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Multicomponent syntheses of functional chromophores

Lucilla Levi,[a] and Thomas J. J. Müller*,[a]

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Multicomponent reactions are a valuable tool for the synthesis of functional π-electron systems. Two different approaches can be taken into account for accessing the target structures. In the more conventional *scaffold* approach an already existing chromophore is coupled with other components to give the complex functional π-system. Here, also electronically monotonous components can be introduced, which may exert synergistic electronic effects within the novel compound. The more demanding *chromophore* concept generates the complete π-electron system and the scaffold concurrently. The latter approach is particularly stimulating for methodologists since π-systems might be accessible from simple starting materials. This review encompasses the advances in the preparation of functional π-electron systems *via* multicomponent processes during the past years, based both on the scaffold and chromophore concepts. Besides the synthetic strategies the most important properties, i.e. redox potentials, absorption and emission maxima or fluorescence quantum yields, of the synthesized molecules are highlighted.

1 Introduction

Chromophores are functional π-electron systems that lay the molecular foundation of modern organic electronics and solar energy conversion with tailored small molecules.[1] For instance they find application in organic light-emitting diodes (OLEDs),[2] dye-sensitized solar cells (DSSCs),[3] organic photovoltaics (OPV),[4] organic field effect transistors (OFETs),[5] or sensor arrays in bio or environmental analytics.[6] Hence, the efficient and rapid preparation of these novel functional organic molecules with specific photophysical and electrochemical properties remains an ultimate goal and challenge for researchers both in organic chemistry and materials science. Inevitably, prerequisites for productivity and efficacy are represented by selectivity criteria, i.e. chemo-, regio-, and stereoselectivity, in combination with economic and ecological aspects. Therefore, the creation of concise and conceptually novel syntheses that intelligently concatenate fundamental organic reactions in one-pot sequences defines the paramount goal.[7]

In particular, multicomponent processes[8] exactly tackle these synthetic challenges and, therefore, they have received considerable interest both in academia and industry, predominantly for synthetizing biologically active molecules.[9] By definition a multicomponent process is a reaction of more than two starting materials leading to a product that contains most of the employed atoms.[7,8] More specifically, multicomponent reactions (MCR) as a reactivity based concept[10] can be divided in three different categories. In domino-type MCR all reagents have to be present from the very beginning of the process. A sequential MCR implements the subsequent addition of components in a well-defined order without changing the reaction conditions. Finally, the consecutive MCR implements the subsequent addition of reagents with changing the conditions from step to step. All three types of processes assure high structural and functional diversity and bear an immense explorative potential. At best, MCR will commence with easily accessible and variable starting materials to warrant convenient, interesting and occasionally unusual results.[7] The implementation of MCR in diversity-oriented syntheses of chromophores, fluorophores and redox-active molecules has just started in the past one and half decades and represents a fruitful concept for exploring large structural and functional molecular spaces.[11,12] By the nature of MCR they can be either employed to introduce a preformed chromophore to a scaffold (scaffold approach) or the MCR acts as a chromogenic event (chromophore approach) (Scheme 1). While the scaffold approach is the more traditional concept for ligating functional chromophores with concomitant formation of an electronically innocent molecular framework, the chromophore approach generates the functional π-system and the scaffold simultaneously.

[a.] *Institut für Organische Chemie und Makromolekulare Chemie, Heinrich-Heine-Universität Düsseldorf, Universitätsstr. 1, D-40225 Düsseldorf, Germany*

† Footnotes relating to the title and/or authors should appear here.

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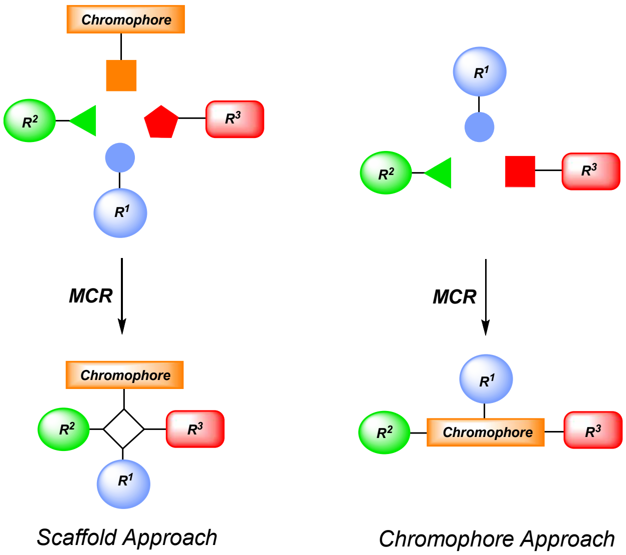


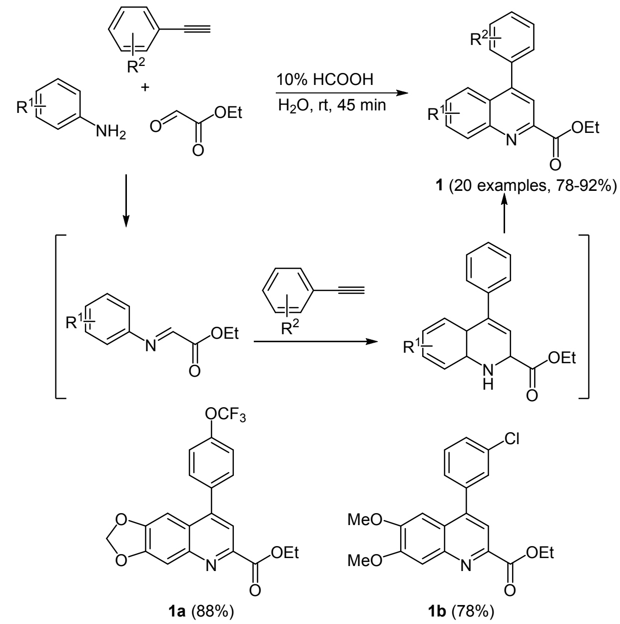
Scheme 1. Conceptual MCR formation of functional chromophores by scaffold and chromophore approaches.

Synthetically this review focuses on scaffold and chromophore approaches based new MCR syntheses of chromophores and functional π-systems that have been developed in the past decade. However the outline is oriented at the functionality of the chromophores and comprises redox systems, including PET (photo-induced electron transfer) systems, and fluorophores, including NLO- (nonlinear optical) chromophores. As clearly defined by MCR methodology only those processes have been considered that are conducted in a one-pot fashion in sensu stricto, i. e. without isolation of intermediate products, filtrations, or intermediate evaporation and change of solvents.

2 Redox Systems

Redox-active systems can undergo a change of the oxidation state, often in a fully reversible fashion, and they have received attention both for biomedical applications and as functional materials. For the former by oxidation or reduction reactivity can be induced that affects protein action, whereas in the latter the change of the oxidation stage can induce intra and intermolecular electron transfer that ultimately leads to material (semi)conductivity and macroscopically to current flow.

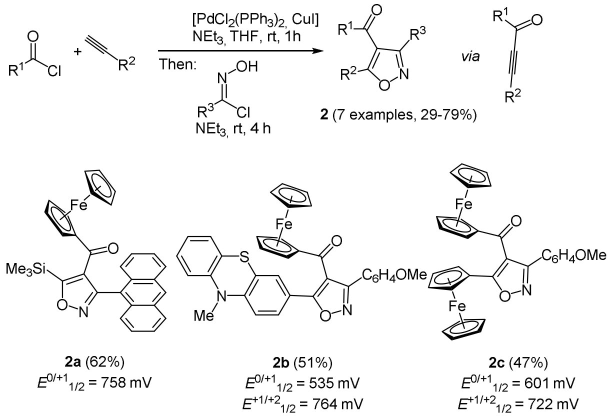
Antioxidants have shown promising results in medicinal chemistry, for instance in devising Alzheimer's disease therapies.[13] The reduced accumulation of certain proteins affects a slower decline of the brain function in mice. Therefore, the search for powerful antioxidants for disease treatment is an ongoing task both in academia and industry. Barate et al. recently reported on the antioxidant activity of 4-arylquinolines in Alzheimer treatment.[14] In the sense of the chromophore concept, a multicomponent, metal-free approach was developed by reacting substituted anilines with terminal alkynes and ethyl glyoxolate to rapidly furnish the ethyl 4-arylquinolinyl-2-carboxylates 1 at room temperature in excellent yields (Scheme 2).



Scheme 2. Domino three-component synthesis of redox active 4-arylquinolines **1**.

The efficiency of the molecule to reduce iron, the so called iron-reducing power, and free-radical scavenging activity determine the antioxidant potential of the prepared 4-arylquinolines. In comparison to ascorbic acid (set at 100% as a standard) the quinolines **1a** and **1b** show the highest Fe-reducing power with approximately 45%. The molecules only possess a low free radical scavenging activity.

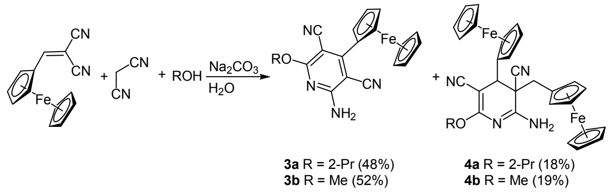
Ferrocenyl derivatives are organometallic redox systems and exhibit a broad range of biological activity, ranging from antitumor, antimalaria to anti-HIV active compounds.[15] By a consecutive three-component synthesis ferrocenyl isoxazoles **2** were readily synthesized according to the scaffold concept (Scheme 3).[16] Interestingly, the isoxazole core is obtained by Sonogashira coupling of acyl chlorides with alkynes to give alkynones, which react as dipolarophiles in subsequent (3+2)-cycloadditions with nitrile oxides (in situ generated from hydroxyiminoyl chlorides by 1,3-elimination) in the same reaction vessel. By choice of the alkyne and the acid chlorides ferrocenyl moieties can be placed at two points of diversity in this coupling-1,3-dipolar cycloaddition sequence.



Scheme 3. Consecutive three-component synthesis of ferrocene substituted isoxazoles **2**.

The MCR proceeds with excellent regioselectivity always placing the carbonyl group at the 4-position of the isoxazole. Cyclic voltammetry reveals slightly anodically shifted oxidation potentials compared to ferrocene ($E^{0/+1}_{1/2}$ = 450 mV). This can be rationalized by the electron withdrawal of the conjugated carbonyl group. For compounds **2b** and **2c** second oxidation waves are detected, which can be assigned to the phenothiazinyl moiety (**2b**) or a second ferrocenyl substituent (**2c**). Interestingly the strongly electron donating character of phenothiazine attenuates the carbonyl capacity on the metallocene potential, leading to a smaller anodic shift in the first oxidation potential.

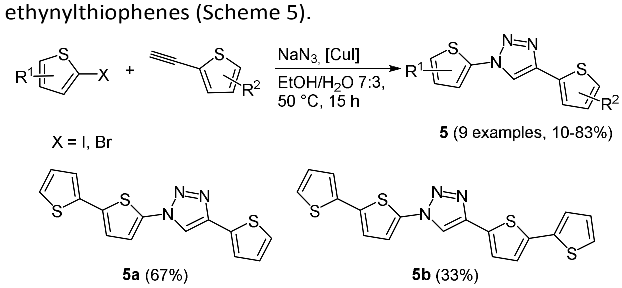
Ferrocenyl-substituted pyridines have also been applied in drug research[17] and find use as potential bio-receptor ligands.[18] The desired ferrocenyl pyridines **3** can be isolated after the multicomponent condensation of malononitrile, 2-cyano-3-ferrocenyl acrylonitrile and an alcohol in the sense of the scaffold concept (Scheme 4). As an inevitable side reaction a twofold addition of the ferrocenyl moiety results in the formation of 3,4-dihydropyridines **4** as byproducts.[19]



Scheme 4. Three-component synthesis of ferrocenyl pyridines **3** and 3,4-dihydropyridines **4**.

The cyclic voltammograms of the aromatic compound **3a** reveals a single reversible Nernstian oxidation potential at around 215 mV deriving from the ferrocenyl substituent. Expectedly a second oxidation potential can be detected for dihydropyridine **4a**, originating from the second ferrocenyl moiety. Surprisingly this second oxidation is irreversible.[20]

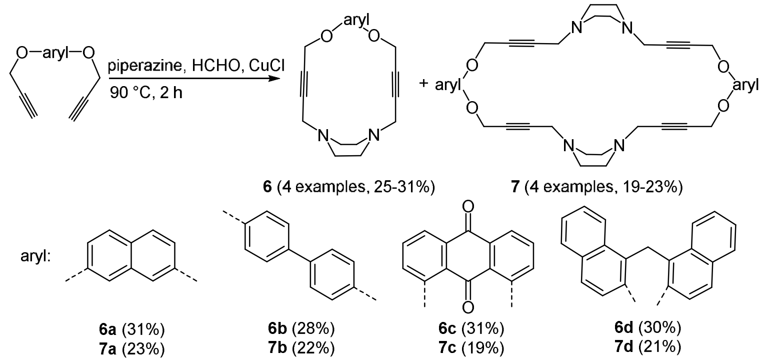
In organic electronics the use of oligothiophenes as organic semiconducting materials is ubiquitous.[21] According to the chromophore concept Bäuerle and coworkers presented a domino three-component synthesis of thiophene-1,2,3-triazole co-oligomers **5** as novel donor-acceptor-donor models.[22] 1,2,3-Triazoles are most conveniently accessed by Cu(I)-catalyzed alkyne-azide cycloaddition (CuAAC).[23] This regiospecific reaction generally produces the 1,4-disubstituted triazole with high yields, moderate reaction times and tolerates many functional groups. For the synthesis of co-oligomers azidothiophenes are formed in situ from halothiophenes with sodium azide, which complete the CuAAC-based MCR[24] with 2-ethynylthiophenes (Scheme 5).



Scheme 5. Domino three-component synthesis of thiophene-1,2,3-triazole co-oligomers **5**.

The absorption spectra show several broad bands, which can be assigned to the different constituting subunits of the oligomers. The longest wavelength absorption bands around 280 nm correlate with the triazole core, while the thienyl substituent at the 1-position of the triazole shows a maximum at around 250 nm. Longer oligomer chains display bathochromically shifted longest wavelength absorption bands and symmetrical oligomers give more structured spectra. The length of the chain also affects the oxidation potentials of the compounds, where shorter oligomers possess higher potentials. A reduction potential for the triazole were not detected in the cyclic voltammograms under the given conditions.

Oxygen and nitrogen containing macrocycles with large cavities have a high binding affinity to numerous anion and cation receptors,[25] proteins[26] and organic guest molecules.[27] The use of these ligands as model compounds for biological processes results from the possible complexation with biologically relevant anions.[28] The preparation of piperazinophanes **6** and the expanded cyclic dimers **7** was realized via an amine-aldehyde-alkyne (A^3) reaction[29] of piperazine and formaldehyde with aromatic bispropargylic ethers in the sense of the scaffold approach (Scheme 6).[30]



Scheme 6. Amine-aldehyde-alkyne (A^3) synthesis of piperazinophanes **6** and **7**.

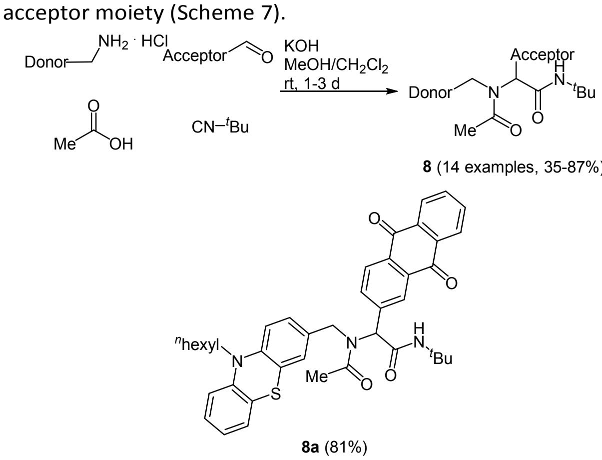
The absorption maxima of the piperazinophanes **6** and **7** appear between 243 and 356 nm. Systems with anthraquinone as an aromatic moiety also show a second weaker absorption band at 284 nm. In addition all macrocycles display intense luminescence with emission maxima between 432 and 501 nm. In the cyclic voltammograms irreversible reductions can be readily identified. Again the anthraquinone substituted macrocycles **6c** and **7c** possess several reduction peaks. The UV/Vis spectra of the compounds after complexation with 7,7,8,8-tetracyanoquinodimethane show strongly red-shifted absorption bands at around 730, 750 and 770 nm, which were assigned to charge-transfer transitions between macrocycle and guest molecule. The complexation ratio was photospectrometrically determined to result in a 1:1 complex.

3 Photoinduced Electron Transfer (PET) Systems

Effective systems in molecular electronics and optoelectronics are often based upon donor-acceptor (D-A) conjugate motifs.[31] These systems can be classified by the nature of ligation of the functional units. Constitutionally, they are distinguished in conjugated, non-conjugated, and non-covalently bound D-A molecules. For non-conjugated topologies, a photoinduced electron transfer (PET) causing a persistent charge separation represents the primordial step in photovoltaics and permits a light-to-current conversion.[32] This is also reminiscent of the most important electron transfer reaction in nature, i. e. photosynthesis converting sunlight into electrochemical potential. Here, sunlight is absorbed, funneled by an antenna complex and followed by an electron transfer to the reaction center which leads to a charge separation. Inspired by this process many studies were directed towards porphyrin induced charge separation in organic solar cells. First simple porphyrin-quinoline-dyads were first reported by Tabushi et al. in 1979,[33] followed by many other research groups.[34] Astoundingly, only very few one-pot syntheses of porphyrins were reported to date. The standard procedures deal with the decoration or extension of porphyrin rings in a multicomponent fashion followed by metalation in a one-pot reaction.[35]

In 1959, Ugi presented a new four-component reaction (Ugi-4CR) condensing an acid, an isonitrile, an aldehyde, and an amine.[36] This event set the stage for an eager search for novel MCRs.[8,9,37] Due to the concomitant formation of two amide bonds in the course of this process the Ugi-4CR was established as a flexible and rapid access to peptides, peptoids and a series of many biologically active compounds.[38] Although this powerful process found entry in modular syntheses of bioactive ingredients only in recent years the Ugi-4CR has been explored for the preparation of electronic and photoactive systems.

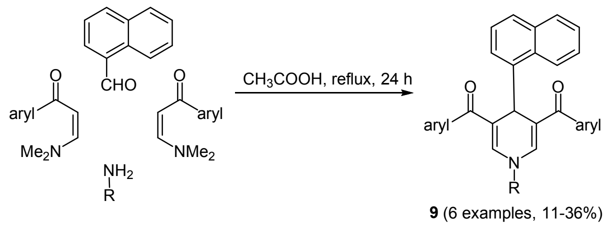
Just recently the Ugi reaction was applied to access donor-acceptor-systems in a novel and straightforward fashion. Due to their tunable and reversible oxidation potentials phenothiazine derivatives are particularly interesting as electron donor moieties.[39] On the other hand 9,10-anthraquinone has a distinct electron deficiency, which makes it an important electron acceptor.[40] When employing the donor as an amine, the acceptor as an aldehyde, acetic acid and *tert*-butyl isocyanide in the Ugi-4CR the desired condensation products **8** are obtained in good to high yields in the sense of a scaffold approach.[41] A scope of 14 examples were realized via this method by varying the donor or/and the acceptor moiety (Scheme 7).



Scheme 7. Ugi-4CR synthesis of donor-acceptor dyads **8** and structure of the phenothiazine-anthraquinone system employed in transient absorption studies.

Phenothiazine based dyads **8** show absorption characteristics in solution that support the absence of an electronic communication in the electronic ground state, as expected for non-conjugated D-A systems. Most strikingly, the D-A conjugates display considerable intramolecular fluorescence quenching caused by an excited state communication between phenothiazine and acceptor moieties. Femtosecond spectroscopy unambiguously elucidated that in the excited state an ultrafast electron transfer to the anthraquinone accounts responsible for the observed emission quenching. Thereby, in the dyads rapid electron transfer proceeds with ps rate constants via excited singlet or triplet states to terminate in a short lived singlet and a long lived triplet charge separated state.

Dihydropyridines already found application as dyads in biosensors and photosensitive polymers, due to their ability to modulate vectorial transport of energy or charge transfer upon photoexcitation.[42] The synthesis of 2-unsubstituted dihydropyridines with strong UV absorption characteristics was achieved via a Hantzsch-type pseudo-four-component reaction with enaminones as starting materials in the sense of the chromophore approach.[43] The introduction of suitable electron-acceptor moieties in the molecule affects the intramolecular PET characteristics. The reaction gives excellent results when performed with sterically undemanding aromatic aldehydes, for instance with benzaldehyde, furnishing the corresponding dihydropyridines within 2 min under microwave irradiation in 84-95% yield. With sterically more demanding substituents such as naphthalene, conventional heating has to be applied for extended times giving the desired heterocycles **9** only in moderate yields (Scheme 8).



Scheme 8. Pseudo four-component reaction for the synthesis of naphthyl substituted dihydropyridines **9**.

The UV/Vis spectra display two distinct absorption bands in the regimes of 277-306 and 383-406 nm, respectively. The higher energy absorption maximum is assigned to the aryl moieties, whereas the longest wavelength absorption maximum is ascribed to the dihydropyridine. The emission spectra exhibit maxima between 454 and 486 nm with fluorescence quantum yields of up to 50%.

4 Fluorophores

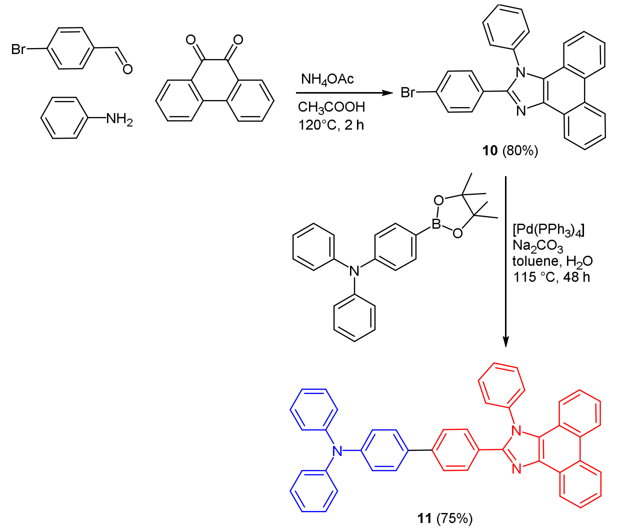
Luminescent dyes exhibit intense light emission upon light excitation. The underlying chromophore is called the fluorophore.[44] Ultimately the electronic properties of the fluorophore determine excitation wavelengths. In addition, fluorophores often display pronounced sensitivity for the environment (solvent polarity, hydrophobic media, pH). Interestingly, due to numerous interactions and processes the spectral properties can often be altered, switched and controlled. Therefore, fluorophores are highly interesting as functional π-electron systems. The emission range lies between UV and NIR with lifetimes varying from nanoseconds (fluorescence in a broader sense) to micro- and milliseconds (generally referred to as phosphorescence), strongly depending on the structures and excited states' characteristics. Fluorescent molecules are often employed for DNA or protein labeling, enabling unique sensitivity and highly selective diagnosis in biomedical analytics.[45]

As a consequence of this manifold of scientific applications and motivated by the demand for stable tailor-made fluorophores, novel and concise syntheses of this class of functional chromophores are currently a hot topic and the synthetic activity is steadily increasing. Various approaches have been followed to date ranging from consecutive over sequential to domino MCR. In many cases the spectral properties of the fluorophores primarily depend on the (hetero)aromatic or polyene core structure. By the choice of the delocalized π-electron system the excitation in the visible region can be achieved and fine-tuned.

4.1 MCR Formation of Nitrogen Heterocycles

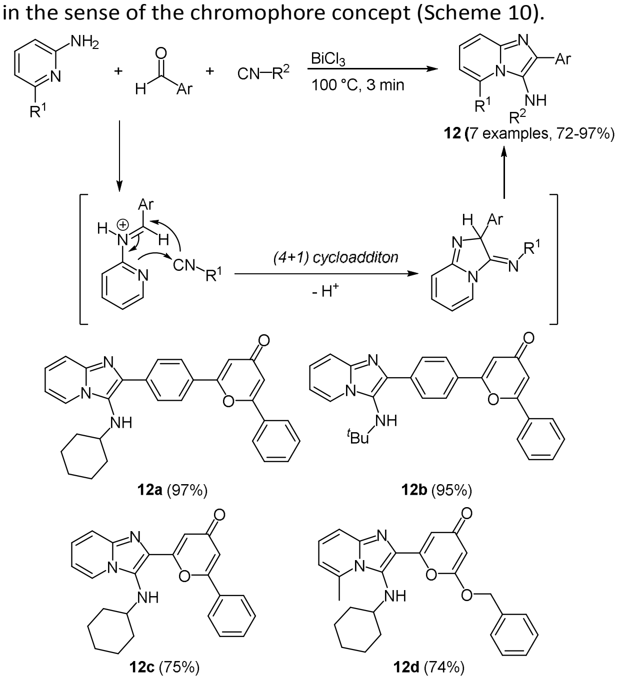
Five-membered N-heterocycles like pyrazoles and imidazoles display a multifold chemical reactivity accompanied by multiple types of application.[46] Much interest resides in the broad spectrum of biological activity but also in unique electronic and optical properties of these classes of heterocycles.[47] Depending on the substitution pattern different photophysical and electrochemical properties can be addressed. As a consequence they find use as optical brighteners, as UV stabilizers, and as constituents in photoinduced electron transfer systems.[48]

Studies on OLED proved that excited states with charge transfer (CT) character are very valuable for increasing the efficiency of the module. Many chromophores, based on both covalent donor-acceptor structure and complexes, have already been synthesized and their electronic properties were tested. Predominantly red and green emissive fluorophores have been reported.[49] CT excited-states typically exhibit a narrower band gap than normal locally excited states, while blue, non-CT emitters usually retain a wider band gap.[50] A deep-blue electroluminescent chromophore **10** with a current efficiency of >5.0% was recently reported by Ma and coworkers.[51] The acceptor moiety **10** was synthesized by a four-component reaction of an aldehyde, an amine, ammonium acetate, and phenanthryl quinone derived from the reaction presented by Sun.[52] Suzuki coupling of the donor as a boronic acid ester and the acceptor **10** resulted in the desired push-pull chromophore **11** following the scaffold concept (Scheme 9).



Scheme 9. Synthesis of the deep-blue emitting donor (blue)-acceptor (red) chromophore **11**.

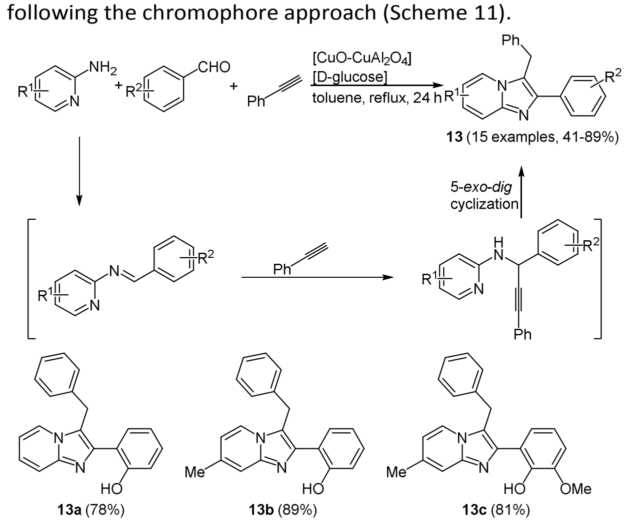
An interesting multicomponent approach to imidazo-pyridines under bismuth catalysis was very recently presented by Esmati and coworkers.[53] In a Groebke-Blackburn-Bienaymé (GBB)[54] multicomponent condensation 4-pyrone carbaldehydes react with isonitriles and 1-amino pyridines under bismuth chloride catalysis furnishing the desired imidazo[1,2-a]pyridines **12** within a reaction time of 3 min and in good to excellent yields in the sense of the chromophore concept (Scheme 10).



Scheme 10. GBB multicomponent synthesis of imidazo[1,2-a]pyridines **12**.

A distinct influence of the benzene spacer between imidazo-pyridine core and 4-pyrone can be observed in the absorption spectra of these chromophores. A blue shift can be detected in the strongest maxima, ascribed to the π-π* transition, of the compounds without spacer (λ_{max} = 265-273 nm) compared to the benzene substituted systems (λ_{max} = 283 nm), which possess an extended conjugated system. More remarkable is the difference in the shape of the absorption bands. The compounds containing a spacer show very broad, shapeless spectra with an intense maximum at 356 nm, whereas clearly a less intense but more structured longest wavelength absorption band is observed for the spacer-free compounds. Also in the emission spectra a hypsochromic shift can be determined for the compounds without the benzene spacer. The compounds display intense blue to green fluorescence with maxima between 500-515 nm for **12a-12b** and 475-478 nm for **12c-12d**.

Imidazo[1,2-a]-pyridines **13** with a similar structure were prepared under copper and glucose catalysis, resulting in systems with excited state intramolecular proton transfer (ESIPT) characteristics.[55] The reaction between phenylacetylene, 2-aminopyridines and benzaldehydes give the desired products in 24 h with yields between 41-89% following the chromophore approach (Scheme 11).



Scheme 11. Three-component synthesis of imidazo[1,2-a]-pyridines **13** under copper and *D*-glucose catalysis and selection of examples showing ESIPT characteristics.

The longest wavelength absorption maxima of the compounds **13** lie between 305 and 360 nm, reaching extinction coefficients up to 22000 $M^{-1}cm^{-1}$. The substituents do not reveal any systematic influence on the absorption characteristics. With very large Stokes shifts of 12400 to 14700 cm^{-1} the compounds bearing a 2-(2'-hydroxyphenyl) substituent clearly show excited state intramolecular proton transfer (ESIPT) characteristics with low fluorescence quantum yields (Figure 1). The emission maxima of all the synthesized molecules are found between 371 and 556 nm.

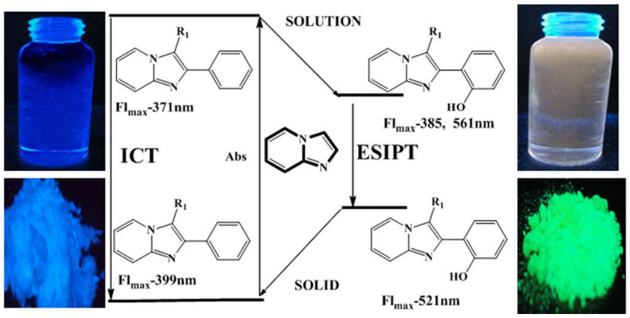
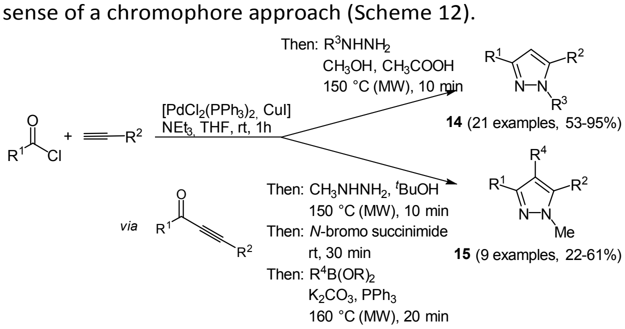


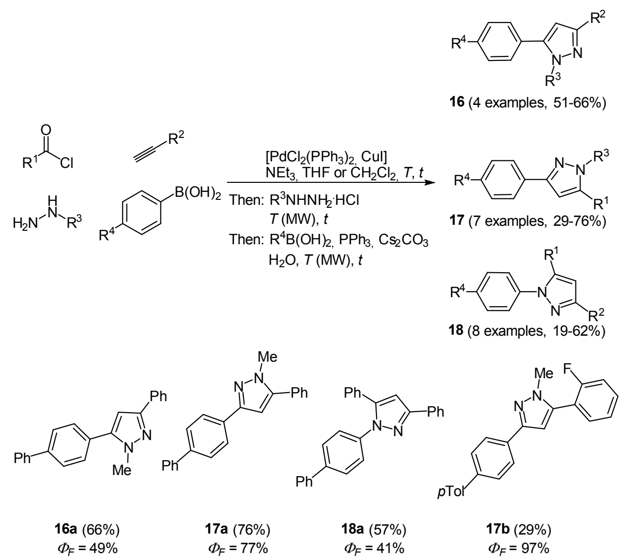
Figure 1: ESIPT characteristics of imidazo[1,2-a]-pyridines **13**. Reprinted from *Dyes and Pigments*, *121*, B. Umamahesh, K. I. Sathiyanarayanan, CuO–$CuAl_2O_4$ and *d*-glucose catalyzed synthesis of a family of excited state intramolecular proton transfer imidazo[1,2-a]pyridine analogues and their optical properties, 88-98, Copyright (2015), with permission from Elsevier."

Various one-pot multicomponent syntheses of pyrazoles are found in literature, however, predominantly for accessing biologically active compounds.[56] Highly fluorescent pyrazoles can be synthesized in an efficient and straightforward fashion by consecutive three- or four-component reactions.[57] Sonogashira coupling between acyl chlorides and terminal alkynes results in reactive alkynone intermediates, which can readily react with all kinds of binucleophiles in a one-pot fashion.[58] Hence, after addition of hydrazines 1,3,5-trisubstituted pyrazoles are formed in a regioselective fashion. A step by step synthesis of these compounds was already known, however only a moderate scope of substituents could be introduced and despite of the high regioselectivity the isolation of both isomers was inevitable.[59] Therefore, the advantages of the multicomponent approach lie in easier experimental handling as well as in better chemical results. An extension of the sequence allows for the efficient de novo synthesis of even more complex tetrasubstituted pyrazoles. After the formation of the pyrazole by coupling-addition-cyclocondensation the 4-position can be halogenated by an *N*-halosuccinimide, still in the same reaction vessel. A subsequent concluding Suzuki coupling with boronates gives the desired products in good yields in a one-pot fashion in the sense of a chromophore approach (Scheme 12).



Scheme 12. One-pot 3- and 4-component synthesis of tri- and tetrasubstituted pyrazoles **14** and **15**.

This diversity-oriented one-pot approach allows for the introduction of many electronically different substituents, generating a broad scope for the investigation of the spectroscopic behavior of pyrazoles. The absorption maxima for the trisubstituted pyrazoles **14** are found between 260 and 385 nm, whereas for tetrasubstituted derivatives **15** values between 240 to 311 nm were determined. It is noteworthy that these molecules display intense fluorescence with emission maxima between 320 and 395 nm and quantum yields of up to 74%. An even higher fluorescence quantum yield of up to 97% could be achieved by the introduction of a biaryl system at one of the substituent positions for the 1,3,5-substituted pyrazoles **14**.[60] Therefore the Suzuki coupling was concatenated directly after the cyclization reaction. Three different isomers **16-18** were prepared by variation of the arylbromides as substituents in the starting materials giving 19 examples in up to good yields (19-76%). The best results both in reaction and in fluorescence quantum yield were achieved when the biaryl moiety was placed at the position of the alkynyl fragment (Scheme 13).



Scheme 13. Palladium catalyzed four-component synthesis of biaryl-substituted pyrazoles **16-18**.

For all substitution patterns large Stokes shifts, between 6000 and 11300 cm^{-1}, were recorded. The longest wavelength absorption maxima of the substances lie between 257 and 311 nm with molar extinction coefficients of up to 44000 $M^{-1}cm^{-1}$. The simultaneous deprotection of three alkyne functionalities on a 1,3,5-triazine core and subsequent CuAAC[23] with aromatic azides results in the formation of highly substituted strongly luminescent chromophores **19** with low reduction potentials in a pseudo multicomponent reaction in the sense of a scaffold approach (Figure 2).[61] Absorption spectra in solution and as thin films display almost the same maxima for the longest wavelength absorption bands, however, with considerably higher extinction coefficients for the solution spectra. The compounds are strongly blue fluorescent with quantum yields of up to 43%. Furthermore a liquid crystalline behavior could be observed, showing columnar mesophases at room temperature.

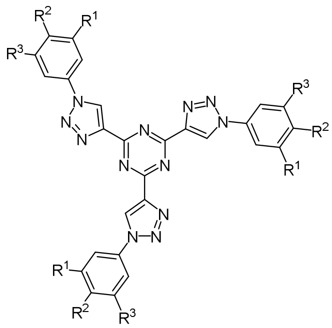
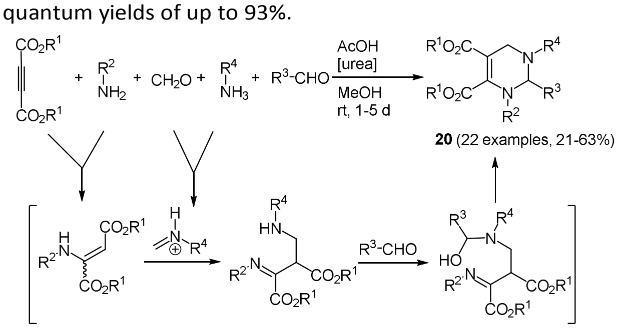


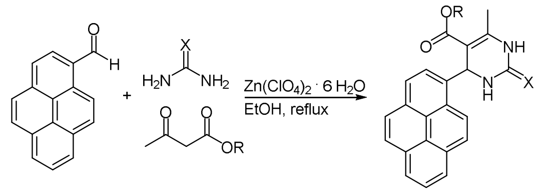
Figure 2. Structure of 2,4,6-tris(triazolyl)-1,3,5-triazine chromophores **19**.

Tetrahydropyrimidines are another noteworthy class of biologically active compounds. Additionally some derivatives show interesting magnetic[62] and photophysical[63] properties. Recently, a novel, efficient five-component synthesis of tetrahydropyrimidines was presented by Liu and coworkers.[64] Here, two different amines, formaldehyde, an aromatic aldehyde and acetylene dicarboxylic acid ester are coupled with urea as an organo catalyst (Scheme 14). The reaction proceeds chemoselectively furnishing the desired C-4 unsubstituted product **20** between 21 and 63% yield according to the chromophore concept. The chromophores show aggregation-induced emission (AIE)[65] and are almost nonfluorescent in solution. The strong green to blue luminescence in the solid state and in suspension reveals quantum yields of up to 93%.



Scheme 14. Five-component synthesis of C-4 unsubstituted tetrahydropyrimidines **20**.

Due to the steadily growing industrialization the detection of toxic heavy metal ions in the environment is an important task.[66] Chemosensors with defined optical and mechanistic properties are the most elegant method for the recognition of metal ions.[67] Effective fluorescent chemosensors for mercury ions are already well represented in literature,[68] but often with inefficient synthetic routes.[69] The Biginelli reaction[70] allows for a straightforward preparation of pyrene substituted 1,2,3,4-tetrahydropyrimidine chromophores with sensor characteristics for Hg^{2+} recognition.[71] The zinc catalyzed multicomponent reaction of pyrene-1-carboxaldehyde, methyl (or ethyl) acetoacetate and (thio)urea yields the two desired chromophores **21** in 79 and 89% in the sense of a scaffold approach (Scheme 15).

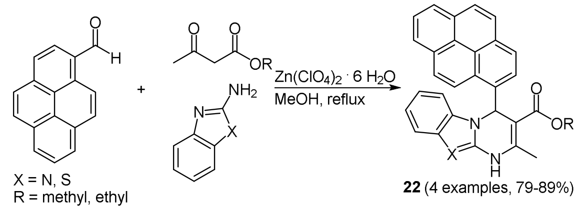


21a: R = methyl, X = S; 89%
21b: R = ethyl, X = O; 79%

Scheme 15. Biginelli reaction for the synthesis of tetrahydropyrimidine based fluorescent Hg^{2+} chemosensors **21**.

The characterization of the cation recognition properties of these chromophores was performed by a number of different fluorescence measurements and the ratiometric detection of anions was determined via a counterion displacement assay.[72] By screening 13 different metal salts the metal binding ability of the sensors **21a** and **21b** was determined. A possible kinetic influence on the fluorescence spectra was excluded by a second measurement of the probes after one hour. The original emission maximum of **21a** at around 395 nm assigned to the pyrene corpus was completely quenched by addition of Hg^{2+} and a new maximum at 460 nm evolved, while no relevant influence was detected with other cations. The bathochromic shift was ascribed to excimer formation by two pyrene rings that come into close proximity by coordination to the mercury ion.

Singh and coworkers used the above mentioned Biginelli reaction to prepare even more complex and multifunctional pyrene based chemosensors **22** always based on the scaffold concept.[73] Thereby zinc ions can be detected in organic media, whereas iron ions are selectively recognized in aqueous medium (Scheme 16).

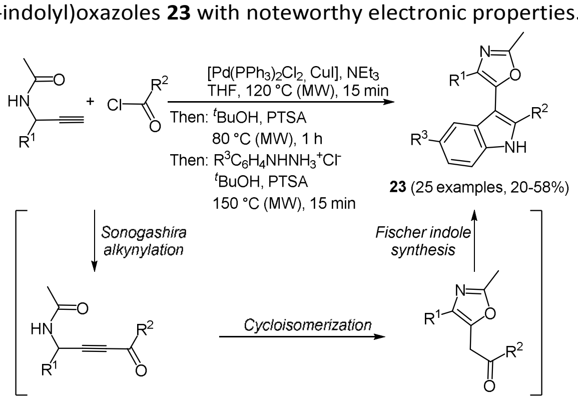


Scheme 16. Pyrene based chemosensors **22** for the selective detection of zinc or iron cations.

Similar fluorescence measurements with different metal salts were performed with the tetrahydropyrimidines **22**. Instead of mercury ions zinc(II) showed the highest variation in the UV/Vis spectra in acetonitrile. Here, the original absorption maximum at around 470 nm was hypsochromically shifted to 370 nm.

Indoles display a high reactivity in the 3-position in electrophilic aromatic substitutions. This aspect has often been exploited to access molecules with remarkable biological activities.[74] In addition indoles are particularly interesting as structures and auxochromes in chromophores.

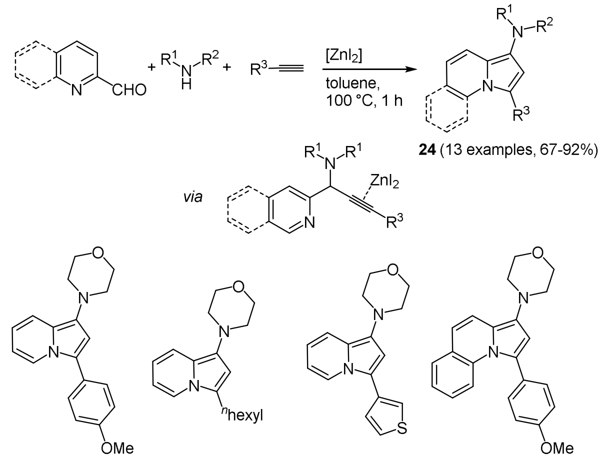
The scaffold of indolyl oxazoles, both with simple but also very complex substitution patterns, is often encountered in naturally occurring alkaloids showing a broad spectrum of biological activity.[75] Although many synthetic strategies were developed searching for more biologically active derivatives, the interesting photophysical properties of this class of fluorophores have been completely neglected. A microwave assisted consecutive three-component alkynylation-cycloisomerization-Fischer indole synthesis offers a concise access to 5-(3-indolyl)oxazoles in good yields.[76] Starting with a Sonogashira coupling of acid chlorides and 1-(aryl) *N*-(prop-2-yn-1-yl)acetamides the formed ynones directly undergo an acid catalyzed cycloisomerization to furnish the oxazole core.[77] Subsequent addition and reaction with aryl hydrazine hydrochloride concludes the sequence by a Fischer indole synthesis (Scheme 17). The multicomponent strategy with a chromophore approach furnished 25 diversely substituted 5-(3-indolyl)oxazoles **23** with noteworthy electronic properties.



Scheme 17. 5-(3-indolyl)oxazoles **23** via the microwave assisted coupling-cycloisomerization Fischer indole sequence.

All indolyl oxazoles **23** display similar absorption and emission behavior. The longest wavelength absorption band is broad and unstructured and appears between 298 and 328 nm. Therefore, only a minor electronic influence of the aryl substituents on the maxima can be deduced. All the emission maxima are found between 426 and 445 nm, resulting in an intense blue luminescence and accompanied by massive Stokes shifts ranging from 7700 to 10600 cm^{-1}. The fluorescence quantum yields lie in the range of 10 to 25%.

An interesting constitutional isomer of indole is indolizine, where the nitrogen atom is positioned at the bridge head. The fusion of an electron-poor pyridine and an electron-rich pyrrole moiety results in an intriguing scaffold with respect to bioactivity.[78] Hence, the synthesis of these heterocycles gained considerable significance and already numerous novel syntheses evolved.[79] However, novel multicomponent accesses have not been explored. An interesting approach presented by Mishra et al. takes advantage of cheap and non-toxic zinc salts as catalysts.[80] Zinc iodide has turned out to be the most active catalyst for the sequential three-component coupling-cycloisomerization reaction in the sense of the chromophore concept. The A^3-reaction[29] of an aromatic aldehyde, a secondary amine, and an alkyne with zinc iodide as a catalyst results in the desired aminoindolizines **24** in good to excellent yields at short reaction time (Scheme 18).



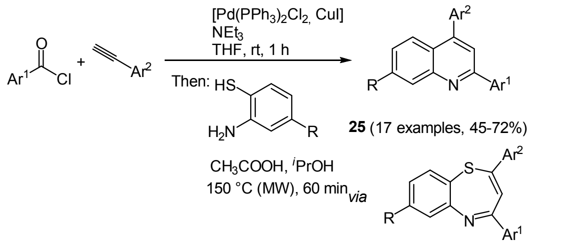
24a (87%) **24b** (74%) **24c** (71%) **24d** (88%)

Scheme 18. Zinc catalyzed 3-component synthesis of aminoindolizines and pyrrolo[1,2-*a*]-quinolines **24**.

The introduction of an aliphatic terminal alkyne proceeds also successfully. Likewise employing quinoline-2-carboxaldehydes allows for the preparation of the corresponding pyrrolo[1,2-*a*]-quinolines **24d** in very good yields. Especially these compounds showed interesting photophysical properties, for instance high fluorescence quantum yields of up to 47% and large Stokes shifts, as important characteristics for biological probes. Both absorption and emission solvatochromicity studies were performed with the pyrrolo[1,2-*a*]-quinoline **24d**. While only a minimal shift can be detected in the absorption spectra, the emission spectra show maxima change from 514 and 541 nm with increasing solvent polarity.

Quinoline and quinoxaline derivatives are well known as biologically and pharmaceutically relevant heterocyclic cores,[81] and many new efficient syntheses have been reported.[82] In addition, these molecules show inherent fluorescence, with a substantial solvent effect on the efficiency and energy of the emission bands, thereby fueling the search for novel emissive chromophores.[83] Consequently, many novel push-pull systems were prepared and analyzed pertaining to their spectroscopic behavior.[84] However, only very few one-pot multicomponent reactions have been found.

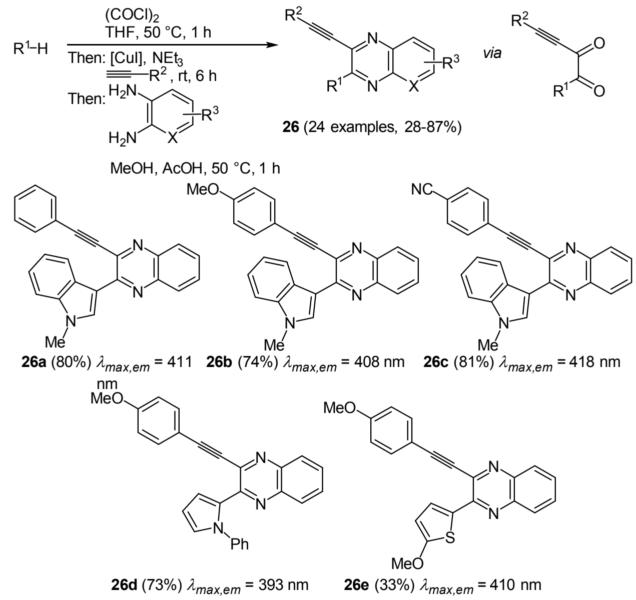
2,4-Diaryl substituted quinolines **25** can be synthesized efficiently by a regiospecific consecutive three-component reaction starting from commercially available acyl chlorides and alkynes.[85] First the Sonogashira conditions furnish the corresponding alkynones[86] that are subsequently reacted with 2-aminothiophenols. The condensation is accompanied by a concomitant sulfur extrusion upon microwave irradiation giving the desired quinolines in moderate to good yields in the sense of the chromophore concept (Scheme 19).



Scheme 19. Consecutive 3-component synthesis of 2,4-diaryl substituted quinolines **25**.

Comparison of the electronic properties of 2,4-diaryl substituted quinolines **25** evidently shows that 2-substitution on the quinoline core only has a minor influence on the electronic properties. In general, all 2,4-aryl substituted quinolines show similar absorption and emission spectra with just small shifts of the maxima. Only strong donor substituents result in a bathochromic shift in the absorption spectra as a consequence of the push-pull system. The molecules display variable Stokes shifts ranging from 600 to 4000 cm^{-1}. In addition, quantum chemical calculations were performed to qualitatively assign the absorption bands in the electronic spectra.

The implementation of another nitrogen atom in the heterocycle, which leads to the class of quinoxalines, even further intensifies the interesting biological and photophysical properties of the π-system.[87-89] Many studies have been conducted with this heterocyclic core, but ethynylquinoxalines are remarkably underexplored. The few reported approaches to ethynylquinoxalines either just furnished intermediates or the obtained substitution pattern was very restricted.[88] The novel glyoxylation-alkynylation-cyclocondensation sequence opened an attractive pathway for the preparation of this chromophore in a consecutive four-component reaction.[89] As reactive intermediates ynediones are generated by glyoxylation with oxalyl chloride and subsequent Stephens-Castro coupling with a terminal alkyne. The cyclocondensation of a 1,2-diaminoarene concludes the one-pot sequence to give 3-ethynylquinoxalines **26** in moderate to excellent yield in the sense of the chromophore concept (Scheme 20). Interestingly all four components are applied in strictly equimolar ratios, thereby warranting a high degree of process economy.



Scheme 20. Glyoxylation-alkynylation-cyclocondensation sequence for the synthesis of 2-substituted 3-ethynylquinoxalines **26**.

A considerable scope becomes apparent by variation of one or more of the components. The glyoxylation is in principle limited to electron-rich π-nucleophiles that ultimately end up in the 2-position. While good results were obtained with aryl- and silyl-substituted alkynes, aliphatic alkynes were no substrates in the Stephens-Castro coupling. Furthermore the photophysical properties of selected derivatives were studied (Scheme 21, **26a**-**26e**). The absorption maxima lie in a narrow range between 393 and 418 nm. The ethynyl substituent only has a minor effect on the spectral properites, while a distinct influence is exerted by the substituents in the 2-position of the quinoxalines. Here, the more electron-rich 1-phenylpyrrol-2-yl substituent causes a blue shift of the longest wavelength absorption band. The emission spectra show a similar behavior, where the shortest wavelength emission band is situated between 474 and 520 nm. Again the electron donating character of the 2-position substituent affects a hypsochromic shift. Furthermore 3-ethynyl quinoxalines display large Stokes shifts of 4400 to 4800 cm^{-1} and an intense emission solvatochromicity (Figure 3).

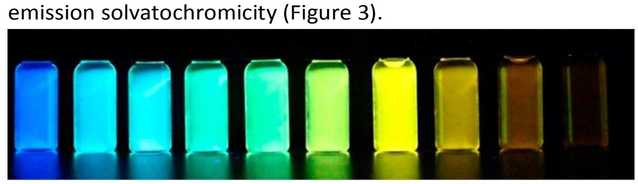
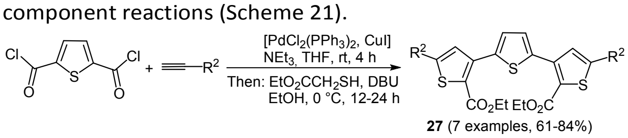


Figure 3. Emission solvatochromism of compound **26b** (recorded in cyclohexane, toluene, THF, EtOAc, acetone, CH_2Cl_2, MeCN, iPrOH, EtOH, MeOH (from left to right); T = 293 K; c(**26b**) = 10^{-4} M; λ_{excit} = 356 nm, hand-held UV lamp). Reprinted with permission from *J. Org. Chem.*, **2014**, *79*, 3296–3310. Copyright 2014 American Chemical Society.

4.2 MCR Formation of Sulfur Heterocycles

Thiophenes and oligomers are particularly electron rich heteroarenes, a characteristic giving them peculiar relevance as functional π-electron systems in organic materials science.[21] They already find application as hole transport materials in OLED, OFET, and OPV.[90] Electropolymerization is one of the well-established methods to prepare 2,5-linked polythiophenes in a resourceful fashion.[91] The employment of functionalized monomers to increase the solubility of these systems is also possible. Nevertheless with this method only polydisperse product mixtures are obtained, leaving out the possibility of preparing oligomers with a defined number of chain links. Therefore, a multicomponent approach could allow for variable substitution patterns on thiophenes within an oligomer. This commutability results in different extensions of the π-electron conjugation, strongly influencing the photophysical and electronic properties.

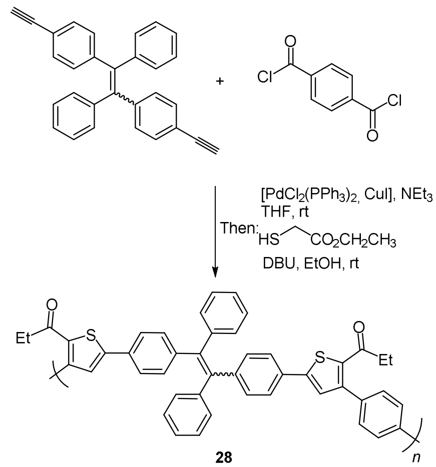
A simple way for enabling different substitution patterns on the heterocycle core is the de novo formation of the thiophene core from easily accessible starting materials. The Fiesselmann cyclocondensation[92] between alkynones and ethyl mercapto acetate was corroborated and implemented in a chromophore approach based MCR strategy.[93] Here, simple acid chlorides or a thiophene dicarbonyl chloride first react with terminal alkynes under Sonogashira conditions setting the stage for a terminal Fiesselmann reaction in a one-pot fashion. A large number of (un)symmetrically substituted (oligo)thiophenes **27** were synthesized by these consecutive three- and pseudo-five-component reactions (Scheme 21).



Scheme 21. Consecutive multicomponent synthesis of ter- and quinquethiophenes **27**.

The symmetrically substituted ter- and quinquethiophenes **27** cover a broad range of absorption maxima (305 to 398 nm) in the near UV whereas the shortest wavelength emission bands are located around 445 nm for all compounds. This behavior results in very large Stokes shifts of 10000 cm^{-1}.

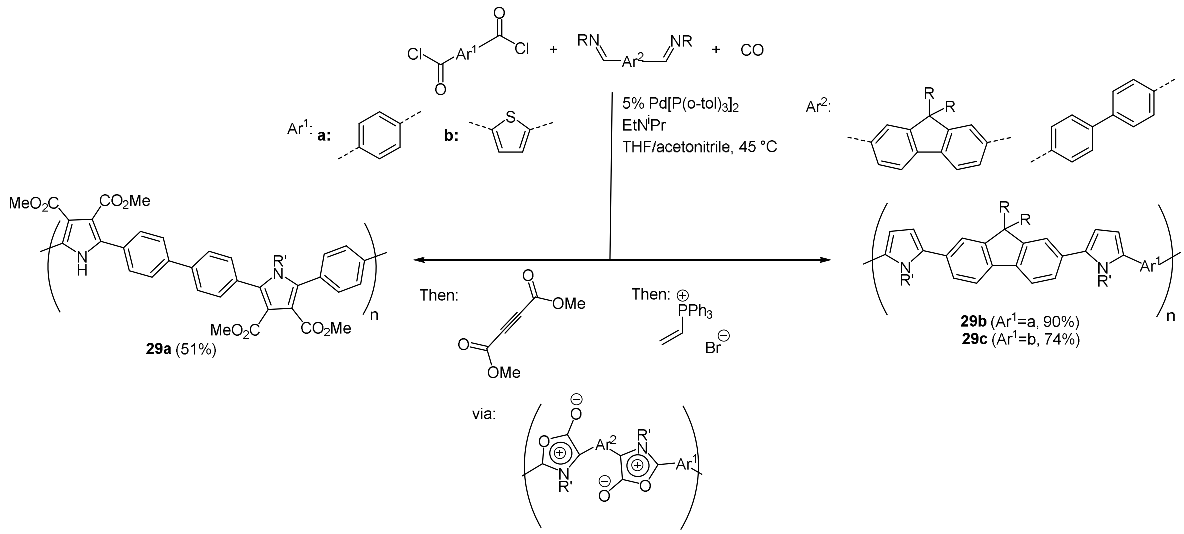
An enhancement of the photophysical properties was achieved by building thiophene functionalized macromolecules via the scaffold approach. A tandem polymerization was developed based on this three-component synthesis of oligothiophenes resulting in structurally regioregular polymers **28** with advanced functionality.[94] Tetraphenylethene was chosen as a dialkyne component due to its strong aggregation induced emission characteristics which should enhance the polymer emission.[95] High molecular weights are obtained with the polymerization of diyne, diaroyl chloride and 2-mercaptoacetate under mild conditions (Scheme 22).



Scheme 22. Three-component polymerization synthesis of regioregular AIE polymers **28**.

Measurements of the photophysical properties with respect to possible AIE characteristics showed a bright green emission for the nanoaggregates. The emission spectra were recorded in THF/water-mixtures displaying a remarkable enhancement of the intensity in an 80% water solution with a small decrease at higher water concentrations, confirming that the strong emission characteristics originate from aggregates.

Another multicomponent reaction to synthesize various poly(heterocycles) takes advantage of the reactivity of 1,3-dipoles which easily undergo cycloaddition reactions.[96] This approach is an important development in polymer chemistry for the construction of highly substituted molecules consisting in a simple variant. Besides overcoming usual tedious multistep syntheses simultaneously rapid and easier tuning of the structures becomes possible.[97] An aromatic bis(acid chloride) and a diimine react with CO as a monomer in a palladium-catalyzed polymerization reaction in the sense of the scaffold concept. Upon generating poly(1,3-dipoles) the cycloaddition with various dipolarophiles results in a large number of poly(heterocycles) **29**. By variation of the monomers avenues to larger scopes of polymers are opened. In Scheme 23 three representative polymers prepared via this multicomponent reaction with interesting photophysical properties are shown.

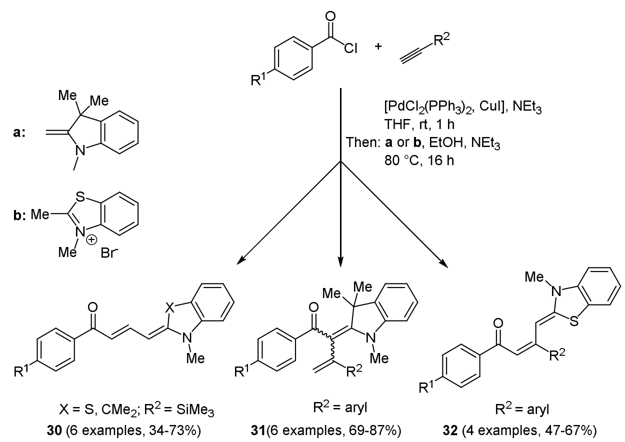


Scheme 23. Selection of possible reactions for the synthesis of poly(heterocycles) **29**.

The longest wavelength absorption maxima of the polymers **29** are found between 280 and 368 nm. Expectedly, the polymer **29a** without heterocyclic bridge between the monomer units displays the maximum at highest energy, whereas polymers **29b** and **29c** are red shifted. A similar behavior is found in the emission spectra, where the maxima lie between 413 and 501 nm with fluorescence quantum yields of up to 47%, however, polymer **29a** does not fluoresce.

4.3 MCR Formation of Merocyanines

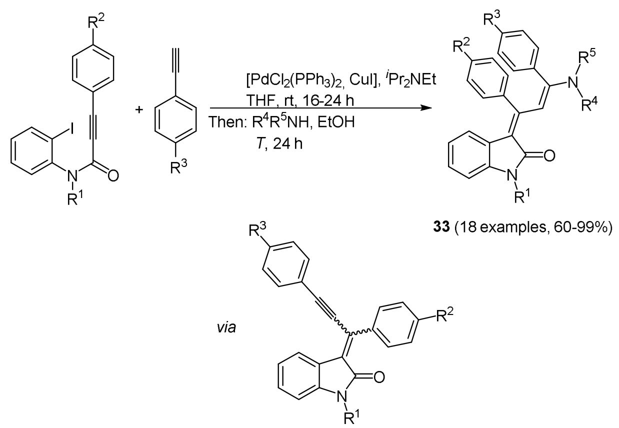
Merocyanines are categorized as polymethine chromophores and they are typically composed of an auxochrome (donor) and an antiauxochrome (acceptor) at the termini of an even-numbered polymethine chain.[98] Due to their tunable photophysical, photochemical and electrochemical properties by modification of the end groups, the substituents and the length of the polymethine chain, merocyanines have found entry as functional dyes in the design of new materials for solar cells, optoelectronics and optical carriers. In the field of organic photovoltaics, both in bulk heterojunction[99] and dye sensitized solar cells,[3] merocyanines can be employed as visible light absorbing materials. With very few exceptions,[100] most syntheses of merocyanines have not been accessed in a multicomponent and a one-pot fashion. Therefore, the search for novel, efficient reaction routes is an ongoing task. An reactivity-based approach takes advantage of the inherent electrophilicity of an intermediary formed Michael system, where an enamine can attack as a nucleophile.[101] This consecutive three-component reaction commences with Sonogashira coupling of an aryl acid chloride and a terminal alkyne. The subsequent concluding Michael addition on the ynone intermediate with different enamines gives the desired butadienyl merocyanines **30/32** and 2-styryl enaminones **31** in moderate to good yields in the sense of the chromophore approach (Scheme 24).



Scheme 24. 3-Component syntheses of butadienyl merocyanines **30** and **32**, and 2-styryl enaminones **31**.

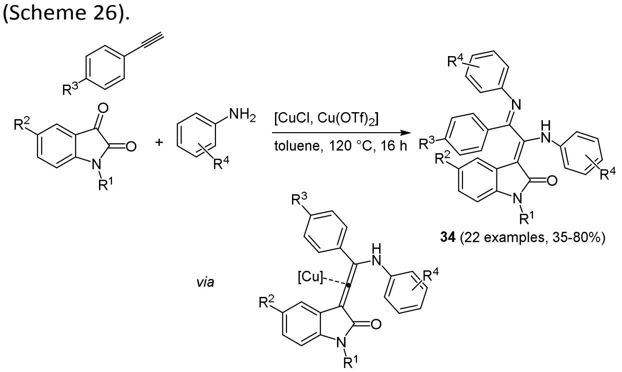
Due to the electronic differences of enamines and ketene acetal intermediates 2-styryl enaminones **31** originate from a (2+2)-cycloaddition with subsequent electrocyclic ring opening. The absorption spectra of the merocyanines **30/32** underline the strong influence of the electronic substituent effects on the photophysical properties of the chromophores. A bathochromic shift of the longest wavelength absorption band occurs for electron-withdrawing substituents on the aroyl moiety. Thereby, the dipolar character of the π-system can be considerably enhanced. This feature can even be enhanced by introducing a more electron-rich donor on the opposite side of the conjugated π-system. This trend is consistently observed for all three merocyanine series **30**, **31**, and **32**. The solution absorption maxima are found between 395 and 516 nm and just a small bathochromic shift can be detected for the thin films prepared by dropcasting.

Indolone based solid-state luminescent merocyanine chromophores **33** can be readily synthesized in a consecutive three-component reaction, based on the chromophore concept, with excellent yields (60-99%) (Scheme 25).[102] By reacting alkynoyl *o*-iodo anilides with a palladium complex a cyclization takes place after insertion of the triple bond in the aryl-metal bond. The following alkynylation under Sonogashira conditions allows for a subsequent Michael-type addition of primary or secondary amines concluding the insertion-coupling-addition sequence. The obtained push-pull butadienes display intense orange to red solid state luminescence (λ = 622-644 nm), while no emission can be detected in solution.



Scheme 25. Insertion-coupling-addition sequence for the synthesis of 4-aminoprop-3-enyliden indolones **33**.

Many heterocycle syntheses based on copper catalysis can be found in the literature,[103] including the combination of both Cu(I) and Cu(II) salts in the same process.[104] Recently, a novel pseudo four-component synthesis of merocyanine analogues by binary Cu(I)/Cu(II) catalysis in the sense of the chromophore approach was reported.[105] The coupling of *N*-methyl isatin with an amine and an alkyne is catalyzed by Cu(I) chloride and Cu(II) triflate, giving rise to merocyanines in 35-80% yield (Scheme 26).

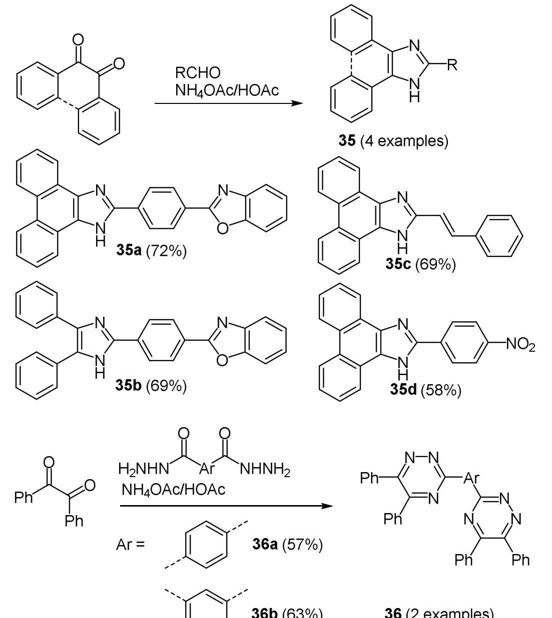


Scheme 26. Binary copper catalysis for the pseudo four-component synthesis of merocyanine analogues **34**.

Interestingly, these compounds show blue luminescence (438-487 nm) with quantum yields of up to 20%, significantly different in comparison to 4-aminoprop-3-enylidene indolones **33**. The absorption spectra possess two major bands at 250-275 and 350-380 nm, resulting in large Stokes shifts of up to 6500 cm^{-1}. The substituent on the aniline rings has the largest influence on the photophysical properties of the merocyanine dyes, for instance larger Stokes shifts can be observed for electron deficient systems.

4.4 MCR Formation of NLO-Chromophores

The term NLO property summarizes a variety of different effects.[106] Most important for organic NLO materials are photorefractive or multiphoton effects. Although the phenomenon of two-photon absorption has been known for a long time,[107] the conceptual design of easily accessible and effective molecules with this characteristic started only in the past two decades.[108] The first step beyond normal spectroscopic usage was taken due to a ubiquitous request for novel imaging and data storage technologies.[109] For the application in biological imaging most requested molecules are green and red emitters, nevertheless also blue emitting chromophores are interesting, when more than two probes have to be introduced. Blue light emitting small molecules were indeed easily prepared by using various one-pot multicomponent syntheses. The reaction of 9,10-phenanthraquinone or diaryl 1,2-diones with an appropriate aromatic aldehyde and ammonium acetate as a third component in glacial acetic acid under microwave irradiation results in the formation of imidazole (and oxazole) based chromophores **35**.[52] By replacing the aldehyde with an aryl bis(hydrazide) also 1,2,4-triazine based derivatives **36** can be prepared in the sense of the scaffold approach (Scheme 27).



Scheme 27. Synthesis of imidazole (**35**) and 1,2,4-triazine (**36**) based two-photon absorption chromophores.

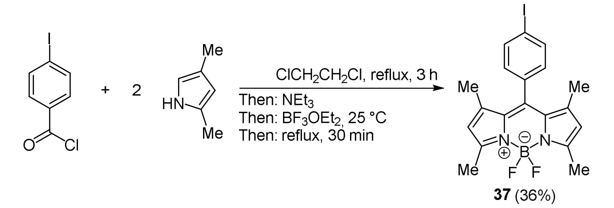
The imidazole based chromophores **35** show strong blue emission maxima at around 443-476 nm after two-photon excitation, whereas the triazoles **36** clearly display weak non-linear optical characteristics, where fluorescence is essentially absent. Also the single-photon absorption properties reveal a pronounced influence of the nature of the *N*-heterocycle. In the absorption spectra a considerable bathochromic shift is found by replacing the triazine core (λ_{max} = 275-276 nm) with an imidazole moiety (λ_{max} = 357-376 nm). In contrast, the one-photon excited fluorescence of both series shows similar shortest wavelength maxima in a range between 434 to 483 nm. Hence, huge Stokes shifts for the triazine systems (14600-15500 cm^{-1}) and considerably smaller shifts for the imidazole based chromophores (4200-6400 cm^{-1}) are found.

4.5 MCR Formation of Complexes

Initially, a wide range of metal complexes was synthesized due to their interesting dye characteristics. However, since the early 1990s these systems gained increasing importance due to their peculiar electronic and photophysical properties. In particular, the development of DSSC by Grätzel was decisive.[110] Complexes with various metals as core elements were prepared and applied in DSSCs giving overall efficiencies of up to 13%.[111]

Organoboron complexes have been known since the end of the 19th century,[112] nevertheless, it was not before the 1950s that the chemistry of these particular compounds has been strongly developed.[113] The interest of researchers aroused due to their immense fluorescence, making them important candidates for the application in OLEDs as emitting components.[114] Due to the increasing significance of these luminescent systems in materials science, the quest for novel straightforward multicomponent reactions became evident.

BODIPY (boron dipyrrin) complexes are the best known and mostly investigated boron containing fluorophores. These boron chelates have already found application in a variety of functional materials, for instance as luminescent biomolecular labels, as laser dyes, light harvesters and fluorescent switches.[115] Furthermore, dipyrrins can form mono- and dinuclear chelates with many different transition metals, resulting in distinct characteristic properties.[116] In 2000 a simple one-pot methodology to prepare these organoboron complexes has been presented by Burgess and coworkers following the chromophore concept. First an aromatic acyl chloride reacts with two equivalents pyrrole derivatives. After addition of triethylamine as a base and boron trifluoride etherate the desired BODIPY complex **37** can be isolated (Scheme 28).[117]



Scheme 28. One-pot synthesis of a BODIPY complex **37** according to Burgess.

This synthesis became well established and many different complexes were prepared also for other systems than dipyrrin ligands (Figure 5).[118] All boronic systems display strong fluorescence in solution or solid state and they are often accompanied by large Stokes shifts.

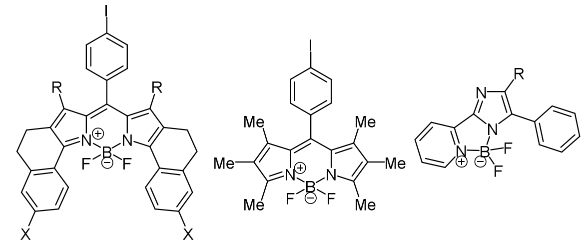
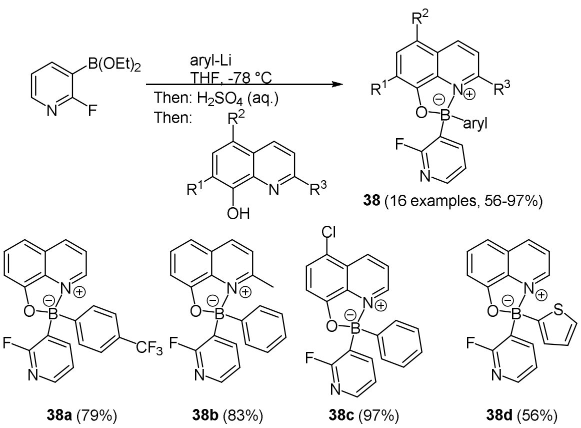


Figure 4. Examples for organoboron complexes by Burgess (left),[117] Bröring (middle),[118] and Xiao (right).[118]

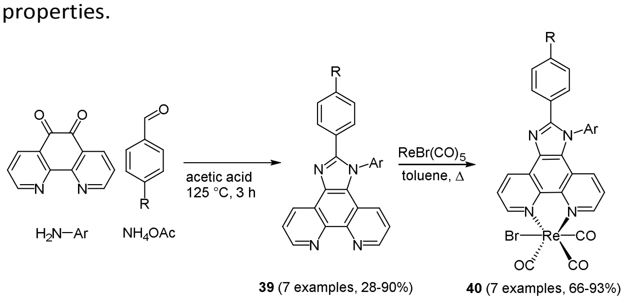
In the past decades investigations on boronic complexes were mostly concerned with fine-tuning of the fluorescence wavelength and with increasing the stability.[114,119] Another attractive ligand with respect to emerging photochemical properties is the 8-oxyquinolinato ligand. For these compounds the emission color can be tuned by chemical functionalization of the heterocycle corpus. Both homo-[120] and heteroleptic diarylboron complexes are known. More interesting are unsymmetrically substituted 8-oxyquinolinato diarylboron derivatives **38** which can be prepared via consecutive three-component synthesis in the sense of the chromophore concept (Scheme 29).[121]



Scheme 29. Synthesis of heteroleptic 8-oxyquinolinato diarylboron complexes **38**.

Most advantageously, a second heterocycle in addition to the 8-oxyquinoline core can be introduced. Here, diethyl 2-fluoro-3-pyridineboronate reacts with aryl lithium to give the diarylborinic acid "ate" complex which after hydrolysis results in the free diarylborinic acid. After addition of the quinolinato ligand the colorful crystalline product can be isolated in good to excellent yields (56-97%). It is also possible to introduce further complexation by addition of zinc chloride. This complexation occurs at the pyridine nitrogen coordinating two boron complexes to the zinc ion. All compounds show absorption maxima between 378 and 407 nm with extinction coefficients of the zinc complexes up to 8900 $M^{-1}cm^{-1}$. The shortest wavelength emission band lies in a range of 502 to 525 nm with fluorescence quantum yields of up to 20%. For the zinc complexes the quantum yields drop to 2 or 3%.

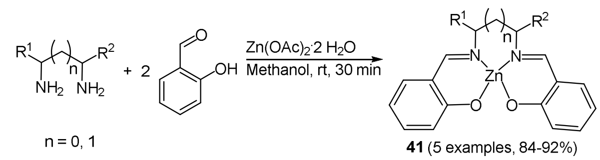
Rhenium(I)-complexes with coordinated diimine ligands often show interesting photophysical properties. Therefore, their use as responsive probes for a variety of analytes[122] and the local medium,[123] or in fluorescence microscopy cell imaging studies has already been established.[124] In metal complexes luminescent properties usually originate from metal-to-ligand charge transfer in the excited state.[125] Consequently, large Stokes shifts and reasonably long luminescence lifetimes can be reached, which are particularly relevant for bioanalytical application. The synthesis of phenanthroline based chromophore ligands can be performed in a domino four-component reaction following the scaffold approach starting from the corresponding 1,10-phenanthroline-5,6-dione.[126] The condensation of the dione with an amine, an aldehyde and ammonium acetate gives rise to imidazo-phenanthroline ligands **39** in moderate to excellent good yields (28-90%) (Scheme 30). The complexation to luminescent [ReBr$(CO)_3$L] complexes **40** was achieved by stirring the ligand with [Re$(CO)_5$Br] overnight. The substituent variation on the ligand core only shows moderate influence on the fluorescence properties.



Scheme 30. Four-component synthesis of chromophoric imidazo-phenanthroline ligands **39** for the complexation with Re(I) to complexes **40**.

The photophysical properties of both free ligands and complexes revealed significant differences. While the emission of the ligands **39** appears around 370 nm, the complexes **40** fluoresce around 580 nm. Even more remarkable is the enlargement of the Stokes shifts (up to 7000 cm^{-1}) caused by complexation to rhenium, as a consequence of metal-to-ligand charge transfer.

For modern technology the preparation of white organic light-emitting diodes (WOLED) is an ongoing task. Their potential application in full color displays or backlights for liquid crystals and the prospect of energy saving systems are only some of their advantages.[127] Mixing the three primary colors, red, green and blue, with a single layer or the combination of two complementary colors are two strategies developed to realize white light emission. Zinc complexes turned out to be promising candidates for these systems bringing along high efficiency, low cost, easy tunable colors and high thermal stability as advantageous characteristics.[128] In the sense of the chromophore concept a pseudo four-component reaction allows for a straightforward synthesis of blue fluorescent zinc-complexes with white-light emitting properties when doped on 4,4',4''-*tris*(*N*-carbazolyl)triphenylamine in OLEDs.[129] Here, a substituted aliphatic diamine reacts with zinc acetate and salicylaldehyde resulting in the desired zinc(II) complexes **41** with chelate ligands in excellent yields (84-92%) (Scheme 31).



Scheme 31. Synthesis of fluorescent zinc(II) complexes **41** via a pseudo four-component synthesis.

All complexes **41** display two distinct absorption maxima in the UV/Vis-spectra, the first at around 260 nm and the second at around 360 nm, which can be assigned to the metal-to-ligand charge transfer. Furthermore, a strong similarity is observed in the emission characteristics, where the maxima lie in a narrow range between 441 and 447 nm showing a more or less intense blue luminescence. The electroluminescence of the compounds was also studied. Here, the compounds revealed typical diode characteristics emitting a sky-blue to white light in the devices (Figure 6).

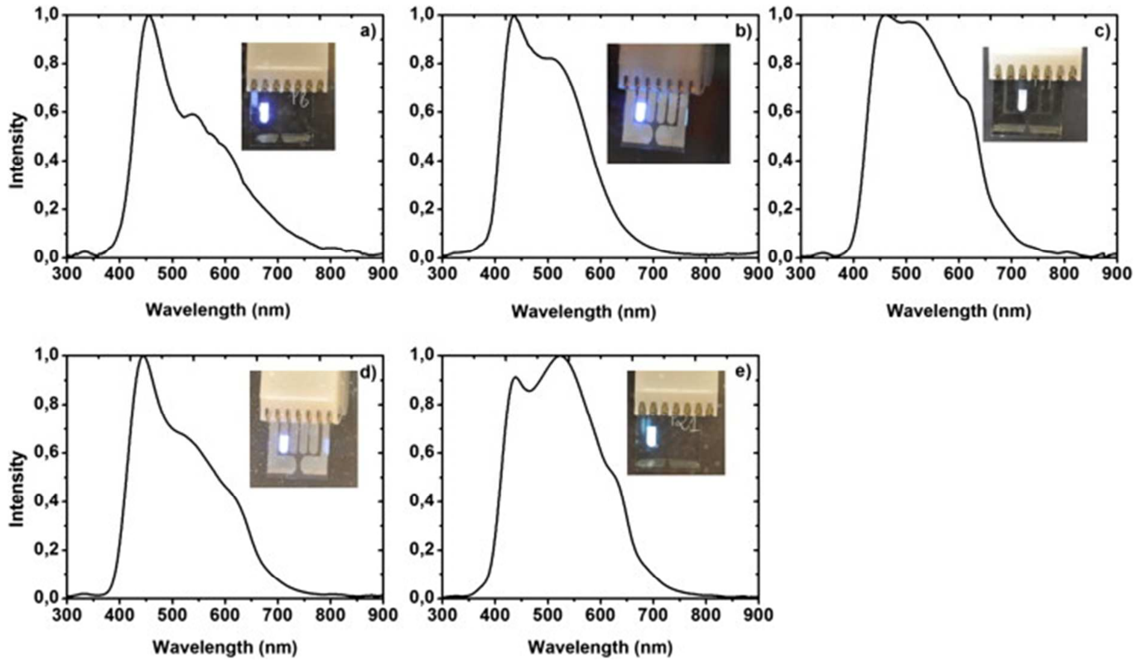


Figure 5. Electroluminescence spectra of sky-blue and white OLEDs of the doped device with zinc complexes **41**. Reprinted from *Thin Solid Films*, *564*, F. Dumur, L. Beouch, M.-A. Tehfe, E. Contal, M. Lepeltier, G. Wantz, B. Graff, F. Goubard, C. R. Mayer, J. Lalevée, D. Gigmes, Low-cost zinc complexes for white organic light-emitting devices, 351-360, Copyright (2014), with permission from Elsevier.

4.6 Miscellaneous

The preparation of chromophore families appended to macrocycles was reported by Main et al. in 2008.[130] These novel DOTA (1,4,7,10-tetra-azacyclododecane-1,4,7,10-tetraacetic acid) monoamide ligands were synthesized by Ugi condensation as the key step, starting from an acid functionalized macrocycle. The complexation of the DOTA-ligands with lanthanides gives luminescent complexes as agents for the imaging of biological systems (Figure 6).[131]

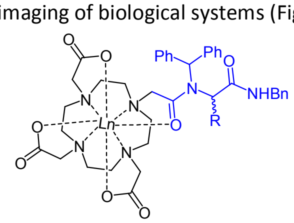
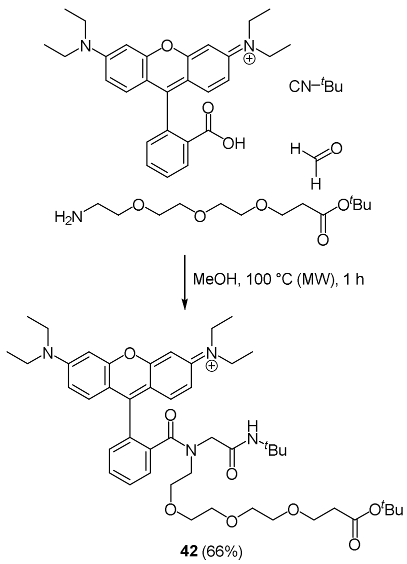


Figure 6. DOTA-lanthanide complexes with an Ugi-4CR product as side chain (highlighted in blue).

These most intensively luminescent complexes show two emission maxima, the first appearing between 250 and 337 nm and the second between 545 and 980 nm. But also free ligands have received great interest for biological studies. Actually, the isolation, identification and, characterization of metabolites, generally referred to as metabolomics, plays a key role for disease diagnosis.[132] The facile mass determination of metabolites can be achieved by chemical derivatization, whereupon the attained novel physicochemical properties simplify both LC-MS and GC-MS analyses.[133] For instance, the chemoselective derivatization of aldehydes and ketones as imines, hydrazones and oximes or the reaction of amines with electrophilic reagents is often employed.[134] By employing the Ugi-4CR for derivatizing more than a single functional group, different classes of metabolites were derivatizes in high yields and with excellent chemoselectivity. Gratifyingly, the MCR can be performed in water giving stable and UV-active products which can be easily identified via LC-MS.[135]

The investigation of the protein composition is an important issue for understanding complex biological processes, such as protein-protein interactions. The studies are predominantly performed with biomarkers in biomedical sciences.[136] For this purpose an activity-based protein profiling (ABPP)[137] was developed among other more biological approaches.[138] The probes employed in this analysis consist of a reactive group for the attachment to the protein, a group for specific target recognition and a reporter-tag for target detection, for instance a fluorophore. Westermann and coworkers developed rhodamine based reporter-tags **42** with different bioorthogonal functional systems as a side chain.[139] In the sense of a scaffold approach the Ugi-4CR[36] turned out to be the excellent method of choice to prepare these chomophores by reacting rhodamine B, i. e. a carboxylic acid, formaldehyde, an amino ether with *tert*-butyl isocyanide (Scheme 32).

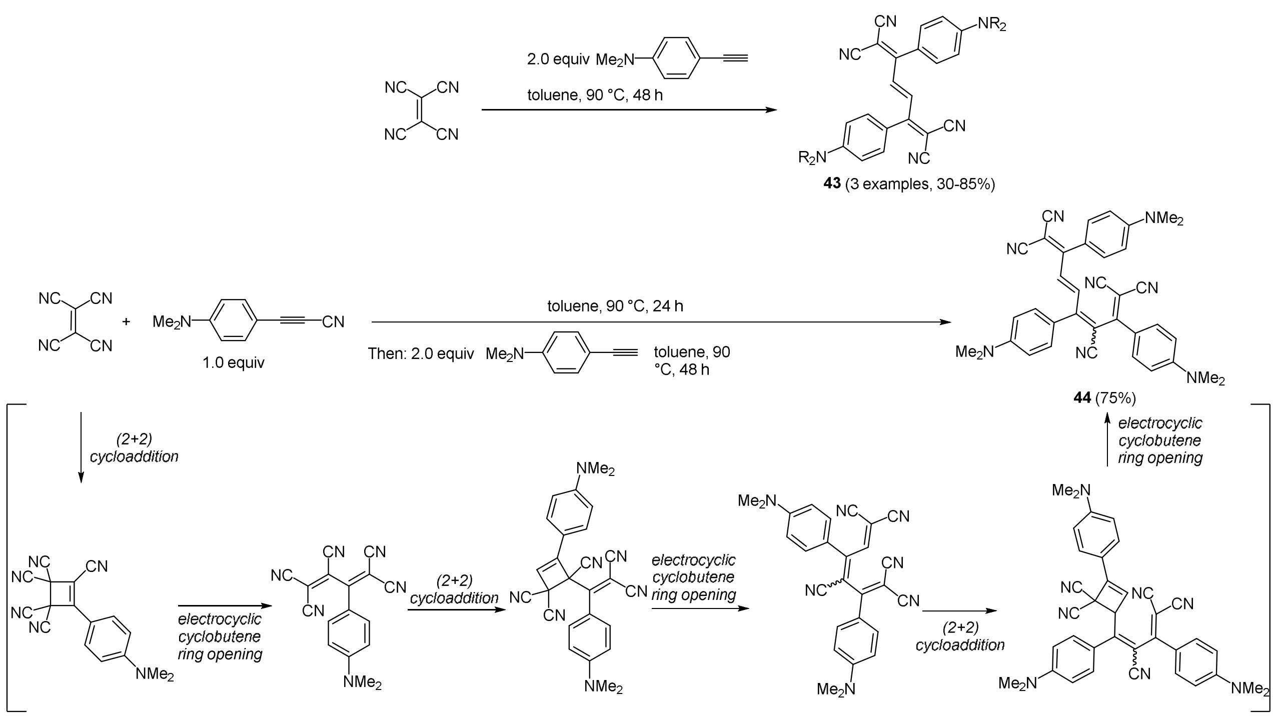
The typical p*H*-dependency of the rhodamine emission characteristics was absent with this substitution pattern, the compound showing emission both under acidic and basic conditions. The compounds show absorption maxima between 532 and 586 nm with high extinction coefficients of up to 72000 $M^{-1}cm^{-1}$ and emission maxima between 550 and 600 nm. The photophysical properties are not altered compared to the starting material rhodamine B, which shows the longest wavelength maximum at 554 nm and the emission maximum at 576 nm.



Scheme 32. Ugi-4CR for the preparation of modified rhodamine dyes **42** for protein detection.

Pericyclic processes, such as cycloadditions and electrocyclic reaction, are particularly suited for accessing conjugated systems.[140] Interestingly, electrocyclic ring opening following a cycloaddition not only lead to the formations of two new carbon-carbon σ-bonds but also to a rearrangement of the π-system. Conjugated arylalkynyl systems can be considered as simple rigid molecular wires that enable fast electron transfer processes between the two redox termini.[141] By reaction of the alkynyl moiety with tetracyanoethylene (TCNE) biscyanomethylene moieties can be readily introduced by the above mentioned mechanistic scenario.[142] Therefore, the combination of (2+2) cycloaddition and electrocyclic cyclobutene ring opening represents a powerful methodology for the preparation of tetracyanohexatrienes and –octatetra-enes.[31,143] The repetitive (2+2)-cycloaddition-cyclobutene sequence has been elaborated into a consecutive (pseudo)-multicomponent reaction with differently substituted alkynes furnishing trienes **43** (3 examples, 30-85%) and tetraene **44** (75%) in the sense of the chromophore concept (Scheme 33).

The trienes **43** exhibit simple UV/Vis spectra with two major bands at around 350 and 560 nm, where the maxima at the lowest energies correspond to intramolecular charge-transfer transitions (ICT). In contrast to PET processes, in ICT the electron transfer instantaneously takes place upon absorption of a photon. Although the two configurational isomers of the tetraene **44** display more complex absorption spectra, the positions of the intense ICT-bands do not alter significantly. These results encouraged other research groups to synthesize further donor-acceptor molecules. For instance the introduction of sterically and structurally more demanding alkynes and also dialkynes separated by a spacer were successfully accomplished.[144]



Scheme 33. [2+2]-Cycloaddition-electrocyclic cyclobutene opening sequence for the synthesis of tretracyano-trienes **43** and tetracyano-tetraene **44**.

5 Conclusion

As highlighted in this review, multicomponent reactions as an ongoing task in organic synthetic chemistry have turned out to be a valuable tool in the preparation of functional chromophores. A broad spectrum of domino and consecutive MCR has already found entry to the literature. Besides concatenation of reactions with diverse reactivity patterns, sequentially catalyzed processes are increasingly gaining attention, in particular, due to their process efficiency and catalyst efficacy.

Classical MCR, such as the Ugi-4CR and the Biginelli-3CR, are particularly useful for accessing functional materials in the sense of the scaffold concept. This approach is very favorable for applications, where covalent ligation and nonconjugated placements chromophores are important, e. g. for fluorescent probes with molecular recognition tags or in general for photo-induced electron transfer. In turn, the in situ formation of the functional chromophore by an MCR, as outlined in the chromophore concept, requires novel processes with the major challenge to tackle concise syntheses of special functional targets. Fascinating results have been unraveled and molecules with tailor-made electrochemical and photophysical properties can be designed, systematically studied and optimized by skillfully applying this powerful tool of diversity oriented synthesis.

Many synthetic pathways and structures are still unexplored in the world of multicomponent reactions. The unique combination of synthetic creativity, programmed reactivity, and systematic exploration of functional chromophores will stimulate the development and rational design of functional materials by MCR as an intellectual challenge in the topical field of organic materials science in the years to come.

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