MASARYKOVA UNIVERZITA
PŘÍRODOVĚDECKÁ FAKULTA
ÚSTAV CHEMIE

Diplomová práce

Brno 2016 Tomáš Pastierik

MASARYKOVA UNIVERZITA

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ÚSTAV CHEMIE

Vývoj nových chromoforů pyroninového typu

Diplomová práce

Tomáš Pastierik

Vedoucí práce: prof. RNDr. Petr Klán, Ph.D. **Brno 2016**

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Abstrakt

V této diplomové práci je prezentována syntéza vybraných analogů pyroninu. U připravených derivátů byla změřena absorpční a emisní spektra a získaná absorpční maxima byla použita pro ověření TD-DFT výpočtů, které provedl kolega. Výsledkem této práce je potvrzeni kvalitativního modelu, který vysvětluje absorpční vlastnosti chromoforů pyroninového typu.

Abstract

In this work, the synthesis of selected pyronin derivatives is presented. The UV-vis absorption and emission spectra of the prepared compounds were measured and the resulting absorption maxima were used to validate the TD-DFT calculations performed by a co-worker. As a result, the qualitative model aimed at understanding the absorption properties of pyronin-type chromophores was confirmed.

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"Do. Or do not. There is no try."

- Yoda

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Prohlášení

Prohlašuji, že jsem svoji diplomovou práci vypracoval samostatně s využitím informačních zdrojů, které jsou v práci citovány.

Brno 16.5.2016 …….

Jméno a příjmení

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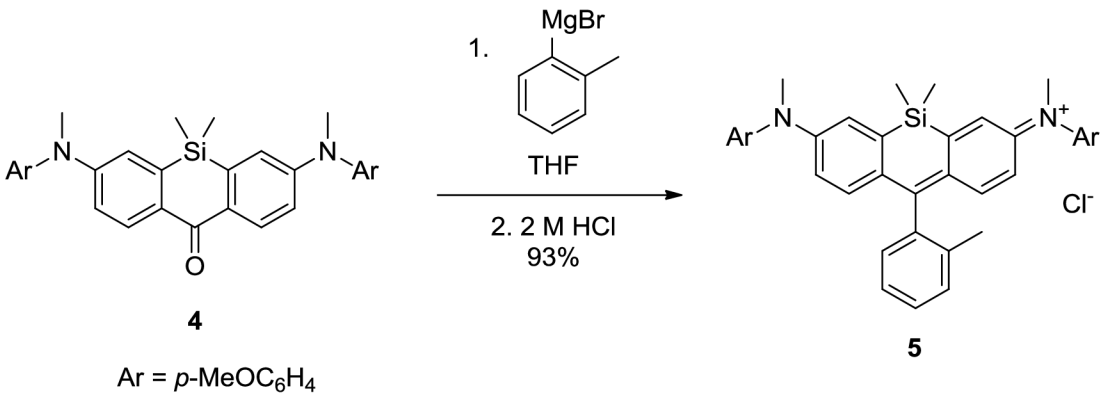
1 Literature Part

1.1 Introduction

Design of new organic molecules derived from fluorescein[1] is currently an important topic in bioorganic and biological research, because they are extensively used as markers and sensors for *in vivo* and *in vitro* biological and medical applications.

1.2 Synthesis of Rhodamine Derivatives

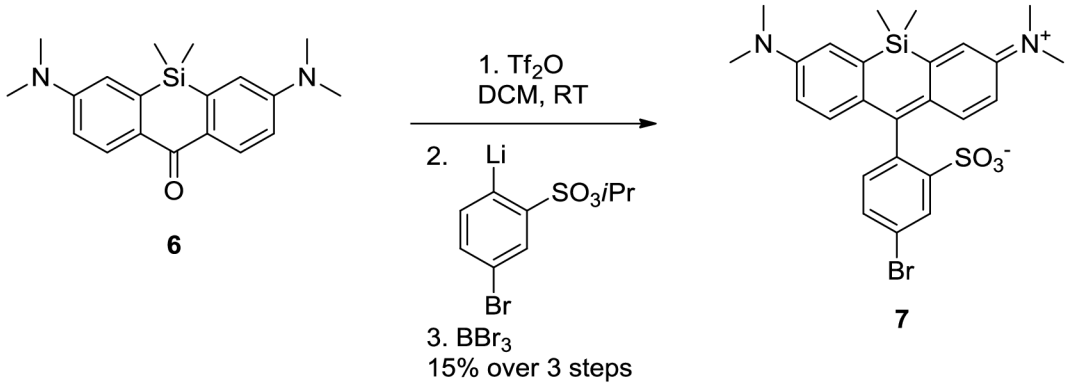
In general, three major pathways for preparation of rhodamine derivatives are described in the literature. In the first one, the derivatives are prepared from xanthenone intermediates by nucleophilic addition of aryllithium[2] or arylmagnesium halide[3,4] to a carbonyl group of xanthenone followed by elimination of water under acidic conditions. The driving force for this elimination, which usually proceeds in order of minutes at ambient temperature, is the formation of a large aromatic system. This method is widely spread and is used for preparation of differently substituted rhodamines. Scheme 1 depicts preparation of **5** published by Urano *et al.*[3]



Scheme 1 - Preparation of 5

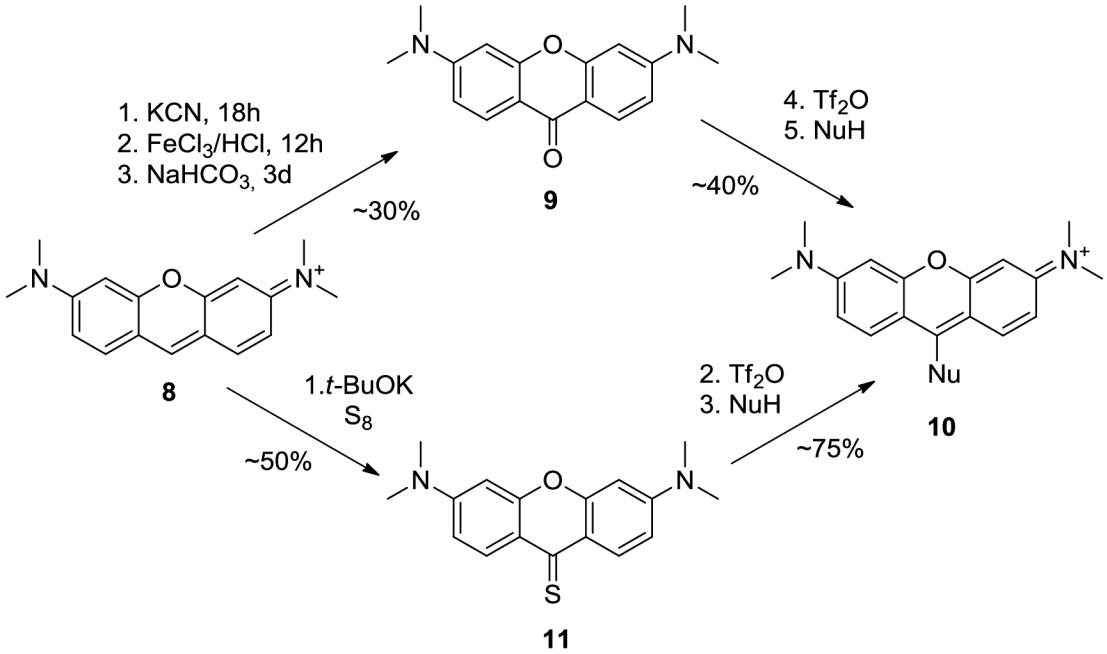
Another approach deals with the conversion of the carbonyl group of xanthenone **6** to its triflate derivative in the first step, followed by addition of aryllithium with the subsequent expulsion of triflate group to form the product **7** (Scheme 2). [5–7] This method is chosen because the resulting triflate-substituted rhodamine is activated towards even

poorer nucleophiles and the subsequent elimination of the triflate is irreversible, allowing for the formation of otherwise inaccessible derivatives. Scheme 2 describes such a step, which is followed by the deprotection of isopropyl ester group by BBr_3.[7]



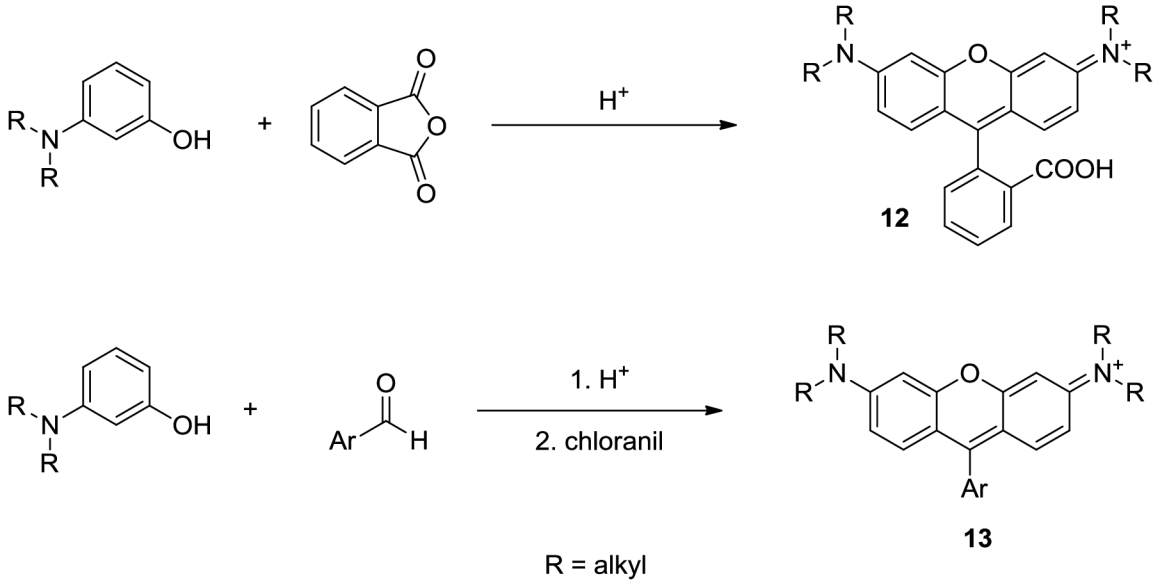
Scheme 2 - Preparation of 7

Recently, an alternative preparation of rhodamines, which bypasses a low-yielding five-step procedure (Scheme 3; upper pathway), has been published. The procedure published by Yoon *et al.*[8] involves deprotonation of the pyronin **8** to form a carbine,[9,10] which reacts with sulfur to form a more reactive thioketone **11**. In analogy to the previous method, the thioketone **11** is subsequently activated with triflic anhydride and subjected to a reaction with nucleophile to form the rhodamine **10**.



Scheme 3 - Preparation of rhodamines *via* the thioketone 11

In a different approach, the rhodamine derivatives can be also constructed *via* a one-pot condensation of smaller building blocks (Scheme 4), however, these pathways are conducted under strongly acidic conditions with poor yields. Moreover, only rhodamines with oxygen in the position 10 can be prepared in this manner.[11–14]

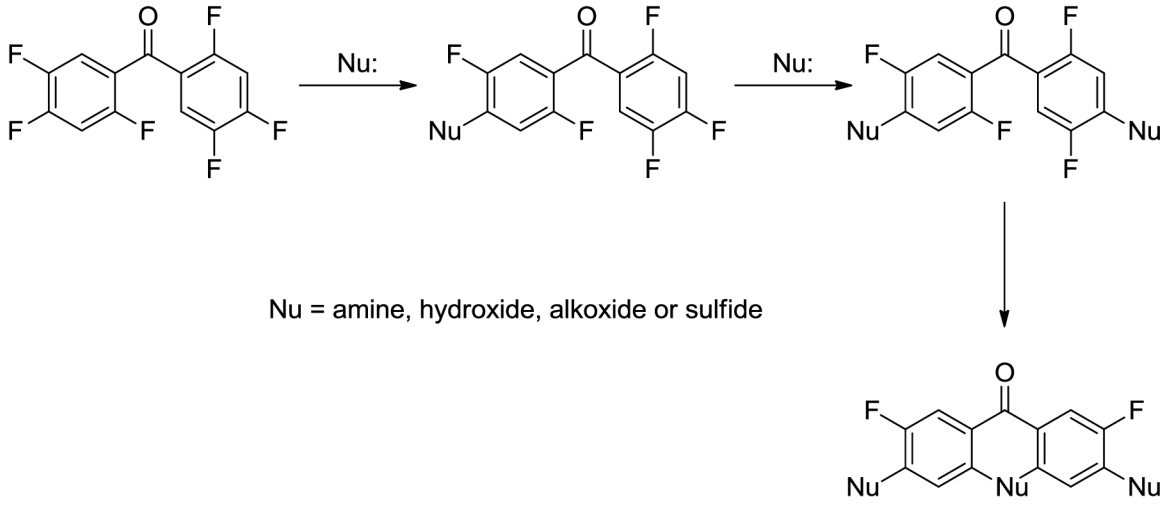


Scheme 4 - Preparation of rhodamines 12 and 13

1.3 Synthesis of 3,6-Diaminosubstituted Xanthenones

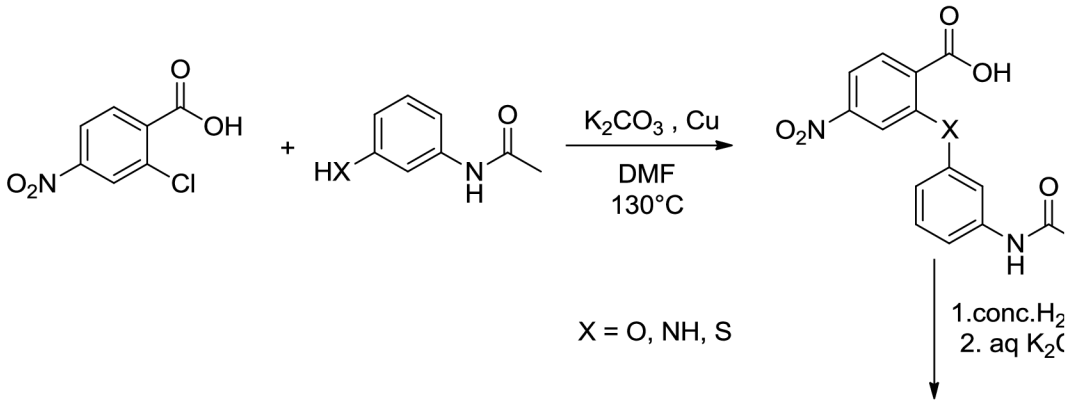
1.3.1 S, Se and Te-Xanthenone

Peterson in his work describes the preparation of fluorinated xanthenones with nitrogen, oxygen or sulfur in the position 10. [15] Preparation is based on sequential attacks of various amines, hydroxides or sulfides as nucleophiles *via* nucleophilic aromatic substitutions (Scheme 5). Fluorination of pyronin and rhodamine dyes can enhance their photostability and improve spectroscopic properties.[15]



Scheme 5 - Preparation of difluoro xanthenones according to Peterson

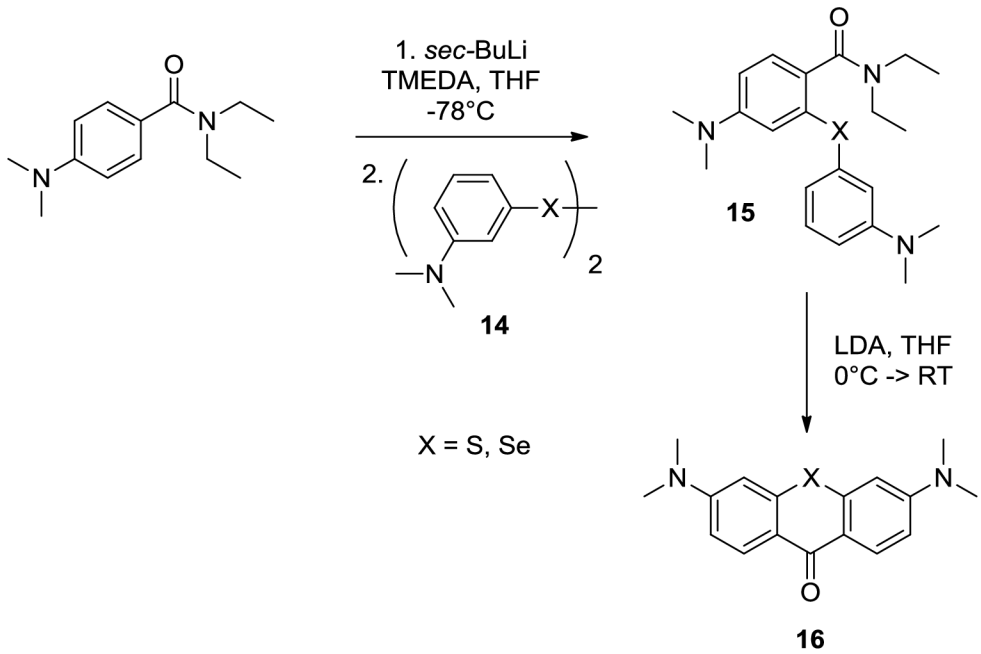
Chang and coworkers have published variable synthesis of xanthenone scaffold which allows for the preparation of xanthenones with N, O or S in the position 10 using the same pathway (Scheme 6).[16] The three-step sequence could be further extended to provide a diverse group of non-symmetrically substituted xanthenone cores. Strongly acidic conditions are required to carry out the intramolecular Friedel-Crafts cyclization to form the desired ketone.



Scheme 6 - Preparation of xanthenones according to Chang *et al.*

The research of Detty is partially focused on the development of chalcogenorhodamine-based inhibitors of P-glycoprotein[17] and photosensitizers for photodynamic therapy.[18]

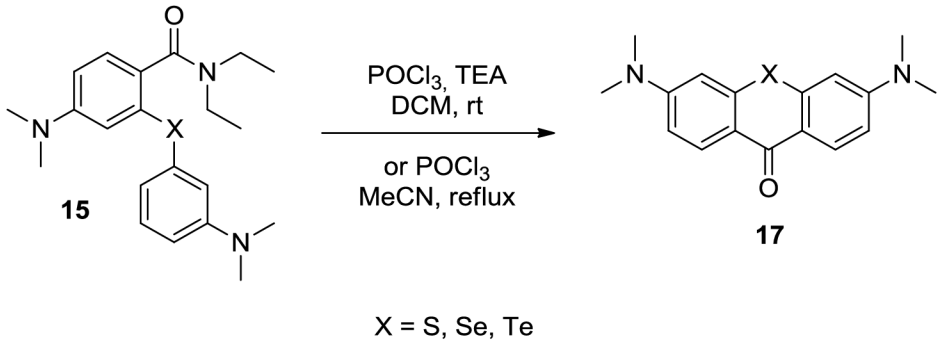
His work involves synthesis of symmetrical[19] and unsymmetrical[18,20] seleno, thio and telluro-rhodamines chalcogeno-rhodamines. In the first step of the synthesis, *ortho*-lithiation takes place, followed by addition of an electrophilic disulfide or diselenide **14** to form the indermediate **15** (Scheme 7). The key step of the synthesis is the cyclization of **15** to give the final ketone **16**. Because of Bronsted and Lewis acidity of the present amino groups, usual Friedel-Cratfs conditions ($AlCl_3$, MsOH) fail in the preparation of target xanthenones. However, **15** could by cyclized using LDA in 13-30% yields, depending on the amount of LDA used.[19]



Scheme 7 - Synthesis of 16

This yield was significantly improved when $POCl_3$ was employed as a cyclization agent.[20] The methods describes use of $POCl_3$ in dichloromethane with TEA to give products in 77-97% yields, but the reaction times reach up to 48 h (Scheme 8). Unsatisfied with the extended reaction times, the authors found that **17** is formed in refluxing MeCN within 90 minutes. On the other hand, lower yields (73-77%) have been observed under

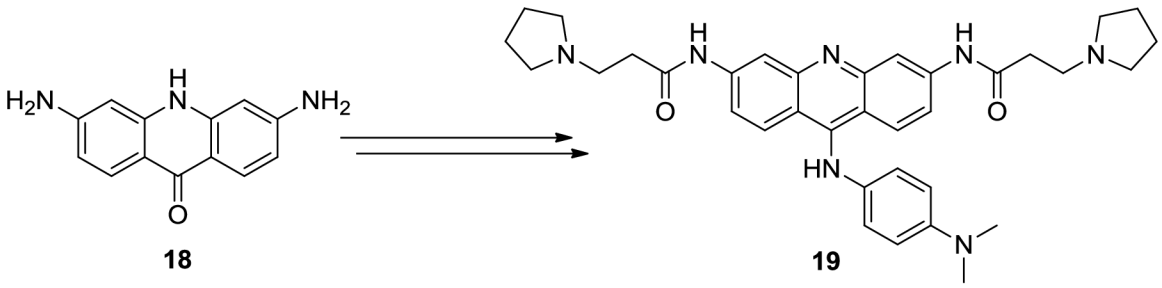
these conditions. The important feature of all cyclization reactions is that the correct regioisomer of cyclization is formed exclusively.



Scheme 8 - Preparation of 17

1.3.2 *N*-Xanthenone

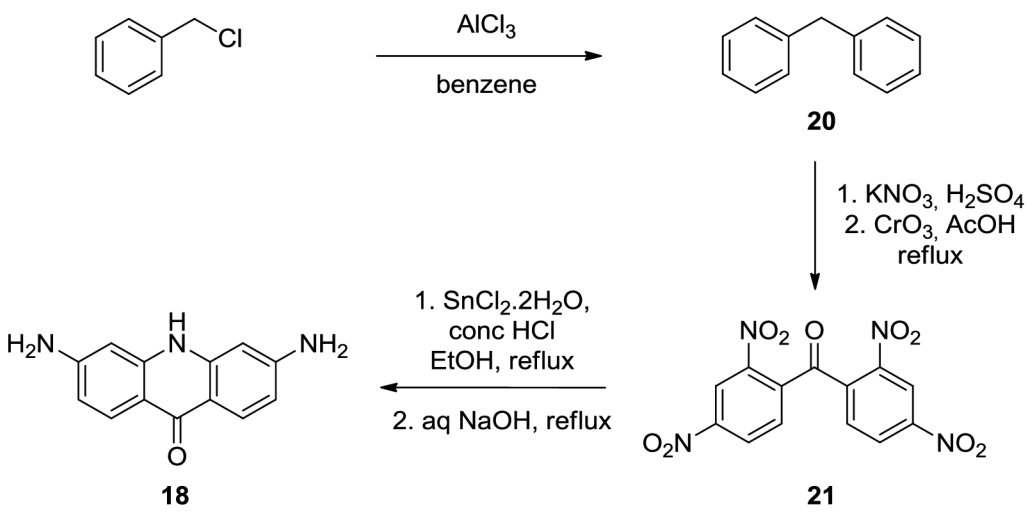
Derivatives of 3,6-diaminoacridine are used in medicinal chemistry as ligands for telomeric DNA, which makes them potential regulators of telomeres of tumor cells. Trisubstituted acridines such as BRACO-19 (**19**) are potent selective G-quadruplex binders.[21–23] They are, in general, synthetically accessed from 3,6-diaminoacridone **18** (Scheme 9).



Scheme 9 - The intermediate 18 in the synthesis of G-quadrouples ligand BRACO-19 (19)

Despite the fact, that applications of BRACO-19 analogues are studied nowadays, almost a 90-year old work of Matsumura[24] is still used[21,22,25–27] to this day as the main synthetic route for preparation of **18**. Matsumura was inspired by the work of Schoppf[28] and Staedel[29] from the end of 19th century and provided a well reproducible synthetic pathway (Scheme 10). In the first step, diphenylmethane **20** is prepared using the Friedel-Crafts reaction. The intermediate **20** is then nitrated and oxidized at the benzylic position

to provide tetranitrobenzophenone **21**, which is subjected to a reductive cyclization in the presence of $SnCl_2$ to provide **18.**

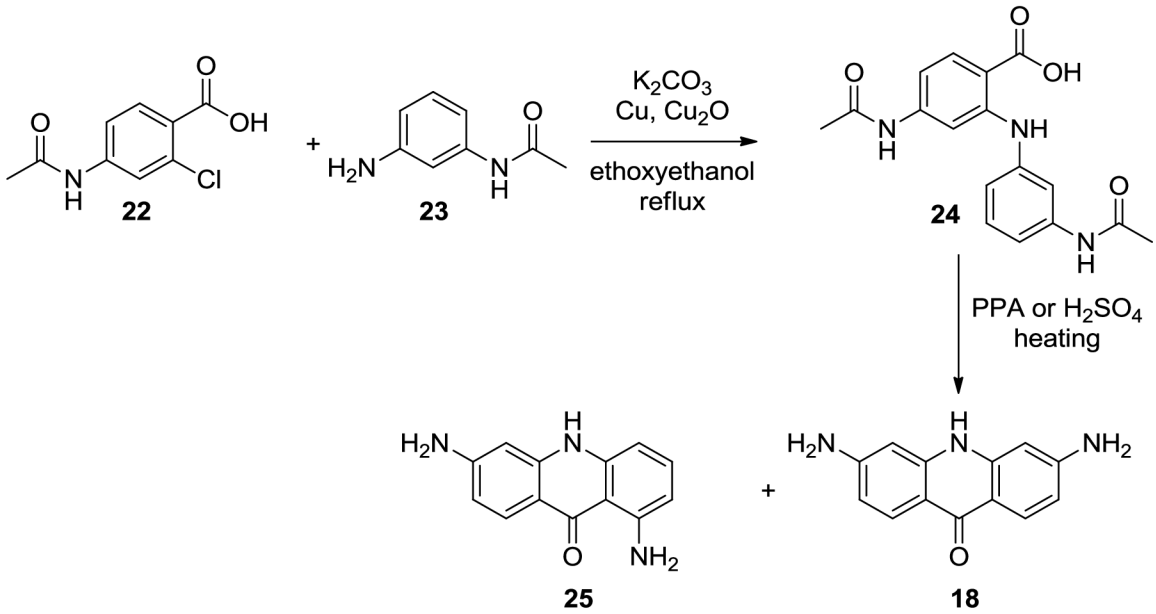


Scheme 10 - Preparation of 18 according to Matsumura

Besides the fact that all steps of this pathway provide pure compounds after recrystallization and do not require other purification, another interesting aspect is the reductive cyclization of **21**. Unfortunately, the mechanism of this transformation is not proposed by any of the authors of the original publications.

Another approach to the synthesis of **18** is described in Section 1.3.1. Chang *et. al.*[16] reported a two-step preparation of the unsymmetrical xanthenone, which could be further reduced to give the symmetrical 3,6-diaminoacridone **18**.

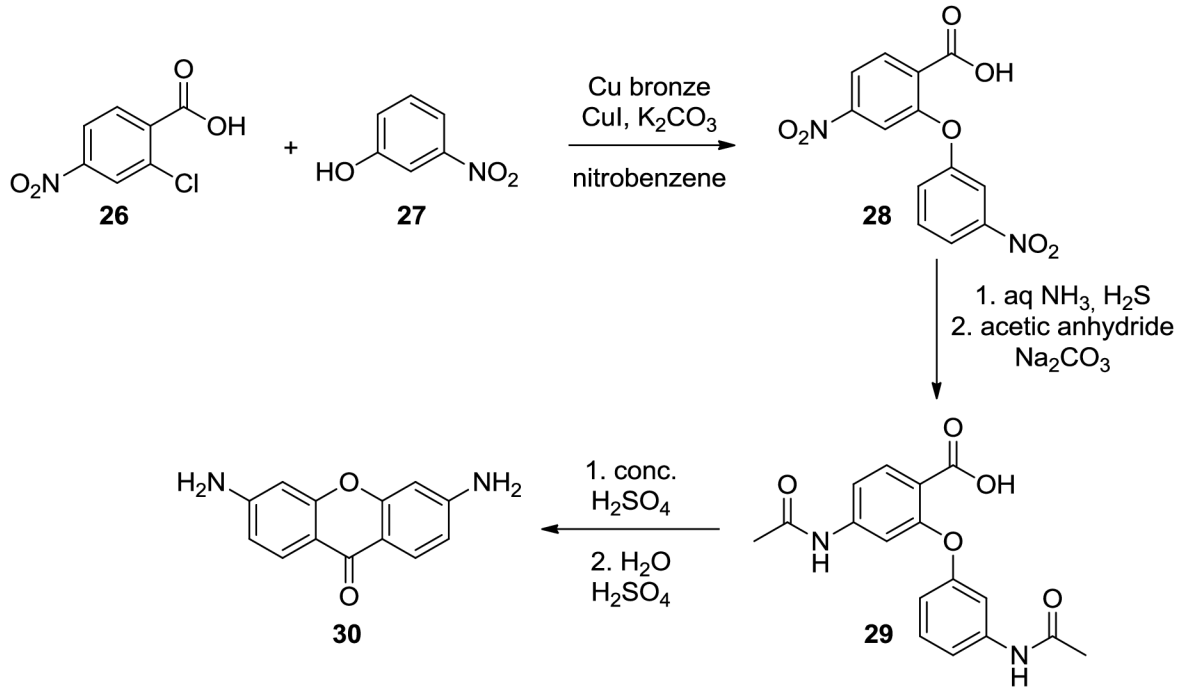
In a similar procedure published by Kozurkova *et. al.*,[30] Ullmann coupling of the two building blocks **22** and **23** was employed in the first step with subsequent cyclization of the diarylamine **24** in the presence of polyphosphoric acid or concentrated sulfuric acid to provide a mixture of regioisomers **18** and **25** (Scheme 11). An experimental study revealed that heating of **24** in conc. H_2SO_4 at 100 °C is the most sufficient method, because it results in a 4:1 ratio of the regioisomers **18** and **25**.



Scheme 11 - Preparation of 18 according to Kozurkova

1.3.3 O-Xanthenone

Preparation of the xanthenone **30** was described already in Chapter 1.3.1 in the work of Chang.[16] A similar approach can be recognized in the work of Goldberg and Walker (Scheme 12).[31] At first, the two building block **26** and **27** are connected *via* Ullmann coupling to give **28**. The nitro groups of **28** are reduced by aq. NH_3/H_2S, and the resulting amino groups are protected with the acetyl groups to give **29**, which is further cyclized in the presence of concentrated H_2SO_4. Finally, the acetyl protecting groups are removed in diluted H_2SO_4 to provide the target xanthenone **30**.

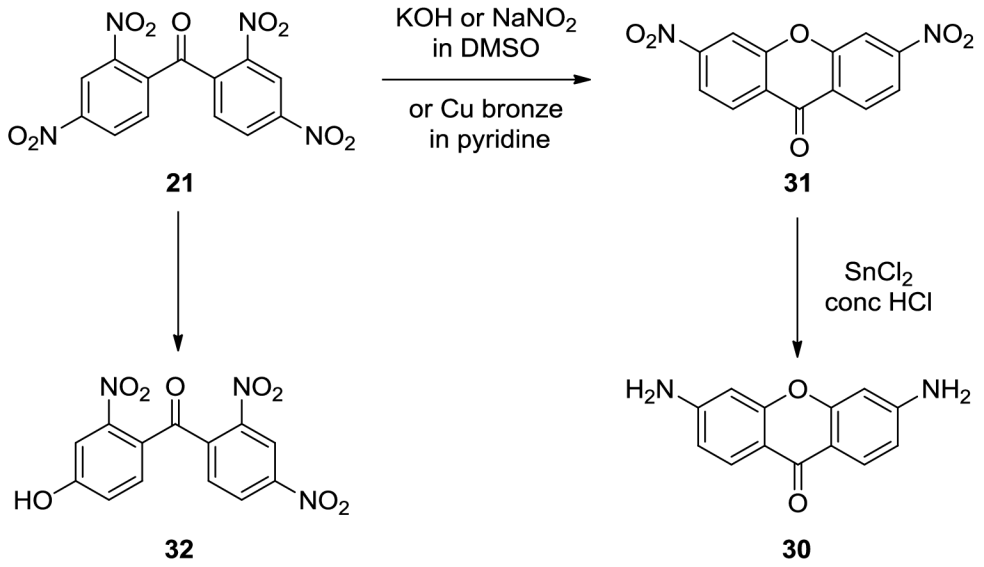


Scheme 12 - Preparation of 30 according to Goldberg

Another method for preparation of **30** was described by Gorwin and Whaley (Scheme 13).[32] The work was aimed to prepare acridine derivatives from some nitrobenzophenones, however, formation of O-xanthenones as byproducts was observed in the process.

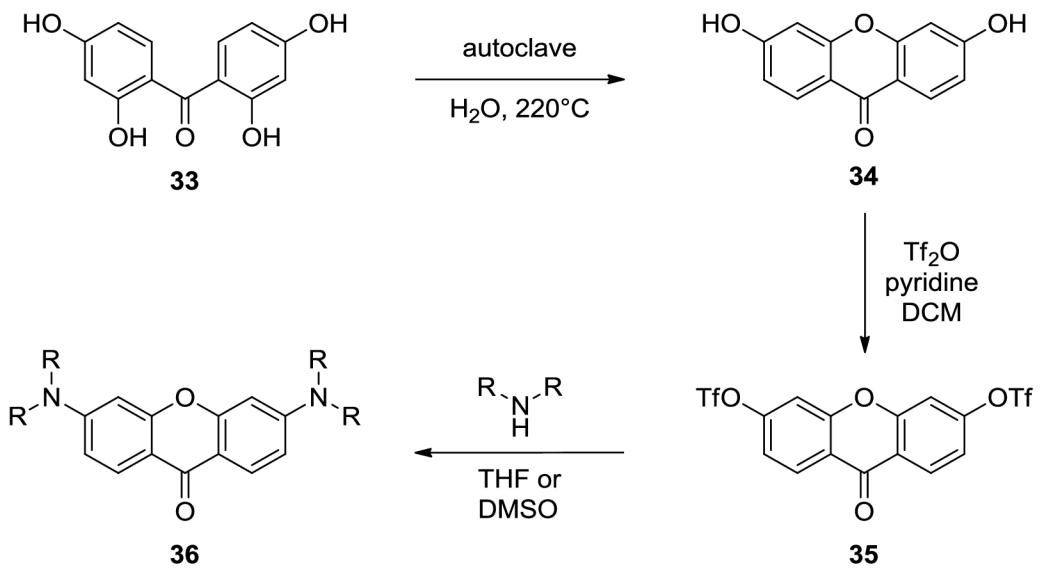
These reactions were carefully examined and showed a potential application as a method for the preparation of **30**. After treatment of **21** with KOH in DMSO or $NaNO_2$ in DMSO or Cu bronze in pyridine, **31** is obtained in 38%, 31% and 18% yield, respectively. Further reduction of **31** by $SnCl_2$ in conc. HCl provide **30**.

In the conversion of **21** to **31**, the undesired side-product **32** is formed in approximately equal yields. Fortunately, the dinitroxanthenone **31** is isolated after filtration of reaction mixture as a solid, while the side-product **32** remains in the solution.



Scheme 13 - Preparation of 30 and observed side reaction

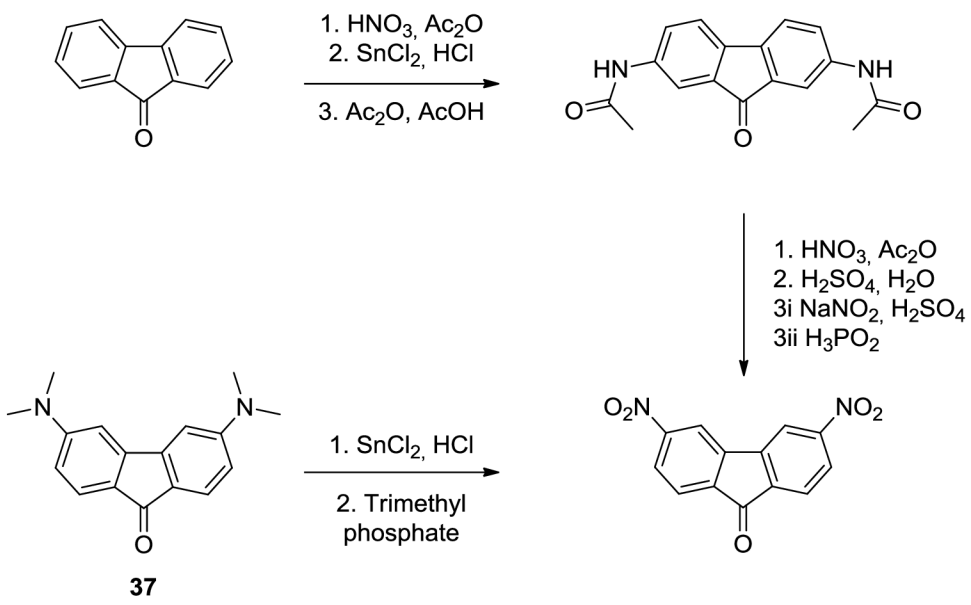
A different methodology for the preparation of O-xanthenones is depicted in Scheme 14. [33–37] First, dihydroxyxanthenone **34** is prepared from the 2,2′,4,4′-tetrahydroxybenzophenone **33** in autoclave at high temperature and subsequently converted to its bistriflate analogue **35** in almost quantitative yield, and the intermediate **35** is transformed *via* nucleophilic aromatic substitution into the differently substituted 3,6-diaminoxanthenones **36**.



Scheme 14 - Preparation of substituted 3,6-diaminoxanthenones

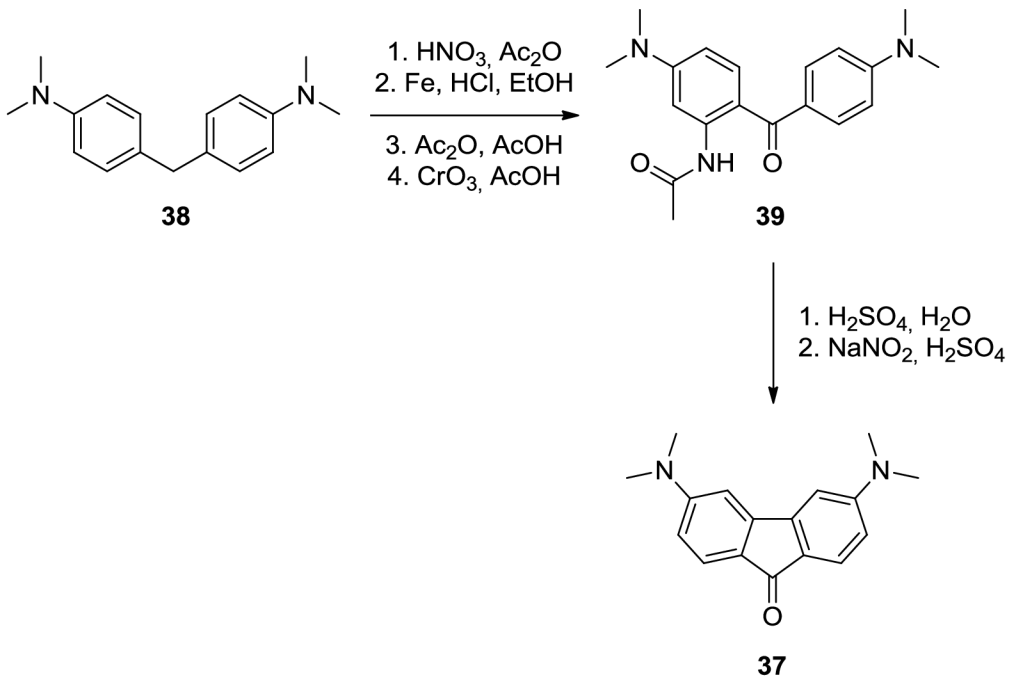
1.3.4 Fluorenone

Synthesis of the 3,6-bisdimethylamino fluorenone **37** is described by Barker and Barker[38–40] who prepared it in nine steps from the commercially available fluorenone (Scheme 15). Lack of methodologies allowing formation of the Ar-Ar bond at that time forced them to use a longer synthetic pathway. At first, temporary directing groups are installed into the position 2 and 7 in three steps, then nitro groups are introduced to the positions 3 and 6, while directing groups are removed in another three steps. Finally, the nitro groups are converted into the desired dimethylamino groups in two steps.



Scheme 15 - Preparation of 37 according to Barker and Barker

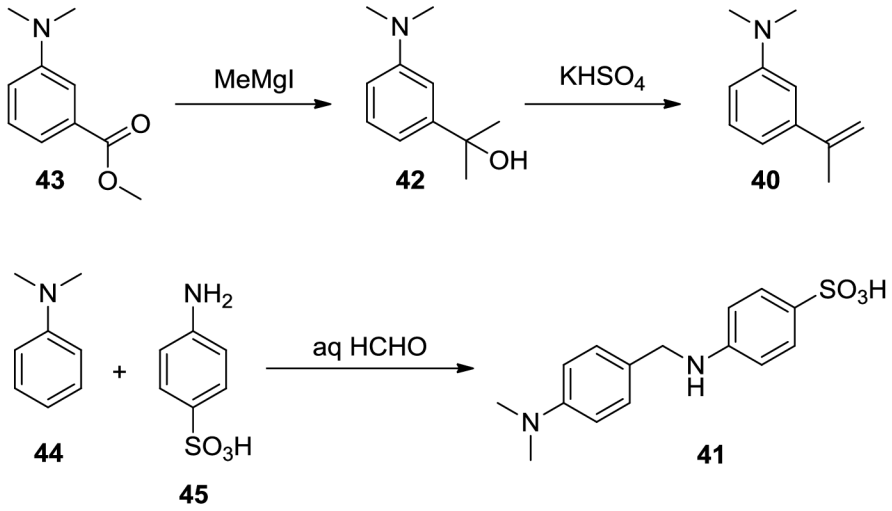
Barker and Barker in their publications introduce also a shorter synthetic pathway, where the fluorenone **37** is prepared in five steps (Scheme 16). The synthesis started by mononitration of **38**, followed by reduction to the amino group with Fe/HCl, which is then protected with acetyl protecting group to allow benzylic oxidation. The amino group in the ketone **39** is deprotected and converted to diazonium salt in the presence of $NaNO_2$, which undergoes intramolecular S_E^{Ar} to provide the target fluorenone **37**.



Scheme 16 - Alternative synthesis of 37 published by Barker and Barker

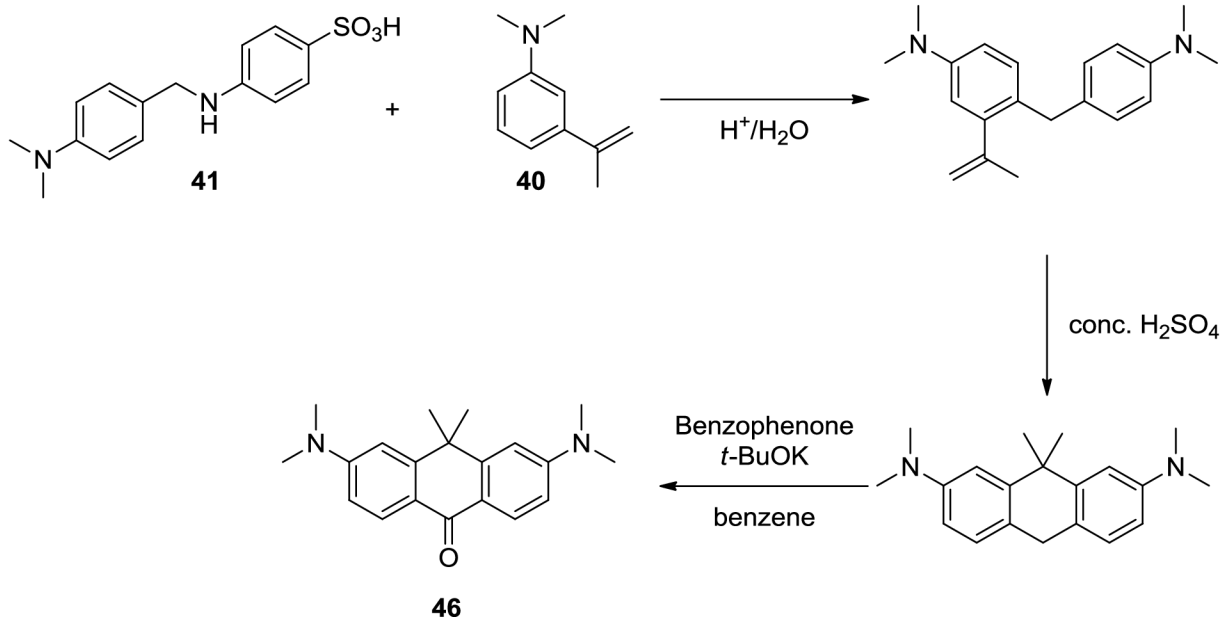
1.3.5 C-Xanthenone

C-xanthenone **46** was synthesized by Aaron and Barker[41] from the two building blocks **40** and **41**. The building block **40** was prepared from tertiary alcohol **42**, which was constructed by reaction of the methyl ester **43** with methylmagnesium iodide (Scheme 17). The second building block **41** was prepared by a condensation of *N,N*-dimethylaniline **44** with sulfanilic acid **45** and formaldehyde.



Scheme 17 - Preparation of building blocks 40 and 41

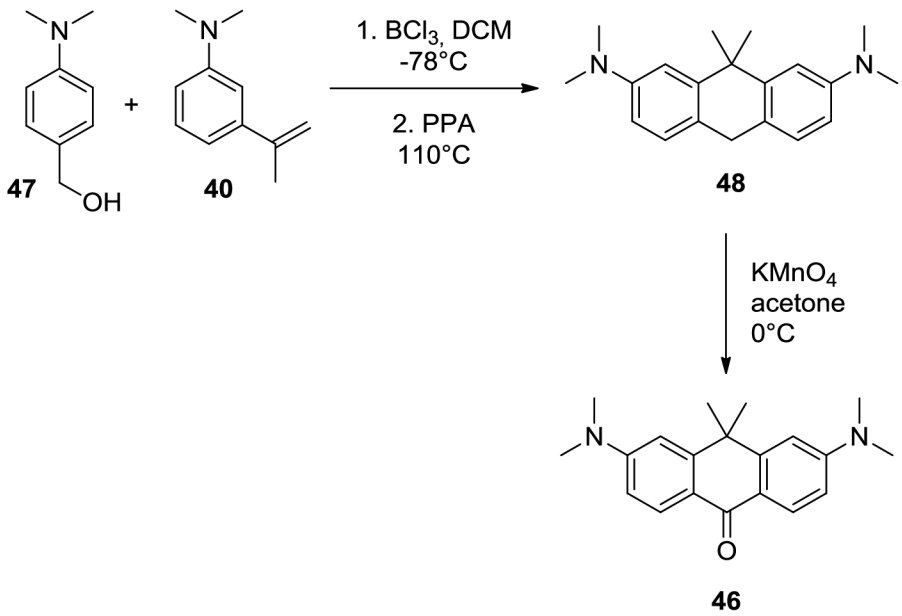
C-xanthenone **46** was prepared from the two building blocks **40** and **41** (Scheme 18) by a two-step acid-catalyzed condensation, followed by oxidation in the presence of *t*-BuOK.



Scheme 18 - Preparation of 46 according to Aaron and Barker

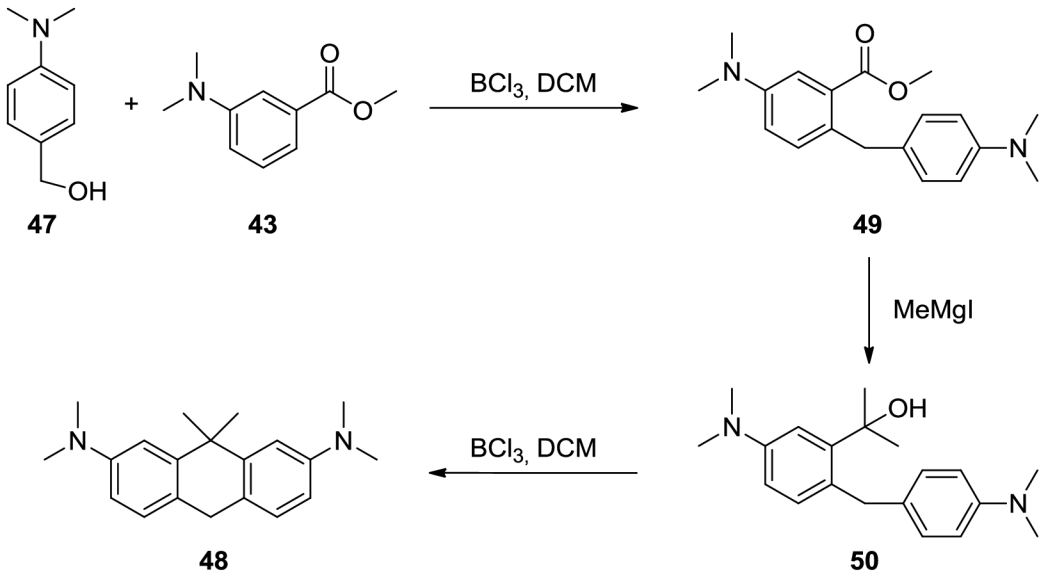
This 60-year old method has recently been conducted in a somewhat improved fashion.[36,42,43] Hell and *et. al.*[42] followed the general idea of the original procedure, however they used different reagents and greatly improved and simplified the procedure (Scheme 19).

In the first stage, the benzylalcohol **47** is condensed with the building block **40** in the presence of a Lewis acid instead of a Brønsted acid. Intramolecular cyclization of the middle ring proceeding *via* S_E^{Ar} is performed in the presence of phosphoric acid instead of sulfuric acid. In the last step, the intermediate **48** is oxidized by $KMnO_4$ in acetone to give the final C-pyronin **46**.



Scheme 19 - Preparation of 46 modified by Hell and co-workers

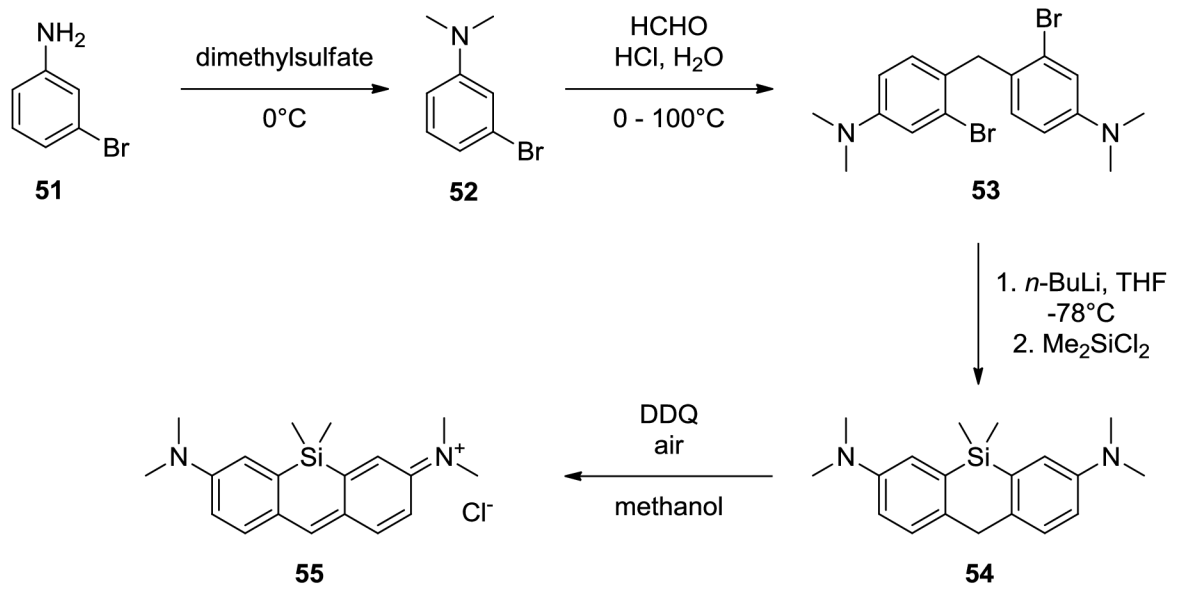
A similar pathway to construct the intermediate **48** is depicted in Scheme 20.[44] The benzyl alcohol **48** is condensed with **43** to give the ester **49**, which is converted into the tertiary alcohol **50** using Grignard reagent. The alcohol **50** is subjected to an intramolecular cyclization in the presence of a Lewis acid to provide final intermediate **48**.



Scheme 20 - Preparation of 48 according to Bai and co-workers

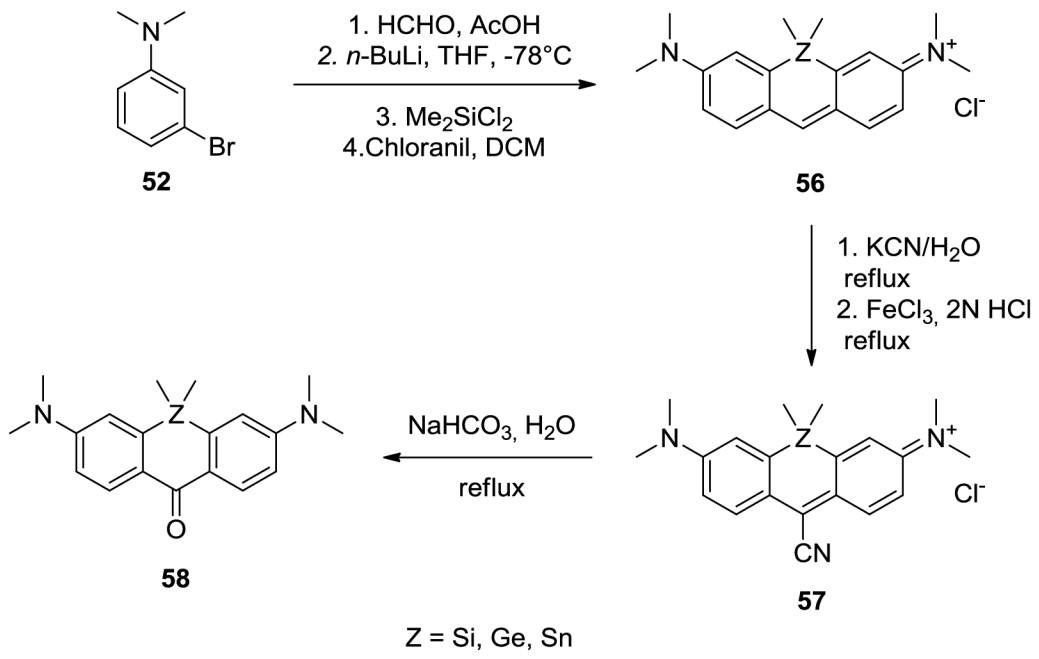
1.3.6 Si, Ge and Sn-Xanthenone

The silicon atom in the pyronin scaffold has appeared for the first time in work of Xu and co-workers[45] who demonstrated that the compound displays a bathochromic shift of its absorption maximum relative to that of pyronin with oxygen in the position 10. TMDHS (**55**) is prepared from *m*-bromoaniline **51** in five steps. The aniline **51** is methylated by DMS to provide **52**, which is condensed with formaldehyde to **53**. The dibromide **53** is cyclized in an intramolecular fashion to form **54**, which is subsequently oxidized to TMDHS (Scheme 21).



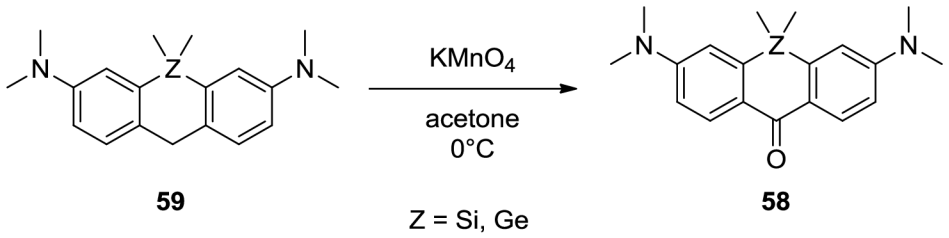
Scheme 21 - Preparation of 55 according to Xu

Koide *et. al.*[2] describes xanthenones with Si, Ge and Sn in the position 10. The preparation of these compounds is based on the synthesis of TMDHS (Scheme 22). Pyronins **56** are converted into the xanthenones **58** in a complicated manner. At first, cyanopyronin **57** is formed by a nucleophilic attack of cyanide on pyronin, and then it is hydrolyzed to the unstable carboxylic acid[46], which decomposes to the target xanthenone **58**. Si-xanthenone[47] and Ge-xanthenone[34] were isolated, but Sn-xanthenone is described to be unstable and its existence is confirmed only by HRMS.



Scheme 22 - Preparation of xanthenones 57 according to Koide *et al.*

An alternative way to prepare xanthenone **58** from the cyclic intermediate **59** is described (Scheme 23).[34,43,48–50] The cyclic intermediate **59** is oxidized by $KMnO_4$ in acetone to furnish the target xanthenone **58**.



Scheme 23 - An alternative preparation of 58

2 Results and Discussion

3 Experimental Part

4 Conclusion

List of Abbreviations

AcOH	acetic acid
Ac_2O	acetic anhydride
Chloranil	tetrachloro-*p*-benzoquinone
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
Deoxo-Fluor®	bis(2-methoxyethyl)aminosulfur trifluoride
DMF	*N*,*N*-dimethylformamide
DMS	dimethylsulfate
DMSO	dimethylsulfoxide
EDG	electron donating group
EtOH	ethanol
EWG	electron withdrawing group
FGI	functional group interconversion
FMO	frontier molecular orbital
HOMO	highest occupied molecular orbital
HPFC	high-pressure flash chromatography
HPLC	high-performance liquid chromatography
HRMS	high-resolution-mass spectrometry
IR	infra-red
LUMO	lowest unoccupied molecular orbital
LDA	lithium diisopropylamide
MeCN	acetonitrile
MeOH	methanol
MsOH	methanesulfonic acid
NIR	near infra-red
NMR	nuclear magnetic resonance
Nu, NuH	nucleophile
PPA	polyphosphoric acid

RT, rt	room temperature
TD-DFT	time-dependent density functional theory
TEA	triethylamine
THF	tetrahydrofuran
TLC	thin layer chromatography
TMDHS	2,7- *N,N,N′,N′*-tetramethyl-9-dimethyl-10-hydro-9-silaanthracene
TMEDA	*N,N,N′,N′*-tetramethylethylenediamine
TsOH	4-methylbenzenesulfonic acid, *p*-toluenesulfonic acid
Tf_2O	triflic anhydride, Trifluoromethanesulfonic anhydride

References

(1) Baeyer, A. *Chem. Ber.* **1871**, *5*, 555–558.
(2) Koide, Y.; Urano, Y.; Hanaoka, K.; Terai, T.; Nagano, T. *ACS Chem. Biol.* **2011**, *6* (6), 600–608.
(3) Myochin, T.; Hanaoka, K.; Iwaki, S.; Ueno, T.; Komatsu, T.; Terai, T.; Nagano, T.; Urano, Y. *J. Am. Chem. Soc.* **2015**, *137* (14), 4759–4765.
(4) Crovetto, L.; Orte, A.; Paredes, J. M.; Resa, S.; Valverde, J.; Castello, F.; Miguel, D.; Cuerva, J. M.; Talavera, E. M.; Alvarez-Pez, J. M. *J. Phys. Chem. A* **2015**, *119* (44), 10854–10862.
(5) Wu, L.; Burgess, K. *Org. Lett.* **2008**, *10* (9), 1779–1782.
(6) Liu, J.; Sun, Y.-Q.; Zhang, H.; Huo, Y.; Shi, Y.; Guo, W. *Chem. Sci.* **2014**, *5* (8), 3183–3188.
(7) Huang, Y.-L.; Walker, A. S.; Miller, E. W. *J. Am. Chem. Soc.* **2015**, *137* (33), 10767–10776.
(8) Zhou, X.; Zeng, Y.; Liyan, C.; Wu, X.; Yoon, J. *Angew. Chem. Int. Ed.* **2016**, *55* (15), 4729–4733.
(9) Gómez-Bujedo, S.; Alcarazo, M.; Pichon, C.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *Chem. Commun.* **2007**, No. 11, 1180–1182.
(10) Sugawara, S.; Kojima, S.; Yamamoto, Y. *Chem. Commun.* **2012**, *48* (78), 9735–9737.
(11) Woodroofe, C. C.; Lim, M. H.; Bu, W.; Lippard, S. J. *Tetrahedron* **2005**, *61* (12), 3097–3105.
(12) Ioffe, I.; Otten, V. *Zhurnal Obshchei Khimii* **1962**, *32* (5), 1477–1480.
(13) Bandichhor, R.; Petrescu, A. D.; Vespa, A.; Kier, A. B.; Schroeder, F.; Burgess, K. *Bioconjug. Chem.* **2006**, *17* (5), 1219–1225.
(14) Jiao, G.-S.; Castro, J. C.; Thoresen, L. H.; Burgess, K. *Org. Lett.* **2003**, *5* (20), 3675–3677.
(15) Woydziak, Z. R.; Fu, L.; Peterson, B. R. *J. Org. Chem.* **2012**, *77* (1), 473–481.
(16) Ahn, Y.-H.; Lee, J.-S.; Chang, Y.-T. *J. Am. Chem. Soc.* **2007**, *129* (15), 4510–4511.
(17) Hill, J. E.; Linder, M. K.; Davies, K. S.; Sawada, G. A.; Morgan, J.; Ohulchanskyy, T. Y.; Detty, M. R. *J. Med. Chem.* **2014**, *57* (20), 8622–8634.
(18) Kryman, M. W.; Schamerhorn, G. A.; Hill, J. E.; Calitree, B. D.; Davies, K. S.; Linder, M. K.; Ohulchanskyy, T. Y.; Detty, M. R. *Organometallics* **2014**, *33* (10), 2628–2640.
(19) Detty, M. R.; Prasad, P. N.; Donnelly, D. J.; Ohulchanskyy, T.; Gibson, S. L.; Hilf, R. *Bioorg. Med. Chem.* **2004**, *12* (10), 2537–2544.
(20) Del Valle, D. J.; Donnelly, D. J.; Holt, J. J.; Detty, M. R. *Organometallics* **2005**, *24* (15), 3807–3810.
(21) Montalvo-Quirós, S.; Taladriz-Sender, A.; Kaiser, M.; Dardonville, C. *J. Med. Chem.* **2015**, *58* (4), 1940–1949.
(22) Martins, C.; Gunaratnam, M.; Stuart, J.; Makwana, V.; Greciano, O.; Reszka, A. P.; Kelland, L. R.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2007**, *17* (8), 2293–2298.
(23) Debray, J.; Zeghida, W.; Jourdan, M.; Monchaud, D.; Dheu-Andries, M.-L.; Dumy, P.; Teulade-Fichou, M.-P.; Demeunynck, M. *Org. Biomol. Chem.* **2009**, *7* (24), 5219–5228.
(24) Matsumura, K. *J. Am. Chem. Soc.* **1929**, *51* (3), 816–820.
(25) McConnaughie, A. W.; Jenkins, T. C. *J. Med. Chem.* **1995**, *38* (18), 3488–3501.

(26) Harrison, R. J.; Gowan, S. M.; Kelland, L. R.; Neidle, S. *Bioorg. Med. Chem. Lett.* **1999**, *9* (17), 2463–2468.
(27) Moore, M. J. B.; Schultes, C. M.; Cuesta, J.; Cuenca, F.; Gunaratnam, M.; Tanious, F. A.; Wilson, W. D.; Neidle, S. *J. Med. Chem.* **2006**, *49* (2), 582–599.
(28) Schoppf, M. *Chem. Ber.* **1884**, *27*, 2318.
(29) Staedel, W. *Justus Liebigs Ann. Chem.* **1883**, *218* (3), 339–361.
(30) Ungvarsky, J.; Plsikova, J.; Janovec, L.; Koval, J.; Mikes, J.; Mikesová, L.; Harvanova, D.; Fedorocko, P.; Kristian, P.; Kasparkova, J.; Brabec, V.; Vojtickova, M.; Sabolova, D.; Stramova, Z.; Rosocha, J.; Imrich, J.; Kozurkova, M. *Bioorganic Chem.* **2014**, *57*, 13–29.
(31) Goldberg, A. A.; Walker, H. A. *J. Chem. Soc.* **1953**, No. 0, 1348–1357.
(32) Gorvin, J. H.; Whalley, D. P. *J. Chem. Soc. Perkin Trans.***1979**, No. 0, 1364–1370.
(33) Štacko, P.; Šebej, P.; Veetil, A. T.; Klán, P. *Org. Lett.* **2012**, *14* (18), 4918–4921.
(34) Horváth, P.; Šebej, P.; Šolomek, T.; Klán, P. *J. Org. Chem.* **2015**, *80* (3), 1299–1311.
(35) Wu, L.; Burgess, K. *J. Org. Chem.* **2008**, *73* (22), 8711–8718.
(36) Butkevich, A. N.; Mitronova, G. Y.; Sidenstein, S. C.; Klocke, J. L.; Kamin, D.; Meineke, D. N. H.; D'Este, E.; Kraemer, P.-T.; Danzl, J. G.; Belov, V. N.; Hell, S. W. *Angew. Chem. Int. Ed.* **2016**, *55* (10), 3290–3294.
(37) Chai, X.; Cui, X.; Wang, B.; Yang, F.; Cai, Y.; Wu, Q.; Wang, T. *Chem. – Eur. J.* **2015**, *21* (47), 16754–16758.
(38) Barker, A.; Barker, C. C. *J. Chem. Soc.* **1953**, No. 0, 2034–2036.
(39) Barker, A.; Barker, C. C. *J. Chem. Soc.* **1954**, No. 0, 870–873.
(40) Barker, A.; Barker, C. C. *J. Chem. Soc.* **1954**, No. 0, 1307–1309.
(41) Aaron, C.; Barker, C. C. *J. Chem. Soc.* **1963**, No. 0, 2655–2662.
(42) Kolmakov, K.; Belov, V. N.; Wurm, C. A.; Harke, B.; Leutenegger, M.; Eggeling, C.; Hell, S. W. *Eur. J. Org. Chem.* **2010**, *2010* (19), 3593–3610.
(43) Pastierik, T.; Šebej, P.; Medalová, J.; Štacko, P.; Klán, P. *J. Org. Chem.* **2014**, *79* (8), 3374–3382.
(44) Gu, L.; Yang, B.; Liu, F.; Bai, Y. *Chin. J. Chem.* **2009**, *27* (6), 1199–1201.
(45) Fu, M.; Xiao, Y.; Qian, X.; Zhao, D.; Xu, Y. *Chem. Commun.* **2008**, No. 15, 1780–1782.
(46) Antony, L. A. P.; Slanina, T.; Šebej, P.; Šolomek, T.; Klán, P. *Org. Lett.* **2013**, *15* (17), 4552–4555.
(47) Myochin, T.; Hanaoka, K.; Komatsu, T.; Terai, T.; Nagano, T. *J. Am. Chem. Soc.* **2012**, *134* (33), 13730–13737.
(48) Umezawa, K.; Grazvydas, L.; Johnsson, K. Cell Permeable, Fluorescent Dye. WO2013029650 (A1), March 7, 2013.
(49) Kim, S.; Tachikawa, T.; Fujitsuka, M.; Majima, T. *J. Am. Chem. Soc.* **2014**, *136* (33), 11707–11715.
(50) Kim, S.; Fujitsuka, M.; Tohnai, N.; Tachikawa, T.; Hisaki, I.; Miyata, M.; Majima, T. *Chem. Commun.* **2015**, *51* (58), 11580–11583.
(51) Pastierik, T. Bachelor Thesis, Masaryk University, 2014.
(52) Colon, I.; Kelsey, D. R. *J. Org. Chem.* **1986**, *51* (14), 2627–2637.
(53) Sprinzak, Y. *J. Am. Chem. Soc.* **1958**, *80* (20), 5449–5455.
(54) Zhang, X.; Ji, X.; Jiang, S.; Liu, L.; Weeks, B. L.; Zhang, Z. *Green Chem.* **2011**, *13* (7), 1891–1896.
(55) Brennan, N. K.; Donnelly, D. J.; Detty, M. R. *J. Org. Chem.* **2003**, *68* (8), 3344–3347.

(56) van Dijken, D. J.; Chen, J.; Stuart, M. C. A.; Hou, L.; Feringa, B. L. *J. Am. Chem. Soc.* **2016**, *138* (2), 660–669.
(57) Štacko, P.; Feringa, B. L. Unpublished results, 2015.
(58) Chang, Y.; Tewari, A.; Adi, A.-I.; Bae, C. *Tetrahedron* **2008**, *64* (42), 9837–9842.
(59) Lal, G. S.; Pez, G. P.; Pesaresi, R. J.; Prozonic, F. M.; Cheng, H. *J. Org. Chem.* **1999**, *64* (19), 7048–7054.
(60) Mussons, M. L.; Raposo, C.; Anaya, J.; Grande, M.; Morán, J. R.; Caballero, M. C. *J. Chem. Soc. [Perkin 1]* **1992**, No. 22, 3125–3127.
(61) Bahrami, K.; Khodaei, M. M.; Sheikh Arabi, M. *J. Org. Chem.* **2010**, *75* (18), 6208–6213.
(62) Fukazawa, A.; Suda, S.; Taki, M.; Yamaguchi, E.; Grzybowski, M.; Sato, Y.; Higashiyama, T.; Yamaguchi, S. *Chem. Commun.* **2016**, *52* (6), 1120–1123.
(63) Beija, M.; Afonso, C. A. M.; Martinho, J. M. G. *Chem. Soc. Rev.* **2009**, *38* (8), 2410–2433.
(64) Šolomek, T.; Pastierik, T.; Klán, P. Unpublished results, 2016.

Appendix

In this section, ^{1}H, ^{13}C and ^{19}F NMR spectra of prepared compounds are attached.