STUDIES ON THE SYNTHESIS OF EXTENDED $\pi$-SYSTEMS:
WILLGERODT-KINDLER DOMINO ANNULATION
AND
$S_NAr$-REACTIONS

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Abstract

A domino annulation process under Willgerodt-Kindler conditions, which transforms a butanone side chain of arene and hetarenes into at least tricyclic annulated thieno(3,2-b)thiophenes with yields in the range of 7 to 46%. The resulting main product depends on the experimental conditions. Moreover, we have examined a variety of substrates under various reaction conditions for thionation. In some cases thionation was better achieved with Lawessons reagent. Further studies about the Willgerodt-Kindler reaction and annulation of new substrates are now in progress. The reaction of a multidentate thioamide with AuCl₃ afforded a gold(III)complex.

Triarylmethylium salts with a sterically shielded cationic center reacted with selected C-nucleophiles under nucleophilic aromatic substitution. The resulting dipolar para-quinoid final products represent highly functionlized extended π-systems. LDA, arylmagnesium and alkyllithium as sterically hindered bases (and nucleophiles at the same time) also reacted with triarylmethylium salts. We obtained dimerization products through coupling of intermediary trityl radicals. Both, symmetrical and quaternary centered dimers were found. Our results represent a straightforward and efficent access to polar p-quinoid compounds, useful for the construction of extended π–systems.
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ABBREVIATIONS

Å    Angstrom (= 0.1 nm)
Abs  Absolutely
Ac   Acetyl
Ar   Aryl
Bu   n-Butyl
br   broad
°C   Temperature in degrees Centigrade
Cat. Catalyst
Conc. Concentrate
COSY Correlated Spectroscopy
calcd Calculate
d   Day
distn Distillation
DMSO Dimethylsulfoxide
DMF  N,N-Dimethylformamide
EI   Electron-Ionization
eq.  Equivalent
Et   Ethyl
eV   Electronvolt
g   gram
h   hour
HMBC Heteronuclear Multiple Bond Correlation
HMQC Heteronuclear Multiple Quantum Coherence
HPLC High Pressure Liquid Chromatography
HRMS High Resolution Mass Spectroscopy
Hz   Hertz
i   Iso
IR   Infrared
J   Coupling constant
L   Liter
LR   Lawessons reagent
Lit. Literature
LDA Lithium diisopropylamide
m  Meta
M  Molecule
M⁺  Molecule ion peak
Me  Methyl
min  Minute
mmol  Millimole
MS  Mass Spectroscopy
mp  Melting point
MTBE  Methyl-tert-butylether
n  Normal
NBS  N-bromosuccinimide
NMR  Nuclear magnetic resonance
NOE  Nuclear Overhauser
NOESY  Nuclear Overhauser effect spectroscopy
O  Othro
p  Para
PE  Petroether
Ph  Phenyl
ppm  Parts per million
Pr  Propyl
RT  Room temperature
TEA  Triethylamine
THF  Tetrahydrofuran
tert  Tertiary
TMEDA  Tetramethylethylenediamine
pTSOH  p-Toluenesulfonic acid
UV  Ultraviolet
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I. THEORETICAL PART
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1.1 Introduction

The organic chemistry of sulfur is based on numerous stable functional groups with sulfur in various oxidation states. It is a very large and currently highly active field, interesting for its theoretical implications and for the diversity of its synthetic applications. Compounds with carbon-sulfur bonds are useful chemical intermediates. Carbon-sulfur bonds are found in many molecules of biological pharmaceutical and materials interest. Therefore sulfur chemistry has become essential in many fields such as pharmaceutical chemistry and industrial chemistry.\[^{[1]}\]

The formation of carbon-sulfur bonds is usually achieved by the reaction of sulfur at high temperature with organic compounds. We have studied the reaction of sulphur in the presence of a secondary amine with organic compounds having reactive groups, particular with a carbonyl and an alkyl group, a transformation which is known as the Willgerodt-Kindler reaction. The Willgerodt reaction was first discovered by Conrad Willgerodt in 1887\[^{[2]}\] and converts aryl alkyl ketones $1$ to terminal amides $2$ and to ammonium salts $3$, respectively, applying yellow ammonium sulphide as reagent. The number of carbon atoms remains constant throughout the process (Scheme 1). Obviously a migration of the carbonyl functionality has taken place, driven by complex redox processes\[^{[3]}\].

\[
\begin{align*}
\text{Ph}-(\text{CH}_2)_n-\text{CH}_3 & \quad \xrightarrow{\text{(NH}_4\text{)}_2\text{S}_x, \text{H}_2\text{O}} \quad \text{Ph}(\text{CH}_2)_n-\text{CO} \equiv \text{NH}_2 \\
\text{Ph}(\text{CH}_2)_n-\text{CO}^- \quad & \quad + \quad \text{Ph}(\text{CH}_2)_n-\text{CO}^- \equiv \text{NH}_4^+
\end{align*}
\]

Scheme 1: Willgerodt reaction of aryl alkyl ketones.
Scheme 2: Willgerodt-Kindler reaction of phenyl methyl ketone (4).

When the alkyl group is an aliphatic chain (n typically 0 to 5), multiple reaction steps always give the terminal thioamide as a result of oxidation and rearrangement (Scheme 2).[4] The Willgerodt reaction has a wide scope and can be conducted with a variety of substrates and modified reagents. Karl Kindler suggested a modification of Willgerodt’s procedure - with sulfur and an amine I - such as morpholine - as reagents, which leads to the formation of thioamides as final products. This reaction is nowadays called Willgerodt-Kindler reaction and has significantly increased the synthetic scope of this type of process. The Willgerodt-Kindler reaction has been extended from the original alkyl aryl ketones as substrates to aldehydes, hydrocarbons, amines, imines and numerous other compounds. Recently, our research group became interested in studying domino processes under Willgerodt-Kindler conditions as a powerful method for CH-tranformation[5,6] Neckers et al.[7] reported that the reaction of the acetyl-substituted substrate 7 with modified reagents (sulfur, DMF and an amine) resulted in the formation of functionalized arenes to benzothiophenes 8

Scheme 3: Mono-annulation reaction under Willgerodt-Kindler conditions according to Neckers et al.[6]
Obviously, the acetyl group undergoes several redox steps, finally ending up as C₂-unit within the thiophene moiety after an intermolecular nucleophilic aromatic substitution with an intermediary thiolate as key step. In continuation of our independent investigation on this type of reaction, we have started a project to study a variety of arenes and heteroarenes which are transformed to annulated ring systems in a domino redox process under Willgerodt-Kindler conditions. This domino annulation reaction, which oxidatively transforms up to 6 CH bonds, is giving rise to tri- and tetracyclic ring systems with thieno[3,2-b]thiophene moieties. The resulting main product depends on the experimental conditions. Mechanistic pathways to the various reaction products are proposed.

1.2 Literature Reviews

The synthesis of thioamides has been reviewed many times. In 1975, Ellis V. Brown reported on the Willgerodt-Kindler reaction from a synthetic standpoint, including types of various compounds for starting material and conditions of operation. The Kindler modification and its usefulness was also indicated. The behavior of heterocyclic compounds in the reaction was mentioned, followed by a number of interesting special compounds prepared. The results obtained by applying the reaction conditions to cyclic ketones were covered. Various examples were recorded in the overviews. Some of these with general character are listed below.

**Willgerodt reaction of ketones:**

\[
\begin{align*}
\text{O} & \quad \text{S / NH}_4\text{OH} \quad \text{NH}_2 \\
\text{4} & \quad \text{31 \% Yield} \\
\end{align*}
\]
Willgerodt reaction of aldehydes and acetals:

10 \[ \text{C}=\text{H} \] \[ \text{S} / \text{NH}_4\text{OH} \] \[ \text{C} \] \[ \text{NH}_2 \] \[ 75 \% \text{ Yield} \]

12 \[ \text{OCH}_3 \text{CH}_2 \text{OCH}_3 \] \[ \text{S} / \text{NH}_4\text{OH} \] \[ \text{O} \] \[ \text{NH}_2 \] \[ 80 \% \text{ Yield} \]

Willgerodt reaction of unsaturated hydrocarbons:

14 \[ \text{C}=\text{C} - \text{CH}_3 \] \[ \text{S} / \text{NH}_4\text{OH} \] \[ \text{CH}_3 \text{C}=\text{CH}_2\text{CO-NH}_2 \] \[ 75 \% \text{ Yield} \]

16 \[ \text{C}=\text{CH} - \text{CH}_2 \] \[ \text{S} / \text{NH}_4\text{OH} \] \[ \text{C} \] \[ \text{CO} \] \[ \text{NH}_2 \] \[ 24 \% \text{ Yield} \]
Willgerodt reaction of aromatic hydrocarbons:

\[
\text{phenyl} \quad \xrightarrow{S / \text{NH}_4\text{OH}} \quad \text{CO-NH}_2
\]

20 % Yield

Thiomorpholides from ketones via the Willgerodt-Kindler reaction.

\[
\text{phenyl ketone} \quad \xrightarrow{S / \text{H-N-O}} \quad \text{N-S-S-N}
\]

72 % Yield

\[
\text{bromo phenyl ketone} \quad \xrightarrow{S / \text{H-N-O}} \quad \text{N-S-S-N}
\]

10 % Yield

\[
\text{nitro phenyl ketone} \quad \xrightarrow{S / \text{H-N-O}} \quad \text{N-S-S-N}
\]

7 % Yield
Dimethylthioamides from ketones via the Willgerodt-Kindler reaction:
In 2004, Darabi et al.\cite{10} reported, that the Willgerodt-Kindler reaction of acetone with sulfur and morpholine gives selectively one of the products $29$, $30$, $31$, $32$ depending upon the proper choice of the reaction conditions.

![Chemical structures of 29, 30, 31, 32](image)

In 2007, Okamodo et al.\cite{11} reported that Willgerodt-Kindler reactions between anilines and benzaldehydes readily proceed in the presence of catalytic amounts of Na$_2$S·9H$_2$O to give thiobenzanilides in moderate to good yield. The base catalyst was also available for preparation of primary thiobenzamide and was applicable for the preparation of various thiobenzanilides. The reaction of aromatic amines and aryl aldehydes with Na$_2$S·9H$_2$O in the presence of sulfur under the condition of the conventional Willgerodt-Kindler reaction afforded the corresponding products as listed below.

![Chemical reactions and yields](image)
1.3 Goal of the Research Project

1. The aim of this research is to study domino processes under Willgerodt-Kindler conditions.
2. In the focus of this research is the synthesis of annulated ring systems by Willgerodt-Kindler reactions with functionalized aryl ketones as staring materials.
3. The butanone 42 and the hexanone 44 were chosen as model compounds for domino annulation processes under Willgerodt-Kindler conditions.
4. Scope and limitations of Willgerodt-Kindler domino annulation reactions should be examined.
5. Mechanistic details of the domino annulation process should be investigated.

1.4 Results and Discussion

We started the synthesis of model compound 4-chloro-3-(3-oxobutyl)benzonitrile (42a) by oxidative iodination of 4-chlorobenzonitrile (39) with H₂SO₄, H₂O, NaIO₄ and KI as reagents to give aryl iodide 40 as a white solid in 68% yield; since the cyano group had

Scheme 4: The sequence of reactions for the synthesis of 4-chloro-3-(3-oxobutyl)-benzonitrile (42a)
been hydrolyzed under the reaction conditions 40 had to be dehydrated back to nitrile 41a by a palladium-catalysed process: by using PdCl$_2$ in water/acetonitrile as solvent water was found to be formally transferred from the substrate to excess acetonitrile. This dehydration of the primary amide gave a satisfactory result: 41a was obtained as a brown solid in 34% yield, and reacted with allylic alcohol by a Heck-type reaction (Pd(OAc)$_2$, LiCl, Et$_3$N, DMF, 3 d at 120 °C ) to give aryIbutanone 42a as a yellow solid in 76% yield.

The mechanism of the Heck-type reaction of 41a with the allylic alcohol 43 is illustrated below.

L$_2$PdX$_2$ or Pd(0) precatalyst

\[
\text{41a} \xrightarrow{\text{Pd(0)}} \text{complex A} \xrightarrow{\text{Et}_3\text{N}} \text{complex C} \xrightarrow{\text{H}} \text{complex B} \xrightarrow{\text{OH}} \text{42a}
\]
**Preactivation**

The palladium(0) complex activates the organic halide by oxidation addition of the carbon-halogen bond. Thus, palladium(0) is needed for this reaction as the active catalyst. The oxidation of triphenylphosphine to triphenylphosphine oxide is one of several pathways to the formation of Pd(0) in *situ* by reduction of palladium(II) acetate (see below).\[12\]

\[
PPh_3 + \text{Pd(OAc)}_2 \xrightarrow{\text{ligand exchange}} PPh_3 \text{PdOAc} \]

\[
\text{AcO} \quad \text{PPh}_3
\]

\[
\text{PPh}_3 \text{O} \quad \text{PPh}_3 \text{PdOAc}
\]

\[
\text{Ph}_3\text{P} \quad \text{Ph}_3\text{OAc}
\]

Step 1. Oxidative addition; the aryl iodide (Ar = 2-chloro-5-cyanophenyl) reacts with the active palladium catalyst Pd(0)L₂ (generated from Pd(OAc)₂ by reduction with PPh₃) gives the active palladium(II) complex A, ArPd(OAc)₂I as a cis-trans isomer. Step 2. Olefin insertion; the reaction proceeds by insertion of the palladium(II) complex A into the terminal double bond of allylic alcohol to afford the complex B as intermediate. Step 3. β-hydride elimination; the palladium and hydride must be coplanar for the reaction to take place as the *syn*- elimination process is leading to the *trans*-double bond in the product. In this case, the subsequent isomerization of the allylic alcohol is particularly important as the conjugated enol is formed, finally tautomerizing zu give the carbonyl compound. Step 4; in the final step the palladium(II) complex C is released in a reductive elimination with regeneration of Pd(0).
As a typical example the $^1$H NMR spectrum of 4-chloro-3-(3-oxobutyl)benzonitrile (42a) is presented:

![NMR Spectrum Image]

**Figure 1**: $^1$H NMR spectrum of 4-(2-chloro-5-cyanophenyl)butan-2-one (42a)

Overall three aromatic protons could be detected as the singlet signal at $\delta_H$ 7.56 (1H) and as the singlet signal at $\delta_H$ 7.44 (2H). Two triplet signals at $\delta_H$ 2.78 and $\delta_H$ 3.02 were found for four protons of two methylene groups and the singlet signal at $\delta_H$ 2.17 was ascribed for three protons of the methyl group.

The synthesis of 4-(2-chloro-5-nitrophenyl)butan-2-one (42b) with nitro-functionality by Sandmeyer-type reaction of 2-chloro-5-nitro-1-benzaniline 44 was achieved with H$_2$SO$_4$, NaNO$_2$ and KI as reagents. The iodo functionality was introduced via the diazonium salt as intermediate to give compound 41b as yellow solid in 12% yield and reacted with allylic alcohol 43 in a Heck-type process to give arylbutanone 42b as slightly orange solid in 60% yield.
Scheme 5: The sequence of reactions for the synthesis of 4-(2-chloro-5-nitrophenyl) butan-2-one (42b).

Figure 2: $^1$H NMR spectrum of 4-(2-chloro-5-nitrophenyl)butan-2-one (42b)

Three aromatic protons could be detected as the doublet of doublets signal at $\delta_H$ 7.42 and as the doublet at $\delta_H$ 7.84 and “d” at $\delta_H$ 7.88. Two triplet signals at $\delta_H$ 3.25 and $\delta_H$ 3.89 were ascribed for eight protons of four methylene groups of morpholine, respectively. The synthesis of 4-(2-chloropyridine-3-yl)butan-2-one (42c) by Sandmeyer-type reaction of 3-amino-2-chloropyridine with NaNO$_2$, KI, MeCN, $p$-TsOH as reagents.
The iodo functionality was introduced via the diazonium salt as intermediate to give compound 41c as yellow solid in 32% yield. The reaction of 41c with allylic alcohol 43 in a Heck-type process to give 4-(2-chloropyridine-3-yl)butan-2-one (42c) as slightly yellow oil in 73% yield.

**Scheme 6:** The sequence of reactions for the synthesis of 4-(2-chloropyridine-3-yl)butan-2-one (42c)

![Scheme 6 Diagram](image)

**Figure 3:** $^1$H NMR spectrum of 4-(2-chloropyridine-3-yl)butan-2-one (42c).
The synthesis of 4-(4-chloropyridine-3-yl)-hexan-3-one (48d) by iodination of 4-hydroxy-pyridine (46) succeeded in the presence of base, soda-alkaline aqueous media with iodine. The product had been obtained by direct iodination of 4-hydroxy-pyridine, substituted at C(3) to afford the mono-substitution product, 4-hydroxy-3-iodopyridine (47) as brown solid in 43%, followed by conversion of the hydroxy group at C(4) of 47 to 4-chloro-3-iodopyridine (41d) by the chlorination with PCl₅ and POCl₃. Then, 4-chloro-3-iodopyridine (41d) reacted with hex-1-ene-3-ol (49) by a Heck-type reaction process to give 48d as yellow solid in 15% yield.

![Scheme 7: Synthesis of arylhexanone with a pyridine functionality](image)

**Figure 4:** ¹H NMR spectrum of 4-(4-chloropyridine-3-yl)-hexan-3-one (48d)
The $^1$H NMR spectrum of 48d displayed three signals of three aromatic protons of pyridine, indicating two singlet signals at $\delta_H$ 7.24, 8.43 and the doublet signal at $\delta_H$ 8.32 ($J = 5.3$ Hz). Eight methylene protons were observed with two multiplet signals at $\delta_H$ 1.57 and 2.73, two triplet signals at $\delta_H$ 2.36 ($J = 7.4$ Hz) and 2.98 ($J = 7.3$ Hz). A triplet signal of the methyl group was observed at $\delta_H$ 0.87 ($J = 7.4$ Hz).

The Willgerodt-Kindler reaction with arylbutanones and an arylhexanone

The arylbutanones 42a, 42b, 42c and the arylhexanone 48d were examined as substrates in the domino annulation under various Willgerodt-Kindler conditions such as: A: morpholine, sulphur (6 eq), DMF at 130 °C, 14 h; B: morpholine, sulphur (6 eq), DMF at 100 °C, 12 min, C: morpholine, sulphur (6 eq), at 130 °C, 6 h without DMF. The domino processes are depicted below, respectively.
Scheme 8: Arylbutanones and arylhexanones under Willgerodt-Kindler reaction conditions; A: morpholine, sulphur (6 eq), DMF at 130 °C, 14 h; B: morpholine, sulphur (6 eq), DMF at 100 °C, 12 min, C: morpholine, sulphur (6 eq), at 130 °C, 6 h without DMF.

In our first attempt for a Willgerodt-Kindler reaction with 4-chloro-3-(3-oxobutyl)benzonitrile (42a) the cyano group in the para-position obviously sufficiently activates for a domino process including bond-forming reactions at the aromatic ring system (nucleophilic armotac substitution): the Willgerodt-Kindler conditions transform the benzonitrile (42a) to a rather complex product mixture via oxidation and rearrangement. We were able to isolate the highly functionalized thieno[3,2-b][1]benzothiophene (50a) as a tricyclic ring system, resulting from a domino annulation process, albeit obtained in low yield (15%).
The $^1$H NMR spectrum of 50a in Figure 5 displayed three signals of three aromatic protons of the pyridine moiety, identified as the double of doublets signal at $\delta_H$ 7.42 and the doublet at $\delta_H$ 7.84 and “d” at $\delta_H$ 7.88. One proton of methine group was observed as the singlet signal at $\delta_H$ 6.34. Two triplet signals at $\delta_H$ 3.25 and $\delta_H$ 3.89 were ascribed for eighth protons of four methylene groups of morpholine.

In the $^{13}$C NMR spectrum in Figure 6 overall thirteen signals displayed at $\delta$ = 50.74 ppm (t), 65.97 (t), 97.31 (s), 108.03 (s), 119.26 (s), 120.57 (d), 122.69 (d), 123.98 (d), 124.51 (d), 133.49 (s), 139.37 (s), 144.38 (s), 162.92 (s), being in accord with 2-morpholine-4-yl-thieno[3,2-b][1]benzothiophene-7-carbonitrile (50). The mass spectrum registered the molecular ion of the compound at m/z = 300 (100%), corresponding to the molecular ion of 50a. Additional proof of the identity of 50a was obtained by HRMS (ESI-TOF) C$_{15}$H$_{12}$N$_{2}$O$_{2}$ (300.04 g/mol) calcd 300.03909 g/mol and found 300.03955 g/mol. Therefore, this spectroscopic data collection clearly confirms the identity of 50a.
**Figure 6** $^{13}$C NMR of 2-morpholine-4-yl-thieno[3,2-b][1]benzothiophene-7-carbonitrile (50a)

**Scheme 9:** Willgerodt-Kindler reaction of 42b with condition B: morpholine, sulphur (6 eq), DMF at 100 °C, 12 min and C: morpholine, sulphur (6 eq), at 130 °C, 6 h without DMF
In the case of a nitro group in the para-position to the chlorine, such as in substrate $42b$, the synthesis of the corresponding tricyclic hetarene with Willgerodt-Kindler conditions C is successful, giving rise to the tricyclic ring system of 7-amino-2-(morpholine-4-yl)thieno(3,2-b)(1)benzothiophene ($51b$) in 22% yield, despite the nitro group is reduced to aniline group. The $^1$H NMR spectrum of $51b$ is presented in Figure 7.

![Molecular Structure](image)

Figure 7 $^1$H NMR of 7-amino-2-(morpholine-4-yl)thieno-(3,2-b)(1)benzothiophene ($51b$)

The $^1$H NMR spectrum of 7-amino-2-(morpholine-4-yl)thieno(3,2-b)(1)benzothiophene ($51b$) in Figure 7 showed a broad signal of an amino proton at $\delta_H$ 1.7-1.4. Two triplet signals at $\delta_H$ 3.18 and $\delta_H$ 3.85 were ascribed for eigth protons of four methylene groups of morpholine. The singlet signal at $\delta_H$ 6.29 was ascribed for one proton of a methine group. Three aromatic protons could be detected at $\delta_H$ 6.62 (dd, $J = 8.58$, 2.28 Hz, 1H), 6.90 (“d”, $J = 2.02$ Hz, 1H), 7.50 (d, $J = 8.60$ Hz, 1H). The IR spectrum of $51b$ showed several strong absorption bands: at 1521 cm$^{-1}$, a medium band at 2216 cm$^{-1}$ and week band at 1113, 1444, 1473 cm$^{-1}$. The mass spectrum displayed the molecular ion of the compound at m/z = 290 (100%), corresponding to the molecular ion of $51b$ in the HRMS found at 290.05515 g/mol and calculated as 290.05474 g/mol. From above results, it could clearly be indicated that tricyclic ring system of $51b$ was formed as a major product.
Indeed, under moderate reaction conditions B (dilute with DMF as solvent at 100 °C for 12 min), being special for a rather short reaction time, the domino annulation process remained uncomplete: the transformation stopped at the monocyclization product \(53b\), albeit with reduction of the nitro group to an amino group in 23%. The by-product is the thioamide \(52b\), isolated in 17% yield. According to orientating experiments, this type of acetyl benzo thiophenes can indeed be oxidatively cyclized under the rather harsh reaction conditions A. Therefore, we regard \(53b\) as an intermediary product on the way to tricycle \(51b\).

![Chemical structures](image)

**Figure 8:** \(^1\)H NMR spectrum of \(54c\)
Under conditions A (morpholine, sulfur at 130 °C without additional solvent) with the prolonged 6 hours reaction time 4-(2-chloropyridine-3-yl)butan-2-one (42c) undergoes the domino annulation process, including the nucleophilic aromatic substitution step. Again a rather complex product mixture via oxidation and rearrangement was obtained as crude product. We were able to isolate a highly functionalized tricyclic ring system 54c in 28 mg (10% yield). The 1H NMR spectrum of 54c is presented in Figure 8.

The 1H-NMR spectrum of tricycle 54c in Figure 8 showed three aromatic protons detected at $\delta_H$ 6.62 (dd, $J = 8.58, 2.28$ Hz, 1H), 6.90 (“d”, $J = 2.02$ Hz, 1H), 7.50 (d, $J = 8.60$ Hz, 1H). Two triplet signals at $\delta_H$ 3.18 and $\delta_H$ 3.85 were ascribed for eight protons of four methylene groups of morpholine. The singlet signal at $\delta_H$ 6.29 was ascribed for one proton of a methine group, respectively. From above results, it could clearly be indicated that the tricyclic ring system of 54c was formed as major product.

The Willgerodt-Kindler reaction of 4-(4-chloropyridine-3-yl)-hexan-3-one (42d) under the relatively harsh reaction conditions A (morpholine, sulfur, 6h at 130 °C without additional solvent) gave the monocyclization thioamide product 55d, resulting from an incomplete domino annulation process. It is still an interesting question, why the process stops with the monoannulation in this case, since it is clear that the thioamide is the terminal functional group (the usual terminal group in Willgerodt-Kindler processes). The 1H NMR spectrum of 55d is presented in Figure 9.
The $^1$H-NMR spectrum of 55d in Figure 9 showed three aromatic protons detected at $\delta_H$ 7.64 ppm (d, $J = 5.6$ Hz, 1H), 8.33 (d, $J = 5.6$ Hz, 1H), 8.90 ppm (s, 1H). Three multiplet signals at $\delta_H$ 2.06-2.28 ppm, 2.78-2.88 and $\delta_H$ 2.96-3.07 ppm were ascribed for six protons of three methylene groups of the carbon chain. The singlet signal at $\delta_H$ 7.08 was ascribed for one proton of a methine group. Two multiplet signals at $\delta_H$ 3.67-3.79 ppm, 4.24-4.32 ppm were indicated approximately for eight protons of four methylene groups of morpholine. Thus, orientating result gave sample of signals clearly belonging to the structure of 55d. From above results, it could clearly be indicated this product has the structure of 55d.

In addition, our research group reported the butanone chain model compound which is readily introduced in good to excellent yields by a Heck-type reaction of aryl iodides 41 with allylic alcohol 43 (Scheme 10$^{[13]}$), providing a C$_4$-unit for the Willgerodt-Kindler redox process. In this process, the Pd catalyst selectively reacts with the iodoarenes in the presence of chloro substituents. Obviously, also nitro groups are tolerated.
Scheme 10: Heck-type synthesis of 2-arylbutanones 42; a: 5% Pd(OAc)$_2$, LiCl, Et$_3$N, DMF, 3 d at 120 °C.$^{[13]}$

Products from the transformation of 2-arylbutanones 42 under Willgerodt-Kindler reaction conditions: morpholine, sulfur, 6 h at 130 °C (see experimental: conditions A, reducing nitro groups); a: moderate reaction conditions; morpholine, sulfur, diluted with DMF, shorter reaction time, 12 min at 100 °C; (see experimental: conditions B), giving rise to tri- and tetracyclic ring systems (scheme 11).

Various products from the transformation of 2-arylbutanones 42 under Willgerodt-Kindler reaction support the feasibility of a domino annulation reaction, which oxidatively transforms up to 6 CH bond, giving rise to tri- and tetracyclic ring systems as reported in literature$^{[8]}$. The 2-chlorophenyl group of 42f was inert towards nucleophilic aromatic substitution even under the relatively harsh reaction conditions A (morpholine, sulfur, 6 h at 130 °C without additional solvent). However, two products were isolated in satisfactory yield: the thioamide 56f as ordinary Willgerodt-Kindler product, and the aminothiophene 57f, a type of product frequently observed earlier (Scheme 11).$^{[14]}$ The 4-chloropyridine moiety of 42g is also electrophilic enough for intramolecularly intercepting thiolate intermediates of the Willgerodt-Kindler reaction, thus leading to the isomeric tricyclic arenes 58g and 59g in rather good yields. Both spectroscopically characterized regioisomers were distinguished by NMR spectroscopy: in the HMBC spectrum of the major regioisomer the thiophenyl hydrogen is correlated with two quaternary carbons via two bonds ($^2J$-correlation) and with a third quaternary carbon via three bonds ($^3J$-correlation), being in accord with structure 58g. Moreover, for this isomer a signal at 162.9 ppm is registered in the $^{13}$C NMR spectrum, typical for the N,S-acetal
moiety. In contrast to a chloride group, the methoxy group of substrate 42h is inert under the reaction conditions. Therefore no annulation reaction takes place and the usual thioamide 56h is the result. Consequently we concentrated on other aryl chlorides for our

**Scheme 11**: Products from the transformation of 2-arylbutanones (42) under Willgerodt-Kindler reaction. [14]
test reactions. As anticipated, 4-chloroquinoline (42i) was transformed to the tetracyclic annulation product 60i, which could be of interest as potential DNA-intercalator\textsuperscript{[15]}

**Single crystal X-ray structure determination**

In addition, from compound 60i single crystals of the monohydrate were grown successfully. According to the X-ray crystal analysis the tetracyclic hetarenes are stacked at a separation of 3.572(5) Å and, in addition, cramped by hydrogen bonds to the crystal water molecules. While one hydrogen bond might be regarded as ordinary linear also typical for pyridine water complexes\textsuperscript{[17]} the other one is somewhat unusual: the OH-bond points perpendicularly towards the sp\textsuperscript{2}-hybrid orbital of the free electron pair of the next

![Figure 10: Structure of the monohydrate of 60i in the crystal\textsuperscript{[16]}](image)
quinoline nitrogen. According to DFT calculations of the infinite periodic crystal this arrangement represents at least a local energy minimum, which allows two positively polarized hydrogen atoms to simultaneously coordinate to one free electron pair: with fixed positions of the hetarene atoms the position of the water molecule does not change qualitatively during geometry optimization.

Figure 10 illustrates the electronic structure of the crystal in terms of the electron localisation function (ELF). Focusing on the water molecule bridging the two nitrogen hetarene atoms, the two lone pairs on the water oxygen and the rather diffuse lone pair on nitrogen can be clearly seen. In addition, on each of the water hydrogen atoms there is a basin of attraction whose shape is typical of hydrogen bonds. The nitrogen lone pair is seen to lean towards the closer water hydrogen (at a calculated NH distance of 1.82 Å), rationalizing the fact that the other hydrogen bond is significantly longer (the calculated NH distance is 2.75 Å). With a nitro group in meta-position to the chloride, such as in substrate 42j, the nucleophilic aromatic substitution is of course not favoured, however, instead of the usually major thioamide a good yield of the morpholino-thiophene 61j was obtained in this case. Simultaneously, the nitro group is reduced resulting in the aniline function of 61j.

Our general mechanistic rationale[18] is depicted in scheme 12: a suitable leaving group X and an activating, electron-withdrawing functional group G are prerequisite for the domino annulation process to take place. The first sulphur atom is oxidatively introduced via an intermediary enolate to give thioketones 63, whose corresponding thioenolate is prone to cyclize by nucleophilic aromatic substitution, thus giving rise to an acetyl benzothiophenes 64 and explaining the isolation of 53b as result under moderate reaction conditions. For subsequent studies within this thesis, the reactivity of acetyl benzothiophenes 68 was to be studied under forcing Willgerodt-Kindler conditions C, trying to verify the transformation to 67 via thiols 66 and 65 on a preparative scale. Thus, as model substrates acetylbenzothiophenes were synthesized with various methods.
**Scheme 12**: Mechanistic rationale for the domino annulation process; X = leaving group, G = functional group activating for nucleophilic aromatic substitution.

**Method A**

Acylation of benzothiophenes (68) by electrophilic aromatic substitution using aluminium chloride and an acid chloride (Friedel-Crafts acylation) allows the synthesis of acylated product 69 in good overall yield (78%). In obtaining the mixture of 2- and 3-substituted benzo(b)thiophene (69), it is clear, that the Friedel-Crafts acylation of benzothiophene is of minor regioselectivity.

\[
\text{AlCl}_3 / \text{CH}_2\text{Cl}_2 \quad \text{CH}_3\text{COCl} \quad \text{O} \quad \text{69}
\]
The mechanism of Friedel-Crafts acylation is not completely understood, but at least two mechanistic pathways are reasonable and might both be followed:

**Mechanism of Friedel-Crafts acylation I** \(^{[19]}\)

Step 1: The acyl chloride reacts with the Lewis acid to form an highly electrophilic complex.

\[
\begin{align*}
\text{H}_3\text{C}-\text{C}-\text{Cl} & \quad \text{AlCl}_3 & \quad \text{H}_3\text{C}-\text{C}-\text{Cl}^2+ \\
\text{H}_3\text{C}-\text{C}-\text{Cl} & \quad \text{AlCl}_3 & \quad \text{H}_3\text{C}-\text{C}-\text{Cl}^2+
\end{align*}
\]

Step 2: The \(\pi\)-electrons of the aromatic \(\text{C}=\text{C}\) act as a nucleophile, attacking the electrophilic complex. From the final result, the mixture of regioisomers, it is clear that this Friedel-Crafts acylation is rather unselective. To keep the schemes simple only one regioisomer is shown.

Step 3: The intermediary cation is deprotonated at position 2 or 3 of benzothiophenes reform the \(\text{C}=\text{C}\) and the aromatic system, generating \(\text{HCl}\) and to form the complex.
Step 4: The final step, the complex was decomposed by treatment with water to afford the corresponding of mixture isomer 69 which was used as the substrate in the next reaction without purification.

Mechanism of Friedel-Crafts acylation II:
In the mechanism II, the acylchloride reacts with the Lewis acid to form an acylium ion (RCO⁺).

Step 1. Lewis acid polarizes an acid chloride, might be followed by the complex dissociation to form E⁺ as formal electrophile[20]

Step 2. The π-electrons of the aromatic C=C between α-intermediate and β-intermediate act as a nucleophile, attacking the electrophile E⁺ (here shown exemplarily for the 3-regioisomer).
The product 69 was identified by $^1$H NMR and confirmed by MS = 176 (M$^+$) (57%) after purifying further by HPLC separation. The $^1$H NMR spectrum is presented in Figure 10.

![Figure 10: $^1$H NMR spectrum of 2- and 3-substituted benzo(b)thiophene 69](image1)

**Figure 11: $^1$H NMR spectrum of 2- and 3-substituted benzo(b)thiophene 69**

The $^1$H NMR spectrum of 69 in Figure 11 exhibits five aromatic protons detected at $\delta_H$ 8.69 (d, 1H), 8.23 (s, 1H), 7.80 (d, 1H), 7.37-7.53 (m, 2H). The singlet signal at $\delta_H$ 2.49 (s, 3H) was ascribed for three protons of methyl group, respectively.
The $^{13}$C NMR spectrum of 69 in Figure 12 displayed two peaks at $\delta_C$ 26.82, 28.21 indicating two carbon signals from methyl group as the mixture of two regioisomers (69b:69a, 2:1), the important carbon signals of carbonyl group showed at $\delta_C$ 193.08. Another signal detected approximately around at $\delta_C$ 123.03-139.87 could be designated for eight carbon aromatic ring. From above results, it is clear that 69 is a mixture of isomeric products. Therefore we have chosen to try again the preparation of 69 as pure regioisomers by applying more selective methods.

**Method B**

The metallation of benzothiophene (68) with nBuLi in dry THF proceeds at -40 °C for 1 h and at -30 °C for 10 min to give lithiumbenzothiophenes, which was slowly transferred via canula to the stirring solution of dry acetic anhydride as electrophile in THF. The reaction mixture was heated to reflux within 1 h to afford 2–acetylbenzo(b)thiophene (69a) in a 66% overall yield.

---

**Figure 12:** $^{13}$C NMR spectrum of 2- and 3-substituted benzo(b) thiophene 69
Figure 13 $^1$H NMR (200 MHz, CDCl$_3$, 25 °C) : 2-acetylbenzothiophene (69a).
The $^1$H NMR spectrum of Figure 13 exhibited five aromatic protons detected at $\delta_H$ 7.99 (d, 1H), 7.83-7.94 (m, 2H), 7.37-7.53 (m, 2H). The singlet signal at $\delta_H$ 2.70 (s, 3H) was ascribed for three protons of methyl group, respectively.

Figure 14 $^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 2-acetylbenzothiophene (69a).

The $^{13}$C NMR spectrum of 69a in Figure 14 displayed one peak at $\delta_C$ 27.44 (indicating the carbon signal from methyl group). The important signal of the carbonyl group showed up at $\delta_C$ 192.20. Other signals detected at $\delta_C$ 123.07, 125.05, 125.94, 127.47, 129.64, 139.20, 1242.72, 144.07 could be designated for eight carbons belonging to the aromatic ring. From above results, it could be indicated that 69a was formed as a major product.

2-Acetylbenzothiophene 69a was subjected to the Willgerodt-Kindler reaction with conditions C (130 °C, 6 h) and was indeed oxidatively cyclised to give 58k (11% yield isolated by flash-chromatography) as shown below. The structure of this cyclic N,S-acetal of a ketene was assigned in analogy to preceding results, in which these acetals were the main regioisomers. However, in the NMR spectrum of the crude product, we detected a minor isomer presumably with the morpholinyln group in β-position: the
diagnostic signal is the singlet at 6.45 ppm and the isomer ratio was determined to be 1:2.3 in favour of 58k.

The $^1$H NMR spectrum of 2-(morpholine-4-yl)thieno(3,2-b)(1)benzothiophene (58k) (Figure 15) showed five aromatic protons detected at $\delta_H$ 7.82 (t, $J = 9.1$ Hz, 1H), 7.63 (dd, $J = 19.5$ Hz, 7.5 Hz, 1H), 7.38 (ddd, $J = 15.1$ Hz, 10.4 Hz, 4.6 Hz, 1H), 7.18-7.31 (m, 1H) and $\delta_H$ 6.39 (s, 1H). Two triplet signals at $\delta_H$ 3.90 and $\delta_H$ 3.23 were ascribed for eighth protons of four methylene groups of morpholine, respectively. The mass

Figure 15: $^1$H NMR spectrum of 2-(morpholine-4-yl)thieno(3,2-b)(1)benzothiophene (58k)
spectrum displayed the molecular ion of the compound at m/z = 275 (100%), corresponding to the molecular ion of 58k in the HRMS calculated as 275.3900 g/mol and found at 275.04321 g/mol. From above results, it could clearly be indicated that tricyclic ring system of 58k was formed as a major product.

To compare this result, we have prepared 3-acetylbenzothiophenes via the bromination of benzothiophene (68) by electrophilic aromatic substitution using N-bromosuccinimide in the presence of dried acetic acid at room temperature 24 h. This bromination was successful, giving 3–bromobenzo(b)thiophene in 78% yield, which was allowed to react with magnesium in THF to the corresponding Grignard reagent. Immediate reaction with acetic anhydride as electrophile afforded 3-acetylbenzothiophenes (69b) as shown below, respectively.

\[
\begin{align*}
\text{N-bromosuccinimide (NBS)} & \quad \xrightarrow{\text{CH}_3\text{COOH}} & \text{protonation of carbonyl oxygen} \\
68 & \quad \xrightarrow{\text{Br}} & 71 \\
72 & \quad \xrightarrow{\text{CH}_3\text{COOH}} & 73 \\
74 & & \text{enol-like tautomer}
\end{align*}
\]

\[
\begin{align*}
68 & \quad \xrightarrow{\text{Br}} & 76 \\
76 & \quad \xrightarrow{\text{Br}} & 71 \\
75 & & \text{carbonyl tautomer}
\end{align*}
\]

Scheme 13: The mechanism for the formation of 3-bromobenzothiophene (71) by electrophilic bromination.
The first step: protonation of carbonyl oxygen of NBS, further polarizing the N-Br bond and resulting in a bromine cation as electrophile (must not necessarily be a free bromine cation). The second step: the bromine cation attacks as electrophile on to the aromatic ring. This initial addition reaction leads to carbocation formation under loss of aromatic stabilization. The third and final step is the deprotonation, regaining aromatic stability. Therefore, net result is substitution to give 3-bromobenzothiophenes (71) which was allowed to react with Mg in THF to the corresponding Grignard reagent immediately with acetic anhydride as electrophile to afford 3-acetylbenzothiophene (69b) as shown below.

![Chemical structure](image)

**Figure 16**: $^1$H NMR spectrum of 3-acetylbenzothiophene (69b)
The $^1$H NMR spectrum of 69b in Figure 16 exhibited five aromatic protons detected at $\delta_H$ 8.69 (d, 1H), 8.23 (s, 1H), 7.80 (d, 1H), 7.37-7.53 (m, 2H). The singlet signal at $\delta_H$ 2.49 (s, 3H) was ascribed for three protons of methyl group, respectively. 3-acetylbenzothiophenes (69b) was further examined to be establish as substrate in the Willgerodt-Kindler reaction with conditions C (145 °C, 3 h) to give 80 in 43 mg (6% yield).

![Scheme 14: 3-Acetylbenzothiophenes (69b) under Willgerodt-Kindler reaction conditions](image)

**Figure 17:** $^1$H NMR spectrum of 2-(benzo(b)thiophen-3-yl)-1-morpholinoethanethione (80)
The $^1$H-NMR spectrum of 80 in Figure 17 showed five aromatic protons detected at $\delta_H$ 7.75-7.89 ppm (m, 1H), 7.64-7.74 (m, 1H), 7.25-7.41 (m, 2H) and the singlet signal at $\delta_H$ 7.23 (s, 1H) was ascribed for one proton of a methine group. Three multiplet signals at $\delta_H$ 3.45-3.49 ppm, 3.54-3.58, 4.38-4.43 ppm and the doublet signal at $\delta_H$ 4.42 ppm were indicated approximately for eight protons of four methylene groups of morpholine. One multiplet signals at $\delta_H$ 3.77-3.82 ppm was indicated for two protons of one methylene groups of carbon chain. Thus, orientating result gave sample of signals clearly belonging to the structure of 80. From above results, it could clearly be indicated this product 80 as original willgerodt-Kindler reaction product.

**Proposed Mechanism**

The main steps of the proposed mechanism of the annulation between 2-acetylbenzothiophene (69a) and morpholine (5) are in accordance with the general proposal of B.P Mundy$^{[21]}$ as shown below in Scheme 15.

In the first step the secondary amine 5 reacts as a nucleophile attacking the carbonyl group of 69a, followed by elimination of H$_2$O to form an enamine 81. Subsequently, this adduct could react with sulfur to produce an iminium cation 82 as an intermediate, through a reaction introduced via iminium-aziridinium 85 to give enamine thiol 88a, which cyclizes intramolecularly by electrophilic aromatic substitution, resulting from a domino annulation process giving the tricyclic arenes 58k. From the above results we we conclude, that 53b is an intermediary product on the way to 51b as shown in Scheme 16, albeit 53b can be isolated under suitable reaction conditions.
3-position highly nucleophilic, reacts with electrophilic sulfur

Scheme 15: Mechanistic rationale for the formation of 2-(morpholine-4-yl)thieno(3,2-b)(1)benzothiophene (58k) by the Willgerodt-Kindler reaction.
Its important to notice, that under slightly more moderate conditions, the cyclization of 69a fails, but the typical Willgerodt-Kindler redox process still occurs:

We started the reaction of 2-acetylbenzothiophenes (69a) with pyrrolidine under moderate Willgerodt-Kindler reaction conditions to afford 2-(benzo(b)thiophene-2-yl)-1-(pyrrolidin-1-yl)ethanethione (90) as ordinary Willgerodt-Kindler product with 22 mg (8%) yield and 1,4-di(pyrrolidin-1-yl)butane-1,4-dithione (91) as by-product with 29 mg yield. In this case, using of pyrrolidine was used instead of morpholine. The reaction proceeded smoothly, providing the thioamide product and by-products 91, which arises from the action of the sulfur on the pyrrolidine itself. Therefore, the nature of the by-products depends on the amine. The $^1$H NMR spectrum of 91 (Figure 18) showed four aromatic protons detected at $\delta_H$ 8.69 (dd, $J = 7.3$, 1.5 Hz, 1H), 8.23 (d, $J = 11.1$ Hz, 1H, 7.37 (m, 2H). 7.80 (ddd, $J = 7.6$, 6.4, 2.9 Hz, 1H). The singlet signal at $\delta_H$ 7.80 (ddd, $J = 7.6$, 6.4, 2.9 Hz, 1H) was ascribed for one proton of a methine group, respectively. The multiplet signal at $\delta_H$ 2.49 was ascribed for three protons of methyl group, respectively. Therefore, it was clearly found, that the corresponding thioamide was attained. However, pyrrolidine was further examined to its reactivity with sulfur to corresponding 1,4-di(pyrrolidin-1-yl)butane-1,4-dithione (91).
The reaction of pyrrolidine (92) with sulfur under the Willgerodt-Kindler reaction at 130 °C 4 h afforded 1,4-di(pyrrolidin-1-yl)butane-1,4-dithione (91) as a small amount. The formation of 91 was confirmed by the $^1$H NMR spectrum and the mp 156-159 °C by comparison from lit.$^{[22]}$ In this case, the reaction was still smoothly providing the dithioamide product 91 which arises from the action of sulfur on the pyrrolidine itself. Therefore, the nature of the product depends on the amine. The identification data of compound 91 is shown below.

**Figure 18:** $^1$H NMR spectrum of 1,4-di(pyrrolidin-1-yl)butane-1,4-dithione (91)

In additional studies, miscellaneous heterocyclic compounds were chosen to examine the Willgerodt-Kindler reaction under various reaction conditions. Moreover, the Willgerodt-Kindler reaction has been compared with the thionation reaction by using enol and aldehyde derivative compounds as the starting materials as shown below.
Synthesis of enol derivative

Synthesis (E)-2-((2-chlorophenyl)(hydroxy)methyl-2,3-dihydro-1H-inden-1-one as enol-type starting material.

Step 1. Preparation of an acid chloride

Generally, an acid could be converted to an acid chloride with excess of redistilled SOCl₂. The structure of this compound was confirmed by the ¹H NMR spectrum and comparison with an authentic sample. This product was used without further purification.

Step 2. Preparation of enamine
In this case, we prepared enamine as product from the condensation reaction of secondary amine with ketone. The structure of the enamine compound was confirmed by the $^1$H NMR spectrum and comparison with authentic sample. This product was used without further purification.

**Figure 19:** $^1$H NMR spectrum of 4-(1H-inden-3-yl)morpholine (97)

The mechanism for enamine formation is outlined below.
Step 3. Reaction of enamine with an acid chloride

The formation of unsaturated ketone 93 was achieved by condensation of enamine 97 and acid chloride 95 in triethyl amine in 66% yield.

**Figure 20:** $^1$H NMR spectrum of (E)-2(((2-chlorophenyl)(hydroxy)methylene)-2,3-dihydro-1H-inden-1-one (93)
The mechanism is in accordance with the proposal of Stork-enamine reaction.[23] as shown below Scheme 17.

Scheme 16: The mechanism for the formation of 93 by modification from Stork-enamine reaction

The Willgerodt-Kindler-reaction of 93 failed to afford the expected product (105). In contrast, 93 reacted smoothly with excess Lawesson’s reagent as thionation reagent in toluene at 130 °C to give 2-((2-chlorophenyl)(mercapto)methyl)-2.3 dihydro-1H-inden-1-one (106) albeit in poor yield (14%). The structure of the thiol 106 compound was suggested on the basis of 1H NMR-spectroscopy and mass spectrometry. However, other isomers have to be taken into account.
Figure 21: $^1$H NMR spectrum of 2-((2-chlorophenyl)(mercapto)methyl)-2,3 dihydro-$IH$-inden-1-one (106)
2-(Phenylethyl)benzaldehyde (107) was synthesized by Sonogashira reaction of phenylacetylene (111) with 2-bromobenzaldehyde (106) in presence of triethylamine and a catalytic amount of Pd-catalyst in 59% yield. The structure of this compound was confirmed by $^1$H-NMR spectroscopy and mass spectrometry and the product was used without further purification in the Wilgerodt-Kindler reaction.

The mechanism is in accordance with the proposal of Castro-Stephens.[24]

Figure 22: $^1$H NMR spectrum of 2-(phenylethyl)benzaldehyde (107)
Scheme 17: The mechanism for the formation of 107, according to Castro-Stephens

In the first step, the active palladium catalyst Pd(0)L₂ 108 reacts with the arylbromide 106 in an oxidative addition to Pd (II) complex 109. This complex reacts in a rate limiting transmetallation with the (phenylethynyl)copper (110) produced in the copper cycle to complex 113 expelling the copper bromide. Both organic ligands are trans oriented and isomerize to cis-complex 114. In the final step, the product is released in reductive elimination with regeneration of Pd (0).
The synthesized 2-(phenylethyl)benzaldehyde (107) was also tested under the Willgerodt-Kindler-reaction conditions and compared with the thionation by Lawesson reagent.

\[
\text{107} \xrightarrow{\text{S}_8/\text{Morpholine}} \xrightarrow{130 \, ^\circ\text{C}, 1 \, \text{h}} \text{115}
\]

The reaction of 2-(phenylethyl)benzaldehyde (107) under Willgerodt-Kindler conditions failed to afford the expected product 115. In contrast, 2-(phenylethyl)benzaldehyde (107) reacted with 2 equivalents of Lawesson’s reagent as thionation reagent in toluene at 130°C to give crude product with low mass recovery. An attempt to purify the crude product was unsuccessful. Nevertheless, the presence of compound 116 was confirmed by NMR spectroscopy. The $^{13}$C NMR spectrum showed the diagnostic signal of C=S at 227 ppm. Therefore, it was believed to be thioketone 116 in 21% overall yield and was analyzed in detail:
**Figure 23**: $^1$H NMR spectrum of 2-phenyl-2,3-dihydro-$1H$-indene-1-thione (116)

The $^1$H NMR spectrum of 116 (Figure 23) showed nine aromatic protons detected at $\delta_H$ 8.08 ppm (d, $J = 7.9$ Hz, 1H), 7.60-7.69 (m, 1H), 7.46-7.56 (m, 3H) and 7.13-7.42 (m, 4H). The multiplet signal at $\delta_H$ 5.16 ppm was ascribed to one proton of a methine group. The two multiplet signals at $\delta_H$ 3.11, 3.53 were ascribed to two protons of the methylene group, respectively.
**Figure 24:** $^{13}$C NMR spectrum of 2-phenyl-2,3-dihydro-1$H$-indene-1-thione (116)

The $^{13}$C NMR spectrum of 116 (Figure 24) displays two peaks at $\delta_C$ 41.82, 58.59 ppm indicating two carbon signals from methylene group and methine group, respectively. The diagnostic carbon signal of the thiocarbonyl group C=S appears at $\delta_C$ 227.46 ppm. Further signals are detected between $\delta_C$ 124.80-150.18 ppm, where the ten aromatic carbons are expected.

In addition, we tried to synthesize the thioamide 119 with two methods as shown below.

**Method A**

\[
\begin{align*}
\text{117} & \quad + \quad \text{118} \\
& \quad \xrightarrow{\text{S}_8, \text{DMF} \atop 15 \text{ min, } 100 \degree \text{C}} \quad \Rightarrow \\
& \quad \text{119}
\end{align*}
\]
Method B

\[
\text{NH}_2 
\text{NH}_2 + \text{OHC} \xrightarrow{S, \text{DMF}, \text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}} \xrightarrow{\text{reflux, 115 °C, 4 h}} \text{S, DMF, Na}_2\text{S} \cdot 9\text{H}_2\text{O}
\]

In method A; the reaction of 8-aminoquinoline (117) and pyridine-2-carboxaldehyde (118) under Willgerodt-Kindler reaction conditions in DMF at 100 °C failed to afford the expected product (119). In contrast, in method B 8-aminoquinoline (117) and pyridine-2-carboxaldehyde (118) reacted in the Willgerodt-Kindler reaction in DMF at 115 °C when a catalytic amount of Na₂S ·9H₂O was present[11] to give thiobenzanilide (119).

**Figure 25:** ¹H NMR spectrum of N-(quinolin-8-yl)pyridine-2-carbothioamide (119)
The structure of thiol compound was confirmed by mass spectrometry, (MS (EI) m/z = 265 (10) (M⁺)) and the ¹H NMR shows six aromatic protons that could be detected as a doublet of doublets signal at δ_H 9.04 ppm, as the multiplet at δ_H 7.79-7.64 ppm, as the doublet of triplets at δ_H 8.25 ppm and multiplet around δ_H 7.63-7.74 ppm. Four methine protons of pyridine could be observed as the doublet of doublets signal at δ_H 10.18, as the triplet at 8.85 ppm, as the ddd at 8.78 ppm and multiplet at 7.88 ppm. One proton of the amino group detected as the singlet signal at δ_H 14.14 ppm.

Figure 26: ¹³C NMR spectrum of N-(quinolin-8-yl)pyridine-2-carbothioamide (119)

The ¹³C NMR spectrum confirms this compound since the signal of a thiocarbonyl group (C = S) was observed at 187 ppm. Final proof of the structure of 119 was obtained by HRMS (ESI-TOF) C₁₅H₁₁N₃S (265.33 g/mol) calcd 265.06735 g/mol and found 265.06714 g/mol. Therefore, we identified 119 as product. We tried to synthesize a gold(III) complex by reaction of N-(quinolin-8-yl)pyridine-2-carbothioamide (119) and AuCl₃ in acetonitrile. We obtained the blue powder of 120 in 43% yield giving a promising mass spectrum (FAB) with the signal at 460 (73) [M⁺-2Cl], but we didn’t succeed in growing crystals. But also from the ¹H NMR - with signals between 6 and 7 ppm, being shifted upfield, it is clear, that a metal complex has been formed.
An enol 93 and an aldehyde derivative 107 were synthesized to examine the Willgerodt-Kindler reaction by comparison with thionation reaction with Lawesson’s reagent. From the above results, the Willgerodt-Kindler reaction of 93 and 107 compounds were unsuccessful. The substrates were inert under the reaction condition. In contrast, the thionation reactions of 93 and of 107 by Lawesson’s reagent were indeed successful, giving rise to interesting thio compounds, partially unexpected due to the observed cyclization.

1.5 Conclusion

We have studied a domino process under Willgerodt-Kindler conditions, which transforms a butanone side chain of arene and heteroarenes into at least tricyclic annulated thieno(3,2-b)thiophenes with yields in the range of 7 to 46%. The resulting main product depends on the experimental conditions. Mechanistic pathways to the various reaction products are proposed. In additional studies we have examined a variety of substrates under various different reaction conditions for thionation. In some cases thionation was better achieved with Lawesson’s reagent. Further studies about the Willgerodt-Kindler reaction and annulation of new substrates are now in progress in our laboratory to elucidate the reaction mechanism for oxidative hetero-annulation reactions. The synthetic result of the reaction of 119 with AuCl₃ to afford the gold(III) complex 120 was indicated by mass spectrometry.
Extended $\pi$-systems through $S_N$ Ar–reactions at sterically shielded trityl salts

2.1 Introduction

Sterically Stabilized Para-Quinodimethanes by Nucleophilic Aromatic Substitution.

Numerous para-quinoid structures have been found in natural products and have been synthesized, such as in vitamins,\textsuperscript{[25]} proteins and dyes (Scheme\textsuperscript{19}). para-Quinoid compounds have a 6-membered ring of a closed system of conjugated double bonds which can alter the energy in delocalised systems.\textsuperscript{[26]} Therefore, the importance of para-quinoid compounds is based on their general tendency to aromatize.

![Diagram of para-quinoid structures](image)

**Scheme 18:** Examples of ortho and para-quinoid systems in natural products.
The importance of para-quinonoid compounds is based on their general tendency to aromatize, thus exhibiting a high reactivity combined with interesting electronic properties. para-Quinodimethanes, for instance, are regularly generated as reactive intermediates for polymerization or cyclic oligomerization reactions, the latter being a versatile entry to the strained [2.2]paracyclophanes. With the ultimate goal to synthesize extended conjugated \( \pi \)-systems through S_N Ar–reactions at sterically shielded trityl salts sterically, we envisioned the nucleophilic aromatic substitution at triarylmethyl cations to be a versatile entry to dipolar para-quinodimethanes, a concept, which is depicted in scheme 2.

Scheme 19: Reaction pathways for the nucleophilic attack on aromatic cations.
The electrophilicity of triarylmethyl cations 126 is of course strongly influenced by electronic effects of attached functional groups,[29] however, steric influence can be even more important for the regioselectivity of a nucleophilic attack: while structure 128 represents the ordinary product[30] from the reaction with nucleophiles 127 bulky groups R and/or R’ should be able to favour attack in para-position to give intermediates 129. With a remaining hydrogen at the nucleophilic center the final elimination should give the exclusive product 130 and desired para-quinodimethanes 131,[31] which are anticipated to be rather dipolar because of the general acceptor character of the double-bonded “Nu”-group. Triarylmethyl cations were chosen as easily accessible model compounds. Examples for the nucleophilic aromatic substitution at triarylmethyl cations are still very rare in literature,[32] especially with C-nucleophiles.[33] A general preparative investigation of scope and limitations of the concept in Scheme 20 is clearly missing.

2.2 Goal of Research

1. To prepare sterically shielded triarylmethyl cation salts by a modification of the method of M. Hagel and O. Muth.
2. To synthesize extended conjugated \( \pi \)-systems from triarylmethyl cations and from the nucleophilic aromatic substitution at triarylmethyl cations with organometallic reagents.

2.3 Literature Reviews

In 2003 M. Hagel et al.[34] reported that triarylmethyl tetrafluoroborates with a sterically shielded cationic center react with selected C- and N- nucleophile aromatic substitution to give dipolar para-quinodimethanes, representing highly functionalized \( \pi \)-systems. Examples for the nucleophilic aromatic substitution at triarylmethyl cations are very rare in literature. A general preparative investigation of its scope - as shown below – was envisioned as a highly rewarding research project.

The electrophilicity of benzylic cations 132 is of course strongly influenced by electronic effects of attached functional groups,[29] however, steric influence can be even more important for the regioselectivity of a nucleophilic attack: while structure 133 represents the ordinary product[30] from the reaction with nucleophiles 127, bulky groups R and/or R’ should be able to favour attack in para-position to give intermediates 134. With a
remaining hydrogen at the nucleophilic center the final elimination should give the desired \textit{para}-quinodimethanes 136.

Scheme 20: Reaction pathways for the nucleophilic attack on benzylic cations.

Model substrates for the synthesis of conjugated $\pi$-systems with coordinated metals are the ferrocenyl substituted triarylmethylcations and the fluorophenyl group.
In further studies, O.Muth et al.\textsuperscript{[35]} used the same method by M.Hagel to synthesized various \textit{para}-quinod compound which are listed below.
The para-quinoid imine 161 shows interesting redox activity, proven by cyclovoltammetry. Palladium complexes of 161 are currently tested for their catalytic activity (H. E. Riveira, unpublished results).
However, the search for para-quinoid compounds by nucleophilic aromatic substitution has been a matter of continued interest for our group since these structures exhibit highly interesting features: color as well as redox activity.

2.4 Results and discussion

We started the synthesis of triarylmethyl salts which are efficiently accessible in just two preparative steps (scheme 21).

1. BuLi/ THF
2. ArBr

162a Ar = 4-methylphenyl 162b Ar = 2,4-dimethylphenyl 162c Ar = 2,4,6-trimethylphenyl

163a 43% 163b 94% 163c 79%

164a 95% 164b 90% 164c 94%

Scheme 21: The sequence of reactions for the synthesis of triarylmethyl salts 164.

In the first step: Triarylmethyl alcohol 163 was synthesized by the metallation of arylbromide (Ar = 4-methylphenyl 162a, 2,4-dimethylphenyl 162b, 2,4,6-trimethylphenyl 162c with nBuLi in dry THF proceeding at -78 °C, 1 h to give aryllithium compounds, which reacted with a solution of xanthone as electrophile in THF. Triarylmethyl alcohol
163 are obtained with yields in the range of 43 to 94%. Step 2: The transformation to the tetrafluoroborate with tetrafluoroboric acid as reagent proceeds with triarylmethyl alcohol by ionic reaction to give triarylmethyl salts 164 in the range of 90 to 95% as shown Scheme 22, respectively.

![Figure 27: 1H NMR of 9-hydroxy-9-(4-methylphenyl)xanthene (163a).](image)

The 1H NMR spectrum of 9-hydroxy-9-(4-methylphenyl)xanthene (163a) in Figure 27 displayed four signals of thirteen aromatic protons which was indicated of two multiplet signals at $\delta_H$ 7.00-7.03 ppm, 7.31-7.26 ppm and two the doublet of doublets signal at $\delta_H$ 7.19, 7.38 ppm. A singlet signal of methyl group was observed at $\delta_H$ 2.29 ppm and one proton of hydroxyl group was observed from the singlet signal at $\delta_H$ 2.59 ppm, respectively.

The $^{13}$C NMR spectrum of 163a in Figure 28 displayed twelve signals at $\delta_C$ = 21.03 ppm (q), 70.44 (s), 116.43 (d), 123.58 (d), 126.17 (d), 127.48 (s), 128.72 (d), 128.98 (d), 129.03 (d), 136.40 (s), 145.22 (s), 149.77 (s) ppm being in accord with 163a. From above results, it could clearly be indicated that 163a has been formed.
Figure 28: $^{13}$C NMR of 9-hydroxy-9-(4-methylphenyl)xanthene (163a).

Figure 29: $^1$H NMR of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a)
In the $^1$H NMR spectrum of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a) (Figure 29) we detected six signals at $\delta = 2.58$ (s, 3H), 7.59 (t, 4H), 7.92 (dd, 2H), 8.19 (dd, 2H), 8.36-8.54 (m, 4H) ppm, respectively.

**Figure 30**: $^{13}$C NMR of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a)

In the $^{13}$C NMR spectrum of 164a in Figure 30 overall ten signals are displayed at $\delta = 21.78$ ppm (q), 120.20 (d), 123.74 (d), 128.05 (d), 129.28 (d), 130.03 (d), 131.17 (d), 131.94 (d), 143.94 (d), 158.48 (d), being in accord with 164a The mass spectrum displayed the molecular ion of the compound at m/z = 290 (16%). From above results, it could clearly be indicated that 164a has been isolated in pure form.

The $^1$H NMR spectrum of 9-hydroxy-9-(2,4-dimethylphenyl) xanthenylium (163b) in Figure 31 showed a singlet signal of hydroxy proton at $\delta_H$ 2.44 ppm. Two singlet signals at $\delta_H$ 1.48 ppm and $\delta_H$ 2.41 ppm were ascribed for six protons of two methyl groups.

Ten aromatic protons could be detected at $\delta_H$ 6.90 (s, br, 1H), 7.06 (“t”, “J” = 7.8 Hz, 2H), 7.15 (dd, J = 7.8, 1.8 Hz, 2H) 7.24-7.28 (m, 3H), 7.37 (“t”, “J” = 7.8 Hz, 2H), 8.28 (d, J = 7.8 Hz, 1H) ppm. The mass spectrum displayed the molecular ion of the compound at m/z = 302 (13%), corresponding to the molecular ion of 163b.
Figure 31: $^1$H NMR of 9-hydroxy-9-(2,4-dimethylphenyl) xanthenylium (163b)

Figure 32: $^{13}$C NMR of 9-hydroxy-9-(2,6-methylphenyl)xanthene (163b)
In the $^{13}$C NMR spectrum of $163b$ in Figure 31 overall fifteen signals displayed at $\delta = 20.52$ ppm (q), 20.93 (q), 69.85 (s), 116.29 (d), 123.52 (d), 125.88 (d), 125.90 (d), 126.05 (s), 128.77 (d), 129.21 (d), 132.83 (d), 135.46 (s), 137.34 (s), 140.98 (s), 150.10 (s) ppm being in accord with $163b$. From above results, it could clearly be indicated that $163b$ is the main product of this reaction.

Figure 33: $^1$H NMR of 9-(2,4-dimethylphenyl)xanthenylium tetrafluoroborate ($164b$)

The $^1$H NMR spectrum of $164b$ in Figure 33 displayed three signals of eleven aromatic protons were detected at $\delta = 6.95$ ppm (s, 2H, 3-H/5-H), 7.99 ("d", "$J = 4.0$ Hz, 4H), 8.51 (d, $J = 8.8$ Hz, 2H), 8.60-8.66 (m, 2H) ppm. Two singlet signals of methyl group were observed at $\delta_H$

In the $^{13}$C NMR spectrum of $164b$ in Figure 34 overall fifteen signals displayed at $\delta = 20.42$ ppm (q), 55.65 (q), 114.20 (d), 120.55 (d), 122.47 (s), 124.68 (s), 130.35 (d), 130.76 (d), 137.44 (s), 145.37 (d), 158.34 (s), 162.19 (s), 178.76 (s) ppm.
Figure 34: $^{13}$C NMR of 9-(2,4-dimethylphenyl)xanthenylium tetrafluoroborate (164b)

Figure 35: $^1$H NMR of 9-hydroxy-9-(2,4,6-trimethylphenyl)xanthenylium (163c)
The $^1$H NMR spectrum of $163c$ in Figure 35 displayed five signals of twelve aromatic protons, observed at $\delta = 6.83$ (s, br, 2H), 7.02 ($''t'',$ $''J'' = 7.5$ Hz, 2H), 7.16 (dd, $J = 7.8$ Hz, $J = 1.65$ Hz, 2H), 7.20 (dd, $J = 8.25$ Hz, $J = 1.2$ Hz, 2H), 7.31 ($''t'',$ $''J'' = 7.7$ Hz, 2H) ppm. A singlet signal of hydroxyl group was observed at $\delta_H 2.08$ (s, 1H,OH). Two singlet signals of methyl group were observed at $\delta_H 2.13$ (s, br, 6H), 2.28 (s, 3H), respectively. The mass spectrum displayed the molecular ion of $163c$ at m/z = 316 (17%), corresponding to the molecular ion of $163c$.

**Figure 36:** $^{13}$C NMR of 9-hydroxy-9-(2,4,6-trimethylphenyl)xanthenylium ($163c$)

In the $^{13}$C NMR spectrum of $163c$ in Figure 36 overall thirteen signals displayed at $\delta =$ 20.58 ppm (q), 24.20 (q, br), 74.31 (s), 116.39 (d), 123.60 (d), 127.94 (s), 128.35 (d), 129.10 (d), 131.75 (d), 136.61 (s), 137.35 (s), 138.40 (s), 149.45 (s) ppm. From above results, it could clearly be indicated that $163c$ has been formed.

The $^1$H NMR spectrum of $164c$ in Figure 37 displayed three signals of ten aromatic protons were indicated at $\delta = 7.18$ ppm (s, 2H), 7.63, (m, 4H), 8.62 (m, 4H) ppm. Two singlet signals of methyl group were observed at $\delta_H 1.83$ ppm (s, 6H), 2.48 (s, 3H) ppm, respectively.
Figure 37: $^1$H NMR of 9-(2,4,6-trimethylphenyl)xanthenylium tetrafluoroborate (164c)

Figure 38: $^{13}$C NMR of 9-(2,4,6-trimethylphenyl)xanthenyliumtetrafluoroborate (164c)
In the $^{13}$C NMR spectrum of 164c in Figure 38 showed thirteen the carbon signals at $\delta = 20.13$ ppm (q), 21.25 (q), 121.11 (d), 124.43 (s), 127.42 (s), 129.23 (d), 129.93 (d), 130.11 (d), 135.34 (s), 141.71 (s), 145.12 (d), 158.49 (s), 177.90 (s) ppm being in accord with 164c. Therefore, we identified 164c as product

**Reaction of sterically hindered triarylmethyl cations with various nucleophiles:**

In the objective of our studies towards the construction of extended $\pi$–systems with various nucleophiles we tested sterically hindered triarylmethyl salts as substrates for the nucleophilic attack of four model nucleophiles. The reactivity of 164a, 164b and 164c was tested with a simple C-nucleophile (malononitrile), LDA as sterically extremely hindered N-nucleophile or base, aryl magnesium and alkyl lithium as sterically hindered C-nucleophiles or bases. We obtained dipolar para-quinoid compounds in poor yields. This type of products is accessible with hydride as leaving group. Examples are illustrated below.

1. Reaction with C-Nucleophiles (malononitrile)

\[
\begin{align*}
\text{164} & \xrightarrow{\text{NaH,THF}} \text{167} \\
\text{Ar} & \text{BF}_4^{-} \\
\text{165} & \quad \text{166}
\end{align*}
\]

164a. (Ar = 4-methylphenyl)  
164b. (Ar = 2,4-dimethylphenyl)

<table>
<thead>
<tr>
<th>164</th>
<th>165</th>
<th>166</th>
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<tbody>
<tr>
<td>164a</td>
<td>68%</td>
<td>166a</td>
</tr>
<tr>
<td>164b</td>
<td>78%</td>
<td>166b</td>
</tr>
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</table>


Triarylmethyl salts 164 react with malononitrile (167) as C-nucleophile under basic conditions to the corresponding quarternary centered products 165 or the desired para-quinoid products 166, depending on the steric hindrance at the central carbon atom. The reaction of 164a (4-methylphenyl-substituent) with malononitrile (167) gave 165a in 68% yield since the central carbon atom of 164a is not sterically shielded by any methyl groups. Thus, the formation of product 165a as the quarternary product was observed with malononitrile through nucleophilic attack at carbonium ion.
Figure 39: $^1$H NMR of 2-(9-(4-methylphenyl)-9H-xanthen-9-yl)malononitrile (165a)

Figure 40: $^{13}$C NMR of 2-(9-(4-methylphenyl)-9H-xanthen-9-yl)malononitrile (165a)
Figure 41: $^1$H NMR of 2-(9-(2,4-dimethylphenyl)-9H-xanthen-9-yl)malononitrile (165b)

Figure 42: $^{13}$C NMR of 2-(9-(2,4-dimethylphenyl)-9H-xanthen-9-yl)malononitrile (165b)
Figure 43: $^1$H NMR of substituted xanthenylidene-malononitrile 166b

Figure 44: $^{13}$C NMR of xanthenylidene-malononitrile 166b
In contrast 164b (2,4-dimethylphenyl-substituent with one shielding methyl-group) gave two types of products: 165b 78% yield and 166b 17% yield: 165b represents the quarternary centered product while structure 166b represents the para-quinoid structure as effect from the bulky influence of 2,4-methylphenyl-group, however, of course not bulky enough for complete inhibition.

2. Reaction with LDA as sterically hindered base

\[ \text{Ar} \text{O} \text{BF}_4^+ \quad \text{Li} \quad \text{N} \quad \text{170} \quad \text{Ar} \text{O} \quad \text{H} \quad \text{Ar} \text{O} \text{BF}_4^+ \]

164a (Ar = 4-methylphenyl) 168a (9%)
164b (Ar = 2,4-dimethylphenyl) 169b (20%)

Scheme 23: Reaction of 164 with lithium diisopropyl amide (170) to give 168a and 169b (or regioisomer with CC-bond formation in peri-position).

The triarylmethyl salts 164a, 164b react with lithium diisopropyl amide (170) under basic conditions and lead to symetrical dimer product 168a in 9% yield and 169b in 20% yield as the quarternary product. The mechanism presumably started with a single electron transfer process, giving rise to triarylmethyl radicals, followed by dimerization and H-shift; explaining both types of products. The coupling of aryllithium compound 164c with the especially shielding mesityl group did not give a clear result concerning dierization products (monomers were still predominant according to an orientating experiment).
Figure 45: $^1$H NMR spectrum of 9,9'-dip-tolyl-9$H$, 9$H$-3,9'-bixanthene (168a)

Figure 46: $^1$H NMR spectrum of bixanthene 169b
Figure 47: $^{13}$C NMR spectrum of 9,9'-bis(2,4-dimethylphenyl)-9H, 9'H-2,3'-bixanthene (169b)
3. Reaction with Arylmagnesium compounds

The triarylmethyl salt 164a reacted with aryl magnesium 171 as Grignard reagent under reflux, 1h to the corresponding exclusive product 172 since the central carbon of the triarylmethyl system is shielded by one methyl and one hydrogen from the attached xylyl group. Thus, arylmagnesium as nucleophile can not attack at central carbonium ion and therefore attack in para-position is favoured, presumably followed by a multi-step hydrogen transfer to give 9-(2,4-dimethylphenyl)-3-(4-methoxyphenyl)-9H-xanthene product (172) in 40% yield.

Scheme 24: Reaction of 164a with arylmagnesium compound (171) to give 172

Figure 47: $^1$H NMR spectrum of arylated xanthene 172
4. Alkyl lithium as sterically hindered base

Scheme 25: Reaction of 164a and 164b with alkyl lithium compound 175 to give 173 and 174

The triarylmethyl salts 164a, 164b reacted with t-BuLi (175) as organolithium reagent in THF at -78 °C. The solution mixture was allowed to warm up to room temperature affording a yellow oil of 173a in 14% as the quarternary product and a yellow oil of 174b as exclusive product, respectively. Obviously the central carbon atom of 164a is not sterically shielded as proven by the formation of product 173a as quarternary centered product. On the other hand, one additional methyl group in 164b is enough to prevent the formation of a quarternary centered product. The nucleophilic attack takes place in para-position to give (174b) in 30% yield. For this product the singulett of the central double benzylic hydrogen at 5.49 ppm is the diagnostic signal.
Figure 49: $^1$H NMR of $9$-tert-butyl-$9$-$p$-tolyl-$9H$-xanthene (173a)

Figure 50: $^1$H NMR of $3$-tert-butyl-$9$-$p$-tolyl-$9H$-xanthene (174b)
Synthesis of oligopyridines as potential ligands by nucleophilic aromatic substitution at fluoropyridines

Preparation of 183 was achieved in three steps from 2-methylpyridine (181) (Scheme 27). We repeated this experiment similar to the method of O.Muth[35] by nucleophilic aromatic substitution 2-fluoropyridine (179) with deprotonated thus lithiated 2-methylyridine to give dipyridin-2-ylmethane(182) in good yield. The nucleophilic aromatic substitution of difluoropyridine (180) with 182 gives product 183 with overall five pyridine rings in excellent yield. Compound 183 reacts readily with copper(II)perchlorate to give 2,6-bis(2-pyridyl)methyl pyridin-copper(II)perchlorate-acetonitrile complexe (184) in 81% yield. Mass spectrometry confirmed the identities of all these compounds.

Scheme 26: Synthesis of CuPy5 181
Scheme 27 Several synthetic routes to 4-ethynylpyridine (188) have been previously reported by Holmes et al.\cite{36} We started to prepare 2-methyl-4-(pyridin-4-yl)but-3-yn-2-ol (187) using direct palladium/copper catalyzed coupling of 2-methyl-3-butyn-2-ol (186) and bromopyridine (185), which proceeds in excellent yield (92%). Compound 187 was fragmented with base-catalysis to give 4-ethynylpyridine (188) in 64% yield. In this instance, the fragmentation is initiated by the deprotonation of the alcohol, prerequisite for the fragmentation in acetone and a alkynylate.

\[ \text{PdCl}_2/\text{CuBr} \quad 90 \, ^\circ\text{C}, 2 \, \text{d} \quad 87\% \]

Scheme 28: Synthesis of 1, 4-bis(pyridin-4-ylethynyl)benzene (190)
The literature method for the preparation of 190 was used as a guide. Using the conditions reported in the original paper[37] the preparation of 190 has allowed to develop the syntheses of a new linear bidentate ligand. 4-ethylpyridine (188) reacts readily with 1,4-diiiodobenzene(189) by cross-coupling Sonogashira reaction to afford the linear bidentate ligand (190) in 87% yield.

Scheme 29: Synthesis of copper(II)complex 191
The synthesis of complex 191 by a procedure similar to the method of O. Muth\[35\], except that 4-bis(pyridin-4-ylethynyl)benzene (190) was used instead of the bidentate 4,4’-bipyridyl. The complexation of 190 with 2,6-bis(2-pyridyl)methyl pyridin-copper(II) perchlorate-acetonitrile complex (184) by the copper(II)center gave a green solid product, which had some of the characteristics of 191 with high mp 300-304 °C. In the mass spectrum (FAB) the molecular peak of complex 191 was not found, but the masses of partial moieties at 478 (Py5Cu) and at 513(Py5CuCl) have been clearly registered.

2.4 Conclusion

Triarylmethylium salts with a sterically shielded cation center react with selected C nucleophile under nucleophilic aromatic substitution. The resulting dipolar para-quinodimethanes represent highly functionalized extended π-systems. Triarylmethyl salts are efficiently accessible in just two preparative steps, starting from the xanthone (Scheme 3). Triarylmethylium salts (164) react with malononitrile (167) under basic conditions to give a quarternary centered products (165a) and desired para-quinoidal products (166) respectively, depending on the steric hindrance of the central carbon atom. The reaction of 164a (4-methylphenyl-substituent) with malononitrile gave 165a in a good yield (68%) and the reaction of 164b (2,4-dimethylphenyl-substituent) with malononitrile gave 165b in 78% and 166b (the 2,4-dimethylphenyl substituent) in 17%. The structures 165a and 165b represent the quarternary centered products with malononitrile nucleophile attack at carbonium ion while structure 166b represents a para-quinoid structure, due to the steric effect from the bulky 2,4-methyl-phenyl group. However, the structure 164b may be not enough bulky for shielding cause 165b was found in almost quantitative yield. In case of LDA, Arylmagnesium, Alkyllithium as sterically hindered bases (and nucleophiles at the same time) also reacted with triarylmethylium salts. We obtained dimerization products through coupling of intermediary trityl radicals. Both, symmetrical and quarternary centered dimers were found. Our results represent a straightforward and efficient access to polar p-quinoid compounds, useful for the construction of extended π-systems.
II. EXPERIMENTAL PART
1. Domino Annulation Reactions under Willgerodt-Kindler Conditions

1.1 Apparatus and Instruments

$^1$H-NMR-Spectroscopy:

Nuclear magnetic resonance (200.1 MHz), DRX-400 (400.1 MHz) spectra were determined on a Bruker and spectra were recorded by use of CDCl$_3$ as solvent and TMS as the internal standard. The chemical shift reported are given in parts per million down field from tetramethylsilane.

$^{13}$C-NMR-Spectroscopy:

$^{13}$C-NMR DPX-200(50.3.1 MHz), DRX-400(100.1 MHz) spectra were obtained from a Bruker and spectra were recorded by use of CDCl$_3$ as solvent and TMS as the internal standard.

Infrared-Spectroscopy:

The infrared spectra were recorded from potassium bromide disks on a Bruker Equinox 55 and Perkin-Elmer model 983G spectrometer. All samples were prepared in the KBr pellets.

UV/VIS-Spectroscopy:

The ultraviolet spectra were recorded on a Cary 1 UV/VIS spectrometer using acetonitril (CH$_3$CN), dichloromethane (CH$_2$Cl$_2$) as the solvent.

Mass Spectroscopy:

Mass spectra were obtained on a Varian MAT311 A and Bruker BIO TOF II instrument.

Elemental analysis:

Elemental analyses were performed on a Carlo Erba Elemental Analyxser model 1160 bzw and Vario EL Elementar/Hanau carbon-hydrogen analyses were obtained with +/-0.4% of the theoretical values.

Melting point:

Melting points (°C) were determined with Büchi Schmelzpunkt Bestimmungs apparatus and were uncorrected.
Preparative TLC:

Thin layer chromatography (TLC) was carried out with polygram siliga G/UV254 from Macherey & Nagel were used.

Preparative Chromatography:

Flash chromatography was performed employing 0.1-0.4 mm silica gel (Merck) with pressure 80 Kpa.

1.2 Methods and Materials

All commercially available materials were used without further purification. Most of the solvents were purified by distillation. THF was distilled from benzophenone/sodium, and was stored over molecular sieves (3 Å) under argon. Purification of frequently used solvent and other laboratory from the company are described.

1.3 Methods for structures determination

1. Nuclear Magnetic Resonance Spectroscopy (NMR): NMR is technique to identify structure of compounds. It is related to molecular arrangement. The chemical shifts (δ) data provide information concerning the electron density of a giving molecules. The resonance frequency of proton is related to its environment. ¹H NMR spectra exhibit the total number of protons in each compound and their chemical shifts are related to position in complexes which were assigned from ¹H ¹H COSY spectra. Furthermore, the ¹³C NMR signals were assigned from HMQC spectra.

2. Electrospray and Fast atom bombardment mass spectrometry (ES-MS and FAB-MS): Mass spectrometry is useful technique to confirm molecular structure of compounds by considering their m/z values. The ES technique has been developed to study inorganic and organometallic structure.

3. Infrared spectroscopy (IR): IR is commonly used to detect characteristic frequencies of functional groups in compounds. The compounds absorb the infrared frequency range and show vibrational modes of molecule at different frequencies. For this research compound absorb in the IR region (4000-350 cm⁻¹)

3 UV-Visible absorption spectroscopy (UV-Visible): UV-Visible absorption is a roughly technique to characterize complexes but useful for describing colored. The chromopholic group in compounds give rise to absorption to the ultra-violet and visible region (200-800 nm).
1.4 Materials

All commercially available materials were used without further purification. Most of the solvents were purified by distillation. THF was distilled from benzophenone/sodium, and was stored over molecular sieves (3Å) under argon. Purification of frequently used solvent. The reagents used for synthesis were purchased from Fluka, Across or Aldrich Chemical Industries, Ltd.

**Material from Fluka**
2-Fluoropyridine: 98%.
Tetrafluoroboric-diethylether: 54% HBF₄ in diethylether.

**Materials from Merck**
t-Butyllithium 1.6 M in Hexane.
2,6-Fluoropyridine: 99%.
Triethylamine: 99%.

**Materials from Aldrich**
8-Aminoquinoline: > 98%, mp 66-68 °C.
2-Bromomesitylene: > 99.996%.
2-Picoline: 98% mp 128-129 °C.
Xanthone: 97% mp 174-176 °C.
2-chlorobenzonitrile: 98%
4-Bromopyridinehydrochloride: 99%
Thianaphthene: 99%
2-Bromomesitylene: 99%
3-Acetylpyridine: 98%
4-Bromoanisole: 99%
1-indanone

**Materials from Acros**
Pyrrolidine: > 98%
4-hydroxypyridine: 95%
8-Aminoquinolinol: > 98%
3-Amino-2-chloropyridine: 96%
4-Bromo-m-Xylene: 97%
2-Bromobenzaldehyde: 97%
3-Butene-2-ol: 97%
Lawesson’s reagent 97%

**Solvents**

Commercial grad solvents were distilled before use for column chromatography. Solvents for reactions and crystallization were reagent grade and used without purification.
Acetone : Acetone is dried over anhydrous Calcium sulfate and distil. Store over 3 Å molecular sieve.

Acetone –d 6: 99.6% D, Deutero was purchased from GmbH.

Acetic acid : Cool in an ice bath until it solidifies and decant the mother liquor when about 80% of the acid has crystallised; repeat twice.

Acetic anhydride : Stand for 3 h over phosphorus pentaoxide(100 g/l), decant, stand over the same amount of anhydrous potassium carbonate for 3 h, filter and distil in the absence of moisture at 100 torr.

Acetonitril : 99.9% was purchased from Firma Merck.

Abs. Acetonitril : The solvent is dried over phosphorouspentoxide for 2 h, then distil. Store over 3 Å molecular sieve.

Chloroform: Dry with phosphorouspentoxide and distil. Store over 4 Å molecular sieve.

Deuterochloroform: 99.8 %  Deutero was purchased from GmbH.

Dichloromethane: Dry with 3 Å molecular sieve and distil. Store over 3 Å molecular sieve.

Abs. Dichloromethane: The solvent is dried over anhydrous Calciumhydride for 1-2 h then distil. Store over 3 Å molecular sieve.

Diethylether: Reflux with sodium/benzophenone, then distil under argon. Store over 3 Å molecular sieve.

Dimethylsulfoxide (DMSO): 99.8%, Deutero was purchased from GmbH.

Dioxan: Stand for 3 h over anhydrous potassium hydroxide, decant and distil over anhydrous Calciumhydride. Store in argon.

Ethylacetate (EA): Dry with 3 Å molecular sieve and distil. Store over 3 Å molecular sieve.

Ethanol: The solvent is dried over anhydrous Calciumoxide and distil. Store over 3 Å molecular sieve.

Dimethylformamid (DMF): The solvent is dried over anhydrous Calciumhydride and distil. Store over 3 Å molecular sieve.

Petroleuemether: Dry with 3 Å molecular sieve and distil. Store over 3 Å molecular sieve.
**Methanol:** Dry with 3 Å molecular sieve and distil. Store over 3 Å molecular sieve.

**Methyl-tert-butylether (MTBE):** Dry with 4 Å molecular sieve and distil. Store over 4 Å molecular sieve.

**Tetrahydrofuran (THF):** Reflux purified Tetrahydrofuran with sodium/benzophenone until the blue colour formed, then distil under argon. Store over 3 Å molecular sieve.

**Toluene:** Dry with 3 Å molecular sieve and distil. Store over 3 Å molecular sieve.

**Trietylamine:** The solvent is dried over anhydrous Calciumhydride and distil. Store over 3 Å molecular sieve.
1.5 Syntheses

1.5.1 Synthesis of 4-chloro-3-iodobenzamide (39):

Prepared similar to the method described by Kadzimirsz et al.\textsuperscript{[38]} A 250 mL roundbottomed flask was charged with a stir bar and 60 mL conc H\textsubscript{2}SO\textsubscript{4}. Then, sodium (meta) periodate (1.18 g, 5.50 mmol), potassium iodide (2.74 g, 16.5 mmol) were slowly added over 2 min. The reaction mixture was stirred at 25 °C for 45 min to result in a dark brown iodating solution. Afterwards, 4-chlorobenzonitrile (39) (2.74 g, 20 mmol) was added in one portion to the iodating solution. The reaction mixture was stirred at 25-30 °C for 2 h and slowly poured into stirred ice water (300 g). The crude solid products were collected by filtration and washed with cold water until the filtrate was neutral, finally washed with CCl\textsubscript{4} until the filtrate was colorless, and dried in vacuum (50 °C, 0.5 mbar, 2 h). The product was isolated as white solid 40 (3.78 g, 68% yield) with mp 135 °C.

\textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}, 25 °C): \(\delta = 5.53\) ppm, (s, 2H, NH\textsubscript{2}), 7.51 (d, J = Hz, 1H, Aryl), 7.55 (d, J = Hz, 1H, Aryl), 8.30 (s, 1H, Aryl).

\textsuperscript{13}C NMR (400 MHz, CDCl\textsubscript{3}, 25 °C): \(\delta = 98.11\) ppm (s), 128.07 (d), 129.23 (d), 132.81 (s), 139.10 (s), 142.45 (s), 166.45 (s).

MS (EI, 70 eV): m/z (%) = 281 (74) [M\textsuperscript{+}], 265 (100), 237 (21), 110 (25), 75 (32).

IR (KBr): \(\nu = 3374\) cm\textsuperscript{-1} (s), 3197 (s), 1652 (s), 1613 (s), 1582 (m), 1547 (m), 1401 (s), 1258 (w), 1116 (m), 1017 (w), 816 (w), 676 (m), 635 (m).

C\textsubscript{7}H\textsubscript{5}ClINO (281.48 g/mol):

\textit{calcd}: C = 29.87%, H = 1.79%, N = 4.99%

\textit{found}: C = 30.34%, H = 2.13%, N = 5.04%
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 4-chloro-3-iodobenzamide (40):

$^{13}$C NMR (200 MHz, CDCl$_3$, 25 °C): 4-chloro-3-iodobenzamide (40):
1.5.2 Synthesis of 4-chloro-3-iodobenzonitrile (41a):

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{PdCl}_2, \ 50^\circ\text{C}, \ 3 \text{ d} \\
\text{NC} & \quad \text{CH}_3\text{CN}, \text{H}_2\text{O} \\
\text{Cl} & \quad \text{I} \\
40 & \quad \rightarrow \\
\text{CN} & \quad \text{Cl} \\
\text{I} \\
41\text{a}
\end{align*}
\]

Prepared similar to the method described by Kadzimirsz et al.\textsuperscript{[38]} 4-chloro-3-iodobenzamide (40) (2.8 g, 10 mmol) was added in a mixture of water / acetonitrile 1:1 (30 mL) in a screw-capped tube, PdCl\textsubscript{2} (174 mg, 1 mmol) was added in one portion. The reaction mixture was stirred in an oil bath set to 50 °C for 3 d, and the solvent was evaporated, and the residue was dissolved in 50 mL MTBE and filtered through a pod of silica and washed twice with MTBE (20 mL). The organic layer was isolated, dried over MgSO\textsubscript{4}. The solvent of the organic layer was removed at the rotatory evaporator to remain of brown residue. The residue was purified by flash column chromatography (MTBE, \text{R}_f = 0.84) and drying in vacuum (50 °C, 0.5 mbar, 1 h). The product was isolated as brown solid 41a (895 mg, 34%) with mp 55 °C.

\textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}, 25 °C): \(\delta = 5.72 \text{ ppm} \) (s, 2H, NH\textsubscript{2}), 7.4 (d, J = Hz, 1H, Aryl), 7.6 (d, J = Hz, 1H, Aryl), 8.25 (s, 1H, Aryl).

\textsuperscript{13}C NMR (400 MHz, CDCl\textsubscript{3}, 25 °C): \(\delta = 98.43 \text{ ppm} \) (s), 111.87 (s), 116.15(s), 129.68 (d), 132.35 (d), 1143.08 (s), 143.96 (s).

MS (EI, 70eV): m/z (%): 263 (100) [M+], 136 (43), 100 (23), 75 (7), 50 (11).

IR (KBr): \(\tilde{\nu} = 3087 \text{ cm}^{-1} \) (w), 2232 (s), 1450 (s), 1368 (m), 1114 (m), 1021 (w), 885 (w), 826 (m), 598 (w).

C\textsubscript{7}H\textsubscript{3}ClIN (263.46 g/mol):
\[
\begin{align*}
\text{calcd:} & \quad C = 31.91\%, \ H = 1.15\%, \ N = 5.32\% \\
\text{found:} & \quad C = 32.74\%, \ H = 1.47\%, \ N = 5.25\%
\end{align*}
\]

HRMS (ESI-TOF): M+H\textsuperscript{+}
\[
\begin{align*}
\text{calcd:} & \quad 262.89986 \text{ g/mol} \\
\text{found:} & \quad 262.90054, \text{g/mol}
\end{align*}
\]
$^1$H NMR (200 MHz, CDCl₃, 25 °C): 4-chloro-3-iodobenzonitrile (41a):

$^{13}$C NMR (100 MHz, CDCl₃, 25 °C): 4-chloro-3-iodobenzonitrile (41a):
1.5.3 Synthesis of 4-chloro-3-(3-oxobutyl)benzonitrile (42a):

\[
\begin{align*}
\text{CN} & \quad \text{+} \quad \text{Cl} \\
\text{41a} & \quad \text{43} \\
\text{CN} & \quad \text{Cl} \\
\text{42a}
\end{align*}
\]

Prepared similar to the method described by Kadzimirsz et al.\cite{38} A mixture of 4-chloro-3-iodobenzonitrile (41a) (526 mg, 2 mmol), 1-buten-3-ol (43) (0.5 mL, 6 mmol), 1.75 mL triethylamine, lithium chloride (168 mg, 4 mmol), Pd(OAc)$_2$ (46 mg, 0.2 mmol), and 10 mL DMF in a screw-capped tube was stirred for 3 days at 120 °C under an argon atmosphere. After cooling to room temperature, MTBE (80 mL) was added and washed 3 times with water (50 mL), once with brine (50 mL) and filtered through a small pad of silica. The solvent of the organic layer was removed at the rotatory evaporator to remain of yellow solid residue. The residue was purified by flash chromatography (MTBE, $R_f = 0.78$) and dried in the vacuum. The product was isolated as yellow solid 42a (265 mg, 64%) with mp 50 °C.

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): $\delta = 2.17$ ppm (s, 3H), 2.78 (t, 2H), 3.02 (t, 2H), 7.44 (s, 2H, Aryl), 7.56 (s, 1H, Aryl).

$^{13}$C NMR (200 MHz, CDCl$_3$, 25 °C): $\delta$ (ppm) = 27.13 (t), 29.74 (q), 42.14 (t), 110.92 (s), 117.80 (s), 130.34 (d), 130.60 (d), 133.96 (d), 139.02 (s), 140.27 (s).

MS (EI, 70eV): m/z (%) = 208 (16) [M$^+$], 192 (27), 172 (52), 164 (22), 150 (14), 128 (12), 101 (9).

IR (KBr): $\bar{\nu}$ (cm$^{-1}$) = 3103 (w), 2229 (m), 1718 (s), 1471 (m), 1428 (m), 1380 (m), 1167 (m), 1047 (w), 827 (m).

C$_{11}$H$_{10}$CINO (207.66 g/mol):

calcd: C = 63.62%, H = 4.85%, N = 6.75% Cl = 17.07%,

found: C = 63.55%, H = 4.68%, N = 4.68%,
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 4-chloro-3-(3-oxobutyl)benzonitrile (42a):
1.5.4 Willgerodt-Kindler-Synthesis from 4-chloro-3-(3-oxobutyl)benzonitrile (42a):

Prepared similar to the method described by Kadzimirsz et al.\textsuperscript{[38]} A mixture of 4-chloro-3-(3-oxobutyl) benzonitrile (42a) (207 mg, 1 mmol), S\textsubscript{8} (190 mg, 6 mmol), DMF 5 mL and morpholine 10 mL was refluxed under argon for 14 h at 130 °C. The morpholine was removed in vacuum. The crude solid was separated by flash chromatography. The eluents for flash chromatography were 100 mL of the following mixture of PE: MTBE were used: 95:5; 90:10; 80:20; 50:50; 20:80; 0:100. The fraction with 90:10 was isolated by flash chromatography (PE/EA, 5:1). The fraction with R\textsubscript{f} = 0.16 was crystallized from (CH\textsubscript{2}Cl\textsubscript{2}/C\textsubscript{5}H\textsubscript{12},1:3) gave 45 mg (15%) of product as yellow crystals (50a) with mp 205 °C.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, 25 °C): δ = 3.25 ppm (t, J = 4.8 Hz, 4H), 3.89 (t, J = 4.8 Hz, 4H), 6.34 (s, 1H), 7.42 (dd, J = 8.36, 1.52 Hz, 1H), 7.84 (d, J = 8.32 Hz, 1H), 7.88 (“d,” J = 1 Hz, 1H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}, 25 °C): δ = 50.74 ppm (t), 65.97 (t), 97.31 (s), 108.03 (s), 119.26 (s), 120.57 (d), 122.69 (d), 123.98 (d), 124.51 (d), 133.49 (s), 139.37 (s), 144.38 (s), 162.92 (s).

MS (EI, 70eV): m/z (%) = 300 (100)[M\textsuperscript{+}], 258 (29), 242 (43), 228 (9), 215 (20), 202 (6), 170 (14), 121 (12).

IR (KBr): \(\tilde{\nu} = 2928\) cm\textsuperscript{-1} (w), 2216 (m), 1521 (s), 1473 (m), 1444 (m), 1381 (w), 1267 (w), 1221 (w), 1113 (m), 924 (w).

UV/VIS (dichloromethane) \(\lambda_{\text{max}} (\lg \varepsilon) = 217\) nm (3.43), 232 (3.85), 281 (4.11), 288 (4.12), 333 (4.09).

C\textsubscript{15}H\textsubscript{12}N\textsubscript{2}O\textsubscript{2} (300.04 g/mol):

\begin{align*}
\text{calcd:} & \quad C = 59.97\%, H = 4.03\%, N = 9.33\%, S = 21.35\% \\
\text{found:} & \quad C = 59.03\%, H = 7.87\%, N = 8.91\%, S = 20.61\%
\end{align*}

HRMS (ESI-TOF): M+H\textsuperscript{+} ; calcd: 300.03909 g/mol; found: 300.03955 g/mol
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): benzothiophene-7-carbonitrile 50a:
1.5.5 Synthesis 1-chloro-2-iodo-4-nitrobenzene (41b):

\[
\begin{align*}
\text{Cl} & \quad \text{NH}_2 & \quad \text{H}_2\text{SO}_4, \text{KI}, \text{H}_2\text{O} & \quad \text{I} \\
\text{NO}_2 & \quad \text{Cl} & \quad \text{NaNO}_2, \text{reflux 1.30 h} & \quad \text{NO}_2
\end{align*}
\]

Prepared similar to the method described by Kadzimirsz et al.\textsuperscript{[38]} A 250 mL round-bottomed flask was charged with a stir bar and 30 mL water at 0 °C in the ice bath. Conc. \(\text{H}_2\text{SO}_4\) 20 mL was slowly added dropwise over 10 minutes and the mixture was stirred at 0-5 °C. 2-chloro-5-nitro-1-benzoaniline (44) (8.65 g, 50 mmol) was added in one portion to the solution. The solution of \text{NaNO}_2 (3.8 g, 0.06 mmol) in 8 mL water was added dropwise with in 10 min and the reaction mixture was stirred at 0-5 °C until iodide-starch paper reacts positive. The solution of \text{KI} (9.1 g, 0.06 mmol) in 10 mL water was slowly added with cooling and the mixture was stirred for 1 h at room temperature. The reaction mixture was refluxed for 1.30 h. After cooling to room temperature, the organic phase was extracted three times with 60 mL of MTBE and the combined organic layers and once with \text{Na}_2\text{CO}_3 (2 x 50 mL), once with brine 50 mL, and evaporated until the solid formed. The solid obtained was filtered off and purified by flash chromatography (PE/MTBE 10:1; \(R_f = 0.51\)) and drying in vacuum. The product as yellow solid 41b (1.69 g, 12% yield) with mp 50-53 °C.

\(^1\text{H NMR}\) (200 MHz, CDCl\(_3\), 25 °C): \(\delta = 7.61\) ppm (d, \(J = 8.83\) Hz, 1H), 8.16 (dd, \(J = 8.84, 2.52\) Hz, 1H), 8.70 (d, \(J = 2.78\) Hz, 1H).

\(\text{C}_9\text{H}_7\text{ClNO}_2\) (283.45 g/mol).

\(\text{MS(El, 70eV)}\): \(m/z\) (%) = 283 (100) [M\(^+\)], 267 (22), 253 (25), 237 (59), 225 (38), 127 (33), 110 (51), 75 (62), 46 (44).
1H NMR (200 MHz, CDCl₃, 25 °C): 1-chloro-2-iodo-4-nitrobenzene (41b):

2.1.5.6 Synthesis 4-(2-chloro-5-nitrophenyl)butan-2-one (42b):

Prepared similar to the method described by Kadzimirsz et al. \[38\] A mixture of 1-chloro-2-iodo-4-nitrobenzene (41b) (567 mg, 2 mmol), 1-buten-3-ol (43) (0.45 mL, 6 mmol), 1.75 mL triethylamine, LiCl (168 mg, 4 mmol), Pd(OAc)₂ (46 mg, 0.2 mmol), and 10 mL DMF in a screw-capped tube was stirred for 3 d at 120 °C under an argon atmosphere. After cooling to room temperature, MTBE (80 mL) was added and filtered through a small pad of silica. The organic filtrate was washed 3 times with water (50 mL), once with brine (50 mL). The solvent was removed at the rotatory evaporator to remain a brown residue. The residue was separated by flash chromatography (MTBE/PE: 1:10, Rₐ = 0.12) and drying in vacuum. The product was isolated as orange solid 42b (272 mg, 60%) with mp 55-57 °C.
**1H NMR** (200 MHz, CDCl₃, 25 °C): \( \delta = 2.19 \) ppm (s, 3H), 2.85 (t, \( J = 7.58 \) Hz, 4H), 3.10 (t, \( J = 0 \) 7.58 Hz, 4H), 7.50 (d, \( J = 8.58 \) Hz, 1H), 8.05 (dd, \( J = 8.84, 2.54 \) Hz,1H), 8.15 (“d”, \( J = 2.54 \) Hz, 1H).

**13C NMR** (200 MHz, CDCl₃, 25 °C): \( \delta = 27.55 \) ppm (t), 29.95 (s), 42.27 (t), 122.60 (d), 125.38 (d), 130.40 (d), 140.52 (s), 140.91 (s), 146.60 (s), 206.30 (s).

**Ms** (70eV, EI): m/z (%): 227.1(5)(M), 192(4), 186(7), 180(100), 165(44), 152(11), 138(6),1023), 89(25), 76(15), 51(5).

**C₁₀H₁₀ClNO₃** (227.64 g/mol).

**HRMS (ESI-TOF):** M+H⁺
- calcd: 227.03490 g/mol
- found: 227.03442 g/mol

**1H NMR** (200 MHz, CDCl₃, 25 °C): 4-(2-chloro-5-nitrophenyl)butan-2-one (42b):
1.5.7 Willgerodt-Kindler of 4-(2-chloro-5-nitrophenyl)-butan-2-one (42b):

\[
\begin{align*}
\text{NO}_2 & \quad 1. S_8, \text{DMF} \\
\text{Cl} & \quad 2. \text{morpholine, 100 °C, 12 min}
\end{align*}
\]

A mixture of 4-(2-chloro-5-nitrophenyl) butan-2-one (42b) (227 mg, 1.0 mmol), S_8 (190 mg, 6 mmol), NaOAc (246 mg, 3 mmol) DMF 10 mL and morpholine (0.4 mL, 5 mmol) in a screw-capped tube was stirred for 12 min at 100 °C under an argon atmosphere. After cooling to room temperature, the excess morpholine is removed in vacuum. The crude solid was fractionated by flash chromatography (MTBE/PE, 1:1; R_f = 0.1, 0.35) to gave two fractions. The fraction with R_f = 0.1 gave 15 mg (10%) of 1-morpholinoethanethion (52b) as white solid with mp 47-48 °C which was reported. The fraction with R_f = 0.35 gave 1-(5-nitrobenzo[b]thiophen-2-yl)ethanone (53b) as yellow crystals (50 mg, 23%) with mp 175-177 °C.

The first fraction: 1-morpholinoethanethion (52b)

C_6H_{11}NOS (145.22 g/mol).

**MS** (EI, 70eV): m/z (%) = 145 [M^+] (100).

**IR** (KBr): \(\nu = 2957 \text{ cm}^{-1} \text{(m)}, 2863 \text{ (w)}, 1486 \text{ (s)}, 1463 \text{ (w)}, 1434 \text{ (m)}, 1280 \text{ (s)}, 1261 \text{ (s), 591 (s)}.\)

The second fraction: 1-(5-nitrobenzo[b]thiophen-2-yl)ethanone (53b)

**\(^1\text{H NMR}\)** (200 MHz, CDCl_3, 25 °C): \(\delta = 2.77 \text{ ppm (s, 3H)}, 8.00 \text{ (d, J = 9.08 Hz, 1H), 8.06 (s, 1H), 8.30 (dd, J = 9.08, 2.34 Hz, 1H), 8.80 “d”, J = 2.26 Hz, 1H).}\)

**\(^{13}\text{C NMR}\)** (100 MHz, CDCl_3, 25 °C): \(\delta = 26.88 \text{ ppm (s)}, 121.39 \text{ (d)}, 121.56 \text{ (d)}, 123.89 \text{ (d)}, 129.47 \text{ (d)}, 138.86 \text{ (s)}, 145.94 \text{ (s)}, 147.55 \text{ (s)}, 147.81 \text{ (s), 191.65 (s).}\)

**IR** (KBr): \(\nu = 3443 \text{ cm}^{-1} \text{(s)}, 1669 \text{ (s)}, 1523 \text{ (w)}, 1505 \text{ (m), 1340 (s), 1270 (w), 825 (w), 742 (w).}\)

**MS** (EI, 70eV): m/z (%) = 221 (61)[M^+], 206(100), 160(57), 132(18), 43(16).
UV/VIS (dichloromethane): $\lambda_{\text{max}} (\text{lg} \varepsilon) = 218$ nm (3.10), 222 (3.12), 225 (3.12), 280 (4.01).

$\text{C}_{10}\text{H}_7\text{NO}_3\text{S}$ (221.23 g/mol).

HRMS (ESI-TOF): M+H$^+$
calcd: 221.01464 g/mol
found: 221.01566 g/mol

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 1-(5-nitrobenzo[b]thiophen-2-yl)ethanone (53b):
$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 1-(5-nitrobenzo[b]thiophen-2-yl)etanone (53b):

1.5.8 Willgerodt-Kindler-Synthesis of 4-(2-chloro-5-nitrophenyl)-butan-2-one (42b):

A mixture of 4-chloro-3-(3-oxobutyl) benzonitrile (42b) (227 mg, 1.0 mmol), $S_8$ (190 mg, mmol), and morpholine 10 mL was refluxed under argon for 6 h at 130 °C. The morpholine was removed in vacuum. The crude solid was separated by flash chromatography. The eluents for flash chromatography were 100 mL of the following mixture of CH$_2$Cl$_2$/MTBE were used: 100:0; 90:10; 80:20; 50:50; 20:80; 0:100. The fraction with 90:10 was isolated by flash chromatography (PE/EA, 5:1). The fraction with R$_f$ = 0.16 crystallized from CH$_2$Cl$_2$/C$_5$H$_{12}$ (1:3). The product was isolated as yellow crystals 51b (46 mg, 15%) with mp 195-197 °C.
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): $\delta$ = 1.53 ppm (s, 2H, NH$_2$), 3.18 (t, J = 9.84 Hz, 4H), 3.85 (t, J = 9.84 Hz, 4H), 6.29 (s, 1H), 6.62 (dd, J = 8.58, 2.28 Hz, 1H), 6.90 (“d”, J = 2.02 Hz, 1H), 7.50 (d, J = 8.60 Hz, 1H).

MS (EI, 70eV): m/z (%) = 290 (100)[M$^+$], 232 (27), 205 (11), 116 (12).

IR (KBr): $\nu$ = 3418 cm$^{-1}$ (s), 3354 (s), 2826 (m), 1617 (w), 1593 (m), 1523 (s), 1485 (w), 1444 (w), 1428 (m), 1215 (w), 1116 (m).

UV/VIS (dichloromethane): $\lambda_{max}$ (lg $\varepsilon$) = 215 nm (3.59), 232 (3.96), 259 (4.09), 327 (4.15).

C$_{14}$H$_{14}$N$_2$OS$_2$ (290.40 g/mol):
- calcd: C = 57.90%, H = 4.86%, N = 9.65%, O = 5.51%, S = 22.08%
- found: C = 56.46%, H = 5.26%, N = 9.28%, S = 19.53%

HRMS (ESI-TOF): M$^+$H$^+$
- calcd: 290.05474 g/mol
- found: 290.05515 g/mol.

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): of 7-amino-2-(morpholin-4-yl)thieno(3,2-b)(1)benzothiophene (51):
1.5.9 Synthesis 2-chloro-3-iodopyridine (41c):

\[
\begin{align*}
\text{NH}_2 & \xrightarrow{\text{NaNO}_2, \text{KI, MeCN}} \text{I} \\
\text{45} & \xrightarrow{\text{p-TsOH, 20 °C, 50 min}} \text{41c}
\end{align*}
\]

Prepared similar to the method described by Elena et al.\[40\] A 250 mL roundbottomed flask was charged with a stir bar. To a solution of p-TsOH.H₂O (3.42 g, 17.92 mmol) in acetonitrile 20 mL was added the 3-amino-2-chloropyridine (45) (771.36 mg, 6 mmol) at room temperature. The resulting suspension of amine salt was cooled to 5-10 °C and to this was added, gradually, a solution of NaNO₂ (0.818 g, 12 mmol) and KI 2.45 g, 15 mmol) in H₂O 3.6 mL. The reaction mixture was stirred for 10 min then allowed to cool to 20 °C and stirred for 50 min. To the reaction mixture was added water 100 mL, NaHCO₃ 1 M until pH = 9-10 and Na₂S₂O₃ 2 M, 12 mL. The solid obtained was filtered off and dried in vacuum at 100 °C. The product was isolated as yellow solid 41c (457 mg, 32%) with mp 93 °C.

\( \quad \)

\( ^1\text{H NMR} \) (200 MHz, CDCl₃, 25 °C): \( \delta = 7.61 \text{ ppm (d, J = 8.83 Hz, 1H), 8.16 (dd, J = 8.84, 2.52 Hz, 1H), 8.70 (d, J = 2.78 Hz, 1H).} \)

\( ^{13}\text{C NMR} \) (100 MHz, CDCl₃, 25 °C): \( \delta = 99.37 \text{ ppm (s), 125.45 (d), 147.34 (d), 150.25 (d), 158 (s).} \)

\( \text{MS(El, 70eV): m/z (%)} = 239 (100) \left[ \text{M}^+ \right], 267 (22), 253 (25), 237 (59), 225 (38), 127 (33), 110 (51), 75 (62), 46 (44). \)

\( \text{C}_5\text{H}_3\text{ClIN}(239.44 \text{ g/mol).} \)

\( \text{calcd: C = 25.08%, H = 1.26%, N = 5.85%} \)
\( \text{found: C = 25.00%, H = 1.04%, N = 5.80%,} \)
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 2-chloro-3-iodopyridine (41c):

\[ \begin{array}{c|cccc|cccc|cccc}
\text{ppm} & 1.0000 & 0.9393 & 0.9730 & 0.0921 & & & & & & & \\
\end{array} \]

$^{13}$C NMR (100 MHz, CDCl$_3$, 25 °C): 2-chloro-3-iodopyridine (41c):

\[ \begin{array}{c|cccc|cccc|cccc|cccc}
158.2363 & 150.2511 & 147.3379 & 125.4538 & 99.3707 & & & & & & & \\
\text{ppm} & 101 & 20 & 30 & 40 & 50 & 60 & 70 & 80 & 90 & 100 & 110 & 120 & 130 & 140 & 150 & 160 & 170 & 180 & 190 \\
\end{array} \]
1.5.10 Synthesis of 4-(2-chloropyridine-3-yl)butan-2-one (42c):

\[
\begin{align*}
\text{Pd(OAc)}_2, \text{LiCl}, \text{Et}_3\text{N}, \text{DMF} \\
\text{120 °C, 3 d}
\end{align*}
\]

Prepared similar to the method described by Kadzimirsz et al.\[38\] A mixture of 2-chloro-3-iodopyridine (41c) (390 mg, 1.63 mmol), 1-buten-3-ol (43) (0.49 mL, 5 mmol), 3.30 mL triethylamine, LiCl (130 mg, 3 mmol), Pd(OAc)_2 (46 mg, 0.2 mmol), and 10 mL DMF in a screw-capped tube was stirred for 3 d at 120 °C under an argon atmosphere. After cooling to room temperature, MTBE (80 mL) was added and the mixture was filtered through a small pad of silica. The organic filtrate was washed 3 times with water (50 mL), once with brine (50 mL). The solvent was removed at the rotatory evaporator to remain a brown residue. The residue was separated by flash chromatography (MTBE/PE; 1:10, \( R_f \approx 0.11 \)) and drying in vacuum. The product was isolated as yelow oil 42c (223 mg, 74 %).

\[^1H \text{NMR (400 MHz, CDCl}_3, 25 °C): \delta = 2.19 \text{ ppm (s, 3H), 2.85 (t, J = 7.58 Hz, 4H), 3.10 (t, J = 0 7.58 Hz, 4H), 7.50 (d, J = 8.58 Hz, 1H), 8.05 (dd, J = 8.84, 2.54 Hz,1H), 8.15 („d”, J = 2.54 Hz, 1H).}

\[^{13}C \text{NMR (400 MHz, CDCl}_3, 25 °C): \delta = 27.18 \text{ ppm (t), 29.93 (s), 42.27 (t), 122.61 (d), 135.16 (d), 139.49 (d), 147.60 (s), 151.16 (s), 206.83 (s).}

\text{Ms}(70eV, \text{EI}): m/z (%) = 184 (32) [M^+1], 168 (21), 148 (100), 140 (23), 126 (13), 104 (28), 77 (10), 43 (49).

\text{C}_9\text{H}_{10}\text{ClNO (183.63 g/mol).}

\text{HRMS (ESI-TOF): M+H}^+ \\
\text{calcd: 183.04000 g/mol} \\
\text{found: 183.04605 g/mol}
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 4-(2-chloropyridine-3-yl)butan-2-one (42c):

$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 4-(2-chloropyridine-3-yl)butan-2-one (42c):
1.5.11 Willgerodt-Kindler of 2-(2-chloropyridine-3-yl)-butan-2-one (42c):

A mixture of 2-(2-chloropyridine-3-yl) butan-2-one (42c) (223 mg, 1.2 mmol), S₈ (190 mg, 6 mmol), and morpholine (0.4 mL, 5 mmol) in a screw-capped tube was stirred for 6 h at 100 °C under an argon atmosphere. After cooling to room temperature, the excess morpholine is removed in vacuum at 75 °C. The crude solid was fractionated by flash chromatography (MTBE/PE, 1:5; Rf = 0.14, 0.35). Only the fraction with Rf = 0.14 give 2-morpholin-4-yl-3,8-dithia-4-aza-cyclopenta(a)indane (54c) 23 mg (7% yield) as brown solid with mp 175-177 °C. The fraction with Rf = 0.35 could not be isolated in pure form failed.

**¹H NMR** (200 MHz, CDCl₃, 25 °C): δ = 3.14 ppm (dd, J = 6.5, 3.2 Hz, 4H), 3.82 (m, 3H), 6.28 (s, 1H), 7.23 (m, 2H), 7.55 (dd, J = 7.8, 0.5, 1H), 7.73 (m, 1H).

**¹³C NMR** (50 MHz, CDCl₃, 25 °C): δ = 51.27 ppm (t), 66.24 (t), 119.32 (d), 120.72 (s), 122.69 (d), 123.48 (d), 124.36 (d), 133.51 (s), 137.38 (s), 140.01 (s), 161.53 (s).

C₁₃H₁₂N₂O₃S₂ (276 g/mol).
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): compound 54c

$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): of 54c:
1.5.12 Synthesis of 3-iodo-4-hydroxypyridine (47):

Prepared similar and modification from the method described by F.W Broekman et al.\textsuperscript{[41]}

To a solution of 4-hydroxypyridine (46) (4.76 g, 50.1 mol) and Na\textsubscript{2}CO\textsubscript{3} (10.8 g, 100 mmol) in water (200 mL) was added in small portions of I\textsubscript{2} (12.7 g, 50.1 mmol) within 10 minutes. The reaction mixture was stirred for 14 h. Then, the solution was adjusted to pH 5 with concentrate HCl. The solid obtained was filtered and suspended in boiling ethanol 100 mL. The resulting solids were hot filtered. The solvent was removed at the rotatory evaporator and a brown residue remained. The residue was crystallized from methanol and gave 2.91 g (21%) of product as brown solid (47) with mp 280 °C. (Lit.\textsuperscript{[41]} mp 282 °C, dec.). This product was used without further purification.

\textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}, 25 °C): $\delta$ = 3.23 ppm (s, 1H), 6.25 (d, J = 7.1 Hz, 1H), 7.78 (d, J = 7.1 Hz, 1H), 8.35 (s, 1H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}, 25 °C): $\delta$ = 97.33 ppm (s), 118.28 (d), 143.07 (d), 148.86 (d), 178.73 (s).

MS (EI, 70eV): m/z = 221 (100%) [M$^+$], 127 (12), 94 (35) 67 (13), 39 (33).
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 3-iodo-4-hydroxypyridine (47):

$^{13}$C NMR (100 MHz, CDCl$_3$, 25 °C): 3-iodo-4-hydroxypyridine (47):
1.5.13 Synthesis of 3-iodo-4-chloropyridine (41d):

Prepared similar to the method described by A. J Kay et al.\textsuperscript{[42]} To a mixture of dry 3-iodo-4-hydroxypyridine (47) (986mg, 4.46 mmol) in phosphoryl chloride 20 mL was added phosphorus pentachloride (1.47g, 7.05 mmol). The reaction mixture was refluxed for 16 h at 100 °C under an argon atmosphere. The solution was then cooled to room temperature and poured in small portions into water 50 mL. The temperature of the aqueous solution did not rise above 70 °C. The reaction mixture was stirred for 2-3 h. The mixture had cooled to 5 °C and was partially neutralized via the cautious addition 30% NaOH (500-700 mL) and the slurry made slightly basic. The solid was collected by filtration and washed thoroughly with water to give 3-iodo 4-chloropyridine (41d) as a white powder (468 mg, 22% yield).

\[^1\text{H} \text{NMR} \text{ (200 MHz, DMSO, 25 °C): } \delta = 3.48 \text{ ppm (s, 1H), 6.25 (d, J = 7.1 Hz, 1H), 7.78 (d, J = 7.1 Hz, 1H), 8.35 (s, 1H).} \]
$^{13}\text{C NMR}$ (100 MHz, DMSO, 25 °C): $\delta = 99.34$ ppm (s), 125.42 (d), 147.71 (d), 150.39 (s), 158.37 (d).

$^1\text{H NMR}$ (200 MHz, DMSO, 25 °C: 3-iodo-4-chloropyridine (41d).
$^{13}$C NMR (200 MHz, DMSO, 25 °C: 3-iodo-4-chloropyridine (41d):

![Chemical Structure]

1.5.14 Synthesis of 1-hexen-3-ol (49):

\[ \text{Br} + \text{O} \rightarrow \text{OH} \]

120 + 121 → 49

Prepared similar to the method described by F. W. Bailey et al. A solution of 1-bromo-propane (120) (7.38g, 0.06 mmol) and magnesium metal turnings (1.64g, 0.068 mmol) in 20 mL of dry THF was slowly added with freshly acrolein (121) (4 mL, 0.06 mmol) at room temperature under an argon atmosphere. After the reaction mixture was stirred for 24 h, 1M of (NH$_4$)$_2$HPO$_4$ (63 mL) was added and the mixture was extracted 3 times with diethyl ether (20 mL), the organic phase was dried with MgSO$_4$, and solvent was removed. Distillation of the residue gave 2.7 g (45%) of the alcohol 49: bp 45 °C (7.5 mm) which was reported earlier.

$^1$H NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$ = 0.94 ppm (m, 3H), 1.45 (m, 1H), 180 (d, J = 30.8 Hz, OH), 4.13 (m, 1H), 5.08 (m, 1H), 5.23 (m,1H), 5.79 (m,1H).

$^{13}$C NMR (100 MHz, CDCl$_3$, 25 °C): $\delta$ = 13.96 ppm (q), 18.55 (t), 39.20 (t), 72.99 (d), 114.43 (t.), 114.39 (t).
**MS** (EI, 70eV): m/z (%) = 183 (8), 157 (20), 139 (13), 101 (54); 83 (51), 71 (25); 67 (17), 57 (100) [M]+, 41 (30).

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 1-hexen-3-ol (49).
13C NMR (50 MHz, CDCl₃, 25 °C) : 1-hexen-3-ol (49):

![13C NMR spectrum]

1.5.15 Synthesis 1-(4-chloropyridine-3-yl)hexan-3-one (48d):

\[
\begin{align*}
\text{CH₂CH₂OH} & \quad + \quad \begin{array}{c}
\text{Cl} \\
\text{I} \\
\text{N}
\end{array} \\
\xrightarrow{\text{Pd(OAc)}₂, \text{LiCl, Et₃N, DMF}} & \quad \begin{array}{c}
\text{Cl} \\
\text{O}
\end{array} \\
\text{OH} & \quad \text{49} & \quad \text{41d} & \quad \text{48d}
\end{align*}
\]

Prepared similar to the method described by Kadzimirsz et al.\[38]\ A mixture of 4-chloro-3-iodopyridine (41d) (511 mg, 2.14 mmol), 1-hexen-3-ol (49) (427.6 mg, 4.27 mmol), 1.687 mL triethylamine, LiCl (180 mg, 3 mmol), Pd(OAc)₂ (49.2 mg, 0.2 mmol), and 10 mL DMF in a screw-capped tube was stirred for 3 d at 120 °C under an argon atmosphere. After cooling to room temperature, MTBE (80 mL) was added and the organic phase was extracted 3 times with water (50 mL), once with brine (50 mL) and was dried over magnesium sulphate. The solvent was removed at the rotatory evaporator to give a remaining brown residue. The residue was purified by flash chromatography (silica/MTBE/PE; 1:10, Rₜ = 0.2). Yield after drying in vacuo: 395 mg (87%) of 1-(4-chloropyridine-3-yl)hexan-3-one (48d) as a slightly yellow oil. An analytically pure sample was obtained by Kugelrohr distillation (100 °C, 0.75 mbar).
$^1$H NMR (400 MHz, CDCl$_3$, 25 °C): $\delta = 0.87$ ppm (t, $J = 7.4$ Hz, 3H), 1.41-1.69 (m, 2H), 2.36 (t, $J = 7.3$ Hz, 2H), 2.60-2.79 (m, 2H), 2.98 (t, $J = 7.4$ Hz, 2H), 7.24 (s, 1H), 8.32 (d, $J = 5.3$ Hz, 1H), 8.43 (s, 1H).

$^{13}$C NMR (400 MHz, CDCl$_3$, 25 °C): $\delta = 13.72$ ppm (q), 17.31 (t), 24.82 (t), 41.60 (t), 44.64 (t), 124.45 (d), 134.77 (s), 143.64 (s), 148.64 (d), 151.49 (d), 209.01 (s).

MS (EI, 70eV): m/z (%) = 211(12)[M$^+$], 176 (12), 168 (42), 140 (100), 126 (39), 104 (19), 77 (14), 71 (54), 51 (12), 43 (58).

IR (KBr): $\nu = 3440$ cm$^{-1}$ (s), 1710 (s), 1626 (m), 1487 (w), 832 (m).

C$_{11}$H$_{14}$ClNO (211.69 g/mol):

HRMS (ESI-TOF): M+H$^+$

  calcld: 211.07784 g/mol
  found: 211.07791 g/mol.

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 1-(4-chloropyridine-3-yl)hexan-3-one (48d):
$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 1-(4-chloropyridine-3-yl)hexan-3-one (48d):
A mixture of 1-(4-chloropyridine-3-yl)hexan-3-one (48d) (317.5 mg, 1.2 mmol), S₈ (190 mg, 6 mmol), and morpholine 10 mL in a screw-capped tube was stirred for 6 h at 130 °C under an argon atmosphere. Cooling to room temperature and evaporation of the excess morpholine in vacuum at 75 °C gave 528 mg of crude product mixture as a brownish solid. The eluents for flash chromatography were 100 mL of the following mixture of CH₂Cl₂/MTBE were used: 100:0; 90:10; 80:20; 50:50; 20:80; 0:100 and methanol. Only the fraction in methanol showed promising spectra of the expected product 55d which could be identified by ¹H NMR spectroscopy. An attempt to isolate it in pure form failed while NMR signals clearly belong to the structure of expected product 55d.

¹H NMR (200 MHz, CDCl₃, 25 °C): δ = 2.06-2.28 (m, 2H), 2.78-2.88 (m, 2H), 2.96-3.07 (m, 2H), 3.67-3.79 (m, 4H), 4.24-4.32 (m, 4H).
1.5.17 Synthesis 2-and 3-acetylbenzothiophene (69):

\[
\begin{array}{c}
\text{68} & + & \text{O} & \text{Cl} & \xrightarrow{\text{AlCl}_3 / \text{CH}_2\text{Cl}_2} & \text{69}
\end{array}
\]

**Method A:**

Acetyl chloride (122) (0.28 g, 3.6 mmol) was added to a mixture of dichloromethane 30 mL and aluminium chloride (0.52 g, 3.96 mmol) at 10 °C under argon. After 1 h of stirring at this temperature, the solution of benzothaiophene (68) (0.41 g, 3 mmol) in 10 mL dichloromethane were slowly added and stirred for 1 h. To the reaction mixture were added 5.0 mL (2.5 M) of hydrochloric acid and dichloromethane successively, followed by extraction with chloroform (3 x 20 mL). The combined organic layer was washed with brine (20 mL), dried with Na₂SO₄ and concentrated. 84 mg of benzothiophene was recovered by distillation in the kugelrohr oven at 125 °C and 0.5 mbar. The residue was fractionated by flash chromatography (silica, petroleum ether/ethylacetate (10%), R_f = 0.26, 0.1): The fraction with R_f = 0.26 gave 69 329 mg (79%) yield as a white-yellow solid of a mixture isomer containing 2- and 3-acetylbenzothiophene, mp 35-39 °C which was used without further purification.

**1H NMR** (200 MHz, CDCl₃, 25 °C): \( \delta = 2.58 \text{ ppm (d, } J = 3.2 \text{ Hz, } 5\text{H}), 7.38 \text{ (m, } 3\text{H}), 7.81 \text{ (m, } 2\text{H}), 8.20 \text{ (s, } 1\text{H}), 8.70 \text{ (m, } 1\text{H}).

**13C NMR** (200 MHz, CDCl₃, 25 °C): \( \delta = 26.83 \text{ ppm (q), } 28.21 \text{ (q), } 123.03 \text{ (d), } 125.03 \text{ (d), } 125.93 \text{ (d), } 127.45 \text{ (d), } 129.67 \text{ (d), } 135.57 \text{ (d), } 136.50 \text{ (s), } 137.34 \text{ (s), } 139.15 \text{ (d), } 139.88 \text{ (s), } 193.08 \text{ (s).}

**MS** (EI, 70eV): m/z (%) = 176 (57) [M⁺], 169 (100), 133 (25), 89 (32).
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 2- and 3-acetylbenzothiophene (69):

$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 2- and 3-acetylbenzothiophene (69):
Method B:

![Chemical structure]

4.95 mL (8.0 mmol) of n-buthyllithium (15% in hexane) were slowly added to the solution of benzothiophene (68) (1.07 g, 8.00 mmol) in 10 mL of abs. THF at -40 °C. After stirring for 1 h the mixture was allowed to warm up to 10 °C. To this reaction mixture was added the solution of acetic anhydride (9.4 mL, 100 mmmol) in 10 mL of abs. THF at -78 °C. The reaction mixture was stirred for 1 h and allowed warm up to room temperature for 24 h. To the reaction mixture was added 5 mL of NaHCO₃ (1 M), then extracted with MTBE and filtered through a small pad of silica and concentrated. The product was isolated with distillation in the kugelrohr oven at 125 °C, to give a white solid 69a (929 mg, 66%) with mp 37 °C which was used without further purification.

1.5.18 Willgerodt-Kindler-synthesis 2-acetylbenzothiophene (69a):

Condition A.

![Chemical structure]

A mixture of 2-acetylbenzothiophene (69a) (264.3 mg, 1.5 mmol), S₈ (190 mg, 6 mmol), morpholine 10 mL was refluxed under argon for 6 h at 130 °C. The morpholine was removed in vacuum. The crude solid was separated by flash chromatography. The eluents for flash chromatography were 100 ml of the following mixture of PE/MTBE were used: 100:0; 90:10; 80:20; 50:50; 20:80; 0:100. The fraction with Rₘ = 0.26 was fractionated by HPLC (Hexane/MTBE, 1:7) to gave 2-morpholin-4-yl-thieno(3,2-b)(1)benzothiophene 58K 26 mg (11% yield) of product as brown solid with mp 170-175 °C.

**¹H NMR** (400 MHz, CDCl₃, 25 °C): δ = 3.23 ppm (ddd, J = 27.0, 11.0, 5.8 Hz, 4H), 3.90 (dd, J = 5.7, 4.0, Hz, 1H), 6.39 (s, OH), 7.24 (m, 2H), 7.38 (ddd, J = 15.1, 10.4, 4.6,Hz, 1H), 7.63 (ddd, J = 19.5, 7.5 Hz, 1H), 7.82 (t, J = 9.1 Hz, 1H).

**¹³C NMR** (200 MHz, CDCl₃, 25 °C): δ = 51.19 ppm (t), 66.30 (t), 98.63 (s), 119.34 (d), 122.16 (d), 123.51 (d), 124.62 (d), 133.58 (s), 137.28 (s) 140.33 (s) 161.58 (s).
MS (EI, 70eV): m/z (%) = 274.9 (100) [M⁺], 246 (16), 217 (43), 203 (13), 190 (26), 145 (13), 108 (10).

C₁₄H₁₃NOS₂ (275.39 g/mol):

HRMS (ESI-TOF): M+H⁺
calcd: 275.3900 g/mol
found: 275.04321 g/mol.

¹H NMR (200 MHz, CDCl₃, 25 °C) of 58K
$^{13}$C NMR (100 MHz, CDCl$_3$, 25 °C): (58K):

| ppm  | 66.2544 | 51.3629 | 119.2891 | 98.5828 | 122.1165 | 122.6957 | 123.4655 | 124.5553 | 124.5781 | 133.5329 | 137.2291 | 140.2851 | 161.5402 |

Conditions B.

![Diagram]

69a

1. S$_8$ / Morpholine
145 °C, 3 h

A mixture of 2-acetylbenzothiophene (69a) (150 mg, 0.85 mmol), S$_8$ (190 mg, 6 mmol), Morpholine 5 mL was refluxed under argon for 3 h at 145 °C. The morpholine was removed at 150 °C in vacuum for 3 h. The crude solid was separated by flash chromatography. The eluents for flash chromatography were 100 mL of the following mixture of PE /MTBE were used: 100:0; 90:10; 80:20; 50:50; 20:80; 0:100. The fraction with 90:10 was isolated by flash chromatography (PE : MTBE, 5:1). The fraction with $R_f = 0.25$ was fractionated by HPLC (Hexane/MTBE, 1:7) to gave 51 mg (22%) of 2-morpholin-4-yl-thieno(3,2-b)(1)benzothiophene (58K) as brown solid with mp 170-175 °C.
1.5.19 Willgerodt-Kindler-reaction of 2-acetylbenzothiophene (69a): with pyrrolidin

![Reaction Scheme]

A mixture of 2-acetylbenzothiophene (69a) (243 mg, 1.38 mmol), S₈ (190 mg, 6 mmol), pyrrolidin 5 mL was refluxed under argon for 6 h at 120 °C. The pyrrolidin was removed at 50 °C in vacuum for 3 h. The crude solid was separated by flash chromatography. The eluents for flash chromatography were 100 mL of the following mixture of PE/MTBE were used:100:0; 90:10; 80:20; 50:50; 20:80; 0:100. The fraction with 100:0 and 90:10 were isolated by flash chromatography with toluene; R_f = 0.77, 0.58, 0.38, 0.18. The fraction with R_f = 0.18 gave 21 mg (8% yield) of 90 as yellow oil. The fraction with R_f = 0.38 gave 19 mg of by-product 91 as brown solid with mp 156-157 °C. (Lit.[44] mp 156-158 °C, dec.).

**1H NMR (200 MHz, CDCl₃, 25 °C):** \( \delta = 1.93-2.05 \) (m, 4H), 3.63-3.69 (m, 2H), 3.84-3.90 (m, 2H), 7.34 (s, 1H), 7.12 (s, 1H), 7.16-7.31 (m, 2H), 7.51-7.79 (m, 2H).

**C_{14}H_{15}NS_{2}** (261.41 g/mol):

**HRMS (ESI-TOF):** M+H⁺  
  calcd: 261.06467 g/mol  
  found: 261.06473 g/mol.
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C) of (90)
1.5. 20 Synthesis of 3-bromobenzob[b]thiophene (71):

\[
\text{68} + \text{Br} + \text{O} \xrightarrow{\text{CHCl}_3/\text{CH}_3\text{COOH}} \text{Br} \xrightarrow{4 \text{ h}, 0 \degree \text{C}, r.t 24 \text{ h}} \text{71}
\]

Prepared similar to the method described by J. Fournier Dit Chabert et al.\cite{45} To a solution of benzothiophene (68) (5 g, 37.25 mmol) in dry chloroform (37.5 mL) and dry acetic acid (37.5 mL) was added stepwise N-bromosuccinimide (72) (8.3 g, 46.66 mmol) for 4 h at 0 °C and then allowed to stir at room temperature for 24 h. Then chloroform (30 mL) was added and resulting mixture was successively washed with a saturated sodium thiosulphate solution (100 mL), a saturated sodium carbonate solution (100 mL) and water (75 mL). The extracted organic layer was then dried over MgSO₄, filtrated and evaporated. The resulting red liquid was filtered through a pad of silica, eluting with cyclohexane to afford product as a yellow oil 71 (6.17g, 78%) which was used without further purification.

\(^1\text{H NMR}\) (200 MHz, CDCl₃, 25 °C): \(\delta = 7.30 \text{ ppm (m, 3H, Aryl)}\). 7.78 ppm (d, J = 24.1 Hz, 2H).

\(^{13}\text{C NMR}\) (200 MHz, CDCl₃, 25 °C): \(\delta = 107.69 \text{ ppm (s), 122.72 (d), 123.05 (d), 123.47 (d), 125.02 (d), 125.29 (d), 137.52 (s), 138.56 (s)}\).

\(\text{Ms (70eV, EI): m/z (%) = 214 (100) [M^+1], 133 (28), 89 (37).}\)

\(\text{C}_8\text{H}_5\text{BrS (213.09 g/mol).}\)

\text{calcd: C = 45.09%, H = 2.37%}
\text{found: C = 45.01%, H = 2.17%}
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 3-bromobenzo(b)thiophene (71):

![1H NMR spectrum](image)

$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 3-bromobenzo(b)thiophene (71):

![13C NMR spectrum](image)
1.5.21 Synthesis of 3-acetylbenzothiophene (69b):

3-Bromobenzo(b)thiophene (71) 1/5 of the required (4.26 g, 0.02 mol) is added to magnesium turnings (0.48 g, 0.02 mol) in 20 mL of anhydrous THF which are treated with one iodine crystal. As soon as the Grignard reaction starts (heat evolution, disappearance of the iodine color), the remaining 3-bromobenzo(b)thiophene solution is added. The mixture is refluxed an additional 30 min and then cooled in ice. Acetic anhydride (123) (2.04 g, 0.02 mmol) in 20 mL of anhydrous THF is added dropwise followed by refluxing for 24 h. The mixture is cooled to 0 °C and ca. 60 mL of saturated aqueous (NH4)2HPO4 solution is added carefully until the initially formed precipitated of Mg(OH)2 and the mixture was extracted 3 times with diethylether 20 mL), the organic phase was dried with MgSO4 and solvent was removed. Distillation of the residue gave 3.38 g (52%) of 3-acetylbenzothiophene (69b) mp 65 °C which was used without further purification.

1H NMR (400 MHz, CDCl3, 25 °C): \( \delta = 2.70 \text{ ppm (m, 3H), 7.29 (d, J = 9.3 Hz, OH), 7.46 (dtd, J = 14.9, 7.2, 1.2, Hz, 2H), 7.91 (m, 1H), 7.99 (d, J = 19.9, OH).} \)

13C NMR (100 MHz, CDCl3, 25 °C): \( \delta = 27.44 \text{ ppm (q), 123.07 (s), 125.05 (d), 125.95 (d), 127.47 (d), 129.64(d), 139.21 (d), 142.73 (s), 144.08 (s), 192.20 (s).} \)

IR (KBr): \( \bar{\nu} = 3443 \text{ cm}^{-1}(\text{br}), 3046 (\text{m}), 2958 (\text{m}), 2852 (\text{ ), 1588 (m), 1518 (s), 1117 (s), 919 (s), 748 (s), 721 (m), 634 (m).} \)

C10H8OS (176.23 g/mol).

Caled: C = 68.15%, H = 4.58%

Found: C = 68.10%, H = 4.38%
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 3-acetylbenzothiophene (69b).

$^{13}$C NMR (100 MHz, CDCl$_3$, 25 °C): 3-acetylbenzothiophene (69b).
1.5.22 Willgerodt-Kindler-reaction with 3-acetylbenzothiophene (69b):

\[ \begin{align*}
\text{S}_8 / \text{Morpholine} \\
145 \, ^\circ \text{C}, \, 3 \, \text{h}
\end{align*} \] 

3-Acetylbenzothiophene (69b) (176 mg, 1 mmol), S\(_8\) (190 mg, 6 mmol), morpholine 5 mL was refluxed under argon for 3 h at 145 \(^\circ\)C. The morpholine was removed at 150 \(^\circ\)C in vacuo for 3 h. The crude solid was separated by flash chromatography with PE:EA (5:1). The fraction with \( R_f = 0.14 \) gave 43 mg (6\% yield) of product 80 as brown oil.

**\(^1\)H NMR** (200 MHz, CDCl\(_3\), 25 \(^\circ\)C): \( \delta_H = 3.38 \, \text{ppm} \) (dt, \( J = 7.0, \, 2.2 \, \text{Hz}, \, 2H \)), 3.49 (dd, \( J = 5.7, \, 3.2 \, \text{Hz}, \, 2H \)), 3.73 (dd, \( J = 6.3, \, 3.6 \, \text{Hz}, \, 2H \)), 4.28-4.47 (m, 2H), 4.42 (d, \( J = 1.3 \, \text{Hz}, \, 2H \)), 7.23 (s, 1H), 7.25-7.41 (m, 2H), 7.64-7.74 (m, 1H), 7.75-7.89 (m, 1H),
1.5.23 Willgerodt-Kindler-reaction of pyrrolidin (92):

\[
\begin{array}{c}
\text{N-H} \\
\text{92} \\
\end{array}
\xrightarrow{S_8 \text{ 130 }^\circ\text{C, 4 h}}
\begin{array}{c}
\text{N-S-S-N} \\
\text{91} \\
\end{array}
\]

A mixture of pyrrolidin (92) (5 mL, 61 mmol), S\textsubscript{8} (190 mg, 6 mmol) was refluxed under argon for 4 h at 130 °C. The pyrrolidin was removed at 150 °C in vacuum for 1 h. The crude solid was separated by flash chromatography with ethylacetate; \(R_f = 0.24, 0.12\). The fraction with \(R_f = 0.24\) was crystallized from methanol to give product 91 29 mg (1% yield) as brown solid with mp 156-159 °C (Lit.\textsuperscript{[44]} mp 156-158 °C, dec.).

\(^1\text{H NMR (400 MHz, CDCl}_3, 25 ^\circ\text{C}): \delta = 1.94-2.03 \text{ (m, 4H), 2.05-2.15 \text{ (m, 4H), 3.23 \text{ (s, 4H), 3.83-3.90 \text{ (m, 8H).}})}
\]

\(^{13}\text{C NMR (100 MHz, CDCl}_3, 25 ^\circ\text{C):} \\delta = 24.23 \text{ (t), 26.23 \text{ (t), 41.35 \text{ (t), 50.87 \text{ (t), 53.99\textsuperscript{(t)}, 198.60 \text{ (s).}}}}
\]

\textbf{MS (EI, 70eV): } m/z (%) = 256 (74) [M\textsuperscript{+}], 223 (16), 187 (21), 154 (100), 142 (61), 128 (18), 70 (19).

\textbf{1H NMR (400 MHz, CDCl}_3, 25 ^\circ\text{C):} of 91
13C NMR (100 MHz, CDCl3, 25 °C): of 91

1.5.24 Synthesis of 2-chlorobenzoylchloride (95):

\[
\begin{align*}
\text{HOOC} & \quad \xrightarrow{\text{SOCl}_2} \quad \text{Cl} \\
\text{Cl} & \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \ quad
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 2-chlorobenzoylchloride (95):

$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 2-chlorobenzylchloride (95):
1.5.25 Synthesis of 4-(1H-inden-1-yl)morpholine (97):

Prepared similar to the method described by A.R. Katritzky et al.[47] A mixture of 1-indanone (96) (3 g, 22.7 mmol), morpholine (5) (2.2 mL, 24.9 mmol), pTSOH (20 mg) in dry toluene 30 mL was refluxed at 140 °C until the water was completely removed with dean stark trap over 16 h. The toluene was seperated with distillation at 140 °C The product was isolated in the kugelrohr oven at 225 °C gave as sticky oil (97) (1.76 g, 39%) which was used without further purification.

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): $\delta$ = 3.03 ppm (m, 4H), 3.25 (d, J = 2.3 Hz, 2H), 3.82 (m, 4H), 5.59 (t, 1H), 7.26 (m, 5H).

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): 4-(1H-inden-1-yl)morpholine (97).
1.5.26 Synthesis (E)-2-((2-chlorophenyl)(hydroxy)methyl-2,3-dihydro-1H-inden-1-one (93):

A mixture of 4-(1H-inden-1-yl) (97) (1.42 g, 7 mmol), 1.2 mL triethylamine in dry toluene 15 mL was stirred under argon for 24 h at room temperature. To the reaction mixture was dropwise added (1.45 g, 8.4 mmol) 2-chlorobenzoylchloride (95) and stirred at 35 °C for 1 h and allowed cooling to 25 °C for 24 h. To the reaction mixture was added 0.5 mL of HCl (20%) and the mixture was refluxed at 100 °C for 30 minutes. After cooling to room temperature, brine (50 mL) was added and the pH for water layer was adjusted to 5-6 with diluted NaOH, then the organic phase was extracted 3 times with MTBE (50 mL), and filtered through a small pad of silica and finally concentrated. The product was isolated with distillation in the kugelrohr oven at 225-250 °C to give (93) as yellow viscous oil (1.25 g, 66%) which was used without further purification.

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): $\delta = 3.46$ ppm (m, 2H), 7.38 (m, 7H), 7.77 (m, 1H).

Ms(70eV, EI):m/z (%) = 270 (30) [M$^+$], 254 (23), 235 (100), 139 (71), 111 (13).

$^1$H NMR (200 MHz, CDCl$_3$, 25 °C): inden-1-one 93)
1.5.27 Willgerodt-Kindler-reaction of (E)-2-((2-chlorophenyl)(hydroxy)methyl-2,3-dihydro-1H-inden-1-one (93):

\[
\begin{align*}
\text{Cl} & \quad \text{OH} \\
\text{S8, Morpholine} & \quad 130 \, ^\circ\text{C}, 3 \, \text{h} \\
\end{align*}
\]

(E)-2-((2-chlorophenyl)(hydroxy)methyl-2,3-dihydro-1H-inden-1-one (93) (176 mg, 1 mmol), S₈ (190 mg, 6 mmol), Morpholine 5 mL was refluxed under argon for 3 h at 130 °C. The morpholine was removed at 50 °C in vacuo for 1 h to give 1.01 g of sticky black oil which was separated by flash chromatography. The eluents for flash chromatography were 100 mL of the following mixture of PE/MTBE were used: 100:0; 90:10; 80:20; 50:50; 20:80; 0:100. The fraction with 100:0 and 90:10 were isolated by flash chromatography with toluene; \( R_f = 0.71, 0.54, 0.33, 0.16 \). The fraction with \( R_f = 0.16 \) gave 51 mg showed a promising spectra. The NMR-spectra indicated a mixture of the starting material and the methylene groups of morpholine but the structure of the products could not be determined. The expected product 104 was not obtained. Therefore, the reaction of (E)-2-((2-chlorophenyl)(hydroxy)methyl-2,3-dihydro-1H-inden-1-one (93) with WK failed to afford the product.
1.5.28 Thionation reaction of (E)-2-((2-chlorophenyl)(hydroxy)methyl-2,3-dihydro-1H-inden-1-one (92):

\[
\begin{align*}
\text{Cl} & \quad \text{OH} \\
\text{C} & \quad \text{O} \\
\end{align*}
\]

\[
\begin{align*}
\text{Cl} & \quad \text{SH} \\
\text{C} & \quad \text{O} \\
\end{align*}
\]

\[
\begin{align*}
\text{93} & \quad \text{Lawesson's reagent, Toluene} \\
\text{105} & \quad 130 \, ^\circ \text{C}, 4 \, \text{h} \\
\end{align*}
\]

Prepared similar to the method described by T. J Curphey et al.\cite{48} A mixture of 93 (252 mg, 0.93 mmol), Lawesson’s reagent (755 mg, 1.87 mmol) in dry toluene 10 mL was refluxed at 130 °C 4 h. After cooling to room temperature, filtered through a small pad of silica and concentrated. The crude product was separated by flash chromatography (PE : MTBE, 5:1). The fraction with \( R_f = 0.26 \) was to gave 38 mg (14\%) of (E)-2-((2-chlorophenyl)(mercapto)methylene)-2,3-dihydro-1H-inden-1-one (105) as yellow solid with mp 65-66 °C.

\(^1\text{H NMR}\) (400 MHz, CDCl\(_3\), 25 °C): \( \delta = 4.07 \) ppm (s, 2H), 7.28 (s, 1H), 7.51 (m, 1H), 7.67 (m, 3H), 8.70 (dd, \( J = 7.8, 1.7 \) Hz, OH).

\(^1\text{H NMR}\) (200 MHz, CDCl\(_3\), 25 °C): (105).
$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): (105).

1.5.29 Synthesis of 2-(phenylethyl)benzaldehyde (107):

\[
\begin{align*}
\text{Br} & \quad \text{H} \\
\text{O} & \quad \text{O} \\
\text{106} & \quad \text{111} \\
\text{Pd(OAc)$_2$, PPh$_3$, CuI, Et$_3$N} & \quad \text{80 °C, 16 h} \\
\text{107}
\end{align*}
\]

Prepared similar to the method described by D. Hildebrandt ($^{[49]}$) A mixture of 2-bromobenzaldehyde (106) (740 mg, 4 mmol), phenylacetylene (111) (0.54 mg, 5 mmol), 30 mL triethylamine, CuI (35 mg, x mmol), Pd(OAc)$_2$ (22.5 mg, 0.1 mmol) in a screw-capped tube was stirred for 16 h at 80 °C under an argon atmosphere. After cooling to room temperature, MTBE (80 mL) was added and filtered through a small pad of silica. The solvent was removed at the rotatory evaporator to remain a brown residue. The residue was purified by flash chromatography (silica/EA/PE; 1:30, $R_f = 0.1$). The fraction with $R_f = 0.35$ gave 483 mg (59%) of product 107 as yellow oil which was used without further purification.
$^{1}\text{H NMR}$ (200 MHz, CDCl$_3$, 25 °C): $\delta$ = 7.33 ppm (m, 9H), 7.79 (m, OH), 10.50 (m, 1H).

Ms(70eV, EI): m/z (%) = 206 (100) [M$^+$], 178 (41), 152 (16), 122 (10), 105 (10), 76 (12).

$^{1}\text{H NMR}$ (200 MHz, CDCl$_3$, 25 °C): 2-(phenylethyl)benzaldehyde (107):

1.5.30: Willgerodt-Kindler-reaction of 2-(phenylethyl)benzaldehyde (107):

\[
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{S}_8 / \text{Morpholine} \\
\text{130 °C, 1 h} \\
\end{array} \rightarrow
\begin{array}{c}
\text{H} \\
\text{S}_8 \\
\text{Morpholine} \\
\text{130 °C, 1 h} \\
\end{array}
\]

2-(phenylethyl)benzaldehyde (107) (206 mg, 1 mmol), S$_8$ (190 mg, 6 mmol), morpholine 10 mL was refluxed under argon for 1 h at 130 °C. The morpholine was removed at 50 °C in vacuo for 2 h to give 1.01 g of sticky black oil which was isolated by flash chromatography with (silica/ EA/PE; 1:5) The fraction with $R_f$ = 0.16 gave 87 mg showed a promising spectra. The NMR-spectra indicated a mixture of the starting material and the methylene
groups of morpholine but the structure of the products could not be determined. The expected product 115 was not obtained without some doubts.

1.5.31: Lawesson reaction of 2-(phenylethyl)benzaldehyde (107):

\[
\text{H} \quad \text{Toluene, Lawesson's reagent} \quad \text{reflux, 5 h}
\]

\[
\begin{align*}
\text{107} & \quad \text{O} \quad \text{H} \\
\text{116} & \quad \text{S}
\end{align*}
\]

Prepared similar to the method described by T. J Curphey et al.\textsuperscript{[48]} A mixture of 2-(phenylethyl)benzaldehyde (107) (401 mg, 1.94 mmol), Lawesson’s reagent (1.57 g, 3.88 mmol) in dry toluene 15 mL was refluxed at 130 °C 5 h. After cooling to room temperature, the mixture was filtered through a small pad of silica and concentrated. After purification by flash chromatography (PE : CH₂Cl₂, 3:1, \(R_f = 0.26\)) and recrystallization from pentane/diethyl ether (1:3), 90 mg (21%) of 2-phenyl-2,3-dihydro-1H-indone-1-thione (116) were obtained as yellow solid with mp 55-58 °C.

\[^{1}\text{H NMR}\ (200 \text{ MHz, CDCl}_3, 25 \text{ °C})\text{: }\delta = 3.11 \text{ ppm (dt, } J = 31.8 \text{ Hz, } 15.9, 1 \text{H), } 3.53 \text{ (m, } 1 \text{H), } 5.16 \text{ (dd, } J = 9.9, 5.3, 1 \text{H), } 7.30 \text{ (m, } 6 \text{H), } 7.51 \text{ (m, } 1 \text{H), } 7.65 \text{ (m, } 1 \text{H), } 8.08 \text{ (d, } J = 7.9 \text{ Hz,}
\]

\[^{13}\text{C NMR}\ (50 \text{ MHz, CDCl}_3, 25 \text{ °C})\text{: }\delta = 41.82 \text{ ppm (t), } 58.59 \text{ (d), } 124.80 \text{ (d), } 124.92 \text{ (d), } 127.38 \text{ (d), } 128.82 \text{ (d), } 129.07 \text{ (d), } 129.92 \text{ (d), } 132.63 \text{ (d), } 137.75 \text{ (s), } 144.10 \text{ (s), } 150.18 \text{ (s), } 227.46 \text{ (s).}
\]
$^1$H NMR (200 MHz, CDCl$_3$, 25 °C) of 116

$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C) of 116
1.5.32: Synthesis N-(quinolin-8-yl)pyridine-2-carbothioamide (119):

**Method A**

\[
\begin{align*}
\text{NH}_2 & \quad \text{CHO} \\
\text{S}_8, \text{DMF} & \\
15 \text{ min, } 100 \degree \text{C} & \quad \rightarrow \\
\end{align*}
\]

A mixture of 8-aminoquinoline (117) (288.36 mg, 2 mmol), pyridine-2-aldehyde (118) (214.2 mg, 2 mmol), DMF 4 mL was refluxed under argon for 15 min at 100 °C and allowed to warm up to room temperature. The reaction mixture was added with S\(_8\) (400 mg, 12.5 mmol) and was refluxed at 100 °C 15 minutes and cooled to room temperature. After evaporation of the solvent the residue was dried in vacuo (160 °C, 2.5 mbar) to give a yellow solid which was identified by \(^1\)H NMR spectroscopy as 8-aminoquinoline and pyridine-2-aldehyde. The expected product 119 was not obtained. The reaction of 8-aminoquinoline and pyridine-2-aldehyde with WK failed.

**Method B**

\[
\begin{align*}
\text{NH}_2 & \quad \text{OHC} \\
\text{reflux, } 115 \degree \text{C, } 4 \text{ h} & \quad \rightarrow \\
\end{align*}
\]

Prepared by a modification of the procedure described by K. Okamoto et al.\(^{[11]}\) A mixture of 8-aminoquinoline (117) (216.3 mg, 1.5 mmol), Na\(_2\)S \(\cdot\)9H\(_2\)O (216 mg, 0.23 mmol), S\(_8\) (160 mg, 5 mmol), DMF 4 mL was refluxed under argon for 30 min at 115 °C and allowed to room temperature. The reaction mixture was added with pyridine-2-aldehyde (118) (214.22 mg, 2 mmol) and was refluxed at 100 °C 12 h. After cooling to room temperature, sat.aq NH\(_4\)Cl solution (50 mL) was extracted with CH\(_3\)Cl 50 mL, then the organic phase was extracted 2 times with water (50 x 2 mL), and filtered through a small pad of silica and dried with Na\(_2\)SO\(_4\) and concentrated. The DMF was removed in vacuum. The crude solid was separated by flash chromatography (PE : MTBE, 3:1). The fraction with R\(_f\) = 0.26 gave 107 mg (27%) of product 119 as yellow solid with mp 168-170 °C.
**1H NMR** (400 MHz, CDCl₃, 25 °C): δ = 7.54 ppm (m, 2H), 7.71 (m, 2H), 7.92 (m, 1H), 8.25 (dt, J = 17.6, 8.8 Hz, 1H), 8.78 (ddd, J = 4.7, 1.7, 0.9 Hz, 1H), 8.85 (t, J = 1.0, 1H), 9.04 (dt, J = 13.9, 6.9, 1H), 10.18 (dd, J = 7.6, 1.4, 1H), 14.41 (s, NH).

**13C NMR** (100 MHz, CDCl₃, 25 °C): δ = 118.05 ppm (d), 121.91 (d), 124.41 (d), 124.83 (d), 125.68 (d), 126.85 (d), 128.23 (d), 135.33 (s), 136.49 (d), 137.31 (s), 140.55 (d), 147.26 (d), 148.97 (d), 153.27 (s), 187.31 (s).

**MS** (EI, 70eV): m/z (%) = 265 (10) [M⁺], 249 (3), 232 (100), 187 (7), 128 (14), 101 (9), 78 (15).

**C₁₅H₁₁N₃S** (265.33 g/mol):

**HRMS (ESI-TOF):** M+H⁺

*calcd:* 265.0 g/mol
*found:* 265.06714 g/mol.

**1H NMR** (400 MHz, CDCl₃, 25 °C): N-(quinolin-8-yl)pyridine-2-carbothioamide (119).
$^{13}$C NMR (400 MHz, CDCl$_3$, 25 °C): N-(quinolin-8-yl)pyridine-2-carbothioamide (119).

1.5.33: Synthesis of tetradeutate Gold complexes:

Method A

A mixture of N-(quinolin-8-yl)pyridine-2-carbothioamide (119) (26 mg, 0.25 mmol), AuCl$_3$ (75 mg, 0.25 mmol), acetonitrile 4 mL under argon was stirred magnetically 5 min at room temperature. The solution color immediately changed from yellow to red. After having been stand 24 h the solvent was removed to give a brown-black solid 96 mg which was identified by $^1$H NMR spectroscopy as the starting material and therefore reused. The expected product 120 was not obtained.
Method B

\[
\begin{array}{c}
\text{NH}_2 \\
\text{N} \\
\text{OHC} \\
\text{AuCl}_3 \\
\text{CH}_3\text{COOH, reflux 4 h}
\end{array}
\]

Prepared by a modification of the procedure described by W. H. Sun et al.\textsuperscript{[50]} A suspension of pyridine-2-aldehyde (117) (53 mg, 0.5 mmol), 8-aminoquinoline (118) (72 mg, 0.5 mmol), and AuCl\textsubscript{3} (151 mg, 0.5 mmol) in glacial acetic acid (5 mL) was refluxed for 4 h. The precipitate was collected by filtration and washed with diethyl ether (3 x 5 mL). The solid was collected and redissolved in methanol, concentrated, and precipitated with diethyl ether. After washing with diethyl ether the collected solid was recrystallized with ethanol and dried under vacuum. Complex A 120 was obtained as back powder in 89 mg (77\% yield).

\textbf{MS (EI, 70eV): m/z (%)} = 460 (73) [M\textsuperscript{+}], 412 (40), 391 (61), 176 (29).
2. Extended π-systems through $S_N$Ar reactions at sterically shielded trityl salts

2.1 Synthesis of 9-hydroxy-9-(4-methylphenyl)xanthene (163a)

Prepared similar to the method described by M. Hagel.$^{[34]}$: To a solution of 3.70 mL (30.0 mmol) of 4-bromotoluene (162a) in 80 mL of dry THF 23.4 mL (37.5 mmol) of n-buthyllithium (15% in hexane) were added at -78 °C within 5 min. After 30 min additional stirring 5.89 g (30.0 mmol) of xanthone were added and the reaction mixture was allowed to warm up to room temperature 24 h. After hydrolysis with 20 mL of water and extraction with CH$_2$Cl$_2$ (three times 20 mL) the organic layer was concentrated to dryness and the residue recrystallized from pentane. After drying in vaccuo for (2 h at 0.5 mbar and 70 °C): 3.75 g (43%) of xanthenol 163a as a colorless solid mp 140-141 °C was obtained (lit.$^{[13-15]}$ mp between 141 and 150 °C).

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 2.29 (s, 3H), 2.59(s, 1H, OH), 7.09-7.03 (m, 4H), 7.19 (dd, $J = 8.3,1.0$ Hz, 2H), 7.31-7.26 (m, 5H), 7.38 (dd, $J = 8.1, 1.8$ Hz, 2H) ppm.

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ = 21.03 (q), 70.44 (s), 116.43 (d), 123.58 (d), 126.17 (d), 127.48 (s), 128.72 (d), 128.98 (d), 129.03 (d), 136.40 (s), 145.22 (s), 149.77 (s) ppm.
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of xanthene 163a:

$^{13}$C NMR-Spectrum (50 MHz, CDCl$_3$) of xanthene 163a:
2.2 Synthesis of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a)

Prepared similar to the method described by O. Muth et al.\textsuperscript{[35]}: 3.72 g (12.9 mmol) of 9-hydroxy-9-(4-methylphenyl)xanthene (163a) were dissolved in 25 mL of dry CH\textsubscript{2}Cl\textsubscript{2} and 5.0 mL (36 mmol) of HBF\textsubscript{4} etherate (15\% in diethyl ether) were added. After 10 min of stirring at room temperature a layer of 40 mL of diethyl ether was carefully placed on the reaction mixture. Slow diffusion (1 d) led to the formation of a yellow to orange precipitate, which was collected, washed with diethyl ether and dried in vacuo (50 °C, 0.5 mbar, 4 h): The formed yellow solid was removed by filtration, washed with diethyl ether (3x10 mL) and dried in vacuo (100 °C, 0.5 mbar, 3 h): 4.60 g (95\%) of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a) as orange solid (a hydrate according to NMR) with mp 210-215 °C (Lit.\textsuperscript{[13]} mp 200 °C, dec.).

\textsuperscript{1}H\textsuperscript{-} NMR (CDCl\textsubscript{3}, 200 MHz): \(\delta = 2.59\) (s, 3H), 2.80 (broad s, hydrate), 7.58 ("d", \(J = 8.0\) Hz, 2H), 7.62 ("d", \(J = 8.0\) Hz, 2H), 7.92 ("t", \(J = 7.7\)Hz, 2H), 8.18 (dd, \(J = 8.2, 1.3\) Hz, 2H), 8.33 (d, \(J = 8.7\) Hz, 2H), 8.36-8.54 (m, 4H) ppm.

MS (70 eV, EI): \(m/z\) (%) = 290 (19), 271 (39), 199 (100) [M\textsuperscript{+}], 181 (42), 49 (38).
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 164a

$^{13}$C NMR-spectrum (50 MHz, CDCl$_3$) of 164
2.3 Synthesis of 9-Hydroxy-9-(2,4-dimethylphenyl)xanthene (163b)

Prepared similar to the method described by O. Muth et al.[35]: To a solution of 5.55 g (30.0 mmol) of 1-bromo-2,4-dimethylbenzene (162b) in 30 mL of dry THF 40.9 mL (60.0 mmol) of n-buthyllithium (1.6 M in n-hexane) were added at -78 °C within 15 min. The colorless suspension was stirred for 1 h and 5.88 g (30.0 mmol) of xanthone were added in one portion. The reaction mixture was stirred at room temperature for 2 h and was hydrolyzed with 30 mL of water. After extraction with CH₂Cl₂ (three times 30 mL) the combined organic layer was dried over sodium sulfate and was concentrated in vaccuo. The crude product was purified by flash chromatography (silica, ethyl acetate/petrol ether 1:5: Rf = 0.27) and dried in vaccuo (70 °C, 0.5 mbar, 1 h): 8.49 g (94%) of 9-hydroxy-9-(2,4-dimethylphenyl)xanthene (163b) as colorless crystals with mp 172-173 °C.

¹H NMR (CDCl₃, 400 MHz): δ = 1.48 (s, 3H), 2.41 (s, 3H), 2.44 (s, 1H, OH), 6.90 (s, br, 1H), 7.06 (“t”, “J” = 7.8 Hz, 2H), 7.15 (dd, J = 7.8, 1.8 Hz, 2H) 7.24-7.28 (m, 3H), 7.37 (“t”, “J” = 7.8 Hz, 2H), 8.28 (d, J = 7.8 Hz,1H) ppm.

¹³C NMR {¹H} (CDCl₃, 125 MHz): δ = 20.52 (q), 20.93 (q), 69.85 (s), 116.29 (d), 123.52 (d), 125.88 (d), 125.90 (d), 126.05 (s), 128.77 (d), 129.21 (d), 132.83 (d), 135.46 (s), 137.34 (s), 140.98 (s), 150.10 (s) ppm.

IR (KBr): ν = 3510 (m), 2914 (m), 1924 (w), 1700 (w), 1601 (m), 1573 (m), 1477 (s), 1446 (m), 1380 (m), 1357 (m), 1312 (s), 1291 (s), 1237 (s), 1205 (s), 1176 (m), 1153 (m), 1116 (m), 1001(m), 1040(m), 991(s), 946(m), 929(m), 896 (m), 874 (s), 824 (m), 798 (m), 759(s) cm⁻¹.

UV (acetonitrile) λₘₐₓ (log ε): 239 (3.64), 281 (3.45), 289 (3.51) nm.

MS (70 eV, EI): m/z (%) = 302 (13) [M⁺], 286 (4), 285 (20), 198 (13), 197 (100), 181 (3), 141 (4), 115 (4), 77(6).

C₂₁H₁₆O₂ (302.37)  caled:  C 83.42  H 6.00
found:  C 83.38  H 5.98
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 9-hydroxy-xanthene 163b:

$^{13}$C NMR spectrum (50 MHz, CDCl$_3$) of 9-hydroxy-xanthene 163b:
2.4 Synthesis of 9-(2,4-Dimethylphenyl)xanthenylium tetrafluoroborate (164b)

Prepared similar to the method described by O. Muth et al.\textsuperscript{[35]}: To a solution of 9-hydroxy-9-(2,4-dimethylphenyl)xanthene (163b) (180 mg, 0.54 mmol) in 4 mL of dry dichloromethane 0.25 mL (1.8 mmol) of HBF\textsubscript{4} etherate (15% in Et\textsubscript{2}O) were added. After 5 min of stirring at room temperature a layer of 10 mL of diethyl ether is carefully placed on the reaction mixture. Slow diffusion led to the formation of a red precipitate (2 d), which was collected, washed with Et\textsubscript{2}O and dried in vacuo (60 °C, 0.5 mbar, 2 h): 195 mg (90%) of 9-(2,4-dimethylphenyl)xanthenylium tetrafluoroborate (164b) as red solid with mp 293-296 °C.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz): \(\delta = 1.99\) (s, 3H), \(2.52\) (s, 3H), \(7.30\text{-}7.36\) (m, 3H), \(7.90\text{-}7.97\) (m, 4H), \(8.47\) (“d”, \(J = 8.6\) Hz, 2H), \(8.54\) (“t”, \(J = 8.6\) Hz, 2H) ppm.

\textsuperscript{13}C NMR {\textsuperscript{1}H} (CDCl\textsubscript{3}, 125 MHz): \(\delta = 20.16\) (q), \(21.51\) (q), \(120.61\) (d), \(124.37\) (s), \(127.24\) (d), \(127.87\) (s), \(129.53\) (d), \(129.83\) (d), \(131.14\) (d), \(131.98\) (d), \(135.87\) (s), \(142.48\) (s), \(144.45\) (d), \(158.63\) (s), \(176.67\) (s) ppm

IR (KBr): \(\tilde{\nu} = 3512\) (m), \(3073\) (m), \(2923\) (w), \(2854\) (m), \(1625\) (m), \(1598\) (s), \(1577\) (m), \(1537\) (m), \(1508\) (s), \(1432\) (m), \(1422\) (s), \(1372\) (s), \(1211\) (w), \(1097\) (s), \(1053\) (s), \(879\) (s), \(830\) (w), \(805\) (w), \(759\) (s), \(610\) (m)520 (w).

UV (acetonitrile) \(\lambda_{\text{max}}\) (log \(\varepsilon\)): 205 (4.57), 258 (4.60), 290 (2.76), 368 (4.45), 371 (4.46), 449 (3.74).

MS (70 eV, EI): \(m/z\) (%) = 304 (29) [M\textsuperscript{+} - F\textsuperscript{-}], 286 (18), 285 (63), 269 (11), 255 (6), 199 (100), 181 (16), 49 (10).

\begin{align*}
C_{21}H_{17}OB\textsubscript{4} (372.17) & : \\
& \text{calcd. C 67.74, H 4.56; found C 67.74, H 4.74.}
\end{align*}
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 164b

$^{13}$C NMR-Spectrum (50 MHz, CDCl$_3$) of 164
2.5 Synthesis of 9-Hydroxy-9-(2,4,6-trimethylphenyl)xanthene (163c)

\[
\begin{array}{c}
\text{Br} \\
\text{162c} \\
\begin{array}{c}
1. \text{n-BuLi, THF} \\
2. \\
\text{OH}
\end{array}
\end{array}
\]

Prepared similar to the method described by O. Muth et al.\textsuperscript{[35]}: To a solution of 1.49 g (1.13 mL, 7.50 mmol) 2-bromomesitylene (162c) in 17 mL of dry THF 3.30 mL (8.26 mmol) of \textit{n}-butyllithium (2.5 M in hexane) were added at -30 °C. The colorless solution was stirred for 30 minutes and a solution of 0.98 g (5.00 mmol) xanthone in 28 mL of dry dioxane was added dropwise within 15 minutes. The reaction mixture was stirred at room temperature for 24 h and hydrolyzed with 20 mL of saturated aqueous diammonium hydrogen phosphate solution. After extraction with CH\textsubscript{2}Cl\textsubscript{2} (3x 20mL) and concentration of the combined organic layer in vacuo the crude product was purified by flash chromatography (silica, PE/Et\textsubscript{2}O 10:1, R\textsubscript{f} = 0.25) and dried in vacuo (50 °C, 0.5 mbar, 4h): 1.24 g (79%) of 163c as colorless solid with mp 193-194 °C (lit.\textsuperscript{[4, 12]} mp 192.5-193.5 °C dec.). The crude product, without any further purification, was used as the starting material in the next reaction.

\textbf{1H-NMR (CDCl\textsubscript{3}, 500 MHz):} \(\delta = 2.08 \text{ (s, 1H)}, 2.13 \text{ (s, br, 6H)}, 2.28 \text{ (s, 3H)}, 6.83 \text{ (s, br, 2H)}, 7.02(\text{"t"}, \text{"J"} = 7.5 \text{ Hz}, 2H), 7.16 (dd, \text{J} = 7.8 \text{ Hz}, \text{J} = 1.65 \text{ Hz}, 2H), 7.20 (dd, \text{J} = 8.25 \text{ Hz}, \text{J} = 1.2 \text{ Hz}, 2H), 7.31(\text{"t"}, \text{"J"} = 7.7 \text{ Hz}, 2H) \text{ ppm.}

\textbf{13C NMR (CDCl\textsubscript{3}, 125 MHz):} \(\delta = 20.58 \text{ (q)}, 24.20(q, \text{ br}), 74.31 \text{ (s)}, 116.39 \text{ (d)}, 123.60 \text{ (d)}, 127.94 \text{ (s)}, 128.35 \text{ (d)}, 129.10 \text{ (d)}, 131.75 \text{ (d)}, 136.61 \text{ (s)}, 137.35 \text{ (s)}, 138.40 \text{ (s)}, 149.45 \text{ (s)} \text{ ppm.}

\textbf{IR (KBr):} \(\tilde{\nu} = 3518 \text{ (s)}, 3037 \text{ (w)}, 2970 \text{ (m)}, 2921(m), 2859 \text{ (w)}, 1602 \text{ (s)}, 1574 \text{ (m)}, 1479 \text{ (s)}, 1446 \text{ (s)}, 1315 \text{ (s)}, 1293 \text{ (s)}, 1242 \text{ (s)}, 1203 \text{ (m)}, 1099 \text{ (m)}, 1043 \text{ (m)}, 1026 \text{ (m)}, 1002 \text{ (s)}, 894 \text{ (s)}, 874 \text{ (s)}, 747 \text{ (s)}, 629 \text{ (m)} \text{ cm}^{-1}.

\textbf{MS (70 eV, EI):} \(m/z \% = 316 \text{ (14) [M\textsuperscript{+}]}, 299 \text{ (33)}, 197 \text{ (100)}.\)

\(\text{C}_{22}\text{H}_{20}\text{O}_{2} \text{ (316.40)}\)

\textbf{calcd:} C 83.52 \ H 6.37

\textbf{found:} C 83.55 \ H 6.45
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 163c

$^{13}$C NMR-Spectrum (50 MHz, CDCl$_3$) of 163
2.6 Synthesis of 9-(2,4,6-trimethylphenyl)xanthenylium tetrafluoroborate (164c)

Prepared similar to the method described by O. Muth et al. [35]: 0.98 g (3.10 mmol) of 9-hydroxy-9-(2,4,6-trimethylphenyl)xanthene in 40 mL of dry diethyl ether was treated with 1 mL (7.4 mmol) of HBF₄ etherate (15% in Et₂O). After 1h of stirring at room temperature, the slightly yellow precipitate was collected, washed with Et₂O and dried in vacuo (100 °C, 0.5 mbar, 2 h): 1.16 g (98%) of 9-(2,4,6-trimethylphenyl)xanthenylium-tetrafluoroborate as yellow solid with mp 251-254 °C.

**1H NMR (CDCl₃, 200 MHz):** δ = 1.83 (s, 6H), 2.48 (s, 3H), 7.18 (s, 2H), 7.63, (m, 4H), 8.62 (m, 4H) ppm.

**13C NMR (CDCl₃, 50 MHz):** δ = 20.13 (q), 21.25 (q), 121.11 (d), 124.43 (s), 127.42 (s), 129.23 (d), 129.93 (d), 130.11 (d), 135.34 (s), 141.71 (s), 145.12 (d), 158.49 (s), 177.90 (s) ppm.

**IR (KBr):** ν = 3075 (vw), 1623 (w), 1599 (s), 1576 (w), 1536 (w), 1508 (s), 1436 (w), 1373 (s), 1084 (s), 1053 (s), 761 (m) cm⁻¹.

**UV (acetonitrile) λₘₐₓ (log ε):** 197 (4.42), 258 (4.30), 372 (4.20), 444 (3.23) nm.

**MS (70 eV, EI):** m/z (%) = 299 (100) [M⁺-BF₄], 154 (20), 136 (14).

**C₂₂H₁₉OBF₄ (386.20)**

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$^1$H NMR spectrum (200 MHz, CDCl$_3$) of **164c**

$^{13}$C NMR-Spectrum (50 MHz, CDCl$_3$) of **164c**
2.7 Reaction of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a) with malononitrile

264 mg (4.00 mmol) of malononitrile (167) in 20 mL of dry THF were treated with 160 mg (60% in mineral oil, 4.00 mmol) of NaH for 30 min at room temperature. 357 mg (1.00 mmol) of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a) were added and the reaction mixture was stirred at reflux temperature for 2 h. After hydrolysis with 50 mL of water and extraction with CH₂Cl₂ (3 x 50 mL) the organic layer was concentrated and the residue was purified by flash chromatography (silica, petrol ether/methyl tert-butyl ether 1:10, Rf = 0.67): 229 mg (68%) of 2-(9-(4-methylphenyl)-9H-xanthene-9-yl)malononitrile (165a) as a colorless solid with mp 83-85 °C were obtained.

\[
\begin{align*}
\text{1H NMR (CDCl₃, 400 MHz):} & \quad \delta = 2.40 (s, 3H), 4.40 (s, 1H), 6.98 (d, J = 8.2 Hz, 2H), 7.07 (m, 2H), 7.25 (m, 6H), 7.39 (m, 2H) ppm. \\
\text{13C NMR (CDCl₃, 100 MHz):} & \quad \delta = 21.04 (q), 36.09 (s), 50.70 (d), 111.43 (d), 117.05 (d), 122.37 (s), 123.85 (d), 128.63 (s), 129.47 (d), 129.87 (d), 130.28 (d), 138.15 (s), 151.36 (s) ppm, one s is missing;
\end{align*}
\]

MS (70 eV, EI): m/z (%) = 271 (100), 255 (16), 181 (8), 128 (14).

IR (KBr): \(\tilde{\nu} = 2032 \text{ (w)}, 2901 \text{ (w)}, 2265 \text{ (vw)}, 1600 \text{ (w)}, 1673 \text{ (w)}, 1478 \text{ (s)}, 1443 \text{ (s)}, 1313 \text{ (m)}, 1280 \text{ (m)}, 874 \text{ (w)}, 756 \text{ (s)} \text{ cm}^{-1}\).

UV (acetonitrile) \(\lambda_{\text{max}} \text{ (log } \varepsilon)\): = 231 (4.47), 243 (4.44), 268 (3.83), 274 (3.89), 290 (3.99) nm.

\(\text{C}_{23}\text{H}_{16}\text{N}_{2}\text{O} \text{ (336.39 g/mol).} \)

HRMS(ESI-TOF): M + H⁺

\[
\begin{align*}
\text{calcd:} & \quad 336.126250 \text{ g/mol} \\
\text{found:} & \quad 336.126263 \text{ g/mol}
\end{align*}
\]

162
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 165a

$^{13}$C NMR-Spectrum (50 MHz, CDCl$_3$) of 165a
2.8 Reaction of 9-(2,4-dimethylphenyl)xanthenylium tetrafluoroborate (164b) with malononitrile (167)

264 mg (4.00 mmol) of malononitrile in 20 mL of dry THF were treated with 160 mg (60% in mineral oil, 4.00 mmol) of NaH for 1 h at room temperature. 372 mg (1.00 mmol) of the xanthenylium salt 164b were added and the reaction mixture was stirred at reflux temperature for 2 d. After hydrolysis with 20 mL of saturated aqueous diammonium hydrogen phosphate solution and extraction with CH₂Cl₂ (three times 50 mL) the organic layer was concentrated and the residue was fractionated by flash chromatography (silica, toluene: Rf = 0.67, 0.14);

1st fraction: (Rf = 0.67): 274 mg (78 %) of 165b as a white solid with mp 165 °C.

¹H NMR (400 MHz, CDCl₃, 25°C): mixture of rotamers; δ = 1.44 (s, 3H, CH₃), 2.39 (s, br, 3H, CH₃), 4.08 (s, br, 0.38H), 4.51 (s, br, 0.62H), 6.94-7.05 (m, 5H), 7.24-7.28 (m, 3H), 7.37- 7.42 (t, 2H), 7.51 (s, br, 0.62H), 7.90 (s, br, 0.38H) ppm.

¹³C NMR (100 MHz, CDCl₃, 25 °C): mixture of rotamers; δ = 20.82 (q), 21.59 (q, br), 34.88 (br), 38.93 (br), 50.11 (br), 111.60 (s), 116.98 (d), 120.68 (br), 124.00 (d), 125.62 (br), 126.32 (br), 128.26 (br), 129.07 (br), 130.40 (d), 135.01 (d, br), 137.53 (s), 138.00 (s), 151.20 (s) ppm.

IR (KBr): ν ~ = 3044 (vw), 2969 (w), 2932 (m), 2265 (vw), 1600 (w), 1573 (w), 1479 (s), 1143 (s), 1310 (m), 1294 (w), 1250 (m), 1229 (m), 1189 (vw), 1129 (vw), 940 (vw), 908 (vw), 874 (m), 812 (vw), 745 (s) cm⁻¹.

UV (acetonitrile) λ_max (log ε): 220 (4.32), 247 (4.08), 290 (3.58) nm.

MS (EI, 70eV): m/z (%) = 351 (0.3), 350 (1.2) [M⁺], 285 (100), 255 (5), 181 (5), 134 (4).

C₁₂H₁₈N₂O (350.41): calcd. C 82.26, H 5.18, N 7.99
found C 82.17, H 5.30, N 7.80.

¹H NMR spectrum (200 MHz, CDCl₃) of (165b)
$^{13}$C NMR spectrum (200 MHz, CDCl$_3$) of 165b
2nd Fraction: 53 mg (15%) of the para-quinonoid compound 166b as deep violet solid with mp 280-285 °C.

$^1$H NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$ = 2.02 (s, 3H), 2.46 (s, 3H), 6.89 (d, J = 9.6 Hz, 1H), 7.02-7.06 (m, 2H), 7.16 (dd, J = 8.1, 1.5 Hz, 1H), 7.19-7.26 (m, 4H), 7.48 (d, J = 8.3 Hz, 1H), 7.65 ("t", "J" = 7.8 Hz, 1H) ppm.

$^{13}$C NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$ = 19.63 (q), 21.29 (q), 64.63 (s), 102.53 (d), 115.89 (s), 116.04 (s), 117.10 (d), 121.77 (s), 122.77 (s), 125.23 (d), 125.66 (d), 127.08 (d), 128.46 (d), 128.73 (s), 129.17 (d), 129.51 (d), 131.61 (d), 134.43 (d), 136.09 (s), 140.06 (s), 150.39 (s), 152.95 (s), 156.07 (s), 157.26 (s) ppm.

IR (KBr): $\nu$ = 2922 (w), 2203 (s), 1631 (m), 1595 (m), 1523 (w), 1467 (s), 1414 (m), 1361 (w), 1320 (w), 1139 (w), 1113 (w), 840 (w), 754 (w) cm$^{-1}$.

UV (acetonitrile) $\lambda_{\text{max}}$ (log $\varepsilon$): 228 nm (4.38), 297 (3.94), 308 (3.97), 349 (4.09), 369 (3.81), 390 (3.79), 528 (4.35), 562 (4.37), 618 (4.22) nm.

MS (EI, 70 EV): m/z (%) = 349 (28), 348 (100) [M$^+$], 332 (4), 318 (4), 166 (4), 59 (6).

C$_{24}$H$_{16}$N$_2$O (348.40) + 0.5 H$_2$O:

calcd. C 80.65, H 4.79, N 7.84;
found: C 81.01, H 5.00, N 7.45.
$^{1}$H NMR spectrum (200 MHz, CDCl$_3$) of 166b

$^{13}$C NMR spectrum (50 MHz, CDCl$_3$) of 166b
2.9 Reaction of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a) with LDA as sterically hindered bases

To a solution of diisopropylamine (0.28 mL, 2 mmol) in 30 mL of dry THF was added slowly with 1.4 mL (2.2 mmol) of n-buthyllithium (1.6 M in hexane) at -78°C. The colorless solution was stirred for 1 h and 9-(4-methylphenyl)xanthenylium tetrafluoroborate 164a (357 mg, 1 mmol) was added, the reaction mixture was stirred at room temperature for 24 h and hydrolyzed with 20 mL of brine. After extraction with CH₂Cl₂ (3x 20mL) and Na₂SO₄, concentration of the combined organic layer. The crude product was purified by flash chromatography (silica, PE/EA 1:1, Rf= 0.2) and recrystallization with isopropanol to give 47 mg (9%) of the product 168a as white solid with mp130 °C.

¹H NMR (CDCl₃, 200 MHz): δ = 1.63 (s, 3H), 2.17 (s, 3H), 5.46 (s, 1H, br), 6.39-7.36 (m, 23H)

MS (70 eV, EI): m/z (%) = 542 (18) (M⁺), 451 (19), 285 (100), 271 (70), 255 (18), 181 (67).
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 168a
2.10 Reaction of 9-(2,4-dimethylphenyl)xanthenylium tetrafluoroborate(164b) with LDA as sterically hindered base

To a solution of diisopropylamine (0.28 mL, 2 mmol) in 30 mL of dry THF was added slowly with 1.4 mL (2.2 mmol) of \textit{n}-buthyllithium (1.6 M in hexane) at -78°C. The colorless solution was stirred for 1 h and 9-(2,4-methylphenyl)xanthenylium tetrafluoroborate (164b) (372 mg, 1 mmol) was added and the reaction mixture was stirred at room temperature for 24 h and hydrolyzed with 20 mL of brine. After extraction with CH\textsubscript{2}Cl\textsubscript{2} (3x 20mL) and Na\textsubscript{2}SO\textsubscript{4}, concentration of the combined organic layer. The crude product was purified by flash chromatography (silica, PE/EA 1:1, \( R_f = 0.2 \)) and recrystallization with isopropanol to give 113 mg (20\%) of the product 169b as white solid with mp 110°C.

\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 200 MHz): \( \delta = 1.63 \) (s, 3H), 2.18 (s, 3H), 2.30 (s, 3H), 2.35 (s, 3H), 5.44 (s, 1H, br), 6.48 (dd, \( J = 8.2, 2.0 \) Hz,1H), 6.58 (d, \( J = 2.0 \) Hz, 1H), 6.69 (m, 2H), 6.84 (d, \( J = 7.4 \) Hz, 1H), 6.88-7.07 (m, 12H), 7.10-7.18 (m, 3H), 7.28 (m, 3H).

MS (70 eV, EI): \textit{m/z} (%) = 570 (28), (M\textsuperscript{+}), 465 (38), 360 (12), 285 (100), 180 (28).

\textsubscript{C}\textsubscript{42}H\textsubscript{34}O\textsubscript{0.5}H\textsubscript{2}O (588):

\begin{align*}
\text{Cald:} & \quad \text{C} = 87.04\% \quad \text{H} = 6.20\% \\
\text{found:} & \quad \text{C} = 86.99\% \quad \text{H} = 6.20\%
\end{align*}
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 169b

$^{13}$C NMR spectrum (50 MHz, CDCl$_3$) of 169b
2.11 Reaction of 9-(2,4-dimethylphenyl)xanthenylium tetrafluoroborate (164b) with arylmagnesium

A freshly powdered Mg (26.4 g, 1.1 mmol) was added into dried flask set up with a magnetic stirring bar under argon. A small crystal of I₂ was added and heating up until violet color vapors formed within 3 minutes. The reaction mixture was cooled to room temperature and 0.25 mL (2 mmol) of 4-bromoanisol in 10 mL abs THF was added slowly. The reaction mixture was refluxed for 1 h until the color disappeared and was cooled to room temperature. 372 mg (1 mmol) of 9-(2,4-dimethylphenyl)xanthenylium tetrafluoroborate (164b) was added and the mixture refluxed 1 h. After cooling down to 0°C, 10 mL of brine and 30 mL of MTBE were added and the layers were separated. The organic layer was filtered through a small silica pad and solvents were removed by rotary evapororation and dried in vacuum (90 °C, 0.5 mbar, 45 min). The residue was purified by flash chromatography (silica, 1:20, PE/MTBE). The solid product was recrystallized from isopropanol to give 9-(2,4-dimethylphenyl)-3-(4-methoxyphenyl)-9H-xanthene (172) 156 mg (40% yield) as a white solid with mp 155-157 °C.

\[ \begin{align*}
\text{1H NMR (CDCl₃, 200 MHz): } & \delta = 2.12 (s, 3H), 2.23 (s, 3H), 3.78 (s, 3H, OCH₃), 5.45 (s, 1H), 6.79-6.96 (m, 6H), 6.99-7.15 (m, 4H), 7.22 (d, J = 1.8 Hz, 2H), 7.46 (d, J = 8.6 Hz, 2H) \\
\text{13C NMR (CDCl₃, 100 MHz): } & \delta = 19.97 (q), 20.97 (q), 40.80 (q), 55.37 (q), 114.23 (d), 116.23 (s), 121.43 (s), 122.64 (s), 123.11 (s), 124.31 (s), 127.16 (s), 127.74 (d), 129.27 (s), 129.50 (s), 131.04 (s), 132.01 (s), 132.86 (s), 135.78 (s), 136.42 (s), 140.53 (s), 151.01 (s), 151.16 (s), 159.31 (s).
\end{align*} \]

\[ \begin{align*}
\text{MS (70 eV, EI): } & m/z (%) = 392 (82) [M⁺], 377 (14), 287 (100) 244 (13), 196 (9), 181 (12) \\
\text{IR (KBr): } & \nu = 3004 (w), 2956 (w), 2923 (w), 2852 (w), 1609 (m), 1558 (m), 1500 (m), 1485 (s), 1454 (m), 1428 (m), 1401 (m), 1276 (s), 821 (m), 757 (s) cm⁻¹.
\end{align*} \]

\[ \begin{align*}
\text{UV (acetonitrile) } & \lambda_{max} (\log \varepsilon): 208 \text{ nm (4.40), 256 (4.19)} \\
\text{C}_{28}\text{H}_{24}\text{O}_{2}0.5\text{H}_{2}\text{O (392.48):} \\
\text{Cald: } & \text{ C = 85.68% H = 6.16%} \\
\text{found: } & \text{ C = 83.76% H = 6.28%}
\end{align*} \]
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 172

$^{13}$C NMR spectrum (50 MHz, CDCl$_3$) of 172
2.12 Reaction of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a) with alkyllithium as sterically hindered base

\[
\begin{align*}
\text{164a} & \rightarrow \text{t-BuLi}175 \\
\text{THF, -60 °C, r.t} &
\end{align*}
\]

To a solution of 9-(4-methylphenyl)xanthenylium tetrafluoroborate (164a) (357 mg, 1 mmol) in 20 mL of dry THF was added slowly with 1.5 mL (1.5 mmol) of t-buthyllithium (1.5 M in hexane) at -78 °C. After stirring for 1 h at room temperature under an argon atmosphere, bBrine (5 mL) and diethylether 15 mL were added and filtered through a small pad of silica. with diethylether15 mL. The solvent was removed at the rotatory evaporator to remain a brown residue. The residue was purified by flash chromatography (silica/ MTBE/PE; 1:5). The fraction with R_f = 0.15 gave 46 mg (14% yield) of 9-tert-butyl-9-p-tolyl-9H-xanthene (173a) as yellow oil.

\[\text{1H NMR (CDCl}_3, 200 \text{ MHz}:} \quad \delta = 1.08-1.40 \text{ (m, 9H), 2.20 (d, 3H), 6.40-7.37 (m, 12H)}\]

\[\text{MS (EI, 70 EV):} \quad \text{m/z (\%)} = 328 (9) [\text{M}^+], 271 (100) [\text{M}^+], 255 (11), 237 (20), 181 (55).\]
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 173a

PROTON CDCl$_3$ spectrum at 212
2.13 Reaction of 9-(2,4-dimethylphenyl)xanthenium tetrafluoroborate (164b) with alkyllithium as sterically hindered base

To a solution of 9-(2,4-dimethylphenyl)xanthenium tetrafluoroborate (164b) (372 mg, 1 mmol) in 20 mL of dry THF was added slowly with 1.5 mL (1.5 mmol) of t-buthylithium (1.5 M in hexane) at -78 °C. After stirring for 1 h at room temperature under an argon atmosphere, brine (5 mL) and diethylether 15 mL were added and filtered through a small pad of silica. The solvent was removed at the rotatory evaporator to remain a brown residue. The residue was purified by flash chromatography (silica/MTBE/PE; 1:5). The fraction with \( R_f = 0.12 \) gave 104 mg (30%) of 3-tert-butyl-9-(2,4-dimethylphenyl)-9\( H \)-xanthene (174b) as yellow oil.

\(^1\)H NMR spectrum (200 MHz, CDCl\(_3\)) of 174b
2.14 Synthesis of 2,7-dibromo-9H-xanthene-9-one (176)

$$\text{162} \xrightarrow{\text{Br}_2, I_2, \text{AcOH}} \text{reflux, 24 h}} \text{176}$$

Prepared similar to the method described by Piers R.J. Gaffney et al.\[^{[51]}\] To a mixture of xanthon (162) (5 g, 0.025 mol), one crystal of I$_2$ in glacial acetic 20 mL was added bromine(16.5 g, 0.1 mol). The reaction mixture was refluxed for 24 h at 100 °C. The solution was then cooled to room temperature. The cooled products were filtered off. The filtrate was concentrated under reduced pressure to give a red brown solid, which was combined with the residue and dissolved in dichloromethane 100 mL, and resulting mixture was successively washed with a saturated sodium hydrogen carbonate solution (50 mL), a saturated sodium thiosulphate solution (50 mL) and water (75 mL). The extracted organic layer was then dried over MgSO$_4$, filtrated and evaporated. The resulting red solid was then recrystallized with benzene to afford 2,7-dibromoxanthene-9-one (176) 2.12 g (24 % yield) as a white solid mp. 203-204 °C (lit.\[^{[51]}\], 204 °C).

$^1$H-NMR (CDCl$_3$, 200 MHz): $\delta = 7.31$ (d, J = 8.9 Hz, 2H), 7.71 (d, J = 2.5 Hz, 1H), 7.75 (d, J = 2.5 Hz, 1H), 8.34 (d, J = 2.5 Hz, 2H).

$^{13}$C NMR (50 MHz, CDCl$_3$, 25 °C): 118 (s), 118 (d), 120 (s), 129 (d), 138 (d), 155 (s), 175 (s) ppm.

MS (EI, 70eV): m/z (%) = 354 (100), 326 (5), 274 (55), 246 (7), 219 (12), 139 (20).

C$_{13}$H$_6$Br$_2$O$_2$ (353.99):

\[
\text{calcd. C 44.11, H 1.71} \\
\text{found C 43.77, H 1.67}
\]
$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 176

$^1$C NMR spectrum (50 MHz, CDCl$_3$) of 176
2.15 Synthesis of 2,7-dibromo-9-mesityl-9H-xanthene-9-ol (177):

To a solution of 1.37 mL (8.9 mmol) of 1-bromo-2,4,6-trimethylbenzene in 40 mL of dry THF, 1.22 mL (1.96 mmol) of \( n \)-buthyllithium (1.6 M in \( n \)-hexane) were added at -30 °C within 15 min. The colorless suspension was stirred for 30 min and 631 mg (1.78 mmol) of 2,7-dibromoxanthone-9-one (176) were added in one portion. The reaction mixture was refluxed at 66 °C for 24 h and was hydrolyzed with 15 mL of brine. After extraction with MTBE (three times 30 mL) the combined organic layer and was concentrated in vacuo afforded crude product as green solid 572 mg. The crude product can not separate to pure compound 177 and we tried to test in the next step.

2.16 Synthesis of 9-(2,4,6-trimethylphenyl)xanthenylum tetrafluoroborate (178)

The crude product from 2.5.17 (177) 572 mg (1.21 mmol) in 5 mL of dry diethyl ether was treated with 1 mL (7.4 mmol) of HBF4 etherate (15% in Et2O). After 30 min of stirring at room temperature, the slightly red precipitate was collected, washed with Et2O and dried in vaccuo (100 °C, 0.5 mbar, 2 h). It was unsuccessful to obtain 178.
3. Synthesis ligand complex by nucleophilic aromatic substitution with fluoropyridine

3.1 Synthesis of 2,6-bis(pyridin-2-yl(pyridin-4-yl)methylpyridine (183)

Prepared similar to the method described by O Multh et al.\textsuperscript{[35]} To 558 mg (6 mmol) of 2-methylpyridine in 30 mL of dry THF at -78°C was slowly added 3 mL (6 mmol) of n-buthyllithium (15% in hexane) within 5 minute, the reaction mixture was stirred for 30 minute and allowed to warm up to -20°C. The reaction mixture was slowly added with 2-fluoropyridine (179) (97 mg, 1.0 mmol) within 5 minute and allowed warm up to room temperature and was stirred at reflux temperature for 24 h and was cooled to r.t. After hydrolysis with 30 mL of H\textsubscript{2}O and extraction with CH\textsubscript{2}Cl\textsubscript{2} (three times 20 mL) and dried with sodium sulfate. After evaporation of the solvent in vacuo, the crude product was recrystallized from acetone to give 350 mg (87%) of 2-(2-pyridylmethyl)pyridine (182).

Step 2. To 1.02 g (6 mmol) of 2-(2-pyridylmethyl)pyridine (182) in 30 mL of dry THF at -78°C was slowly added 3 mL (6 mmol) of n-buthyllithium (15% in hexane) within 5 minute, the reaction mixture was stirred for 30 minute and allowed to warm up to -20°C. The reaction mixture was slowly added with 2,6-difluoropyridine (180) (115 mg, 1.0 mmol) within 5 minute and allowed warm up to room temperature and was stirred at reflux temperature for 24 h and was cooled to r.t. After hydrolysis with 30 mL of H\textsubscript{2}O and extraction with CH\textsubscript{2}Cl\textsubscript{2} (three times 20 mL) and dried with sodium sulfate. After evaporation of the solvent in vacuo, the crude product was recrystallized from acetone to give 350 mg (87%) of 2,6-bis(pyridin-2-yl(pyridin-4-yl)methylpyridine (183) as a brown solid with mp 144-146°C (Lit.\textsuperscript{[35]} mp 146°C, dec.).
$^1$H NMR (200 MHz, CDCl$_3$): $\delta = 5.99$ ppm (s, 2H), 7.18 (m, 11H), 7.63 (m, 5H), 8.53 (ddd, $J = 4.9$, 1.8, 0.9 Hz, 4H).

MS (EI, 70 eV): $m/z$ (%) = 415 (100) [M$^+$], 414 (99), 337 (48), 246 (38), 169 (31).

$^1$H NMR spectrum (200 MHz, CDCl$_3$) of 2,6-bis(pyridin-2-yl(pyridin-4-yl)methyl)pyridine (183)
3.2 Synthesis of 2,6-bis(2-pyridyl)methyl pyridin-cupper(II)perchlorate-acetonitrile complexes (184)

Prepared similar to the method described by O Multh et al.\textsuperscript{[35]}: To 2,6-bis(pyridin-2-yl(pyridin-4-yl)methylpyridine (183) (91 mg, 0.22 mmol) in dry CH\textsubscript{3}CN 2 mL and CH\textsubscript{3}OH 2 mL was added copper(II)perchlorate (66 mg, 0.22 mmol) in dry CH\textsubscript{3}OH 2 mL. The reaction mixture led to the formation of blue precipitate within 1 d, and the solvents were removed. The formed blue solid was washed with CH\textsubscript{3}CN and dried in vacuo (50 °C, 2.5 mbar, 10 min) to afford 2,6-bis(2-pyridyl)methyl pyridin-copper(II)perchlorate-acetonitrile complex (184) 130 mg (81%) of the blue solid with mp 242-245 °C.

3.3 Synthesis of 2-methyl-4-(pyridin-4-yl)but-3-yn-2-ol (187)

Prepared similar to the method described by Yu et al.\textsuperscript{[36]}: 4-bromopyridine hydrochloride (185) (5.01 g, 25.7 mmol), Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (180 mg, 0.26 mmol), CuI (29 mg, 0.15 mmol) were added into a dried schlenck flask, set up with a magnetic stirring bar under argon. The reaction mixture was stirred at room temperature and 2.6 g (31 mmol) of 2-methyl-3-butyn-2-ol (186), DEA 42.85 mL in 17 mL abs THF was added slowly. The reaction mixture was stirred for 4.5 h at room temperature. The solvent was evaporated to dryness.
and the crude product was dissolved in 100 mL of CHCl₃ and 50 mL of H₂O. The organic layer was separated and dried with NaSO₄. The solvents were removed by rotary evaporation. The residue was purified by chromatography (silica, CHCl₃/EA 1:1) affording a yellow solid 3.96 g of 2-methyl-4-(pyridin-4-yl)but-3-yn-2-ol (187). Recrystallization (CHCl₃/Hexenes) afforded a yellow solid 2.23 g (54% yield) with mp 113-115 °C (Lit.[36] mp 113-114 °C, dec.).

**¹H NMR** (200 MHz, CDCl₃): δ = 1.51 ppm (s, 6H), 2.98 (s, OH), 7.30 (dd, J = 4.4 Hz, 1.7 Hz, 2H), 8.59 (dd, J = 4.5 Hz, 1.6 Hz, 2H).

**MS (EI, 70 eV):** m/z (%) = 161 (13) [M⁺], 146 (24), 118 (11), 104 (15), 59 (12), 43 (42).

¹H NMR spectrum (200 MHz, CDCl₃) of 187
3.4 Synthesis of 4-ethynylpyridine (188):

A mixture of 2-methyl-4-(4-pyridyl)-3-butyn-2-ol (187) (3 g, 18.6 mmol), NaOH (0.8 g, 20 mmol) in toluene 90 mL was refluxed under argon for 3 h at 120 °C and allowed to warm up to room temperature. The resulting mixture was filtered off. The filtrate was concentrated, taking care to minimize the loss of product, which is quite volatile. Kugelrohr distillation at 30 °C, 0.01 mbar afforded a brown solid, which was purified by sublimation in vaccuo (100 °C, 0.1 mbar, 3 h): 4-ethynylpyridine (188).1.22 g (64%) of the white solid with mp 94 °C (Lit.[36] mp 96-97 °C, dec.).

\[ \text{1H NMR (200 MHz, CDCl}_3\text{): } \delta = 3.23 \text{ ppm (s, 1H), 7.28 (dd, J = 4.5, 1.6 Hz, 2H), 8.53 (dd, J = 4.5, 1.6 Hz, 2H).} \]

\[ \text{MS (EI, 70 eV): } m/z = 103 (100) [M^+], 76 (42), 63 (12), 50 (35), \]

\[ \text{1H NMR spectrum (200 MHz, CDCl}_3\text{) of 4-ethynylpyridine (188).} \]
3.5 Synthesis of 1, 4- bis(pyridin-4-ylethynyl)benzene (190):

A mixture of 4-ethynylpyridine (188) (0.32g, 3.1 mmol), Pd(PPh$_3$)$_2$Cl$_2$ (19 mg, 0.027 mmol) 1,4-diiodobenzene (189) (4.95g, 1.5 mmol), CuBr (6 mg,0.042 mol) in triethylamine 19 mL was stirred in oil bath at 60 °C for 1 h and the temperature was slowly increased to 90 °C and the reaction mixture stirred at 90 °C for 48 h, then cooling to room temperature. The solvent was removed by rotary evaporation. The solid residue was dissolved in CH$_2$Cl$_2$. The solution was washed with aqueous K$_2$CO$_3$ and filtered off. The organic layer was dried over Na$_2$SO$_4$. The solvent was removed by rotary evaporation. The product was recrystallized from toluene to give 1, 4- bis(pyridin-4-ylethynyl)benzene (190) 0.36 g (87% yield) as a brown solid with mp 186 °C (Lit.[Tetrahedron Letters 40,1999, 5413-5416] mp 186-187°C, dec.).

$^1$H NMR (200 MHz, CDCl$_3$): $\delta = 7.41$ ppm (d, J = 6.0 Hz, 4H), 7.58(s, 4H), 8.64 (d, J = 6.0 Hz, 4H)

MS (EI, 70 eV): m/z (%) = 280 (100) [M$^+$], 140 (24), 100 (6), 140 (33), 87 (12), 69 (5).
$^1$H NMR spectrum (200 MHz, CDCl$_3$, 25 °C) of 1,4-bis(pyridin-4-yl- ethynyl) benzene (190)
3.6 Synthesis of copper(II) complex with 1,4-bis(pyridine-4-ylethynyl)benzene and 2,6-bis[bis(2-pyridyl)methyl] pyridin-cupper(II)perchlorate (191)

To 6-bis(2-pyridyl)methyl pyridin-cupper(II)perchlorate-acetonitrile complexes (190) (60 mg, 0.08 mmol) in dry CH₃CN 2 mL was added 1,4-bis(pyridin-4-ylethynyl)benzene (184) (14 mg, 0.05 mmol) in dry CH₃CN 2 mL. The reaction mixture (3 d) led to the formation of a brown precipitate, the solvents were removed. The formed brown solid was washed with CH₃CN and dried in vacuo (50 °C, 2.5 mbar, 1 h). The solid product was recrystallized from CH₃CN/CHCl₃ (1:1) to give 56.8 mg of green solid which was analyzed by mass spectrometry (FAB), but could not verify the molecular mass of 191.
III. APPENDIX
References

[16] X-ray crystal structure analysis of 60i: Pale orange prism, 0.32 x 0.28 x 0.23 mm³, monoclinic, P2₁/n, a = 17.056(2), b = 3.9938(5), c = 23.829(3) Å, β = 98.49(1)°, V = 1605.4(3) Å³, ρcalc = 1.483 gcm⁻³, 2θmax = 50.50°, λ = 0.71073 Å, T = 113 K, 8141 measured reflections, 2892 independent reflections (Rint = 0.0368), 2084 observed reflections (I>2σ(I)), μ = 0.345 mm⁻¹, 224 parameters, R1(I>2σ(I)) = 0.0354, wR2(all data) = 0.0846, max./min. residual electron density 0.301/-0.287 eÅ⁻³.


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