1240, 1227, 1172, 1029 (s), 838, 824, 800, 778 (m), 724, 700, 640 (w) 573, 547 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 420 (M^+, 38), 339 (56), 325 (75), 309 (65), 319 (10), 227 (100), 207 (52) 152 (38). HRMS (EI): calcd. for $C_{26}H_{28}O_5$ $[M]^+$: 420.1936; found: 420.193424.

Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (9g):



To a CH_2Cl_2 solution (5 mL) of **4a** (260 mg, 1.0 mmol) and **8c** (0.411 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **6g** as a greenish oil (0.126 g, 33%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.18 (s, 3 H, CH_3), 1.98, 2.05 (s, 3 H, CH_3), 3.82 (s,3 H, OCH_3), 5.84 (s, 1 H, CH), 6.66 (s, 1 H, ArH), 6.89-6.96 (m, 8 H, ArH), 10.50 (s, 1 H, OH), ^{19}F NMR (250 MHz, $CDCl_3$): δ = -116, ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 22.6, 29.6 (CH_3), 49.3 (CH), 52.0 (OCH_3), 112.9 (C), 114.0, 118.4, 130.3 (CH_{Ar}), 137.5, 140.1, 145.0, 159.6, 162.8, 171.8 (C). IR (KBr): $\tilde{\nu}$ = 2949, 2918, 2850 (w), 1650, 1503, 1349, 1328, 1229 (w), 1155, 1072, 857. 822, 795 (w) cm^{-1}.. MS (EI, 70 eV): *m/z* (%) = 428 (M^+, 38), 382 (100), 367 (10), 347 (19), 319 (10), 271 (18), 199 (32) 165 (58). HRMS (EI): calcd. for $C_{23}H_{20}O_3F_2$ $[M]^+$: 382.13750; found: 382.137228.

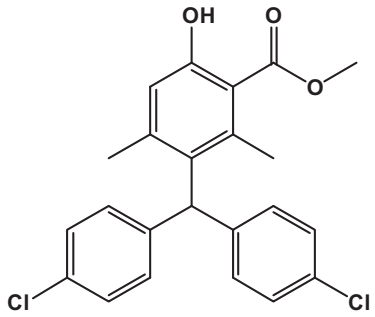
Ethyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (9h):



To a CH_2Cl_2 solution (5 mL) of **4b** (0.274 g, 1.0 mmol) and **8c** (0.411 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give as **9h** as a greenish oil (0.146 g, 37%). ^{1}H NMR

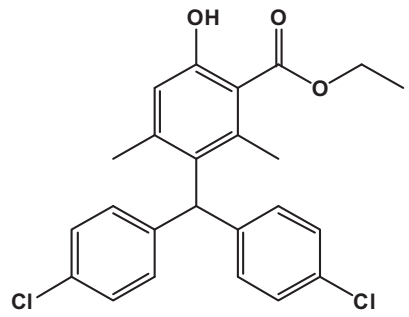
(250 MHz, $CDCl_3$): δ = 1.28 (t, 3 H, CH_3), 1.97, 2.07 (s, 3 H, CH_3), 4.30 (q,2 H, OCH_2), 5.84 (s, 1 H, CH), 6.65 (s, 1 H, ArH), 6.85-6.99 (m, 8 H, ArH), 10.59 (s, 1 H, OH), ^{19}F NMR (250 MHz, $CDCl_3$): δ = -116, ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 21.2, 22.7 (CH_3), 49.3 (CH), 61.6 (OCH_2), 113.0 (C), 114.9, 115.2, 118.0, 130.3 (CH_{Ar}), 137.6, 140.1, 144.9, 159.2, 163.1, 171.3 (C). IR (KBr): $\tilde{\nu}$ = 2959, 2922, 2851 (w), 1650, 1598 (m), 1503, 1220, 1210 (s), 1157, 1151 (m), 794 (s), 727, 716, 632 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 396 (M^+, 45), 350 (100), 335 (20), 255 (12), 201 (19), 183 (20), HRMS (EI): calcd. for $C_{24}H_{22}O_3F_2$ $[M]^+$: 396.15315; found: 396.153067.

Methyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (9i):



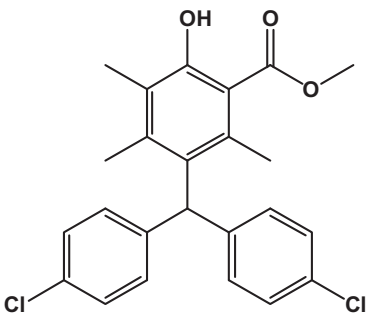
To a CH_2Cl_2 solution (5 mL) of **4a** (0.260 g, 1.0 mmol) and **8d** (0.466 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6−12 h. After stirring for additional 2−6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **6i** as a crystalline solid (0.207 g, 50%) mp 167-168 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 5.82 (s, 1 H, CH), 6.66 (s, 1 H, ArH), 6.90 (d, 4 H, ArH), 7.18 (d, 4 H, ArH), 10.53 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 21.6 (CH_3), 48.6 (CH), 51.1 (OCH_3), 111.9 (C), 117.0, 127.4, 129.3, (CH_{Ar}), 131.0, 139.1, 139.2, 144.0, 159.1, 170.7 (C). IR (KBr): $\tilde{\nu}$ = 2961, 2946 (w), 1650 (m), 1598 (w), 1435 (m), 1326 (m), 1258, 1227 (s), 1088, 1069, 1025, 1009 (s), 796, 776, 735 (s), 707, 687, 584 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 414 (M^+, 78), 382 (100), 367 (15), 347 (23), 165 (49). HRMS (ESI-TOF): calcd. for $C_{23}H_{19}O_3Cl_2$ $[M-H]^-$: 413.07188; found: 413.07167.

Ethyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (9j):



To a CH_2Cl_2 solution (5 mL) of **4b** (0.274 g, 1.0 mmol) and **8d** (0.446 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at –78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **6j** as a crystalline solid (0.226 g, 56%) mp 173-175 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29 (t, 3 H, CH_3), 1.97 (s, 3 H, CH_3), 2.06 (s, 3 H, CH_3), 4.31 (q, 2 H, OCH_2), 5.82 (s, 1 H, CH), 6.66 (s, 1 H, ArH), 6.91 (d, 4 H, ArH), 7.19 (d, 4 H, ArH), 10.63 (s, 1 H, OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.1, 20.4, 21.7 (CH_3), 48.6 (CH), 60.6 (OCH_2), 112.0 (C), 117.0, 127.4, 129.3, (CH_{Ar}), 131.0, 131.1, 139.2, 143.9, 159.2, 170.3 (C). IR (KBr): $\tilde{\nu}$ = 2981, 2958, 2913, 2852 (w), 1647 (s), 1596, 1572 (m), 1487, 1463, 1371. 1321, 1292. 1224. 1009 (s), 853, 839 (m), 815, 799, 784 (s) 754, 734 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 428 (M^+, 38), 382 (100), 367 (10), 347 (19), 319 (10), 271 (18), 199 (32) 165 (58). HRMS (ESI-TOF): calcd. for $C_{24}H_{21}O_3Cl_2$ [M-H]$^-$: 427.08732; found: 427.08796.

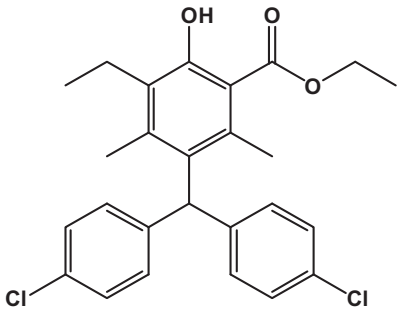
Methyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4,5-trimethylbenzoate (9k):



To a CH_2Cl_2 solution (5 mL) of **4c** (0.274 g, 1.0 mmol) and **8d** (0.446 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at –78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was

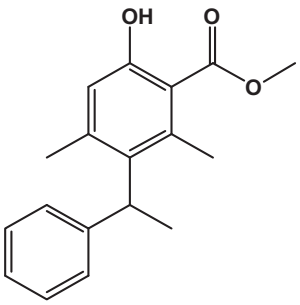
purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9k** as a yellow gummy solid (171 g, 40%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.89, 2.06, 2.10 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 5.88 (s, 1 H, CH), 6.92-7.16 (m, 8 H, ArH), 10.81 (s, 1 H, OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 11.3, 13.0, 20.4, 21.6 (CH_3), 49.0 (CH), 51.1 (OCH_3), 111.1 (C), 116.4, 127.4, 129.3, (CH_{Ar}), 130.8, 139.2, 144.0, 157.1, 159.9, 171.4 (C). IR (KBr): $\tilde{\nu}$ = 2991, 2852 (s), 1669, 1489, 1456, 1439 (m), 1091, 1013 (s), 750, 698, 647 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 428 (M^+, 37), 398 (62), 396 (100), 353 (7), 235 (10), 199 (11), 165 (16), HRMS (ESI-TOF): calcd. for $C_{24}H_{21}O_3Cl_2$ [M-H]$^-$: 427.08732; found: 427.08657.

Methyl 3-(bis(4-chlorophenyl)methyl)-5-ethyl-6-hydroxy-2,4-dimethylbenzoate (9l):



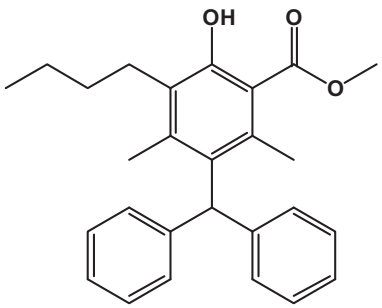
To a CH_2Cl_2 solution (5 mL) of **4d** (0.288 g, 1.0 mmol) and **8d** (0.466 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9l** as a yellow oil (0.191 g, 42%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.02 (q, 2 H, CH_3), 1.28 (t, 3 H, CH_3), 1.93, 2.05 (s, 3H, CH_3), 3.81 (s, 3 H, OCH_3), 5.88 (s, 1 H, CH), 6.93,7.18 (d, 4 H, Ph), 10.83 (s, 1 H, OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.1 (CH_3), 17.0, 18.9 (CH_3), 19.3 (CH_2), 20.2 (CH_3), 49.1 (CH), 60.6 (OCH_3), 111.4 (C), 127.3, 127.3, (CH_{Ar}), 130.8, 135.7, 139.5 141.4, 157.1, 170.9 (C). IR (KBr): $\tilde{\nu}$ = 2962, 2903 (w), 1721, 1651, 1489, 1445 (w), 1257, 1089, 1012, 788 (s), 700, 660 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 456 (M^+, 77), 412 (94), 410 (100), 382 (45), 285 (13), 165 (32). HRMS (ESI-TOF): calcd. for $C_{26}H_{25}Cl_2O_3$ [M-H]$^-$: 455.11862; found: 455.11805.

Methyl 6-hydroxy-2,4-dimethyl-3-(1-phenylethyl)benzoate (9m):



To a CH_2Cl_2 solution (5 mL) of **4a** (0.260 g, 1.0 mmol) and **8e** (0.304 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6−12 h. After stirring for additional 2−6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give as **6m** as a yellow oil (0.156 g, 55%) ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.59 (d, 3H, CH_3, J = 7.4 Hz), 2.12 (s_{brd}, 3 H, CH_3), 2.14(s_{brd}, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 4.57 (q, 1H, CH, J = 7.4 Hz), 6.63 (s, 1 H, ArH), 7.04-7.20 (m, 6 H, ArH), 10.41 (s, 1 H, OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 17.2, 20.1, 22.1 (CH_3), 37.6 (CH), 51.9 (OCH_3), 112.7 (C), 117.6, 125.3, 126.3, 128.3 (CH_{Ar}), 135.9, 139.2, 144.5, 145.4, 159.4, 172.0 (C). IR (KBr): $\tilde{\nu}$ = 3024, 2953 (w), 1659 (s), 1600, 1570 (m), 1439 (m), 1341 (m), 1227 (s), 1154 (m), 1072, 1020 (w), 950, 859, 804, 698 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 284 (M^+, 54), 252 (95), 237 (100), 209 (9), 165 (21). HRMS (EI): calcd. for $C_{18}H_{20}O_3$ $[M]^+$: 284.14070; found: 284.140521.

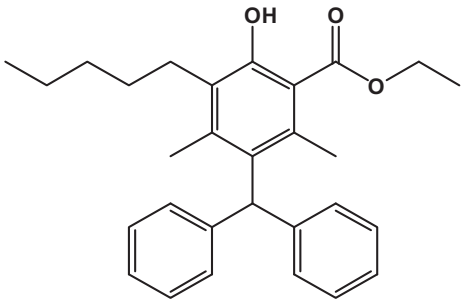
Methyl 3-benzhydryl-5-butyl-6-hydroxy-2,4-dimethylbenzoate (9n):



To a CH_2Cl_2 solution (5 mL) of **4e** (0.316 g, 1.0 mmol) and **8a** (0.372 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6−12 h. After stirring for additional 2−6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give Compound **6n** was synthesized according to the *general procedure A* at as a colourless

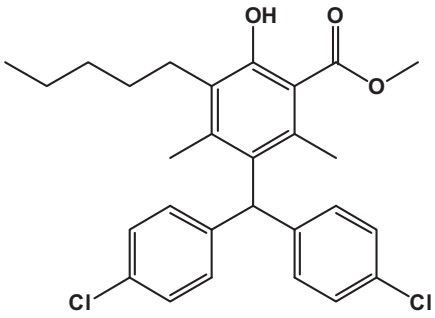
gel (0.172 g, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, 3H, CH_3), 1.25 (m, 4H, $2CH_2$), 1.83, 1.92 (s, 3 H, CH_3), 2.49 (t, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 5.79 (s, 1 H, CH), 6.75-6.88 (m, 10 H, Ph), 10.62 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.2, 19.4, 22.4 (CH_3), 24.2, 27.7, 32.5 (CH_2), 51.0 (CH), 53.2 (OCH_3), 113.4 (C), 116.0, 116.3, 130.3 (CH_{Ar}), 134.3, 138.0, 143.6, 144.3, 159.1, 173.8 (C). IR (KBr): $\tilde{\nu}$ = 2954, 2927 (w), 169, 1598 (m), 1504 (s) 1438, 1397, 1293 (m), 1223, 1200, 1157 (s), 1115, 1015, 823, 819 (m), 796 (s), 731, 670 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 402 (M^+, 100), 370 (83), 353 (22), 328 (37), 279 (16), 165 (14). HRMS (EI): calcd. for $C_{23}H_{22}O_3$ $[M]^+$: 402.21895; found: 402.218714.

Methyl 3-benzhydryl-6-hydroxy-2,4-dimethyl-5-pentylbenzoate (9o):



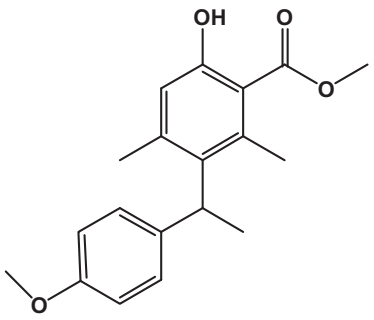
To a CH_2Cl_2 solution (5 mL) of **4f** (0.330 g, 1.0 mmol) and **8a** (0.372 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9o** colourless gel (0.170 g, 41%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, 3H, CH_3), 1.24 (m, 6H, $3CH_2$), 1.84, 1.95 (s, 3 H, CH_3), 2.49 (t, 2 H, CH_2), 3.69 (s, 3 H, OCH_3), 5.89 (s, 1 H, CH), 6.90-7.09 (m, 10 H, Ph), 10.62 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.2, 19.5, 22.4 (CH_3), 24.3, 27.7, 30.8, 32.5 (CH_2), 52.3 (CH), 53.1 (OCH_3), 113.3 (C), 127.0, 129.3, 130.3 (CH_{Ar}), 134.3, 138.0, 143.6, 144.3, 159.1, 173.8 (C). IR (KBr): $\tilde{\nu}$ = 2952, 2924, 2855 (w), 1655 (s), 1596, 1561, 1493 (m), 1437 (s), 1398, 1323, 1290 (m), 1200 (s), 1115, 1022, 805, 725 (m), 697 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 416 (M^+, 100), 370 (83), 353 (22), 328 (37), 279 (16), 165 (14). HRMS (EI): calcd. for $C_{23}H_{22}O_3$ $[M]^+$: 416.21895; found: 416.218714.

Methyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-pentylbenzoate (9p):



To a CH_2Cl_2 solution (5 mL) of **4f** (0.330 g, 1.0 mmol) and **8d** (0.466 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at –78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9p** as yellowish gummy solid (0.218 g, 45%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 3H, CH_3), 1.34 (m, 6H, $3CH_2$), 1.93, 2.01 (s, 3 H, CH_3), 2.59 (t, 2 H, CH_2), 3.82 (s, 3 H, OCH_3), 5.87 (s, 1 H, CH), 6.92 (d, 4 H, ArH), 7.17 (d, 4 H, ArH), 10.75 (s, 1 H, OH). ^{13}C NMR (250 MHz, $CDCl_3$): δ = 12.9, 17.2, 20.3 (CH_3), 22.0, 25.5, 28.6, 30.2 (CH_2) 49.1 (CH), 51.0 (OCH_3), 111.2 (C), 127.3, 129.3 (CH_{Ar}), 130.8, 135.7, 139.5, 141.7, 157.2, 171.4 (C). IR (KBr): $\tilde{\nu}$ = 2941, 2909 (w), 1654 (m), 1554 (w), 1435 (m), 1326 (m), 1258, 1227 (s), 1088, 1069, 1025, 1009 (s), 796, 776, 735 (s), 707, 687, 584 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 485 (M^+, 78), 484 (100), 367 (15), 347 (23), 165 (49). HRMS (EI): calcd. for $C_{28}H_{29}O_3Cl_2$ $[M]^+$: 485.44200; found: 485.441673.

Methyl 6-hydroxy-3-(1-(4-methoxyphenyl)ethyl)-2,4-dimethylbenzoate (9q):

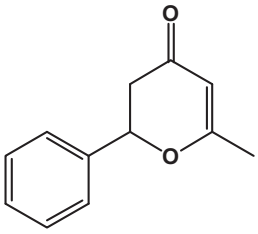


To a CH_2Cl_2 solution (5 mL) of **4a** (0.260 g, 1.0 mmol) and **8f** (0.336 g, 1.1 mmol) was dropwise added $TiCl_4$ (0.12 mL, 1.1 mmol) at –78 °C. The reaction mixture was allowed to warm to 20 °C during 6–12 h. After stirring for additional 2–6 h at 20 °C, hydrochloric acid (10%, 20 mL) was added. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3 x 25 mL). The combined organic layers

were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate) to give **9q** as a yellowish oil (150 g, 48%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55 (d, 3 H, CH_3), 2.11, 2.15 (s, 3 H, CH_3), 3.70, 3.81 (s, 3 H, OCH_3), 4.50 (s, 1 H, CH), 6.62 (s, 1 H, ArH), 6.71-6.97 (m, 8 H, Ph), 10.38 (s, 1 H, OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 16.4, 21.0, 22.8 (CH_3), 35.8 (CH), 50.9, 54.1 (OCH_3), 112.6 (C), 116.5, 123.2, 126.2 (CH_{Ar}), 134.9, 136.3, 143.3, 156.3, 158.2, 170.9 (C). IR (KBr): $\tilde{\nu}$ = 2953, 2923, 2848 (w), 1658 (s), 1608, 1570 (m), 1509(s), 1461, 1439, 1349 (m), 1244, 1227, 1214 (s), 1154, 1032, 908 (m), 829, 803, 729 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 314 (M^+, 35), 252 (95), 237 (100), 209 (9), 165 (21). HRMS (ESI): calcd. for $C_{18}H_{20}O_3$ $[M+H]^+$: 315.15909; found: 315.15944.

General procedure for the synthesis of 3-substituted pentane-2,4-diones: A THF solution of LDA was prepared (25.0 mmol) by addition of *n*BuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stiring for 1h, the solution was cooled to -78 °C and **10a-c** (1.00 g, 10.0 mmol) was added. After stirring for 1 h at -78 °C, **11a-i** (1.06 g, 10.0 mmol) was added and the solution was allowed to warm to 20 °C within 24 h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethyl acetate (3 x 50 ml). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give **14a-m** as our required product.

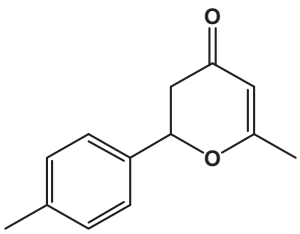
6-Methyl-2-phenyl-2*H*-pyran-4(3*H*)-one (14a):



A THF solution of LDA was prepared (25.0 mmol) was prepared by addition of *n*BuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, **11a**

(1.06 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give **14a** as colourless crystalline solid (1.63 g, 87%), mp 54-56 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.47-2.55 (dd, 1 H_A, *J* = 3.2, 16.7 Hz), 2.66-2.79 (dd, 1 H_B, *J* = 14.0, 16.7, Hz), 5.27-5.34 (dd, 1H, CH, *J* = 3.2, 14.5 Hz), 5.36 (s, 1H, CH), 7.28-7.33 (m, 5H, Ph), ^{13}C NMR (300 MHz, $CDCl_3$): δ = 21.1(CH_3), 42.4 (CH_2), 80.8, 105.2 (CH), 126.1, 128.8 (CH_{Ar}), 138.1,174.3, 192.3 (C). IR (KBr): $\tilde{\nu}$ = 3062, 3033, 2962, 2918 (w), 1661, 1603, 1392, 1327 (s), 1237, 1179, 1023 (m), 999 (s), 950, 808 (m), 755, 696 (s) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 188 (M^+, 2), 170 (8), 155 (6), 145 (36), 104 (100), 91 (2), 78 (16), 77 (12). HRMS (ESI-TOF): calcd. for $C_{12}H_{13}O_2$ $[M+H]^+$: 189.09101; found: 189.09077.

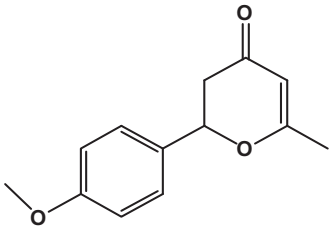
6-Methyl-2-(p-tolyl)-2*H*-pyran-4(3*H*)-one (14b):



A THF solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, p-tolyldehyde **11b** (1.20g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give **14b** as a reddish crystalline solid (0.89 g, 89%), mp 44-46 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 2.45-2.52 (dd, 1 H_A, *J* = 4.5, 16.8 Hz), 2.68-2.78 (dd, 1 H_B, *J* = 14.1, 16.8, Hz), (dd, 1H, CH, *J* = 4.5, 14.1 Hz), 5.34 (s, 1H, CH), 7.13-7.23 (m, 4H, Ph), ^{13}C NMR (300

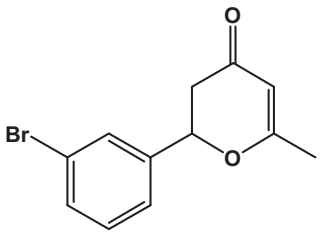
MHz, $CDCl_3$): δ = 21.1, 21.2 (CH_3), 42.2 (CH_2), 80.8, 105.1 (CH), 126.2, 129.4 (CH_{Ar}), 135.2, 138.8,174.4, 192.5 (C). IR (KBr): $\tilde{\nu}$ = 3069, 3027, 2998, 2920 (w), 1661, 1606, 1394 (s), 1224, 1183, 1069, 1029 (m), 1019, 1006, 961 (s), 906, 871 (m), 811 (s) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 202 (M^+, 2), 184 (12), 160 (22), 159 (30), 119 (10), 118 (100), 117 (60), 91 (17), 77 (4). HRMS (EI): calcd. for $C_{13}H_{14}O_2$ $[M]^+$: 202.09883; found: 202.098924.

2-(4-Methoxyphenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (14c):



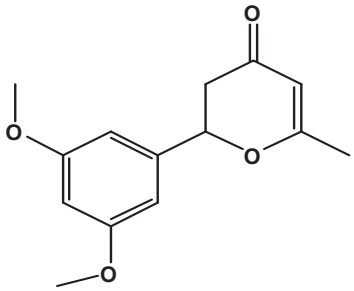
A THF solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, p-methoxybenzaldehyde **11c** (1.36 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give **14c** as a yellow crystalline solid (0.91 g, 84%), mp 45-48 °C. ^1H NMR 300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.44-2.51 (dd, 1 H_A, *J* = 3.4, 16.9 Hz), 2.69-2.80 (dd, 1 H_B, *J* = 14.2, 16.9, Hz), 3.75 (s, 3H, OCH_3), 5.23-529 (dd, 1H, CH, *J* = 3.4, 14.2 Hz), 5.44 (s, 1H, CH), 6.87, 7.27 (d, 4H, CH_{Ar} , *J* =6.7), ^{13}C NMR (300 MHz, $CDCl_3$): δ = 21.1, (CH_3), 42.1 (CH_2), 55.3 (OCH_3) 80.6, 105.1 (CH), 114.1, 127.8 (CH_{Ar}), 130.1, 160.0, 174.4, 192.6 (C). IR (KBr): $\tilde{\nu}$ = 3400, 2998, 2958, 2934, 2836 (w), 1715 (m), 1608, 1511, 1242, 1173, 1149, 1028 (s), 1006, 957, 930, 869 (m), 828, 818 (s), 798, 658 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 218 (M^+, 7), 200 (8), 175 (13), 160 (22), 134 (100), 119 (21), 91 (14), 77 (5). HRMS (ESI): calcd. for $C_{13}H_{14}O_3$ $[M]^+$: 218.09375; found: 218.093796.

2-(3-Bromophenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (14d):



A THF solution of LDA was prepared (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, m-bromobenzaldehyde **11d** (1.83 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50ml). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **(14d)** as a yellow crystalline solid (0.88 g, 67%), mp 59-61 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 2.01 (s, 3 H, CH_3), 2.48-2.54 (dd, 1 H_A, J = 3.3, 16.7 Hz), 2.62-2.73 (dd, 1 H_B, J = 13.9, 16.7, Hz), 5.25-5.31 (dd, 1H, CH, J = 3.3, 13.9 Hz), 5.37 (s, 1H, CH), 7.18, 7.45 (m, 4H, CH_{Ar}), ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.0, (CH_3), 42.3 (CH_2), 79.9, 105.4 (CH), 122.8 (C) 124.6, 129.2, 130.3, 131.8 (CH_{Ar}), 140.4, 174.0, 191.6 (C). IR (KBr): $\tilde{\nu}$ = 3391, 3073, 2968, 2879 (w), 1655, 1604 (s), 1472, 1428 (m), 1388, 1323, 1256, 1002 (s), 881, 866, 854 (m), 778, 694, 681 (s) 621 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 266 (M^+, 7), 250 (11), 248 (11), 184 (98), 182 (100), 144 (30). HRMS (ESI): calcd. for $C_{12}H_{11}O_2Br[M]^+$: 265.99369; found: 265.993520.

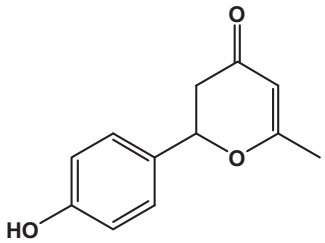
2-(2,5-Dimethoxyphenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (14e):



A THF solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the

solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, 2,4-dimethoxybenzaldehyde **11e** (1.66 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14e** as a pale yellow solid (0.94 g, 76%), mp 108-110 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 2.46-2.53 (dd, 1 H_A, *J* = 3.7, 16.8 Hz), 2.59-2.69 (dd, 1 H_B, *J* = 13.9, 16.8, Hz), 3.74 (s, 6H, OCH_3), 5.33 (s, 1H, CH), 5.58-5.64 (dd, 1H, CH, *J* = 3.7, 13.9 Hz), 6.40-6.48 (m, 2 H, CH_{Ar}), 7.30 (d, 1H, CH_{Ar}), ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.1, (CH_3), 41.7 (CH_2), 55.3 (OCH_3), 75.9, 98.4, 104.5 104.9(CH), 119.2 (C) 127.4 (CH_{Ar}), 157.3, 161.0, 174.8, 193.3 (C). IR (KBr): $\tilde{\nu}$ = 3073, 2971, 2837 (w), 1655, 1603, 1583 (s), 1508, 1461, 1439 (m), 1158 (s), 1031, 1020 (m), 991, 827, 804 (s) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 248 (M^+, 27), 205 (21), 164 (100), 149 (83), 121 (45), 91 (13), 77 (12). HRMS (EI): calcd. for $C_{14}H_{16}O_4$ $[M]^+$: 248.10431; found: 248.104054.

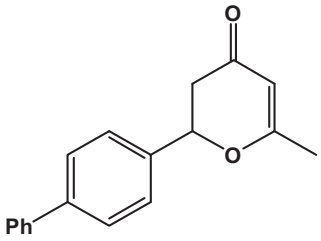
2-(4-Hydroxyphenyl)-6-methyl-2*H*-pyran-4(3*H*)-one (14f):



A THF solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30mL) of diisopropylamine (2.52g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, p-hydroxybenzaldehyde **11f** (1.22 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14f** as a white crystalline solid (0.79 g, 78%), mp

160-161 °C. ^{1}H NMR 300 MHz, CD_3OD): δ = 1.96 (s, 3 H, CH_3), 2.34-2.41 (dd, 1 H_A, *J* = 4.5, 16.9 Hz), 2.72-2.82 (dd, 1 H_B, *J* = 14.1, 16.9, Hz), 5.23-529 (dd, 1H, CH, *J* = 4.5, 14.1 Hz), 5.32 (s, 1H, CH), 6.71, 7.17 (d, 4H, CH_{Ar} , *J* = 8.4), ^{13}C NMR (300 MHz, CD_3OD): δ = 21.1, (CH_3), 42.7 (CH_2), 82.3, 105.1 (CH), 116.3, 129.1 (CH_{Ar}), 130.4, 159.2, 177.8, 195.9 (C). IR (KBr): $\tilde{\nu}$ = 3151, 3069, 2974, 2900 (w), 1630, 1615, 1576, 1515, 1463, 1393, 1251, 1234 (s), 1224, 1188, 1066, 1017 (m), 997, 818 (s), 792, 744, 666 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 204 (M^+, 51), 186 (43), 171 (28), 161 (79), 147 (100), 119 (29), 91 (21), 77 (8). HRMS (EI): calcd. for $C_{12}H_{12}O_3$ $[M]^+$: 204.07810; found: 204.078152.

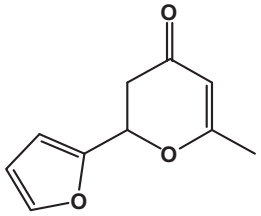
2-(Biphenyl-4-yl)-6-methyl-2*H*-pyran-4(3*H*)-one (14g):



A THF solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30mL) of diisopropylamine (2.52g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, 4-biphenylaldehyde**11g** (1.82 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14g** as a light yellowish solid (1.05 g, 80%), mp 64-66 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 2.01 (s, 3 H, CH_3), 2.52-2.58 (dd, 1 H_A, *J* = 2.9, 16.8 Hz), 2.72-2.82 (dd, 1 H_B, *J* = 14.1, 16.8, Hz), 5.27-5.32 (dd, 1H, CH, *J* = 2.9, 14.1 Hz), 5.37 (s, 1H, CH), 7.26, 7.41 (m, 9H, CH_{Ar}), ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.1, (CH_3), 42.2 (CH_2), 80.6, 105.2 (CH), 126.6, 127.1, 127.5, 127.6, 128.8 (CH_{Ar}), 137.0,140.4, 141.8, 174.3, 192.3 (C). IR (KBr): $\tilde{\nu}$ = 3390, 3056, 3027, 2990, 2836, 1712 (w), 1660, 1601 (s), 1485, 1432 (m), 1394, 1331, 1235, 1000 (s), 951, 899, 872 (m), 763, 730, 701 (s) 657 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 264 (M^+,

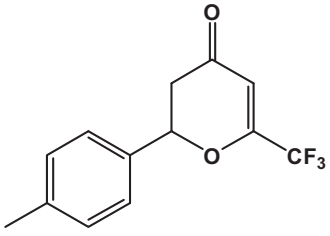
6), 222 (18), 221 (19), 180 (100), 165 (10), 152 (9). HRMS (ESI): calcd. for $C_{18}H_{16}O_2$ $[M]^+$: 264.11448; found: 264.114410.

2-(Furan-2-yl)-6-methyl-2*H*-pyran-4(3*H*)-one (14h):



A THF Solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (0.96g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and **10a** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, 2-furyldehyde **11h** (1.06 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14h** as a yellowish crystalline solid (0.77 g, 87%), mp 57-59 °C. ^{1}H NMR 250 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, CH_3), 2.52-2.59 (dd, 1 H_A, J = 3.1, 10.8 Hz), 2.69-2.80 (dd, 1 H_B, J = 14.0, 10.8, Hz), 3.75 (s, 3H, OCH_3), 5.33 (s, 1H, CH), 5.37 (d, 1H, CH, J = 3.1 Hz), 6.32, 6.37 (m, 2H, CH_{Ar}), 7.40 (s, 1H, CH_{Ar}), ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.0, (CH_3), 38.5 (CH_2), 73.3, 105.2 (CH), 109.4, 110.5, 143.4 (CH_{Ar}), 150.3, 173.6, 191.5 (C). IR (KBr): $\tilde{\nu}$ = 3147, 3126, 3073, 2915 (w), 1657, 1604 (s), 1503, 1439 (m), 1387, 1322, 1183, 1147, 1000 (s), 888, 865, 841, 820 (m), 742 (s), 680, 598 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 178 (M^+, 14), 160 (5), 94 (100), 66 (17), 65 (12), 39 (11). HRMS (EI): calcd. for $C_{10}H_{10}O_3$ $[M]^+$: 178.06245; found: 178.062320.

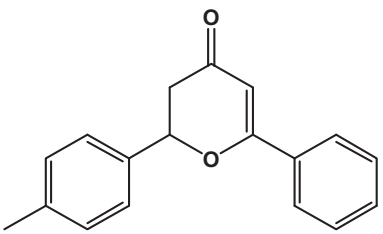
2-p-Tolyl-6-(trifluoromethyl)-2*H*-pyran-4(3*H*)-one (14i):



A THF Solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and 1,1,1-trifluoropentane-

2,4-dione **10b** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, p-tolyldehyde **11b** (1.20 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give **14i** as a blackish solid (0.96 g, 75%), mp 82-84 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 2.65-2.72 (dd, 1 H_A, *J* = 3.1, 16.8 Hz), 2.69-2.80 (dd, 1 H_B, *J* = 13.6, 16.8, Hz), 5.44-5.49 (dd, 1H, CH, *J* = 3.1, 13.6 Hz), 5.87 (s, 1H, CH), 7.15-7.24 (m, 4H, CH_{Ar}), ^{19}F NMR 300 MHz, $CDCl_3$): -73.3, ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.2, (CH_3), 42.5 (CH_2), 82.6, 105.8 (CH), 126.2, 129.6 (CH_{Ar}), 133.2, 139.5, 159.5, 191.4 (C). IR (KBr): $\tilde{\nu}$ = 3039, 2923 (w), 1679, 1633, 1411 (s), 1324 (m), 1271, 1177, 1142, 1069 (s), 990, 959, 937 (m), 810 (s), 719, 709, 602 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 256 (M^+, 7), 187 (8), 159 (8), 118 (100), 117 (51), 91 (15), 69 (12). HRMS (EI): calcd. for $C_{13}H_{11}O_2F_3$ $[M]^+$: 256.07057; found: 256.071111.

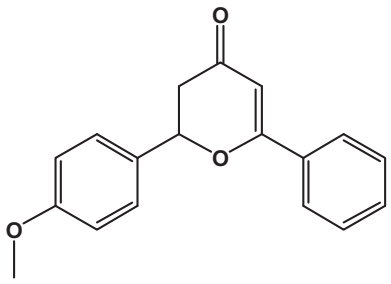
6-Phenyl-2-(p-tolyl)-2*H*-pyran-4(3*H*)-one (14j):



A THF Solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and 1-phenylbutane-1,3-dione **10c** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, p-tolyldehyde **11b** (1.20 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14j** as a dark red crystalline solid (1.04 g, 73%), mp 75-77 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 2.65-2.87 (m, 2H, CH_2), 3.77 (s, 3H, O CH_3), 5.45 (d, 1H, CH), 6.03 (s_{brd}, 1H, CH), 6.81-7.79 (m, 9H, CH_{Ar}), ^{13}C NMR (300 MHz, $CDCl_3$): δ = 42.8

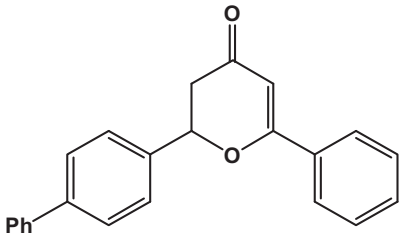
(CH_2), 55.5 (OCH_3), 80.8, 102.3 (CH), 114.2, 126.7, 127.8,128.6, 131.7 (CH_{Ar}) , 135.2, 138.8, 170.4, 193.4 (C). IR (KBr): $\tilde{\nu}$ = 3368, 3029, 2964 (w), 1650, 1593, 1568 (s), 1487,1448,1378, 1365, 1229, 1046, 930, 839 (m), 760, 728, 689 (s), 665, 621, 614 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 280 (M^+, 4), 262 (13) 175 (30), 134 (100), 119 (20), 105 (15), 91 (16), 77 (14). HRMS (EI): calcd. for $C_{18}H_{16}O_3$ $[M]^+$: 280.10940; found: 280.109347.

2-(4-Methoxyphenyl)-6-phenyl-2*H*-pyran-4(3*H*)-one (14k):



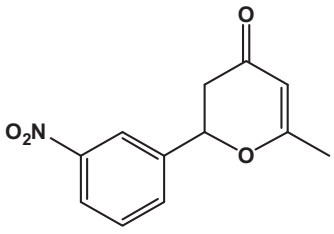
A THF Solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and 1-phenylbutane-1,3-dione **10c** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, p-methoxybenzaldehyde **11c** (1.36 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14k** as a yellowish crystalline solid (1.04 g, 89%), mp 72-74 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 2.62-2.94 (m, 2H, CH_2), 5.43 (d, 1H, CH), 6.04 (s_{brd}, 1H, CH), 7.20-7.41 (m, 9H, CH_{Ar}), ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.2, (CH_3), 42.9 (CH_2), 81.0, 102.3 (CH), 126.2, 126.6, 127.6,129.7, 131.7 (CH_{Ar}), 135.2, 138.8, 170.3, 193.2 (C). IR (KBr): $\tilde{\nu}$ = 3368, 3029, 2964 (w), 1650, 1593, 1568 (s), 1487,1448,1378, 1365, 1229, 1046, 930, 839 (m), 760, 728, 689 (s), 665, 621, 614 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 264 (M^+, 4), 246 (13) 159 (34), 158 (13), 118 (100), 117 (51), 91 (16), 77 (15). HRMS (EI): calcd. for $C_{18}H_{16}O_2$ $[M]^+$: 264.11448; found: 264.114363.

2-(Biphenyl-4-yl)-6-phenyl-2*H*-pyran-4(3*H*)-one (14l):



A THF Solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and 1-phenylbutane-1,3-dione **10c** (1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, 4-biphenylaldehyde **11h** (1.82 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14l** as a reddish brown crystalline solid (1.27 g, 78%), mp 110-112 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 2.68-2.97 (m, 2H, CH_2), 5.53 (d, 1H, CH), 6.08 (s_{brd}, 1H, CH), 7.26-7.50 (m, 13H, CH_{Ar}), ^{13}C NMR (250 MHz, $CDCl_3$): δ = 42.9 (CH_2), 80.8, 102.3 (CH), 126.7, 127.1, 127.6, 128.7, 128.8, 131.8, 132.5 (CH_{Ar}), 137.1, 140.4, 141.8, 170.3, 192.8 (C). IR (KBr): $\tilde{\nu}$ = 3368, 3029, 2964 (w), 1650, 1593, 1568 (s), 1487,1448,1378, 1365, 1229, 1046, 930, 839 (m), 760, 728, 689 (s), 665, 621, 614 (m) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 326 (M^+, 5), 308 (9), 221 (27), 180 (100), 165 (10), 105 (29), 91 (2), 77 (9). HRMS (ESI): calcd. for $C_{23}H_{18}O_2$ $[M]^+$: 326.13013; found: 326.129947.

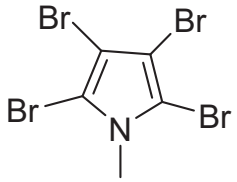
6-Methyl-2-(3-nitrophenyl)-2*H*-pyran-4(3*H*)-one (14m):



A THF Solution of LDA (25.0 mmol) was prepared by addition of nBuLi (10 mL, 25.0 mmol, 2.5 M solution in hexanes) to a THF solution (30 mL) of diisopropylamine (2.52 g, 25.0 mmol) at 0 °C. After stirring for 1h, the solution was cooled to -78 °C and pentane-2,4-dione **10a**

(1.00 g, 10 mmol) was added. After stirring for 1h at -78 °C, m-nitrobenzaldehyde **11i** (1.51 g, 10 mmol) was added and the solution was allowed to warm to 20 °C within 24h. Hydrochloric acid (10%, 25 ml) was added. The organic and aqueous layers were separated and organic layer was extracted with ethylacetate (3 x 50 ml). The combined organic layer was dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/ethyl acetate, 2:1) to give a **14m** as a brown crystalline solid (0.87 g, 75%), mp 71-73 °C. ^{1}H NMR 300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 2.67 (d, 2 H, *J* = 6.6 Hz), 5.19 (t, 1H, CH, *J* = 6.6 Hz), 7.46 (t, 1 H, CH_{Ar} , *J* = 7.9 Hz), 7.65 (d, 1H, CH_{Ar} , *J* = 7.9 Hz), 8.05-8.20 (m, 2H, CH_{Ar}) ^{13}C NMR (250 MHz, $CDCl_3$): δ = 21.0, (CH_3), 42.3 (CH_2), 79.3, 100.8, 105.6 (CH), 119.2 (C) 127.4 (CH_{Ar}), 157.3, 145.1, 173.8, 191.0 (C). IR (KBr): $\tilde{\nu}$ = 3073, 2971, 2837 (w), 1655, 1603, 1583 (s), 1508, 1461, 1439 (m), 1158 (s), 1031, 1020 (m), 991, 827, 804 (s) cm^{-1} MS (EI, 70 eV): *m/z* (%) = 234 (M^+, 6), 176 (11), 174 (6), 152 (25), 150 (22), 100 (58), 91 (8), 85 (100), 77 (29). HRMS (EI): calcd. for $C_{12}H_{11}O_4N[M]^+$: 233.06826; found: 233.067874.

2,3,4,5-tetrabromo-1-methylpyrrole (25):

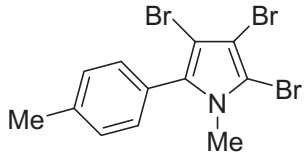


To a THF solution (700 mL) of *N*-methylpyrrole (40.5 g, 44.5 mL, 0.5 mol) was added *N*-bromosuccinimide (504 g, 2.5 mol) at 78 °C and the solution was stirred at this temperature for 8 h. To the mixture was added n-heptane (500 mL) and the tetrahydrofuran was subsequently removed under reduced pressure to give a colourless precipitate of succinimide. The precipitate was filtered off and the solvent of the filtrate was removed in vacuo. To the residue was added a saturated aqueous solution of NaOH and the solution was heated under reflux for 6 h. The aqueous layer and the organic layer were separated. The latter was dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was recrystallized from a 1:1-solution of chloroform and methanol at 18 °C. The crude product (in the form of yellow crystals) was washed with very cold ethyl acetate for several times to give **25** as colourless crystals (174.7 g, 88%), mp = 154–156 °C. 1H NMR (250 MHz, $CDCl_3$): d = 3.65 (s, CH_3). ^{13}C

NMR (75 MHz, $CDCl_3$): d = 37.0 (CH_3), 101.0, 103.5 (CBr). IR (KBr, cm^{-1}): 2940 (w), 2862 (w), 2833 (w), 2664 (w), 1492 (m), 1451 (m), 1311 (m), 1079 (m), 988 (w), 861 (w).

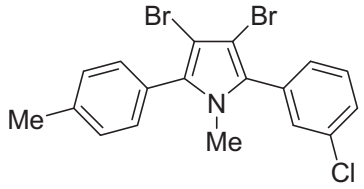
General procedure for synthesis of 3,4-dibromo-2,5-diaryl-1-methylpyrroles: To a solution (4 mL) of **25** (0.199 g, 0.5 mmol) was added $Pd(PPh_3)_4$ (0.058 g, 10 mol %) at 20 °C under argon atmosphere. After stirring for 30 min, the arylboronic **(a-d)** acid (1.25 mmol per Br), K_3PO_4 (4.0 mmol) and water (1.0 mL) were added. The mixture was stirred under reflux for 24 h. After cooling to 20 °C, the mixture was diluted with EtOAc, dried (Na_2SO_4), and filtered through a short Celite pad. The solution was concentrated in vacuo and the residue was purified by flash column chromatography (fine flash silica gel, n-heptane) and subsequent chromatotron chromatography (Marrison Research, ser. no. Y63, n-heptane).

Synthesis of 5-(4-methylphenyl)-2,3,4-tribromo-1-methylpyrrole (26):



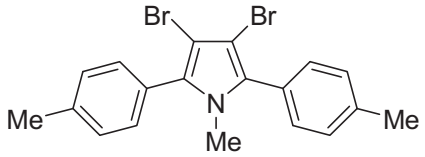
Starting with **25** (0.199 g, 0.5 mmol) and 4-methylphenyl boronic acid (0.075 g, 1.1 mmol), **26** was isolated (0.164 g, 81%) as a white solid, mp 161–163 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, CH_3), 3.47 (s, 3 H, pyrrole-CH_3), 7.21, 7.25 (d, ^3J = 8.2 Hz, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.4 (CH_3), 35.7 (pyrrole-CH_3), 98.0, 101.1, 104.2 (CBr), 129.3, 130.1 (2 CH, Ar), 127.6, 133.7, 138.8 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1702 (w), 1490 (w), 1459 (w), 1373 (w), 1320 (m), 1183 (w), 1112 (w), 1087 (w), 1016 (w), 974 (w), 819 (s), 7.65 (w), 715 (w), 606 (m). MS (EI, 70 eV): *m/z* (%) = 411 (M^+, [^{81}Br,^{81}Br,^{81}Br], 29), 409 (M^+, [^{81}Br,^{81}Br,^{79}Br], 97), 407 (M^+, [^{81}Br,^{79}Br,^{79}Br], 100), 405 (M^+, [^{79}Br,^{79}Br,^{79}Br], 30). HRMS (EI, 70 eV): calcd for $C_{12}H_{10}Br_3N$ (M^+, [^{81}Br ,^{81}Br ,^{81}Br]): 410.82965; found: 410.82950; (M^+, [^{81}Br, ^{81}Br, ^{79}Br]): 408.83170; found: 408.93132; (M^+, [^{81}Br, ^{79}Br, ^{79}Br]): 406.83374; found: 406.83334.

Synthesis of 3,4-dibromo-2-(3-chlorophenyl)-5-(4-tolyl)-1-methylpyrrole (27):



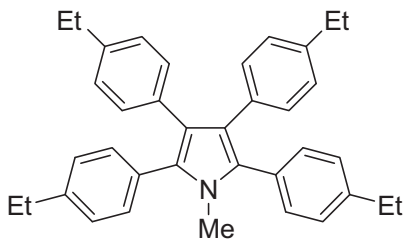
Starting with **26** (0.199 g, 0.5 mmol) and 3-chlorophenyl boronic acid (0.087 g, 1.1 mmol), **27** was isolated (0.098 g, 51%) as a brown solid, mp 97–99 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.39 (s, 3 H, CH_3), 3.53 (s, 3 H, pyrrole-CH_3), 6.79, 7.05 (d, ^{3}J = 8.2 Hz, 2 H, Ar), 7.16 (t, ^{3}J = 8.2 Hz, 1 H, Ar), 7.25 (s, 1 H, Ar), 7.30 (d, ^{3}J = 8.2 Hz, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (CH_3), 33.7 (pyrrole-CH_3), 113.7, 113.9 (CBr), 121.8 (C-pyrrole, overlap), 129.7, 131.5 (2CH, Ar), 128.5, 128.8, 129.7, 130.5 (CH, Ar), 132.0, 134.4, 135.7, 136.0, 156.3 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 2919 (m), 2844 (w), 1660 (m), 1589 (s), 1561 (m), 1509 (s), 1420 (m), 1299 (m), 1249 (s), 1163 (s), 1020 (s), 802 (s), 765 (m), 690 (m). MS (EI, 70 eV): *m/z* (%) = 443 (M^+, [^{81}Br,^{81}Br,^{37}Cl]], 9), 441 (M^+, [^{81}Br,^{79}Br,^{37}Cl], 100), 439 (M^+, [^{79}Br,^{79}Br,^{37}Cl], 41), 437 (M^+, [^{79}Br,^{79}Br,^{35}Cl], 31). HRMS (EI, 70 eV): calcd for $C_{18}H_{14}Br_2ClN$ (M^+, [^{79}Br,^{79}Br,^{37}Cl]): 438.91611, found: 438.91600; (M^+, [^{79}Br,^{79}Br,^{35}Cl]): 436.57146; found: 436.57135.

Synthesis of 3,4-dibromo-2,5-di(4-tolyl)-1-methylpyrrole (28d):



Starting with **25** (0.199 g, 0.5 mmol) and 4-tolyl boronic acid (0.170 g, 2.5 mmol), **28d** was isolated (0.166 g, 79%) as a colourless solid, mp 145–150 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.32 (s, 6 H, $2CH_3$), 3.26 (s, 3 H, pyrrole-CH_3), 7.15, 7.20 (d, ^{3}J = 8.2 Hz, 4 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 34.5 (pyrrole-CH_3), 100.0 (CBr), 129.3, 130.4 (4CH, Ar), 128.8 (C-pyrrole), 133.0, 138.8 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1920 (w), 1910 (w), 1549 (w), 1535 (w), 1493 (m), 1445 (w), 1318 (m), 1222 (w), 1114 (w), 1020 (w), 973 (w), 825 (m), 802 (m), 770 (w), 726 (w). MS (EI, 70 eV): *m/z* (%) = 421 (M^+, [^{81}Br,^{81}Br], 50), 419 (M^+, [^{81}Br,^{79}Br], 100), 417 (M^+, [^{79}Br,^{79}Br], 52), 244 (11). HRMS (EI, 70 eV): calcd for $C_{19}H_{17}Br_2N$ (M^+, [^{79}Br,^{79}Br]): 416.97228; found: 416.97225.

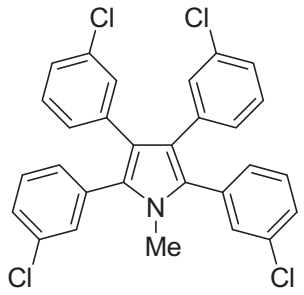
Synthesis of tetra(4-ethoxyphenyl)-1-methylpyrrole (29a):



Starting with **25** (0.199 g, 0.5 mmol) and 4-ethoxyphenylboronic acid (0.374 g, 5 mmol), **29a** was

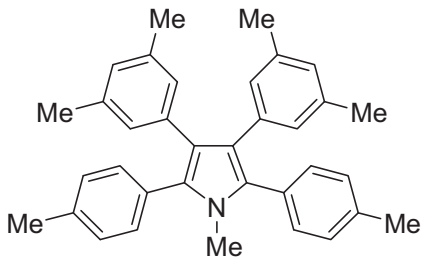
isolated (0.191 g, 78%) as a yellow solid, mp 169–171 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.09, 1.18 (t, ^{3}J = 7.2 Hz, 6 H, $2CH_3$), 2.45, 2.60 (q, ^{3}J = 7.2 Hz, 4 H, $2OCH_2CH_3$), 3.32 (3 H, pyrrole-CH_3), 6.80 (m, 8 H, Ar), 7.09, 1.18 (d, ^{3}J = 8.2 Hz, 4 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0, 15.2 (CH_3), 28.3, 28.5 (CH_2), 33.0 (pyrrole-CH_3), 126.8, 127.5, 130.7, 131.3 (4 CH, Ar), 121.8, 130.3, 131.7, 133.0, 140.4, 142.9 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2962 (m), 2929 (m), 2871 (w), 1704 (m), 1683 (m), 1604 (m), 1508 (m), 1454 (m), 1413 (m), 1356 (m), 1261 (m), 1175 (m), 1085 (m), 1008 (m), 821 (s). MS (EI, 70 eV): *m/z* (%) = 497 (M^+, 100), 411 (5), 369 (4), 299 (2), 91 (14). HRMS (EI, 70 eV): calcd for $C_{37}H_{39}N$ (M^+): 497.30825; found: 497.30813.

Synthesis of 3,4-dibromo-2,5-di(4-chlorophenyl)-1-methylpyrrole (29b):



Starting with **25** (0.199 g, 0.5 mmol) and 4-chlorophenyl boronic acid (0.34 g, 5 mmol), **29b** was isolated (0.149 g, 57%) as a brown solid, mp 165–167 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.43 (s, 3 H, CH_3), 6.74, 7.08 (t, ^{3}J = 8.2 Hz, 1 H, Ar), 6.93, 6.96, 7.06, 7.24 (d, ^{3}J = 8.2 Hz, 2 H, Ar), 6.84, 7.22 (s, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.1 (CH_3), 126.0, 128.0, 128.88, 128.9, 129.4, 129.6, 130.5, 131.0 (2 CH, Ar), 121.5, 131.0, 133.4, 133.7, 134.2, 136.7 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2966 (w), 1925 (w), 1924 (w), 1551 (w), 1529 (w), 1459 (m), 1428 (w), 1351 (m), 1252 (w), 1129 (w), 1010 (w), 971 (w), 820 (m), 814 (m), 771 (w), 709 (w). MS (EI, 70 eV): *m/z* (%) = 529 (M^+, [^{37}Cl,^{37}Cl,^{37}Cl,^{37}Cl], 11), 527 (M^+, [^{35}Cl,^{37}Cl,^{37}Cl,^{37}Cl], 23), 525 (M^+, [^{35}Cl,^{35}Cl,^{37}Cl,^{37}Cl], 100), 523 (M^+, [^{35}Cl,^{35}Cl,^{35}Cl,^{37}Cl], 51), 521 (M^+, [^{35}Cl,^{35}Cl,^{35}Cl,^{35}Cl], 19). HRMS (EI, 70 eV): calcd for $C_{29}H_{19}Cl_4N$ (M^+, [^{35}Cl,^{35}Cl,^{35}Cl,^{37}Cl]): 523.02421; found: 523.02412; (M^+, [^{35}Cl,^{35}Cl,^{35}Cl,^{35}Cl]): 521.02716; found: 521.02707.

Synthesis of 2,5-ditolyl-3,4-di(3,5-dimethylphenyl)-1-methylpyrrole (29c):



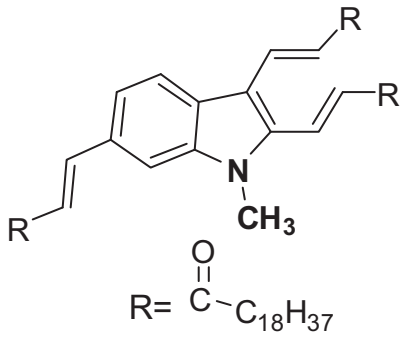
Starting with **25** (0.209 g, 0.5 mmol) and tolylboronic acid (0.34 g, 5 mmol), **29c** was isolated as a yellow

solid (0.199 g, 85%), mp 165–170 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.00 (12 H, CH_3), 2.29 (6 H, CH_3), 3.32 (pyrrole-CH_3), 6.61 (s, 4 H, Ar), 6.69 (s, 2 H, Ar), 7.04, 7.12 (d, ^{3}J = 8.2 Hz, 4 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3, 33.0 (CH_3), 33.7 (pyrrole-CH_3), 126.8 (2 CH, Ar), 128.7, 129.1, 131.2 (4 CH, Ar), 122.1, 130.6, 132.3, 136.2, 136.4, 136.6 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2915 (w), 2859 (w), 1599 (m), 1505 (w), 1449 (w), 1351 (w), 1228 (w), 1111 (w), 1037 (w), 1017 (w), 851 (m), 818 (s), 732 (m), 712 (m), 700 (m), 672 (m). MS (EI, 70 eV): *m/z* (%) = 469 (M^+, 100), 439 (5), 365 (54), 132 (5), 119 (17). HRMS (EI, 70 eV): calcd for $C_{35}H_{35}N$ (M^+): 469.27640; found: 469.27696.

Synthesis of 2,3-dibromo-*N*-methylindole (16). To a THF solution (20 mL) of *N*-methylindole **15** (1.0 mL, 8.0 mmol) was portionwise added NBS (3.30 g, 18.4 mmol) at – 78 ˚C and the solution was stirred at this temperature for 4 h. To the solution was added water (25 mL). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$, dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash silica column chromatography (pure heptanes) to yield **16** as a colourless solid (1.83 g, 90%).

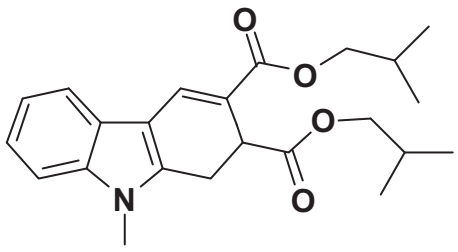
General procedure for Heck cross-coupling reactions. In a pressure tube (glass bomb), a suspension of $Pd(OAc)_2$ (0.012 g, 0.05 mmol, 1.25 mol% per Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl) phosphine (**L**) (0.041 g, 0.10 mmol) in DMF (5 mL) was purged with argon and stirred at 20 °C to get a yellowish or brownish transparent solution. To the stirred solution were added the brominated indole **16, 17** (1.0 mmol), NEt_3 (1.1 mL, 8.0 mmol) and the acrylate (1.25 equiv. per Br). The reaction mixture was stirred at 120 ˚C for 48 h. The solution was cooled to 20 °C, poured into H_2O and CH_2Cl_2 (25 mL each), and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with H_2O (3 x 20 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes/EtOAc).

(2E,2'E,2''E)-Trioctadecyl 3,3',3''-(1-methyl-1*H*-indole-2,3,6-triyl)triacrylate (22):



Starting with suspension of $Pd(OAc)_2$ (0.018 g, 0.05 mmol, 1.25 mol% per Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl) phosphine (**L**) (0.061 g, 0.10 mmol) in DMF (5 mL), brominated indole **17** (367mg, 1.00mmol) was added to stirred solution and heated for 48 h. Reaction mixture was cooled, extraced and purified as yellow oil (0.687 g, 64%).[1]H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, 9H, $3CH_3$), 1.18 (m, 102H, $51CH_2$), 3.62 (s, 3H, CH_3O), 3.75 (s, 3H, OCH_3), 3.79 (s, 3H, CH_3N), 3.82 (s, 3H, CH_3O), 6.24 (d, 1 H, J = 16.1 Hz), 6.43 (d, 1 H, J = 15.9 Hz), 6.42 (d, 1 H, J = 15.9 Hz), 7.23-7.43(m, 2H, ArH), 7.72 (d, 1H, J = 15.9 Hz), 7.83 (d, 1H, J = 16.2 Hz), 7.88 (dd, 1H, J = 1.3, 7.5 Hz, ArH), 7.95 (d, 1H, J = 15.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 ($3CH_3$), 22.6 (CH2), 28.4-29.6 (CH2), 32.8 (CH_3CN), 63.9, 64.6, 65.2 (CH_3O), 108.7 (C), 110.5, 114.2, 115.3, 117.3, 121.3, 123.0 (CH), 125.4 (C), 128.9 (CH), 129.0 (C), 134.2 (CH), 138.3, 139.0 (C), 144.8 (CH), 166.0, 167.1, 167.7 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 1097 (M^+,9), 801 (2), 575 (7), 228 (4), 189 (5), 97 (21), 69 (27), 44 (100); HRMS (ESI-TOF): *m*/*z* calcd for $C_{72}H_{123}NO_6$ $[M]^+$: 1097.93504; found: 1097.935219.

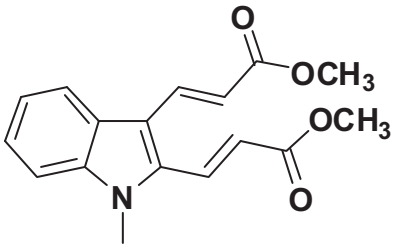
3-(Bis(4-fluorophenyl)methyl)pentane-2,4-dione (19):



Starting with suspension of $Pd(OAc)_2$ (12 mg, 0.05 mmol, 1.25 mol% per Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl) phosphine (**L**) (41 mg, 0.10 mmol) in DMF (5 mL), brominated indole **16** (288 mg, 1.00mmol) was added to stirred solution and heated for 48 h. Reaction mixture was cooled, extraced and purified as yellow oil (0.229 g, 66%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.73 (d, 6H, $2CH_3$), 0.90 (m, 2H, CH), 3.0 (dd, 1 H_α, J = 8.5, 17.3 Hz, C(1)); 3.68 (d, 2H, CH_2O), 3.72 (d, 2H, OCH_2), 3.96 (s, 3H, CH_3N), 4.05 (dd, 1 H_α, J = 2.4, 8.8 Hz C(2)),

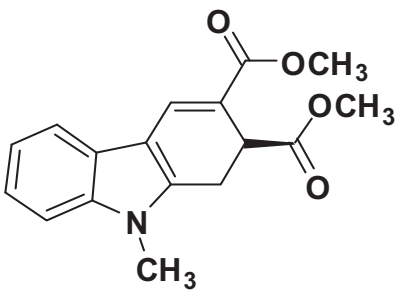
6.43 (d, 1 H, *J* = 16.1 Hz), 7.2-7.4 (m, 2H, ArH), 7.7 (d, 1H, *J* = 15.9 Hz), 7.8 (d, 1H, *J* = 16.2 Hz), 7.8 (dd, 1H, *J* = 1.3, 7.5 Hz, ArH), 7.9 (d, 1H, *J* = 15.9 Hz); ^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.0 (CH_2), 29.7 (C(4)H), 38.7 (CH_3N); 51.6 (CH_3O), 51.8(CH_3O), 52.6(CH_3O), 108.7, 110.4(CH), 114.6, 115.9(CH), 117.3, 120.0CH), 125.8, 127.4, 131.0(CH), 137.2, 141.0, 145.0(CH), 166.5, 166.8, 172.5. IR (KBr): $\tilde{\nu}$= 2958, 2927, 2872 (w), 1727, 1464, 1263, 1194, 1158 (m), 1029, 1010 (m), 737 (s), 711, 660, 573 (w) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%) = 383 (M^+, 60), 309 (21), 282 (54), 226 (100), 208 (80), 182 (77), 167 (22); HRMS: *m/z* calcd for $C_{21}H_{21}NO_6$ $[M]^+$: 383.13634; found: 383.136265

Dimethyl 3,3'-(1-methyl-1*H*-indole-2,3-diyl)diacrylate (20a):



Starting with suspension of $Pd(OAc)_2$ (0.012 g, 0.05 mmol, 1.25 mol% per Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl) phosphine (**L**) (41 mg, 0.10 mmol) in DMF (5 mL), brominated indole **16** (0.288 g, 1.00mmol) was added to stirred solution and heated for 48 h. Reaction mixture was cooled, extraced and purified as yellow oil (0.231 g, 77%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.53 (s, 3H, CH_3O), 3.75 (s, 3H, OCH_3), 3.78 (s, 3H, CH_3N), 6.05 (d, 1 H, *J* = 12.5 Hz), 6.19 (d, 1 H, *J* = 12.8 Hz), 6.25 (d, 1 H, *J* = 15.9 Hz), 6.49 (d, 1 H, *J* = 15.8 Hz), 6.8-7.3(m, 3H, ArH), 7.70(d, 1H, ArH), 7.82 (d, 1H, *J* = 16.6 Hz), 7.93 (d, 1H, *J* = 16.6 Hz) ^{13}C NMR (62 MHz, $CDCl_3$): δ = 30.6, 31.2 (CH_3CN), 51.3, 51.5 (CH_3O), 109.7 (C), 110.0, 116.1, 120.2, 120.8 (CH), 124.2 (C), 131.3 (CH), 135.6 (CH), 136.3, 137.1 (C), 143.2 (CH), 166.4, 168.2 (CO). IR (KBr): $\tilde{\nu}$= 2948, 2841 (w), 1702, 1618, 1433 (s), 1410, 1372, 1341 (m), 1269, 1190, 1165, 1132 (s), 1035, 1013, 967 (m), 739 (s), 648, 560 (w) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%) = 299 (M^+, 60), 240 (67), 209 (64), 181 (100), 120 (32), 77 (19), 41 (19); HRMS (ESI-TOF): *m/z* calcd for $C_{17}H_{17}NO_4$ $[M+H]^+$: 300.12303; found: 383.12291.

Dimethyl 9-methyl-2,9-dihydro-1*H*-carbazole-2,3-dicarboxylate (20b):



Starting with suspension of $Pd(OAc)_2$ (0.012 g, 0.05 mmol, 1.25 mol% per Br) and dicyclohexyl (2',6'-dimethoxybiphenyl-2-yl) phosphine (**L**) (0.041 g, 0.10 mmol) in DMF (5 mL), brominated indole **16** (0.288 g, 1.00mmol) was added to stirred solution and heated for 48 h. Reaction mixture was cooled, extraced and purified as yellow oil (0.212 g, 69%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.99 (dd, 1 H_α, J = 8.6, 17.0 Hz, C(1)); 3.52 (s, 3H, CH_3N), 3.63 (s, 3H, CH_3O); 3.76 (s, 3H, CH_3O), 4.01 (dd, 1 H_β, J = 2.4, 8.7 Hz, C(1)), 7.08-7.22 (m, 4H, ArH), 7.92 (s, 1 H, C(4)); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 23.9 (CH_2), 29.8 (C(4)H), 38.8 (CH_3N); 51.6 (CH_3O), 52.5 (CH_3O), 109.3, 109.6 (CH), 115.7, 117.9 (CH), 117.3, 121.0, 121.9 (CH), 125.1 (C), 132.7 (CH), 138.0, 139.8 (C), 167.7, 173.8 (CO). IR (KBr): $\tilde{\nu}$ = 2949, 2845 (w), 1720, 1692 (s), 1605, 1524, 1467, 1434, 1270 (m), 1234, 1241, 1191 (s), 1048, 750 (m) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 299 (M^+, 58), 268 (6), 240 (73), 208 (92), 181 (100), 152 (31), 104 (5), 76 (22); HRMS: *m/z* calcd for $C_{17}H_{17}NO_4$ $[M+H]^+$ 300.12303; found: 300.122761.

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Table 1. Crystal data and structure refinement for 26

Identification code	av_tung2	
Empirical formula	$C_{12}H_{10}Br_3N$	
Formula weight	407.94	
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 = 7.4990(15) Å	α= 90.46(3)°.
	b = 8.9820(18) Å	β= 97.43(3)°.
	c = 9.4260(19) Å	γ = 97.12(3)°.
Volume	624.5(2) $Å^3$	
Z	2	
Density (calculated)	2.169 Mg/m^3	
Absorption coefficient	9.660 mm^{-1}	
F(000)	388	
Crystal size	0.30 x 0.20 x 0.11 mm^3	
Θ range for data collection	2.29 to 33.74°.	
Index ranges	$-11\leq h\leq 11$, $-13\leq k\leq 12$, $-13\leq l\leq 14$	
Reflections collected	10215	
Independent reflections	4078 [R(int) = 0.0250]	
Completeness to Θ = 29.82°	81.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.1597 and 0.4163	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3475 / 0 / 153	
Goodness-of-fit on F^2	1.054	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0238, wR2 = 0.0561	
R indices (all data)	R1 = 0.0312, wR2 = 0.0576	
Largest diff. peak and hole	0.668 and -0.571 $e.Å^{-3}$	

Table 2. Crystal data and structure refinement for 14a

Identification code	ra164	
Empirical formula	$C_{12}H_{12}O_2$	
Formula weight	188.22	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 4.8646(3) Å	α= 90°.
	b = 9.5579(6) Å	β= 91.934(3)°.
	c = 20.8639(13) Å	γ = 90°.
Volume	969.52(10) $Å^3$	
Z	4	
Density (calculated)	1.289 Mg/m^3	
Absorption coefficient	0.087 mm^{-1}	
F(000)	400	
Crystal size	0.55 x 0.24 x 0.17 mm^3	
Θ range for data collection	2.34 to 29.99°.	
Index ranges	$-6\leq h\leq 6$, $-12\leq k\leq 13$, $-29\leq l\leq 29$	
Reflections collected	12701	
Independent reflections	2809 [R(int) = 0.0291]	
Completeness to Θ = 29.99°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9855 and 0.9540	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2809 / 0 / 133	
Goodness-of-fit on F^2	1.042	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0493, wR2 = 0.1277	
R indices (all data)	R1 = 0.0598, wR2 = 0.1373	
Largest diff. peak and hole	0.948 and -0.327 $e.Å^{-3}$	

Curriculum vitae

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Academics:

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Publications:

1. ***Rasheed Ahmad***, Rasheed Ahmad Khera, Alexander Villinger, Peter Langer*, ***Tetrahedron Lett.* 2009**, accepted. "One-pot synthesis of 2,3-dihydro-4*H*-pyran-4-ones by cyclocondensation of 1,3-diketone dianions with aldehydes".

2. ***Rasheed Ahmad***, Abdolmajid Riahi, Peter Langer*, ***Tetrahedron Lett.*** 2009, *50*, 1419-1492. "Synthesis of functionalized triarylmethanes based on a '$FeCl_3$-catalyzed benzylation/[3+3] cyclocondensation' strategy".

3. Tung Thanh Dang, ***Rasheed Ahmad***, Tuan Thanh Dang, Helmut Reinke, Peter Langer. ***Tetrahedron Lett.*** 2008, *49*, 1698. "Regioselective Suzuki Cross-Coupling Reactions of 2,3,4,5-Tetrabromo-1-methylpyrrole**".**

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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 in the form of a private viva voce and a public presentation.

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Rasheed Ahmad