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Acetylene derivatives of quinones and their transformation products: synthesis, reactivity and applied aspects

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The review summarizes the data on the methods of synthesis, reactivity and practical applications of acetylene derivatives of quinones and their transformation products published for the last 15 years. The specificity of alkynylquinones associated with the activation of the triple bond by the quinoid moiety is addressed. The triple bond activation is responsible for high reactivity of these compounds, which makes it possible to design and perform complex cascade transformations, providing a rational route to multipurpose products. The general patterns and specific features of the reactivity of this class of compounds are systematically reviewed. Particular attention is given to fundamentally important redox processes and new heterocyclization reactions. The mechanisms of these transformations are considered. The prospects of the practical application of alkynylquinones and their transformation products in optics, electronics, medicinal chemistry and other areas of human activity are discussed.
The bibliography includes 141 references.

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1. Introduction

Quinones are an important and unique class of organic compounds. In the 20th century, these compounds were widely used as photographic materials and dyes (*e.g.*, alizarin (1,2-dihydroxyanthraquinone)). Presently, these compounds are attracting attention of chemists and biologists as potential drugs. Thus, the fat-soluble coenzymes ubiquinones are widely present in animal and plant cells and are involved in electron and proton transfer in the respiratory chain.[1,2] Some natural and synthetic naphtho- and anthraquinones and their heterocyclic analogues exhibit high anticancer activity.[3]

Quinones easily undergo reversible redox reactions, due to which these compounds are attractive for applications in nonlinear optics and molecular electronics, in particular as redox switches.[4,5] Simple quinones, such as benzoquinone, chloranil or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), are often used as acceptors in charge-transfer complexes. For example, the first metal complex with chloranil was synthesized back in 2004.[6]

Besides, the unique reactivity of compounds with a carbon – carbon triple bond offer good prospects for their versatile use in many fields of organic synthesis, medicinal chemistry and materials science.[7] That was why acetylene

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derivatives have attracted great attention of organic chemists and biochemists in the past two decades. The state of the art of organic chemistry is characterized by the emergence of new concepts and the development of efficient preparative methods of alkyne synthesis and new reactions with alkynes, including reactions under green chemistry conditions.[8–10]

A striking example of a new efficient methodology in the acetylene chemistry is the addition of acetylene carbanions to the C=N double bond in a potassium *tert*-butoxide–DMSO superbase system (at 40 °C for 10 min), which was discovered by B. A. Trofimov and his research team in 2018.[11] It is worth noting that until recently the C=N bond was considered to be insufficiently electrophilic to be involved in such transformations. Actually, this reaction is an analogue of the Favorsky ethynylation of aldehydes and ketones and it was rightly called as the aza-Favorsky reaction.

Also worthy of mention is the recently discovered complete cleavage of the strong triple bond under metal catalyst-free conditions in the presence of ethylenediamine (EDA) as an organic base giving methyl aryl ketones and 2-substituted imidazolines.[12,13] The atom-economic nickel- or copper-catalyzed direct ethynylation of azoles and polyfluoroarenes, which does not require an inert atmosphere,[14] is an attractive new strategy.

The progress in the acetylene chemistry is reflected in numerous reviews on this subject. Apart from the above reviews,[8–10] let is mention the review by Gilmore and Alabugin,[15] who critically considered and partially revised the universal rules for the cyclization of unsaturated derivatives, including alkynes (Baldwin's rules).[16] It is also known that many acetylenes are widely distributed in nature and exhibit various, including anticancer, activities.[17]

In view of the above, it can be suggested that compounds with a conjugated system, involving a carbonyl group and a triple bond, are highly reactive substrates in various chemical transformations. Besides, alkynylquinones are promising for medicinal chemistry due to the presence of two pharmacophore moieties. A combination of such moieties is of interest for the design of new drugs. Actually, fused alkynylanthraheterocycles, *e.g.*, dynemicin A (**1**), are able to intercalate into duplex DNA.[18] The synthesized analogues of this natural compound, such as yangpumicin A (**2**) and tiancimycin B (**3**), exhibit high anticancer activity.[19]

The previous review on the chemistry of alkynylquinones was published back in 2004,[20] which was an additional impetus for a systematic review on this subject. The present review covers the data published from 2005 to 2020 and seems to be relevant since the trends in this field of chemistry have significantly changed in the past 15 years. New ingenious synthetic strategies were developed, new reactions were discovered and unusual transformations of alkynylquinones were described.[21]

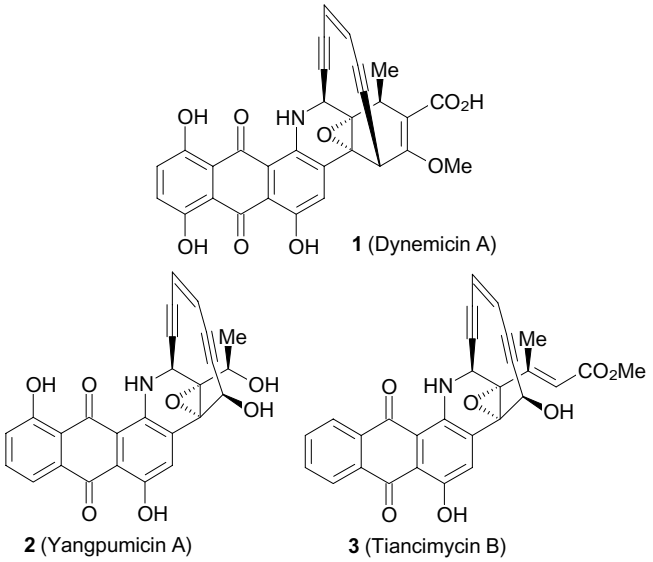
The present review demonstrates the specific features of alkynylquinones, making these derivatives important for both fundamental and applied research in organic chemistry. A combination of the quinoid and acetylene moieties in one molecule leads to a significant increase in the electrophilicity of the triple bond and the enhancement of its response to both external (the reaction temperature, the nature of the solvent) and internal stimuli (the structure of substituents in the quinone core and the acetylene moiety) and provides the diversity of possible transformations. Particular attention is given to the practical significance of the transformation of *peri*-substituted acetylenyl-9,10-anthraquinones in the presence of nitrogen nucleophiles, which provides a route to the synthesis of biologically active analogues of aporphinoid alkaloids.[22] Selected putative mechanisms of unusual reactions of alkynylquinones, which are of great fundamental importance, are discussed.

2. Methods of synthesis of alkynylquinones

Although the Sonogashira reaction was used as the main tool for synthesizing aryl(hetaryl)acetylenes for more than 45 years, procedures for accomplishing this reaction are continued to be improved. The development of new ligands and the design of more efficient catalytic complexes have attracted attention. For instance, Trofimov *et al.*[23] described an environmentally benign method for the synthesis of a palladium complex, which does not require corrosive reagents (PCl_3 or $POCl_3$) and sodium metal or organomagnesium compounds in anhydrous media. This procedure is more cost-effective and is based on the use of available tris(*Z*)-styryl)phosphine (**4**) (Scheme 1).

Ligand **4** was synthesized directly from elemental phosphorus and phenylacetylene in the KOH–hexamethylphosphoramide (HMPA) superbase system. The complex $[(Z)\text{-PhCH=CH})_3P]_2PdCl_2$ (**5**) was synthesized by heating phosphine **4** with $PdCl_2$ in DMF. The efficiency of complex **5** was compared with that of the classical complex $Pd(PPh_3)_2Cl_2$ (**6**) using the cross-coupling reaction of

Structures 1–3

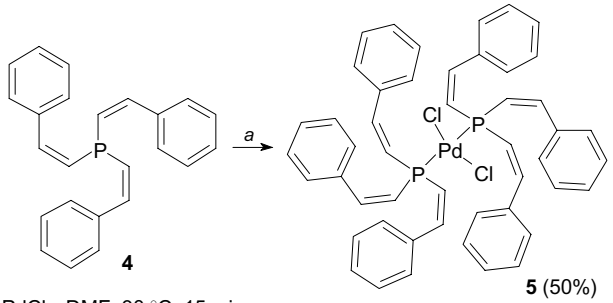


1 (Dynemicin A)

2 (Yangpumicin A)

3 (Tiancimycin B)

Scheme 1

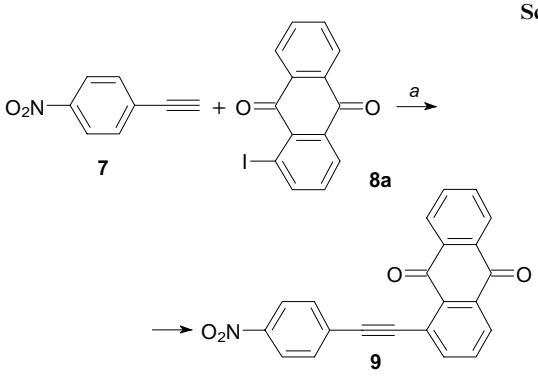


4

5 (50%)

(*a*) $PdCl_2$, DMF, 90 °C, 15 min

Scheme 2



(*a*) Cat, CuI, Et_3N, PhH, 50–60 °C, 1.5 h;
Cat = **5** (92% yield), **6** (95%)

1-ethynyl-4-nitrobenzene (**7**) with 1-iodo-9,10-anthraquinone (**8a**) (Scheme 2).

In both cases, the reaction was completed within 1.5 h to give 1-(4-nitrophenyl)ethynyl-9,10-anthraquinone (**9**) in rather high yields. Therefore, the new complex can be used as an alternative to the conventional catalyst for the Sonogashira reaction due to simplicity and environmental safety of its synthesis.

This Section considers only the general approaches to the synthesis of practically important alkynylquinones and briefly discusses their characteristic features. Other methods, which are not widely used, are considered addressed in detail in Sections 2–4.

The development of methods for the synthesis of acetylene derivatives of quinones is an important and relevant issue taking into account that such compounds serve as a convenient platform for the investigation of the effect of the alkyne and quinoid moieties on their reactivity. Besides, these compounds are practically promising intermediates for electronics, optics, medicinal chemistry and other areas of science and engineering.

2.1. Cross-coupling reactions of bromo- and iodoquinones with alk-1-ynes and their copper salts

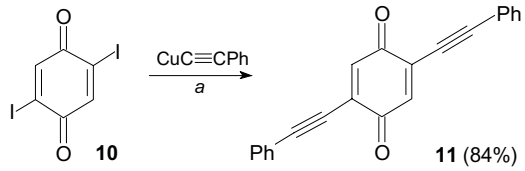
Since the discovery in 1975, the Sonogashira reaction,[24] the cross-coupling of iodo- and bromo(het)arenes with terminal alkynes, served as the main method for the synthesis of aryl- and hetarylacetylenes. The advantages of this reaction are the tolerance of a wide range of functional groups both in the acetylene component and haloarene, the possibility of using various catalysts, solvents and bases, a broad temperature range and generally high yields of cross-coupling products.

The alkynylation is sometimes performed using an alternative method based on the cross-coupling of iodo(bromo)arenes with copper acetylides (Castro reaction).[25] In both types of condensation, the halogen atom may be present both in the quinoid and benzene parts of the molecule. The reactivity of aryl halides in the Sonogashira reaction decreases in the series ArI > ArBr > ArCl.[26] The cross-coupling occurs particularly rapidly when the halogen atom is present in the quinoid ring.

Thus, the condensation of 2,5-diiodo-1,4-benzoquinone (**10**) with copper phenylacetylide is accompanied by self-heating even at 20 °C and is completed within 20 min to form dialkynyl-substituted benzoquinone **11** (Scheme 3).[27]

Bromo-substituted quinones are characterized by higher reactivity compared to that of bromoarenes due to the

Scheme 3

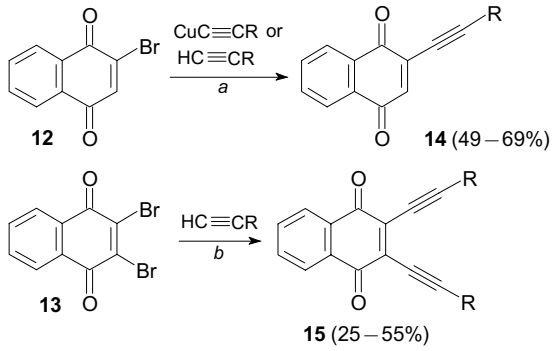


(*a*) $Pd(PPh_3)_2Cl_2$, DMSO, $CHCl_3$, 20 °C, 20 min

electron-withdrawing effect of carbonyl groups. Hence, the synthetic chemists often use cheaper and more readily available bromo derivatives instead of iodoquinones.

It was found[27,28] that the bromine atoms in the quinoid ring are successfully replaced by alkyne groups in the reactions with copper(I) acetylides, which are prepared in advance or *in situ*, in a mixture of DMSO and $CHCl_3$. The cross-coupling of 2-bromo- (**12**) and 2,3-dibromo-1,4-naphthoquinone (**13**) with copper acetylides affords the corresponding 2-alkynyl- (**14**) and 2,3-dialkynyl-1,4-naphthoquinones (**15**) (Scheme 4).

Scheme 4



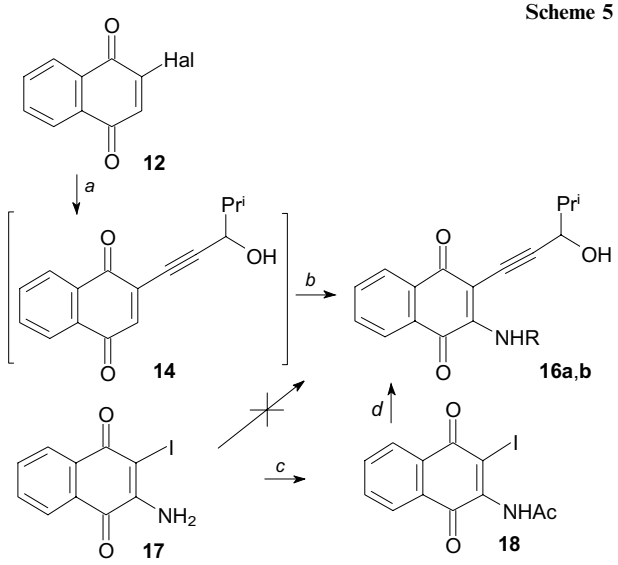
(*a*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, $CHCl_3$, DMSO, 50 °C, 35 min;
(*b*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, $CHCl_3$, DMSO, 28–55 °C, 20 min–12 h;
R = Ph, 4-$O_2NC_6H_4$, 4-$MeOC_6H_4$, C(OH)Me_2, C(OMe)Me_2, $(CH_2)_3OH$, Bu^n, n-C_6H_{13}, n-C_8H_{17}, 1-hydroxycyclohexyl

In the acetylide version, the reaction time is 35 min at 50 °C; in the catalytic version, the reaction occurs in the temperature range of 28–55 °C with a reaction time from 20 min to 12 h.

Acetylenylquinones containing an amino group in the vicinal position to the triple bond are of great interest as convenient precursors for the annulation of the quinoid ring with the pyrrole or pyridine ring. However, an attempt to synthesize 3-alkynyl-2-amino-1,4-naphthoquinones **16** by the cross-coupling of 2-amino-3-iodo-1,4-naphthoquinone (**17**) with terminal alkynes failed because of the deactivation of the iodine atom due to the strong positive mesomeric (+*M*) effect of the electron-donating amino group (Scheme 5).[29]

However, when performing the cross-coupling of bromoquinone lacking amino groups, Kolodina *et al.*[29] ran into problems with the isolation and purification of intermediate acetylene alcohol **14** (resinification, low yield) because of its lability. The authors found a rational approach. They performed the Sonogashira cross-coupling of iodoquinone lacking amino groups and then subjected acetylene **14** to *in situ* oxidative amination at the free position of the

Scheme 5



(*a*) HC≡CCH(OH)Pr^i, $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, $CHCl_3$, DMSO, 50 °C, 20 min; (*b*) aq. NH_3, dioxane; (*c*) Ac_2O, H_2SO_4, $CHCl_3$; (*d*) HC≡CCH(OH)Pr^i, $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, $CHCl_3$, DMSO, 30 °C, 30 min; R = H (**16a**), Ac (**16b**); Hal = Br, I

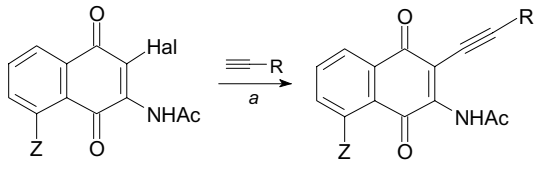
quinoid ring. Target product **16a**, being more stable due to the $+M$ effect of the amino group, was obtained in 44% yield over two steps.

An alternative approach involved the preacetylation of the amino group in starting amino(iodo)quinone **17**. The iodine atom in N-acetyl derivative **18** is less deactivated compared to that in iodide **17** due to a weaker $+M$ effect. Meanwhile, it was sufficient for the stabilization of final product **16b**. More reactive iodonaphthoquinone **18** reacted with copper acetylide, which was derived *in situ* from 3-hydroxy-4-methylpentyne in the presence of $Pd(PPh_3)_2Cl_2$.[29] The yield of acetylated amino alcohol **16b** was 67%.

This method, which has obvious advantages over the former approach, was used to synthesize a large series of 3-acetylamino-2-alkynyl-1,4-naphthoquinones **16** and **20** bearing different substituents starting from substituted 2-bromo(iodo)naphthoquinones **18** and **19** (Scheme 6).[27, 29–31]

The cross-coupling reaction can be performed also using bromonaphthoquinones containing substituents with a moderate $+M$ effect (*e.g.*, the NHAc group), which deactivate the substrate towards the nucleophilic attack.[27, 29, 30]

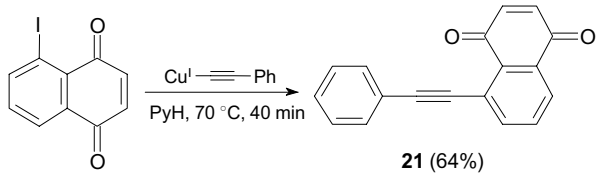
Scheme 6



(*a*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, $CHCl_3$, DMSO, 20–35 °C, 30–180 min; **16**, **18**: Z = H (41–84%); **19**, **20**: Z = NHAc (85–93%); Hal = Br, I; R = Ph, CH_2OTHP, $C(OH)Me_2$,1-hydroxycyclohexyl, 4-$O_2NC_6H_4$, $(CH_2)_2OH$, $CH(OH)Pr^i$, C(cyclo-C_3H_5)(OH)Me; THP is tetrahydropyran-2-yl

It is worth noting that the Sonogashira cross-coupling is inapplicable to the synthesis of 5-phenylethynyl-1,4-naphthoquinone (**21**). This compound was prepared using the Castro reaction (Scheme 7).[32, 33]

Scheme 7

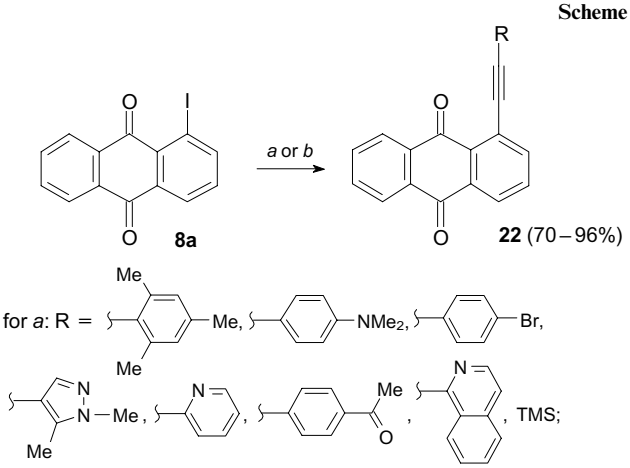


Py is pyridyl

The authors supposed that the Pd-catalyzed cross-coupling involving benzo- and naphthoquinones is a complex process because quinoid substrates can act as an oxidizing agent or a ligand for a Pd complex.[34, 35]

As opposed to 1,4-benzo- and 1,4-naphthoquinones, the introduction of an acetylene moiety into 9,10-anthraquinones causes no difficulties. For benzo- and naphthoquinones, complications arise when these substrates contain one (see Scheme 5) or two (see Scheme 7) free positions in the quinoid part of the molecule. For anthraquinone derivatives, both reactive sides of the quinoid ring are blocked by benzene rings, resulting in that the reaction affords target products in high yields. Actually, a large series of *peri*-acetylenyl-9,10-anthraquinones **22** containing alkyl, aromatic and heteroaromatic substituents of both electron-donating and electron-withdrawing nature were synthesized under typical Sonogashira reaction conditions (Scheme 8).[22, 36–38]

Scheme 8

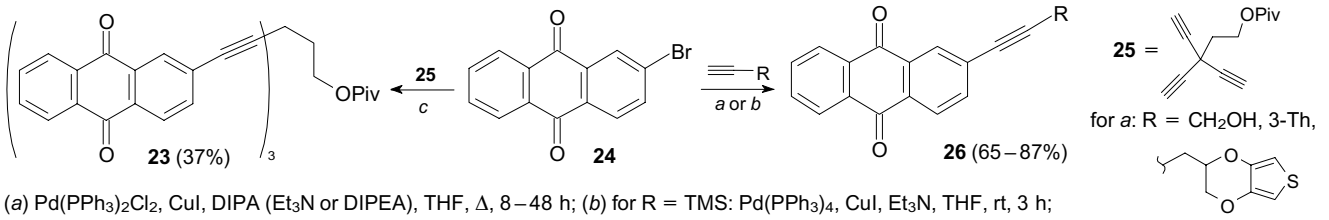


(*a*) HC≡CR, $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, 40–65 °C, 1–9 h; (*b*) for R = n-C_5H_{11}, 2-Th: CuC≡CR, PyH, 65 °C, 0.5 h; DIPA is diisopropylamine, TMS is trimethylsilyl, Th is thienyl

1-Alkynyl-9,10-anthraquinones can also be synthesized by the Castro reaction.[25, 38]

The Sonogashira cross-coupling is often used to introduce an alkyne moiety at the 2 position of the starting 9,10-anthraquinone.[4, 39–41] Chromophore **23** containing three ethynylquinone moieties was synthesized in order to study fluorescence in solutions and films. The reaction was performed using both Pd^0 and Pd^{II} complexes (Scheme 9).[42]

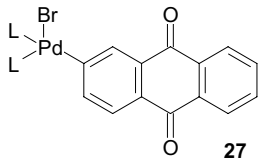
Scheme 9



(*a*) $Pd(PPh_3)_2Cl_2$, CuI, DIPA (Et_3N or DIPEA), THF, Δ, 8–48 h; (*b*) for R = TMS: $Pd(PPh_3)_4$, CuI, Et_3N, THF, rt, 3 h; (*c*) $Pd(PPh_3)_4$, CuI, Et_3N, DMF, 80 °C, 16 h; Piv is pivaloyl, DIPEA is diisopropylethylamine, rt is room temperature

It is worth noting that the reaction of the same starting bromide **24** with triethynyl derivative **25** is less efficient compared to that with monoethynyl substrates (2-R-ethynyl-9,10-anthraquinones **26** were synthesized in moderate to high yields) despite a higher temperature (80 °C) and the use of the more active Pd^0 complex. The factors responsible for a low yield of product **23** were not discussed by the authors. Apparently, this is associated with the steric effect. Three ethynyl groups at one $C(sp^3)$ atom hinder the access to the intermediate bulky complex $L_2Pd(2\text{-AQ})Br$ (**27**) (2-AQ is anthraquinon-2-yl).

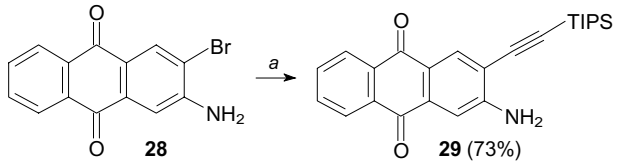
Structure 27



As mentioned above, an attempt to perform the cross-coupling of 2-amino-3-iodo-1,4-naphthoquinone (**17**) with terminal acetylenes failed.[29] Unlike compound **17**, its less reactive bromoanthraquinone analogue **28** is easily subjected to the Sonogashira reaction to form product **29** (Scheme 10).[43]

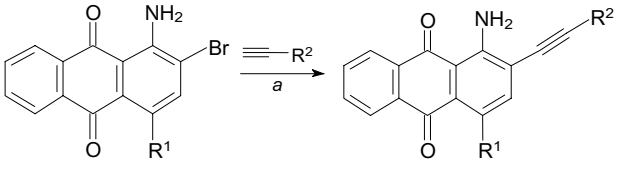
Moreover, even two electron-donating groups do not hinder the alkynylation of 2-bromoanthraquinone **30** giving

Scheme 10



(*a*) HC≡CTIPS, $Pd(PPh_3)_2Cl_2$, CuI, DIPA, THF, 85 °C, overnight; TIPS is triisopropylsilyl

Scheme 11

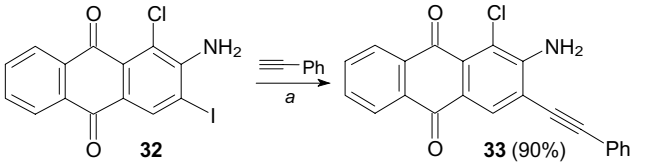


(*a*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, 43–75°C, 1–12 h; R^1 = 3-MeC_6H_4NH, 4-MeC_6H_4NH, OH; R^2 = Ph, 4-$O_2NC_6H_4$, 4-BrC_6H_4, 4-$MeOC_6H_4$, 2,3,5,6-Me_4C_6H, CMe_2OH, TMS, 1,5-dimethyl-1*H*-pyrazol-4-yl, isoquinoline-4-yl

alkynes **31** in moderate to high yields (Scheme 11).[44–46] The terminal TMS group in the product can be removed under basic conditions: K_2CO_3, MeOH, 20 °C, 3 h, 93% yield.

Kolodina *et al.*[47] have achieved success due to a large difference in the reactivity of the chloro and iodo derivatives in the cross-coupling, which made it possible to selectively ethynylate 2-amino-1-chloro-3-iodo-9,10-anthraquinone (**32**) (Scheme 12).

Scheme 12

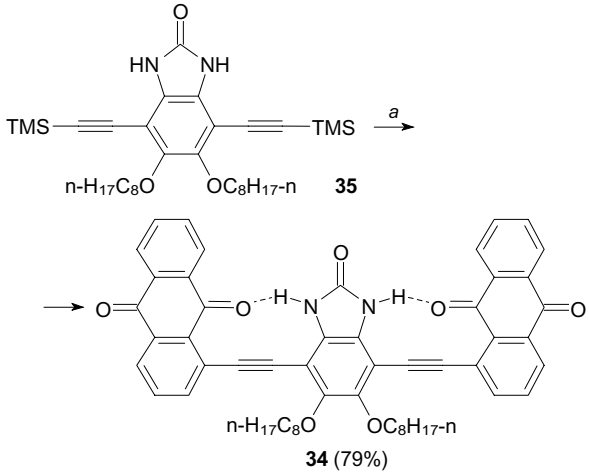


(*a*) $Pd(PPh_3)_2Cl_2$, CuI, Na_2CO_3, dioxane, 85 °C, 15 min

The use of an inorganic base (sodium carbonate) accelerates the reaction, and it is brought to completion at 85 °C within 15 min to form alkyne **33** in high yield.

The Sonogashira reaction with a diethynyl derivative as the acetylene component gave model compound **34** containing two alkynylquinone moieties, which are linked together by intramolecular hydrogen bonds. This compound was intended to be used to investigate the molecular and supramolecular properties (Scheme 13).[48] The reaction was performed in a one-pot fashion. In the first step, the trimethylsilyl protection of dialkyne **35** was removed by the treatment with tetra(n-butyl)ammonium fluoride

Scheme 13

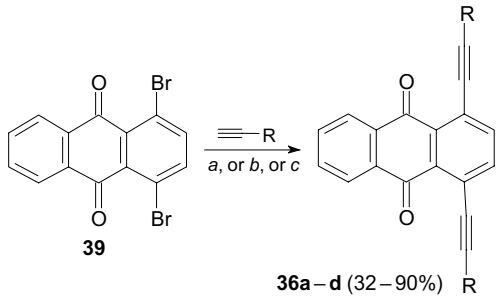


(*a*) 1) TBAF, CH_2Cl_2, MeOH, rt, overnight; 2) **8a**, $Pd(PPh_3)_4$, CuI, Et_3N, 80 °C, 3 days

(TBAF) followed by the condensation of the intermediate with iodoanthraquinone **8a** at 80 °C.[48]

The Sonogashira condensation was successfully applied in the case of dihaloquinones. This method was used to synthesize 1,4-, 1,5- and 1,8-dialkynylquinones **36**–**38**. It should be noted that in the latter case, both triple bonds are in *peri* positions of the anthraquinone. Thus, 1,4-dialkynylanthraquinones **36a**–**d** were synthesized from appropriate 1,4-dibromide **39** (Scheme 14).[4, 49–51]

Scheme 14

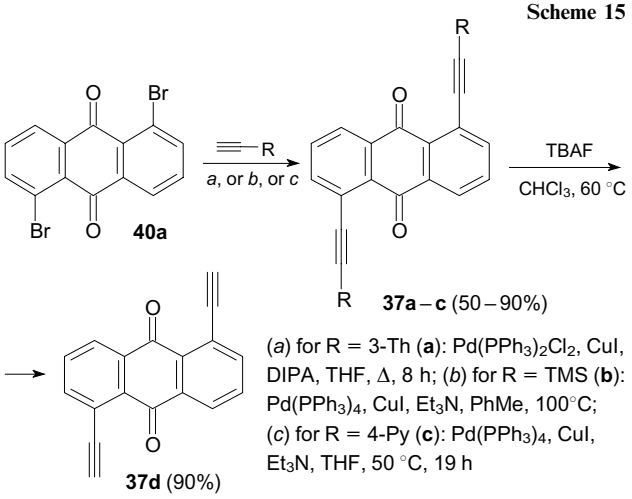


(*a*) for R = 3-Th (**a**), 4-(4-MeOC$_6$H$_4$)$_2$NC$_6$H$_4$ (**b**): Pd(PPh$_3$)$_2$Cl$_2$, CuI, DIPA, THF, Δ, 8 h; (*b*) for R = Fc (**c**): Pd(PPh$_3$)$_2$Cl$_2$, CuI, Et$_3$N, 70 °C, 3 h; (*c*) for R = 4-Py (**d**): Pd(PPh$_3$)$_4$, CuI, Et$_3$N, THF, 50 °C, 20 h; Fc is ferrocenyl

The low yields of the thiophene and aniline derivatives are apparently attributed to low CH-acidity of the starting terminal alkyne due to the $+M$ effect of the 3-thienyl and aminophenyl groups.

Under similar conditions, 1,5-dialkynyl-9,10-anthraquinones **37a**–**c** bearing different substituents in the acetylene moiety were synthesized from 1,5-dibromo-9,10-anthraquinone (**40a**) (Scheme 15).[4, 49, 52, 53] The product containing the TMS group was transformed into the corresponding terminal alkyne **37d** by the treatment with TBAF in refluxing chloroform.

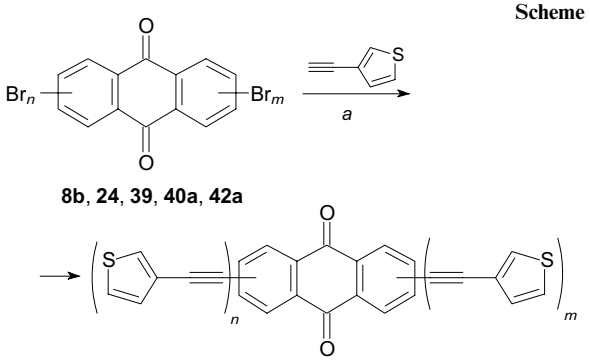
Scheme 15



(*a*) for R = 3-Th (**a**): Pd(PPh$_3$)$_2$Cl$_2$, CuI, DIPA, THF, Δ, 8 h; (*b*) for R = TMS (**b**): Pd(PPh$_3$)$_4$, CuI, Et$_3$N, PhMe, 100°C; (*c*) for R = 4-Py (**c**): Pd(PPh$_3$)$_4$, CuI, Et$_3$N, THF, 50 °C, 19 h

With the aim of searching for compounds suitable for the application in molecular electronics, methods were developed for the synthesis of thiophene-containing 1(or 2)-mono- (**22**, **26a**) and 1,4(or 1,5, or 2,6)-dialkynyl-9,10-anthraquinones (**36a**, **37a**, **41a**) from the corresponding bromides **8b**, **24**, **39**, **40a** and **42a**. These compounds can form monolayers with gold(III) or with semiconductor surfaces, which is a necessary condition for the construction of redox switches (Scheme 16).[4]

Scheme 16

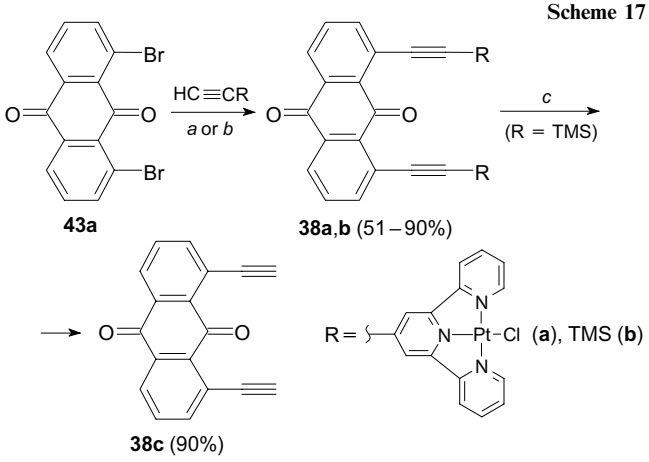


(*a*) Pd(PPh$_3$)$_2$Cl$_2$, CuI, DIPA, THF, Δ, 8 h; m = 0: n = 1 (**8b**, **22a**, **24**, **26a**), 2 (**36a**, **39**); $n = m$ = 1 (**37a**, **40a**–**42a**); substituent positions: 1 (**8b**, **22a**), 2 (**24**, **26a**), 1,4 (**36a**, **39**), 1,5 (**37a**, **40a**), 2,6 (**41a**, **42a**)

Regardless of the position and number of ethynyl groups, the target products are obtained in moderate yields, varying in a narrow range.

Under standard conditions, the Sonogashira reaction of 1,8-dibromo-9,10-anthraquinone (**43a**) gave 1,8-dialkynylquinones **38a**,**b** (Scheme 17).[52, 54] The trimethylsilyl deprotection allowed the synthesis of quinone **38c** containing two terminal acetylene groups at the 1 and 8 positions.

Scheme 17

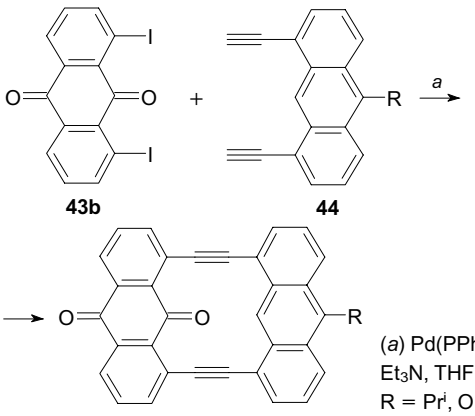


(*a*) Pd(PPh$_3$)$_4$, CuI, Et$_3$N, THF, Δ, 16 h; (*b*) Pd(PPh$_3$)$_2$Cl$_2$, CuI, Et$_3$N, PhMe, Δ, 3 h; (*c*) TBAF, CHCl$_3$, 60 °C, 3 h

The coupling of diiodoanthraquinone **43b** with diethynylanthracenes **44** provides a route to the synthesis of macrocycles **45**, in which the quinoid core is bonded *via* two rigid triple bonds to the anthracene moiety acting as a chromophore. These macrocycles were intended to explore the optical properties in the conjugated cyclic system (Scheme 18).[55, 56]

The replacement of two bromine atoms smoothly occurs even in the presence of two electron-donating methoxy groups. Thus, compound **46** was transformed into diethynylanthraquinone **47** (Scheme 19).[57]

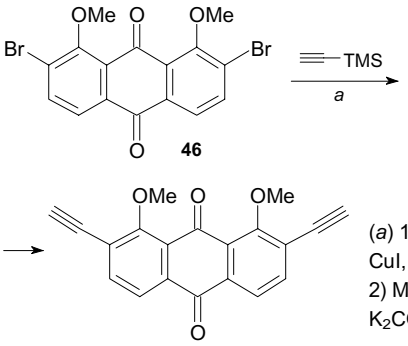
Scheme 18



45 (27 – 79%)

(*a*) $Pd(PPh_3)_4$, CuI, Et_3N, THF, Δ, 3 h; R = Pr^i, OMe, OC_8H_{17}-n

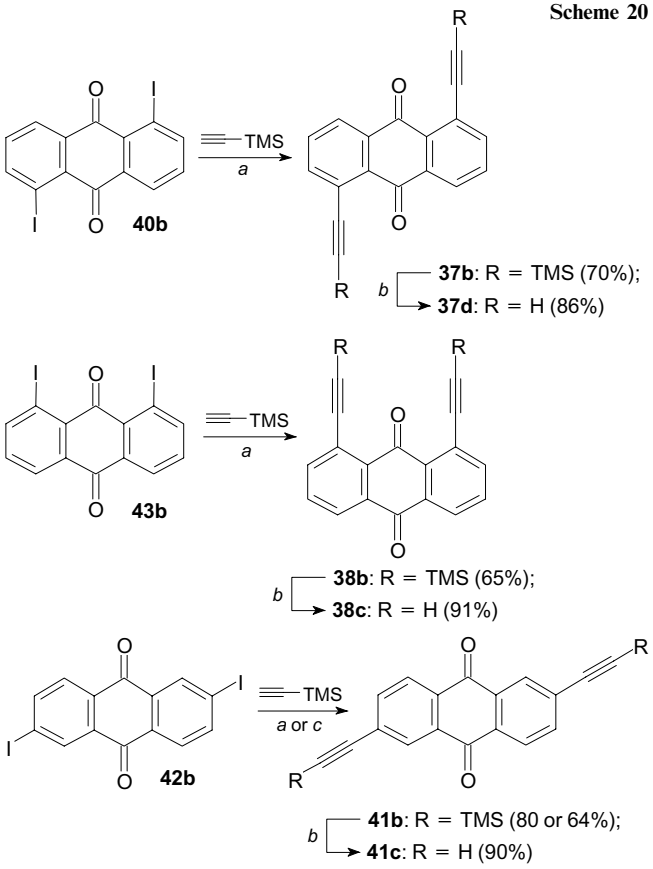
Scheme 19



47 (59% over two steps)

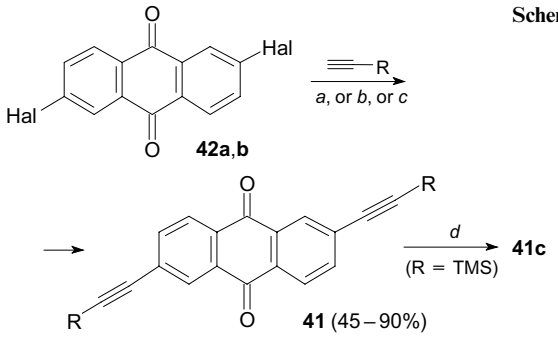
(*a*) 1) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, THF, Δ, 16 h; 2) MeOH – CH_2Cl_2 (5 : 1), K_2CO_3, 0 °C, 1 h

Scheme 20



(*a*) $Pd(PPh_3)_4$, CuI, Et_3N, PhMe, 100 °C, 3 h; (*b*) TBAF, $CHCl_3$, 60 °C, 3 h; (*c*) $Pd(PPh_3)_4$, CuI, Et_3N, THF, rt

Scheme 21



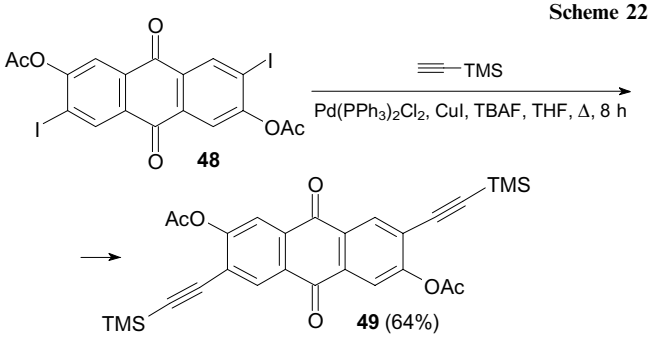
(*a*) for R = 3-Th, 3-hexyl-2-thienyl, 4-(n-C_7H_{15})C_6H_4, 4-$Bu^tSC_6H_4$, 4-$Me_2NC_6H_4$, 4-(n-C_6H_{13})$_2NC_6H_4$, 4-$AcSC_6H_4$, 3,5-$(AcS)_2C_6H_4$, CH_2OH: $Pd(PPh_3)_2Cl_2$, CuI, DIPA (Pr^i_2NH or Et_3N), THF, Δ, 8 – 24 h; (*b*) for R = TMS: $Pd(PPh_3)_4$, CuI, Et_3N, THF, rt, 3 h; (*c*) for R = Fc: $Pd(PPh_3)_4$, Et_3N, PhMe, 90 °C, 15 h; (*d*) TBAF, $CHCl_3$, 60 °C, 3 h

The positional isomers, 1,5- (**37b**), 1,8- (**38b**) and 2,6-bis[(trimethylsilyl)ethynyl)]-9,10-anthraquinones (**41b**), were synthesized by the Sonogashira reaction from diiodides **40b**, **43b** and **42b**, respectively (Scheme 20).[41, 52] The reaction of these isomers with TBAF affords anthraquinones **37d**, **38c** and **41c** containing two terminal acetylene groups in different benzene rings.

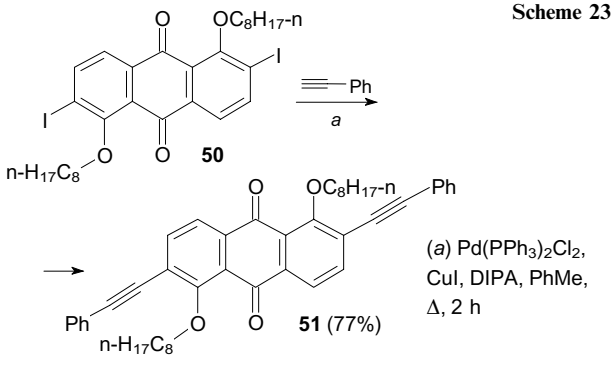
The reaction of 2,6-dibromo- (**42a**) and 2,6-diiodo-9,10-anthraquinones (**42b**) with different terminal alkynes in the presence of a Pd^{II}- or Pd^0-catalyst system gave a series of disubstituted alkynes **41** (Scheme 21).[4, 39, 41, 52, 58 – 62]

In the presence of two acetoxy groups with a moderate electron-donating ability, the reaction required TBAF as a stronger base compared to organic amines.[63] Under these conditions, the reaction of diiodide **48** afforded 2,6-diacetoxy-3,7-dialkynyl-9,10-anthraquinone (**49**) in moderate yield (Scheme 22).

Scheme 22

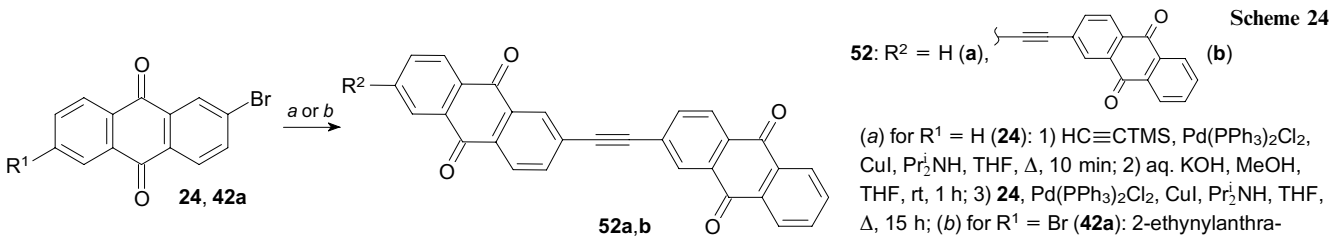


Scheme 23



(*a*) $Pd(PPh_3)_2Cl_2$, CuI, DIPA, PhMe, Δ, 2 h

Scheme 24



(*a*) for R^1 = H (**24**): 1) HC≡CTMS, $Pd(PPh_3)_2Cl_2$, CuI, Pr^i_2NH, THF, Δ, 10 min; 2) aq. KOH, MeOH, THF, rt, 1 h; 3) **24**, $Pd(PPh_3)_2Cl_2$, CuI, Pr^i_2NH, THF, Δ, 15 h; (*b*) for R^1 = Br (**42a**): 2-ethynylanthraquinone, $Pd(PPh_3)_2Cl_2$, CuI, DIPA, THF, Δ, 15 h

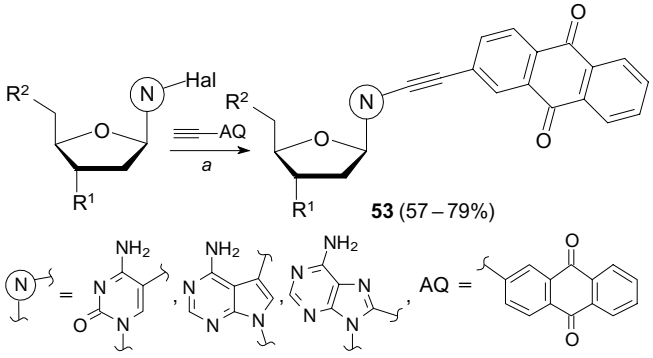
The cross-coupling of diiodo-9,10-anthraquinone **50** containing two strong electron-donating alkoxy groups with phenylacetylene gave product **51** (Scheme 23).[64]

Under certain conditions, the use of trimethylsilylacetylene as the acetylene component allows the one-pot deprotection and the repeated Sonogashira reaction (Scheme 24).[65]

This strategy provides a route to compounds containing two or three acetylene-bridged anthraquinone moieties. Dimer **52a** and trimer **52b** were obtained in a yield of 63% and 47%, respectively.

According to the published data, quinone derivatives generally act as the halogen component. In some cases, taking into account whether the substrates are easily accessible or they are easy to synthesize, the reverse method is used, in which ethynylquinones serve as the acetylene component. For example, this method was applied to introduce the 2-alkynylquinone moiety into the pharmacophore heterocycle to form conjugate **53** in moderate yield (Scheme 25).[66,67] It was shown that these transformations can be performed using not only an expensive Pd^0 complex but also the classical and cheaper complex $Pd(PPh_3)_2Cl_2$, which is insignificantly reflected in the product yield.[67]

Scheme 25

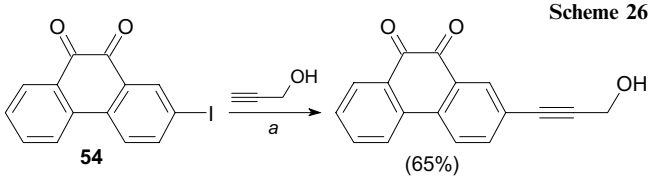


R^1 = OH, $OP(O)(OBn)_2$; R^2 = OH, ODMTr; Hal = Br, I; (*a*) $Pd(PPh_3)_2Cl_2$ or $Pd(PPh_3)_4$, CuI, DIPEA or Et_3N, DMF, 65–75 °C, 1–6 h; DMTr is 4,4′-dimethoxytrityl

The Sonogashira reaction with *ortho*-quinone was also reported.[68] The condensation of 2-iodo-9,10-phenanthrenequinone (**54**) with propargyl alcohol was accomplished in the presence of Pd/C (Scheme 26).

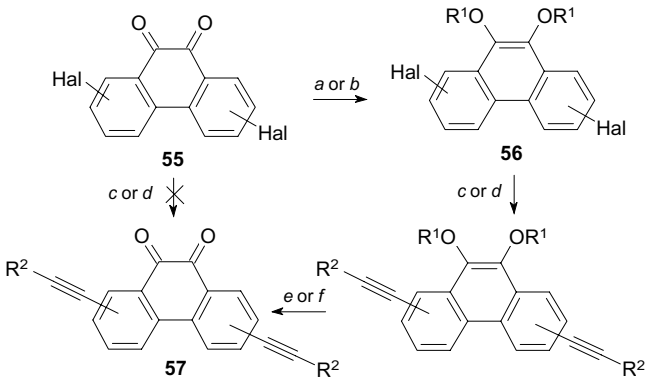
However (a rare case!), the Sonogashira reaction appeared to be inapplicable to the alkynylation of 3,6- and 2,7-dibromo(iodo)phenanthrenequinones **55** (Scheme 27).[69,70] The target product was synthesized using an alternative approach. In the first step, carbonyl groups of dihalophenanthrenequinones **55** were reduced to hydroxyl groups to form ethers **56**. The Sonogashira ethynylation, ether hydrolysis and oxidation of the OH group with CAN afforded target 3,6- and 2,7-dialkynylquinones **57**.

Scheme 26



(*a*) Pd/C, PPh_3, CuI, K_2CO_3, DME, 80 °C, 2 h; DME is dimethoxyethane

Scheme 27



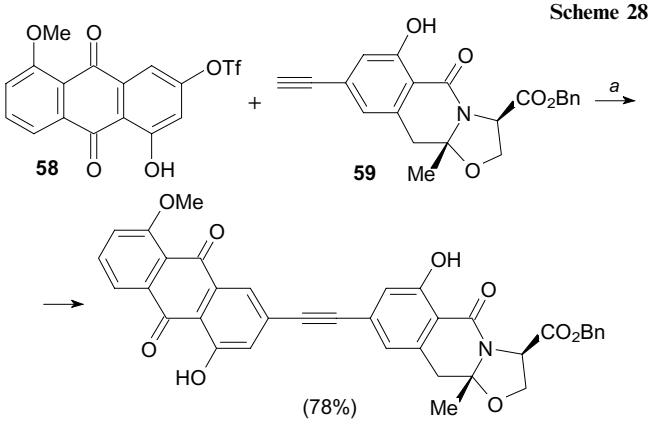
For 3,6-Br_2-isomer, R^1 = Me: (*a*) Me_2SO_4, TBAB, $Na_2S_2O_4$, NaOH, THF, H_2O, rt, 3 min (92%); (*c*) CH≡CTIPS, $Pd(PPh_3)_2Cl_2$, PPh_3, CuI, Et_3N, PhMe, 80°C, 16 h (84%); (*e*) CAN, H_2O, MeCN, CH_2Cl_2, rt, 15 min (84%); for 3,6-I_2-isomer, R^1 = TBS: (*b*) TBSCl, Zn, TMEDA, CH_2Cl_2, rt, 30 h (87%); (*d*) 4-$AcSC_6H_4C{\equiv}CH$, $Pd(PPh_3)_4$, CuI, Et_3N, THF, rt, 5 days up to 45–50 °C, 50 h (76%); (*f*) TBAF, THF, AcOH, air, rt, 10 min; R^2 = TIPS, 4-$AcSC_6H_4$; TBAB is tetra(*n*-butyl)ammonium bromide, CAN is cerium(IV) ammonium nitrate, TBS is *tert*-butyldimethylsilyl

2.2. Cross-coupling reactions of quinone triflates with alk-1-ynes

The cross-coupling reactions with terminal alkynes can be performed using not only halogen derivatives but also triflate derivatives of quinones. In the presence of even two electron-donating groups (OH and OMe) in the anthraquinone ring, the cross-coupling of triflate **58** with terminal alkyne **59** occurs smoothly because the triflate substituent is a good leaving group.[71] The reaction proceeds at room temperature and is completed within 5 min (Scheme 28).

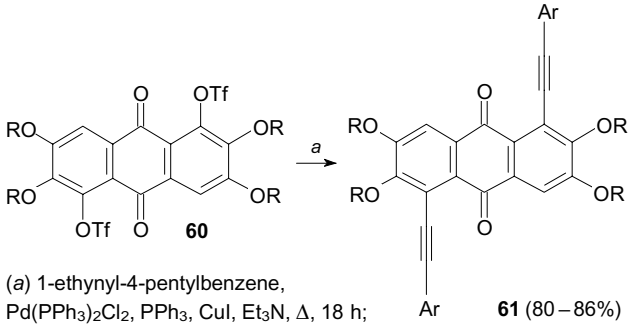
A high reactivity of triflates is convincingly confirmed by the cross-coupling of 1-ethynyl-4-n-pentylbenzene with tetraalkoxy-9,10-anthraquinones **60** containing two triflate

Scheme 28



(*a*) $Pd(OAc)_2$, PPh_3, CuCl, DIPA – DMF (1 : 5), rt, 5 min;
Tf is trifluoromethanesulfonyl (triflyl)

Scheme 29



(*a*) 1-ethynyl-4-pentylbenzene,
$Pd(PPh_3)_2Cl_2$, PPh_3, CuI, Et_3N, Δ, 18 h;
R = n-C_6H_{13}, n-C_8H_{17}, n-$C_{10}H_{21}$,
n-$C_{12}H_{25}$, $CH_2CH(Me)(CH_2)_3Pr^i$; Ar = 4-(n-C_5H_{11})C_6H_4

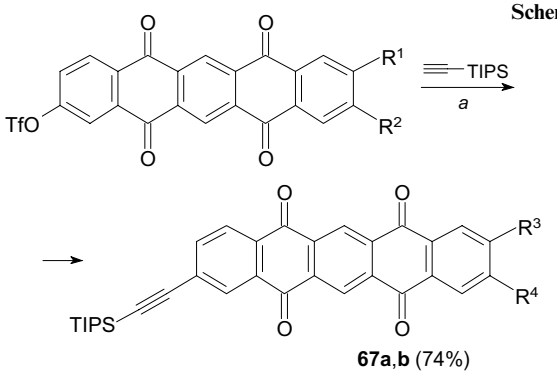
groups. In the presence of even four electron-donating alkoxy groups in the substrate, the synthesis of target 1,5-di(alkynyl)quinones **61** was quite successful (Scheme 29).[53]

The possibility of selective transformation of alkoxy groups into triflate substituents made it possible to sequentially introduce the ethynyl and butadiynyl moieties into the anthraquinone ring.[72] The cross-coupling of anthraquinone triflate **62** with alkyne **63** at 60 °C followed by the selective deacetylation (removal of the AcO group) with $(NH_4)_2CO_3$ in DMF afforded C-glycoside **64**,. Then the triflate substituent was introduced into **64** under standard conditions, and the resulting aryl triflate **65** was used in the cross-coupling with terminal butadiyne to form target diyne **66** (Scheme 30).

Unusual diquinone structures containing two acetylene moieties and two quinone rings, 2,9- and 2,10-bis(silylethynyl)pentacenediquinones **67a**,**b**, were synthesized *via* replacement of triflate groups in the corresponding substrates with triisopropylsilylacetylene (Scheme 31).[73]

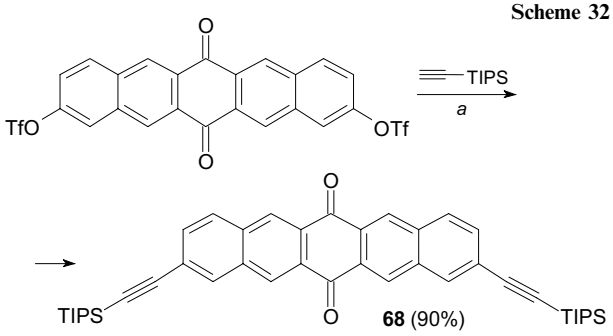
Diethynylpentacenequinone **68** was synthesized under similar conditions (Scheme 32).[73]

Scheme 31



(*a*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, THF, 22 – 67 °C, 16 h;
R^1 = OTf, R^2 = R^4 = H, R^3 = C≡CTIPS (**a**); R^1 = R^3 = H,
R^2 = OTf, R^4 = C≡CTIPS (**b**)

Scheme 32

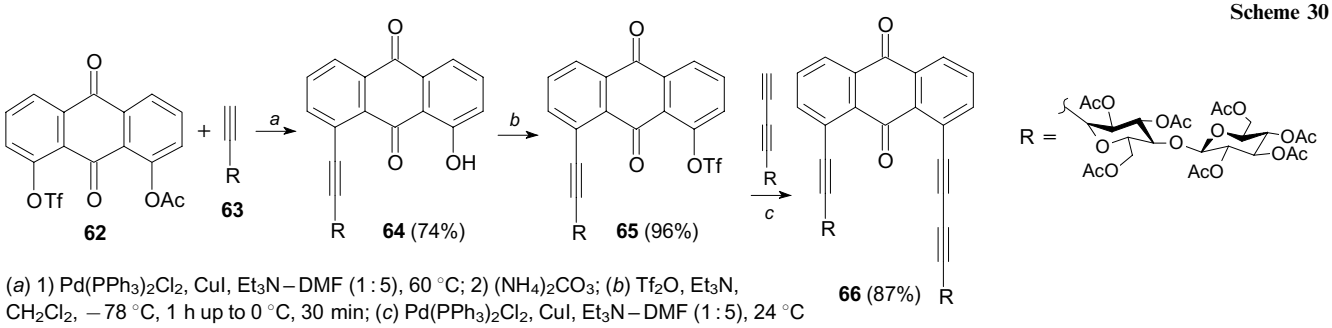


(*a*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, THF, 67 °C, 12 h

2.3. Hydrolysis – oxidation reactions of acetylene derivatives of dialkoxybenzenes, -naphthalenes, -anthracenes and -phenanthrenes

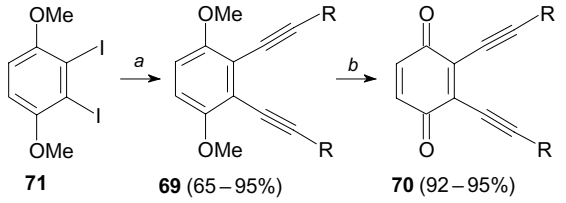
Alkynylquinones can be synthesized not only by cross-coupling reactions but also using other methods, for example, the sequential hydrolysis and oxidation of dialkyloxyarenes **69** already bearing side triple bonds. Generally, the oxidation is performed using CAN as a mild and efficient oxidant leaving the C≡C bond intact. This method was applied to prepare diethynyl derivatives of the simplest benzoquinone, compound **70**, in high yield.[5] 2,3-Bis(alkynyl)-1,4-benzoquinones **70** have attracted interest because they can be employed as molecular switches and sensing devices (Scheme 33).

Scheme 30



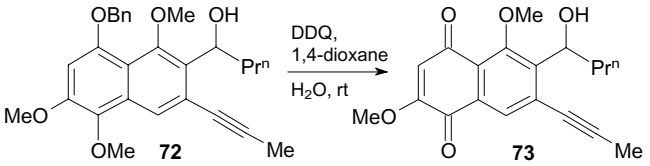
(*a*) 1) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N – DMF (1 : 5), 60 °C; 2) $(NH_4)_2CO_3$; (*b*) Tf_2O, Et_3N,
CH_2Cl_2, −78 °C, 1 h up to 0 °C, 30 min; (*c*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N – DMF (1 : 5), 24 °C

Scheme 33



(*a*) CH≡CR, $Pd(PPh_3)_4$, CuI, Et_2NH, DMF, MW (200 W), 120 °C, 15 bar, 10–20 min; (*b*) CAN, MeCN, H_2O, rt, 5–20 min; R = Bu^n, Bu^t, TMS; MW is microwave irradiation

Scheme 34



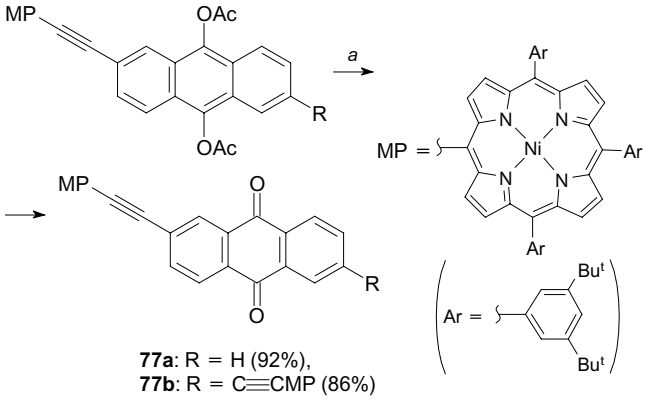
It is worth noting that the Sonogashira cross-coupling involving 2,3-diiodo-1,4-dimethoxybenzene (**71**) with terminal alkynes under standard conditions was found to be not suitable for the synthesis of intermediate dialkynylquinones **69**. The authors did not address this issue but it can be supposed that this is associated with the deactivation effect of two electron-donating alkoxy groups. This problem was tackled using microwave irradiation. The further oxidation of 1,4-dimethoxy groups with CAN was accomplished at room temperature in aqueous acetonitrile giving 2,3-dialkynyl-1,4-benzoquinones **70** in nearly quantitative yield.[5]

Other reagents, for example, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, are sometimes used as mild oxidizing agents (Scheme 34).[74] The selective hydrolysis of ethynylnaphthalene **72** with a water–dioxane solution at room temperature followed by the oxidation of the intermediate with DDQ afforded 3-alkynyl-1,4-naphthoquinone **73**.[74]

An elegant example of the selective sequential hydrolysis–oxidation of dimethoxyarenes was described by Nishinaga *et al.*,[75] who synthesized three complex macrocyclic hexadehydro[18]annulenes containing three butadiynyl bridges. These macrocycles are of interest as precursors for the synthesis of various carbon-rich polymers (Scheme 35).

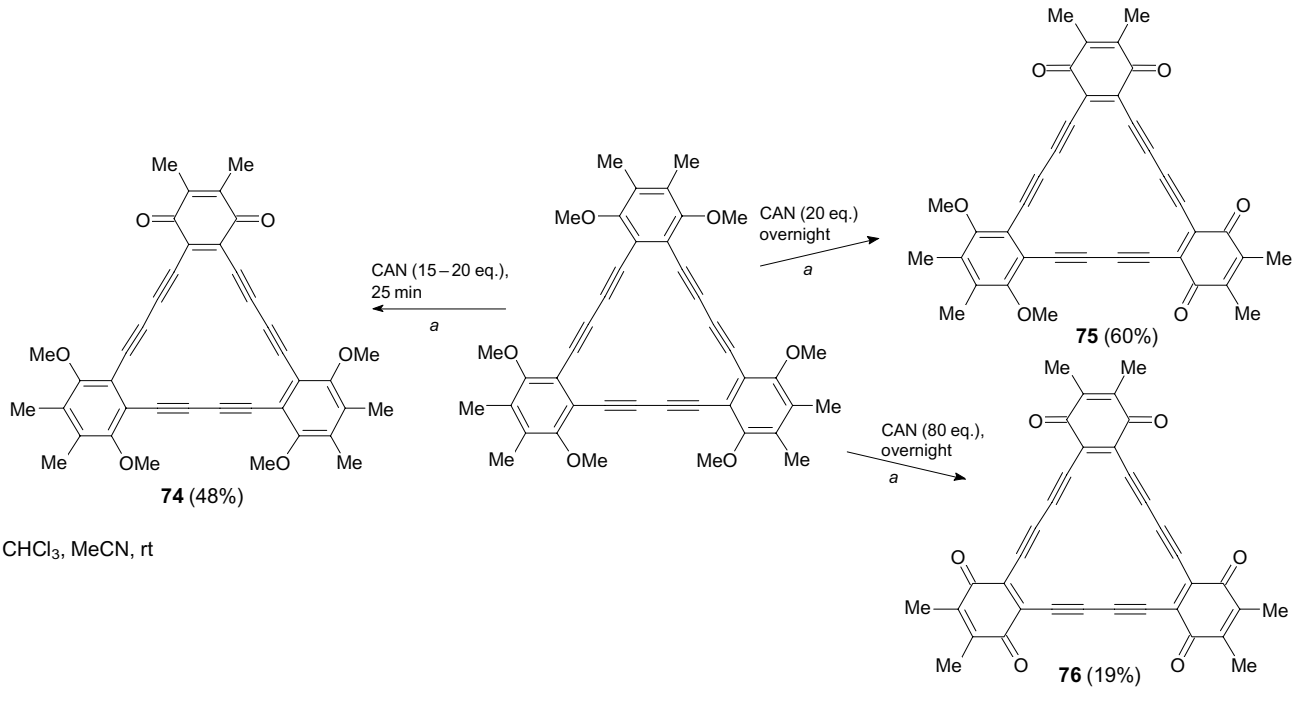
p-Dimethoxybenzene units were transformed into *p*-benzoquinone units using CAN. The selectivity was achieved by varying the amount of the oxidizing agent and the reaction time. Thus, the reaction with 15–20 equiv. of CAN in a $CHCl_3$–MeCN mixture (1 : 01, v/v) at room temperature for 0.5–1 h afforded monoquinone **74** as the major product. The synthesis of bisquinone **75** required the storage of the reagents for a longer time. The synthesis of trisquinone **76** was performed using a larger amount of CAN (80 equiv.), the reaction mixture being kept overnight at room temperature to bring the reaction to completion.[75]

Scheme 36



(*a*) KOH, EtOH, H_2O, THF, N_2, Δ, 0.5 h; MP is metalloporphyrin

Scheme 35

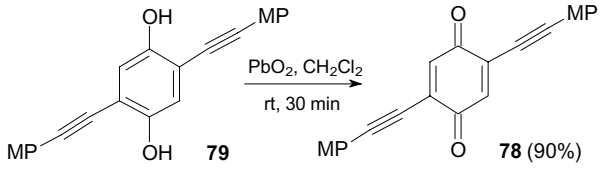


(*a*) $CHCl_3$, MeCN, rt

In some cases, acetoxy rather than alkoxy groups are hydrolyzed; for example, in the synthesis of the alkynylquinone-bridged porphyrin-containing monomer (**77a**) and dimer (**77b**). These compounds, which are promising for the use in electronics, were prepared by Chinese researchers [76] in 2013 (Scheme 36). The hydrolysis was accomplished by refluxing the substrate in an aqueous ethanol solution of KOH.

This research group [77] also synthesized benzoquinone **78** bearing two alkynylporphyrin moieties using another mild oxidizing agent, lead(IV) oxide, which leaves the triple bond intact (Scheme 37). Substrate **79** was oxidized in dichloromethane at room temperature.

Scheme 37



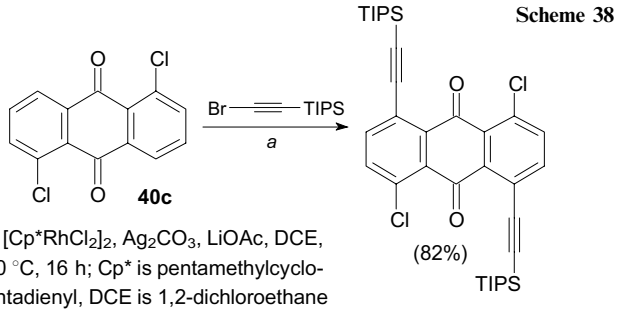
2.4. Miscellaneous methods

This Section covers unique methods, which are not versatile but demonstrate the diversity of approaches to the synthesis of alkynylquinones.

In addition to the conventional method for the synthesis of alkynylquinones by the replacement of an iodine (bromine) atom or a triflate group by acetylene moieties, Tan *et al.*[78] developed a fundamentally new type of cross-coupling. In this reaction, 1-bromoalkyne (C(sp)−Br bond) acts as the halogen component, while an arene with high CH-acidity (C(sp^2)−H bond) rather than alk-1-yne (C(sp)−H bond) serves as the partner. It was found that the Rh-catalyzed cross-coupling can be performed using substrates bearing electron-withdrawing substituents, such as carbonyl, ester and other groups, and also a halogen atom (*e.g.*, quinone **40c** in Scheme 38).

This is the first example of the alkynylation of electron-deficient compounds under relatively mild Rh-catalysis conditions (at 45–70 °C for esters and at 25–90 °C for ketones). Mechanistic investigations demonstrated that the reaction involves the electrophilic substitution through the C−H bond activation.

Scheme 38



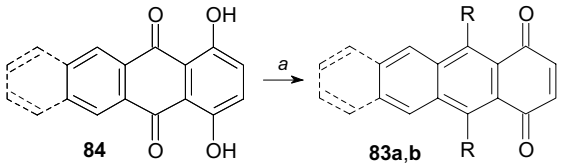
(*a*) $[Cp^*RhCl_2]_2$, Ag_2CO_3, LiOAc, DCE, 100 °C, 16 h; Cp* is pentamethylcyclopentadienyl, DCE is 1,2-dichloroethane

2-Alkynyl-1,4-anthraquinones **80** were synthesized by the hydrolysis–oxidation reactions followed by cycloaddition (Scheme 39).[79, 80] The hydrolysis and oxidation of methoxy groups in disubstituted alkynylarenes **81** with CAN in aqueous acetonitrile afforded ethynylbenzoquinones **82**, which underwent the regioselective cycloaddition to enolate generated from homophthalic anhydride.

Carey *et al.*[81] reported an unusual method for the synthesis of rigid dialkynylanthracenedione **83a** (67% yield) and -tetracenedione **83b** (56%) (Scheme 40). Carbonyl groups in substrates **84** were transformed into alkynyl groups by the treatment with [(triisopropylsilyl)ethynyl]-magnesium chloride. The intermediate diols were treated *in situ* with hydrochloric acid, and their dehydration afforded dialkynylanthraquinone **83a** and -tetracenedione **83b** as the target products.

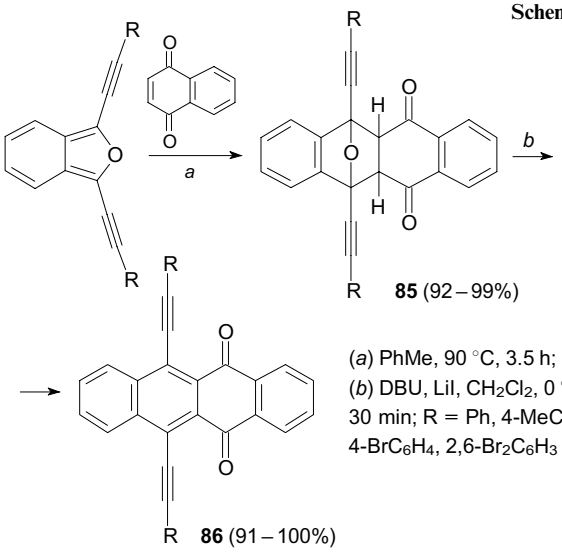
Kitamura *et al.*[82] described a fundamentally different route to ethynyltetracenequinones. The authors utilized the specific ability of quinones to be involved in the Diels–Alder reaction as a dienophile. The synthesis was based on the [4 + 2]-cycloaddition of 1,3-diethynylbenzofurans to 1,4-naphthoquinone followed by the aromatization (Scheme 41). The treatment of adducts **85** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and LiI caused the aromati-

Scheme 40



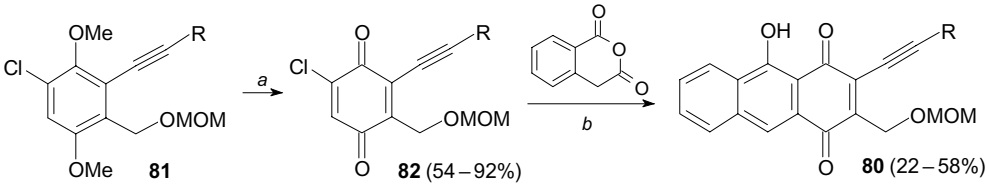
(*a*) 1) RMgCl, PhMe, 80 °C, 24–48 h; 2) HCl, 0 °C;
R = TIPS

Scheme 41



(*a*) PhMe, 90 °C, 3.5 h;
(*b*) DBU, LiI, CH_2Cl_2, 0 °C, 30 min; R = Ph, 4-MeC_6H_4, 4-BrC_6H_4, 2,6-$Br_2C_6H_3$

Scheme 39



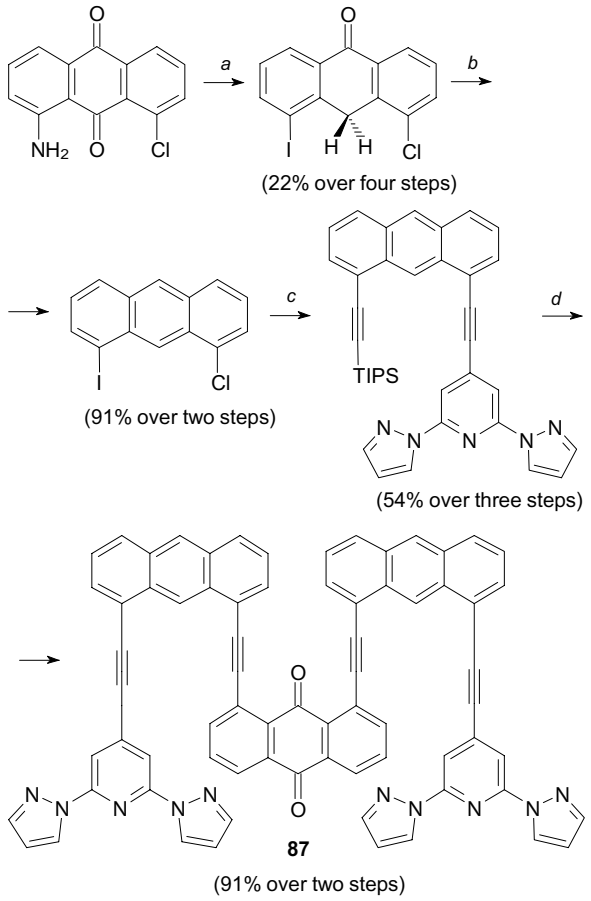
(*a*) CAN, H_2O, MeCN, 0 °C, 20 min; (*b*) LDA, THF, rt, 5 min;
R = TMS, TES, TBS, TIPS;
MOM is methoxymethyl,
LDA is lithium diisopropylamide,
TES is triethylsilyl

zation giving tetracenequinones **86** in yields from 91% to quantitative.[82]

Šalitroš *et al.*[83] constructed original molecule **87** consisting of the anthraquinone skeleton, two pyrazolylpyridine moieties and two anthracene moieties (Scheme 42). The synthesis involved eight steps and gave the product in an 8% overall yield. It should be noted that four of the eight steps are based on the Sonogashira reaction, which reiterates once again its preparative significance. The synthetic assembly of this compound can be compared with a two-dimensional puzzle, which requires the precise spatial arrangement of two iodine atoms and, correspondingly, two terminal hydrogen atoms of ethynyl groups of two ethynylanthracene molecules. The specific structural feature of these ligands is the face-to-face arrangement of the peripheral anthracene moieties, which is a necessary condition for the occurrence of [4 + 4]-photocycloaddition. The authors believed that new types of organic compounds bearing two pyrazolylpyridine groups and moieties of the photoisomerized multianthracene skeleton are promising bis(tridentate) ligands that can be coordinated to transition metal ions and form various oligomeric clusters.

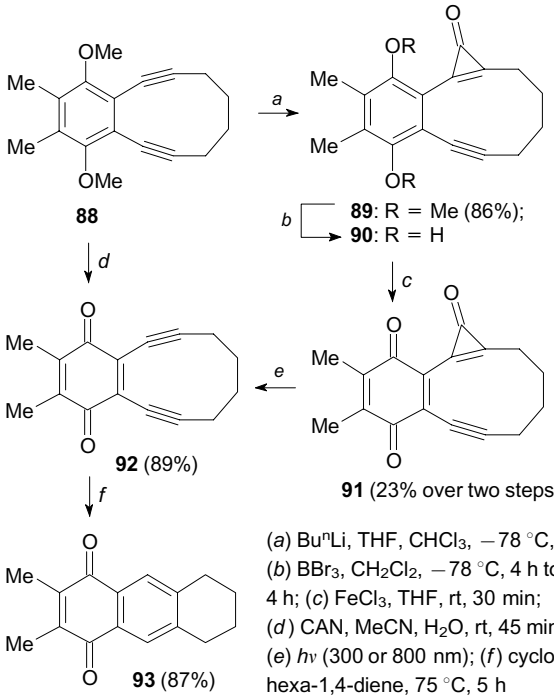
In some cases, apart from conventional chemical methods, photochemical reactions are used for the synthesis of

Scheme 42



(*a*) 1) $NaNO_2$, H_2SO_4, 0 °C, 3 h; 2) KI, 0 °C, 3 h; 3) $NaBH_4$, MeOH, rt, 4 h; 4) HCl, 60 °C, 1 h; (*b*) 1) $NaBH_4$, MeOH, rt, 8 h; 2) HCl, 60 °C, 1 h; (*c*) 1) CH≡CTIPS, $Pd(PPh_3)_4$, CuI, DIPA, rt, 3 h; 2) MgC≡CTMS, PPh_3, $Ni(acac)_2$, THF, 60 °C, overnight; 3) 4-iodo-2,6-di(1*H*-pyrazol-1-yl)pyridine, $Pd(PPh_3)_4$, CuI, Cs_2CO_3, DIPA, THF, rt, 24 h; (*d*) 1) TBAF, THF, rt, 2 h; 2) 1,8-diiodo-9,10-anthraquinone (**43b**), $Pd(PPh_3)_4$, CuI, DIPA, THF, 80 °C, 24 h; acac is acetylacetonate

Scheme 43



(*a*) Bu^nLi, THF, $CHCl_3$, −78 °C, 2 h; (*b*) BBr_3, CH_2Cl_2, −78 °C, 4 h to rt, 4 h; (*c*) $FeCl_3$, THF, rt, 30 min; (*d*) CAN, MeCN, H_2O, rt, 45 min; (*e*) *hν* (300 or 800 nm); (*f*) cyclohexa-1,4-diene, 75 °C, 5 h

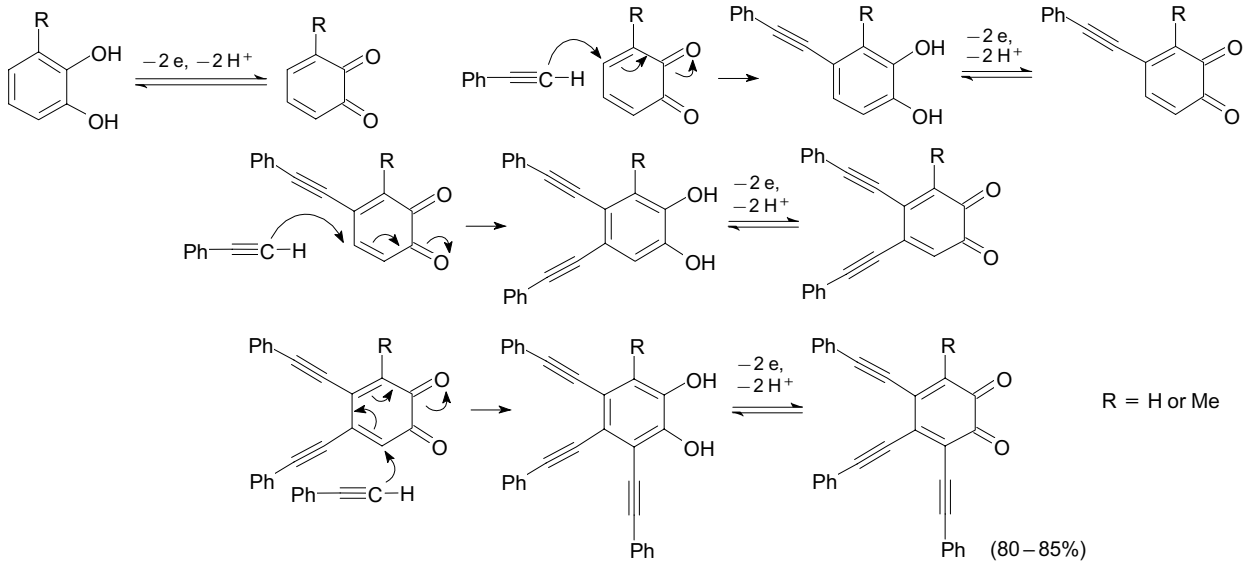
alkynylquinones. Poloukhtine and Popik[84] addressed the advantages and drawbacks of the chemical and photochemical transformations of highly reactive benzoquinonediynes.

The reaction of enediyne **88** with n-butyllithium in a mixture of $CHCl_3$ and THF at −78 °C followed by the treatment with concentrated HCl afforded dimethoxycyclopropenone **89** (Scheme 43). A solution of BBr_3 in CH_2Cl_2 was added to a solution of ether **89** in CH_2Cl_2 at −78 °C. The treatment of hydroquinone **90** with anhydrous $FeCl_3$ gave target cyclopropenone **91**. Diynyl-1,4-benzoquinone **92** was synthesized by the oxidation of methoxy groups in starting diyne **88** with CAN in acetonitrile.

An alternative photochemical route to diyne **92** involved the photolysis of cyclopropenone **91** in a methanol solution. The isolated annulated octadiynyl-1,4-benzoquinone **92** was identical to the product prepared by the chemical method. Tetrahydro-1,4-anthraquinone **93** was produced by heating compound **92** in a benzene–cyclohexa-1,4-diene mixture (4 : 1). Poloukhtine and Popik[84] showed that the two-photon photochemical reaction has advantages over purely chemical transformations because it is not accompanied by side processes.

To conclude this Section, let us consider the study,[85] in which an attractive method was proposed for the synthesis of trialkynyl-*ortho*-quinones. This procedure combines the electrochemical oxidation and chemical reduction of diols in the presence of phenylacetylene under mild conditions (Scheme 44). The electrolysis was performed in phosphate buffer (pH 7.5, the concentration was 0.2 mol L^{-1}) at a potential of 0.3 V (with respect to Ag/AgCl|3 M KCl) in an undivided cell in the absence of an expensive palladium catalyst and a copper salt as the co-catalyst. The reaction occurs with high product yields. The mechanism of the transformation involves the sequential alternation of electrochemical and chemical oxidation of diols in the presence of phenylacetylene. The eight-electron process was confirmed by potential coulometry and spectroscopy.[85] To the best of our knowledge, the electrosynthesis based on the

Scheme 44



Sonogashira-type reaction was accomplished for the first time.

Briefly analyzing the above methods for the synthesis of alkynylquinones, the following conclusions can be drawn. The Pd–Cu-catalyzed cross-coupling of terminal alkynes with the corresponding halides is the most commonly used and attractive procedure for the synthesis of acetylene derivatives of benzo-, naphtho-, anthra- and phenanthreneoquinones. The above examples demonstrate that the Sonogashira reaction has almost no limitations with respect to the structure of substituents both in the acetylene and halogen components. This reaction occurs in a wide temperature range (from room temperature to 100 °C) in the presence of different catalysts and, in some cases, in the absence of catalysts, with organic or inorganic bases. The yields of the target products vary from moderate to high.

These advantages are characteristic also of an alternative cross-coupling of terminal acetylenes with quinone triflates. The choice of a particular method is dictated only by the availability of the corresponding halides or triflates as the substrates.

The third approach, based on a combination of the hydrolysis and oxidation of acetylene derivatives of dialkoxybenzenes, -naphthalenes, -anthracenes and -phenanthrenes, is an essence the Sonogashira cross-coupling involving aryl halides as the key process. In this case, the final oxidation step easily occurs with mild reagents, most often with cerium(IV) ammonium nitrate.

Methods for the synthesis of alkynylquinones with a complex structure, which are not of general importance, are described in Sections 3 and 4 because, in our opinion, it is logical and appropriate to consider them in terms of the discussion of chemical properties of such compounds.

3. Chemical properties of quinones with a triple bond in the side chain

In this review, particular attention is given to the chemical properties of alkynylquinones because the general and specific features of their reactivity define the fundamental significance of this class of compounds and prospects of their applications.

Heterocyclization reactions hold a prominent place in a series of numerous transformations of alkynylquinones.[15]

3.1. Heterocyclization of functionalized vicinal alkynylquinones

The general features of regio- and stereocontrolled cyclization reactions are particularly important for the construction of complex molecules. A concise set of guidelines for the rational design of cyclization reactions known as Baldwin's rules[16] remains one of the most useful tools in the arsenal of organic chemists. In recent years, a need was perceived to critically revise and partially improve these rules, in particular regarding the cyclization of alkynes. This gap was addressed in the review,[15] in which new empirical data, including geometric and orbital parameters of the molecules and stereoelectronic effects, were taken into account. The systematic analysis allowed the authors to make important improvements and general statements, in particular for the cyclization of alkynyl-9,10-anthraquinones.

3.1.1. N-Heterocyclization

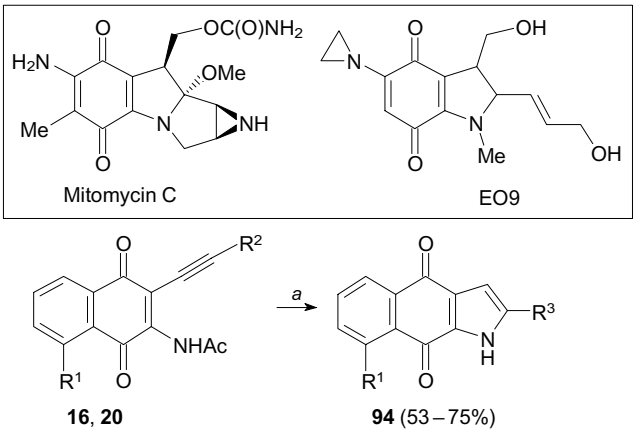
It seems appropriate to consider first the cyclization of vicinal-substituted alkynylquinones involving the simplest functional groups (NH_2, OH, SH), which undergo 5-*endo-dig* cyclization to form fused benzo-, naphtho- and anthraquinonepyrroles and related furan and thiophene derivatives. These annulated quinones are suitable precursors of biologically active compounds, including related natural products.

Russian[30] and Japanese researchers[86] have focused on indole-4,9-diones as promising structures for the design of efficient anticancer agents, analogues of the known drugs mitomycin C and EO9.

Shvartsberg and co-workers[30,31] developed a method for the synthesis of benzo[*f*]indole-4,9-diones **94** *via* the cyclization of 3-acetylamino-2-alkynyl-1,4-naphthoquinones **16** (R^1 = H) and **20** (R^1 = NHAc) in the presence of potassium carbonate in refluxing acetonitrile (Scheme 45).

The intramolecular cyclization of amidoacetylenes **16** and **20** occurs under relatively mild conditions in the presence of an equimolar amount of anhydrous K_2CO_3 in

Scheme 45

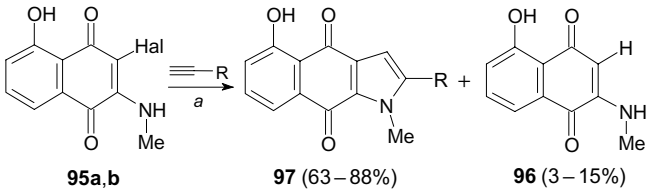


(*a*) K_2CO_3, MeCN, 80 °C, 15–40 min; R^1 = H, NHAc; R^2 = R^3 = Ph, CH_2OTHP; R^2 = CMe_2OH, R^3 = C(Me)=CH_2; R^2 = C(cyclo-C_3H_5)MeOH, R^3 = C(cyclo-C_3H_5)=CH_2; R^2 is 1-hydroxycyclohexyl, R^3 is cyclohex-1-enyl

MeCN at 80 °C. This reaction is accompanied by the deacylation to form 2-substituted benzo[*f*]indole-4,9-diones **94**.

Japanese researchers[86] used a similar approach (Scheme 46).

Scheme 46



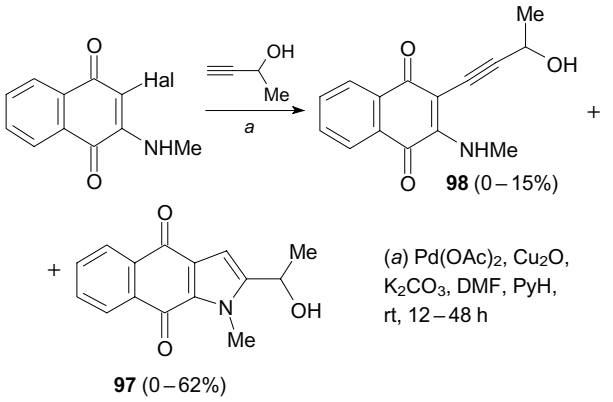
(*a*) $Pd(OAc)_2$, Cu_2O, K_2CO_3, DMF, 80 °C, 1 h; Hal = Br (**a**), I (**b**); R = Ph, CH(OH)Me, CH_2Bn

The reaction of 2-halo-1,4-naphthoquinones **95a**,**b** with terminal alkynes followed by the intramolecular cyclization was performed in a one-pot fashion.[86] As expected, the iodo derivative was significantly more reactive than the bromide although both reactions were accompanied by the formation of by-products through the dehalogenation of the starting haloquinones. The best outcome was achieved in the reaction in pyridine at 80 °C in the presence of Cu_2O, which afforded deiodinated product **96** in 3% yield and target product **97** in 88% yield.[86]

Assuming that the formation of dehalogenation products is associated with high temperature, the authors attempted to prevent the side process by decreasing the temperature to room temperature (Scheme 47).[87] Actually, the formation of dehalogenation products was avoided at room temperature; however, under these conditions, intermediate acetylene alcohol **98** remained unreacted. When attempting to optimize the reaction conditions, it was found that the target products were obtained in higher yields using the bromide to alkyne ratio of 1 : 2 and the pyridine to Cu_2O ratio of 50 : 1.[87]

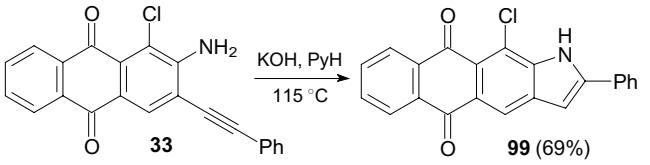
The same strategy involving the base-catalyzed cyclization of *vic*-amino(phenylethynyl)-9,10-anthraquinone **33** was applied in the synthesis of linearly annulated naph-

Scheme 47



(*a*) $Pd(OAc)_2$, Cu_2O, K_2CO_3, DMF, PyH, rt, 12–48 h

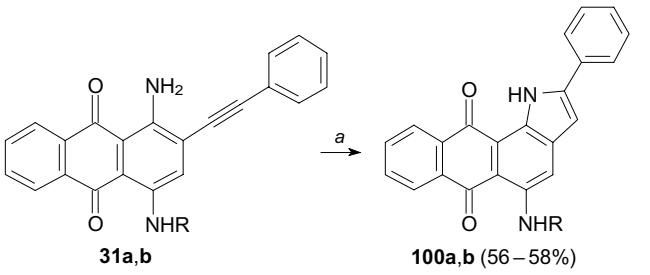
Scheme 48



thoindole **99** (Scheme 48).[47] The heterocyclization of 2-amino-1-chloro-3-phenylethynyl-9,10-anthraquinone (**33**) successfully occurred in the presence of KOH in refluxing pyridine.

Indolonaphthoquinones can be synthesized using CuI–DMF as the catalytic system. Thus, angularly fused naphthoindoles **100a**,**b** were synthesized by the cyclization of *vic*-amino(acetylenyl)-9,10-anthraquinones **31a**,**b** in the presence of CuI (Scheme 49).[44]

Scheme 49

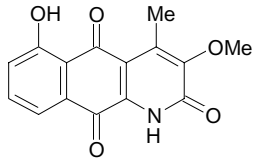


(*a*) CuI, DMF, 155 °C, 2–3 h; R = 3-MeC_6H_4 (**a**), 4-MeC_6H_4 (**b**)

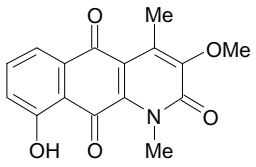
It is worth noting that these data allow the rejection of the conclusion drawn by Shvartsberg *et al.*,[20] who, referring to their own results, claimed that the cyclization of *vic*-amino(ethynyl)-9,10-anthraquinones occurs in the presence of copper acetylide or copper powder (but not copper(I) halides) in pyridine or DMF at 80–153 °C. Apparently, it is more relevant to say that the cyclization of *vic*-amino(ethynyl)-9,10-anthraquinones does not occur under these conditions in the presence of Cu^I halides with a range of compounds used by the authors.

Some natural 1-aza-9,10-anthraquinones exhibit anticancer, antifungal and antibacterial activities.[88] The reaction of alkynylquinones containing the ketoacetylene group as the acetylene substituent can be applied to form fused

Structures of marcanines



Marcanine D

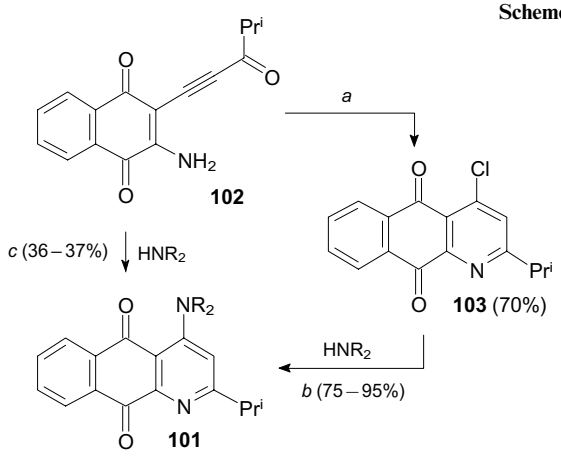


Marcanine E

six-membered heterocycles, benzo[*g*]quinoline-5,10-diones, which are analogues of natural marcanines D and E.[29,89]

An attempt to synthesize benzo[*g*]quinoline-5,10-diones **101** by the direct amination of the starting ketone **102** resulted in the formation of the target products in low yield (Scheme 50).[29] The authors reasonably assumed that this is associated with steric hindrance and(or) with high nucleophilicity (basicity) of the reaction medium. These problems were addressed by applying an alternative two-step method. In the pre-synthesized 4-chlorobenzoquinoline-5,10-dione **103a**, the chlorine atom can easily be replaced by the dialkylamino group. 4-Chloro-1-aza-9,10-anthraquinone **103a** is generated from acetylene **102** through the heterocyclization in the presence of HCl at room temperature. The amination of chloride **103a** was accomplished in the presence of an excess of amine at 20 °C.[29]

Scheme 50



(*a*) HCl, $CHCl_3$, rt, 7 h; (*b*) dioxane, rt, 1–14 h; (*c*) dioxane, rt, 0.5–12 h; R–R = $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$; R = Et

The reactivity of haloquinones towards nucleophilic agents significantly depends on the nature of the halogen atom. For example, the chlorine atom is easily replaced with such nucleophiles as amines and phenols. Meanwhile, bromides and iodides are reactive in the Sonogashira reaction as opposed to related chlorides.[31]

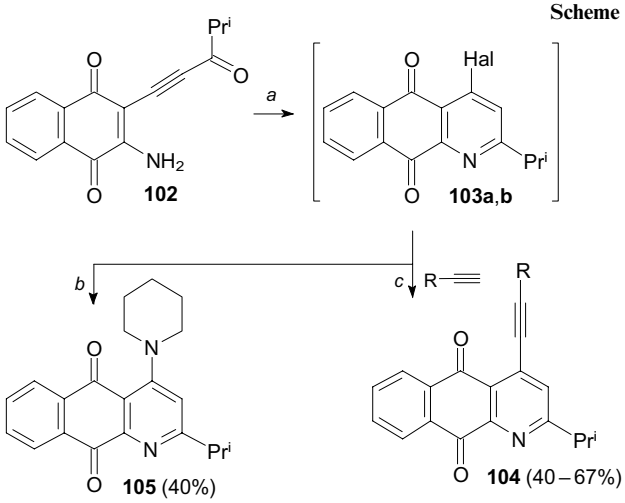
This fact was used in the synthesis of alkynyl-substituted benzo[g]quinoline-5,10-diones **104** by the alkynylation of 4-bromo derivative **103b**; the reaction with chloride **103a** afforded 4-piperidinobenzo[g]quinoline-5,10-dione **105** (Scheme 51).[31,90]

Another route to heterocycles fused to the quinone core is based on the cyclization of vicinal diazonium salts with alkynyl-9,10-anthraquinones.[44–46]

The construction of biohybrid molecules combining two or more pharmacophore groups is often applied to design new synthetic biologically active compounds. For example, annulated 9,10-anthraquinones can intercalate into the DNA helix.[18]

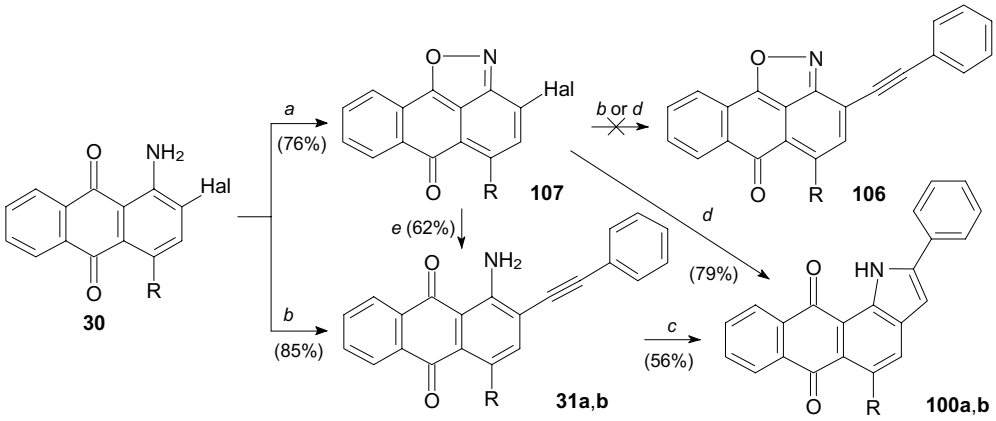
A facile one-pot three-step transformation of diazonium salts of 2-alkynyl-9,10-anthraquinones[44] afforded hybrid molecules combining two pharmacophore moieties, such as 9,10-anthraquinone and azole.[91,92] An attempt to synthesize bioconjugates **106** containing three pharmacophore

Scheme 51



(*a*) HBr or HCl, dioxane or $CHCl_3$, rt, 7–9 h; (*b*) piperidine, dioxane, rt, 30 min; (*c*) $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, 45–50 °C, 40–100 min; Hal = Cl (**a**), Br (**b**); R = CMe_2OH, Ph, CH_2OTHP, $(CH_2)_2OH$, 1-hydroxycyclohexyl

Scheme 52



(*a*) 1) $NaNO_2$, H_2SO_4, AcOH, 5 °C, 30 min; 2) NaN_3, H_2O, rt, 1 h; (*b*) CH≡CPh, $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, PyH, 55°C, 4 h; (*c*) CuI, DMF, Δ, 2 h; (*d*) CuC≡CPh, PyH, Δ, 6 h; (*e*) CH≡CPh, $Pd(PPh_3)_2Cl_2$, PPh_3, CuI, Et_3N, PhH, 45–50 °C, 9.5 h; Hal = Br, I; R = 3-MeC_6H_4NH (**a**), 4-MeC_6H_4NH (**b**)

moieties, such as the ethynyl substituent, the anthraquinone core and the annulated isoxazole ring, by means of the Sonogashira or Castro reaction failed. However, when analyzing the reasons for this failure, an unusual cascade reaction was discovered, which involved the sequential ring opening, cross-coupling and recyclization (Scheme 52).[44–46]

Under the standard Castro reaction conditions, the reaction of 3-iodoisoxazoles **107** (Hal = I) with copper phenylacetylide in refluxing pyridine did not give target anthra[1,9-*cd*]isoxazoles. The reaction produced naphtho[2,3-*g*]indole-6,11-diones **100a**,**b**. This unexpected transformation can be divided into three steps: the Cu-promoted reductive isoxazole ring opening, the cross-coupling of the resulting *vic*-amino iodide with copper acetylide and the nucleophilic addition of the NH_2 group at the C–C bond of aminoalkynes **31a**,**b** in the final step.

To achieve the stated goal, namely to synthesize 3-substituted ethynylanthra[1,9-*cd*]isoxazoles **106**, an alternative approach was applied involving anthraquinone azides **108**.[45] The diazotization of amino-9,10-anthraquinones **109** with a solution of nitrosylsulfuric acid in acetic acid afforded diazonium salts **110**, which reacted with NaN_3 to give azido(alkynyl)anthraquinones **108**. The latter compounds were transformed into 3-ethynyl-6*H*-6-oxoanthra[1,9-*cd*]isoxazoles **106** through the thermal 5-*exo*-*dig* cyclization at 110 °C (Scheme 53).

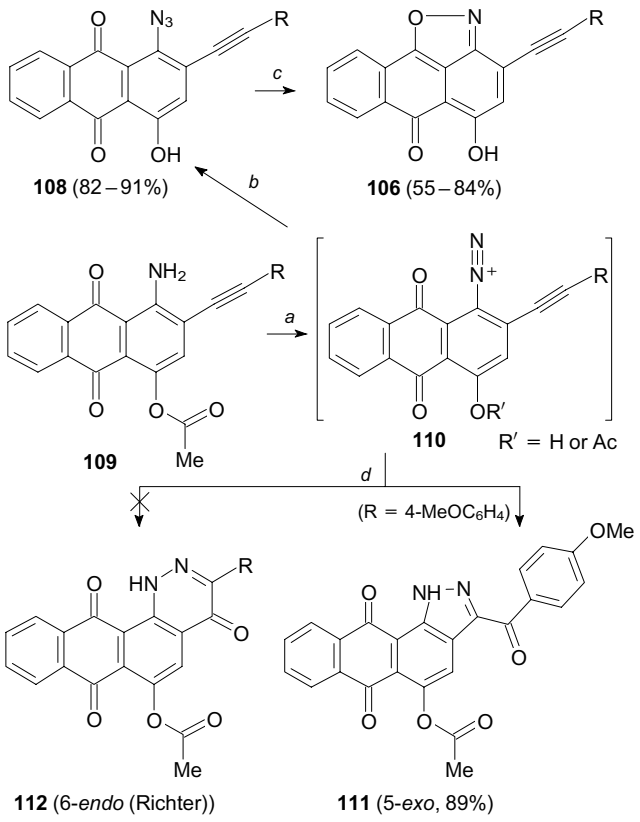
As opposed to substrates containing electron-withdrawing substituents, the cyclization of alkyne **109** bearing the *p*-methoxyphenyl group involved the triple bond to form naphthoisoxazoledione **111**. It is worth noting that of the two possible alternative pathways for the formation of 5-*exo*-*dig* and 6-*endo*-*dig* products, only the former pathway takes place, whereas the conventional Richter synthesis occurs only through the 6-*endo*-*dig* cyclization giving compound **112**.[93]

Such fused systems as naphthoindazoles and naphthocinnolines can be synthesized based on triazenes, which are analogues of diazonium salts in the latent form.[43] Thus, the heterocyclization of *vic*-(acetylenyl)triazene-9,10-anthraquinone **113**, which was generated in three steps from the appropriate amino derivative (Scheme 54), occurs *via* two pathways depending on the reaction conditions. The reaction of ethynyltriazene **113** with CuCl in 1,2-dichloroethane produced annulated isoindazole **114**, while the heating of this compound in *o*-dichlorobenzene (DCB) at 200 °C gave cinnoline **115** containing the six-membered diazine ring. Both products readily undergo ethynylation at the carbonyl carbon atoms. For example, dialkynyldiazatetracene **116** was synthesized from cinnoline **115** (Scheme 55).

3.1.2. O-Heterocyclization

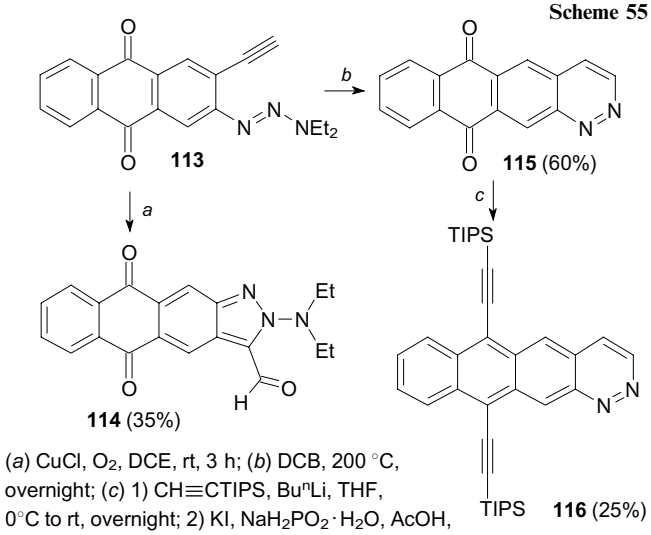
Like nitrogen analogues, vicinal oxygen-containing nucleophilic groups of alkynylquinones also easily undergo intramolecular cyclization. Hayashi *et al.*[63] described the double heterocyclization of 2,6-diacetoxy-3,7-dialkynyl-9,10-anthraquinone **49** (Scheme 56). When treated with TBAF, trimethylsilyl derivative **49** undergoes desilylation followed by the cyclization to anthradifuran-5,11-dione **117**.

Scheme 53



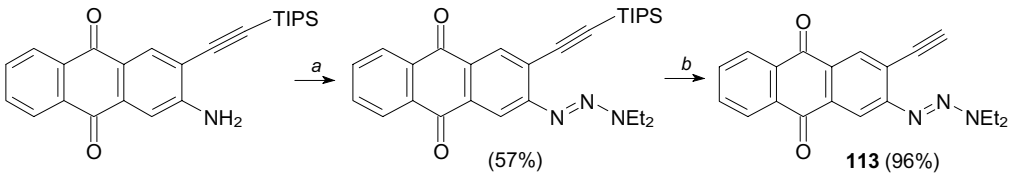
(*a*) $NaNO_2$, H_2SO_4, AcOH, rt, 0.5–2 h; (*b*) NaN_3, H_2O, rt, 30 min; (*c*) PhMe, Δ, 3–40 min; (*d*) H_2O, 70°C, 2 h; R = H, Ph, 4-$O_2NC_6H_4$, 4-BrC_6H_4, 4-$MeOC_6H_4$,isoquinolin-1-yl

Scheme 55



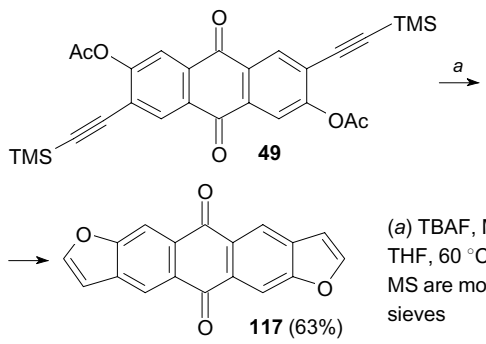
(*a*) CuCl, O_2, DCE, rt, 3 h; (*b*) DCB, 200 °C, overnight; (*c*) 1) CH≡CTIPS, Bu^nLi, THF, 0°C to rt, overnight; 2) KI, $NaH_2PO_2 \cdot H_2O$, AcOH, rt, overnight

Scheme 54



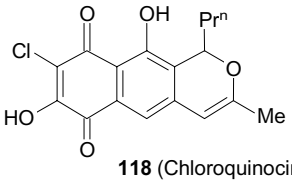
(*a*) 1) Bu^tONO, $BF_3 \cdot Et_2O$, THF, −20 °C, 30 min; 2) Et_2NH, K_2CO_3, DMF, 0 °C, 1.5 h; (*b*) TBAF, THF, MeOH, rt, 10 min

Scheme 56



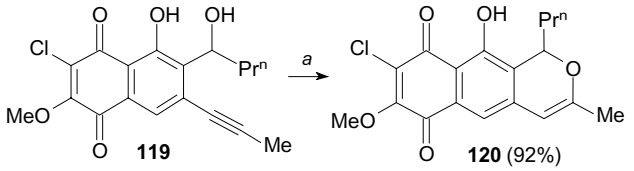
Shimbashi and Nishiyama [74] synthesized natural chloroquinocin **118**, the efficient antimicrobial agent against Gram-positive bacteria, using the cyclization of alkynylnaphthoquinone involving the side-chain hydroxyl group.

Structure 118



Acetylene alcohol **119** readily cyclized to pyranoquinone **120**. in the presence of $Pd(MeCN)_2Cl_2$. The authors believed that the simple synthetic approach to this unique pyranonaphthoquinone offers great opportunities for the synthesis of new therapeutic agents based on this compound (Scheme 57).

Scheme 57



(*a*) $Pd(MeCN)_2Cl_2$, CH_2Cl_2

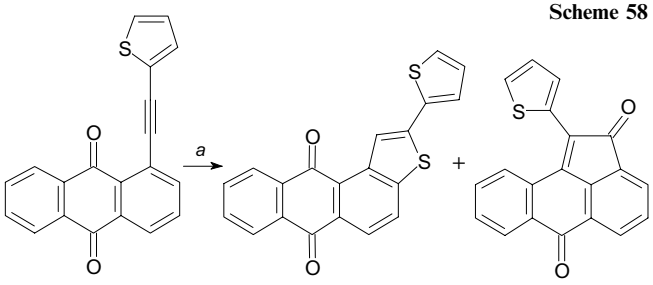
3.1.3. S-Heterocyclization

Methods for the synthesis of quinones annulated to S-containing heterocycles have attracted attention of chemists as a route to promising compounds with anticancer activity.[94] The synthesis of fused anthrathiophenes was designed based on *peri*-alkynylquinones, which readily react with S-nucleophiles. The reaction of sodium sulfide in ethanol with 1-alkynyl-9,10-anthraquinone **22a** is accompanied by the formation of both hetero- and carbocyclization products.[38] Anthrathiophene-6,11-dione **121** and acenthrylene-2,6-dione **122** were isolated from this reaction (Scheme 58).

A more efficient sulfating agent was produced *in situ* by the reaction of elemental sulfur with alkali. This system allowed the direct cyclization of 1-alkynyl-9,10-anthraquinones **22** to the corresponding thienoanthraquinones **123** (Scheme 59).[95]

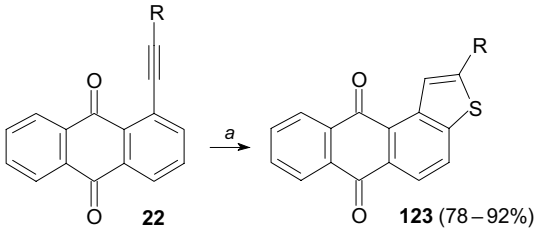
Under similar conditions, the direct CH-cyclization of azaanthraquinones **104** gave benzo[*g*]quinoline-6,11-diones annulated to the thiophene ring (compounds **124**, Scheme 60).[95] The mechanism of cyclization was described by the same research group.[96]

Scheme 58



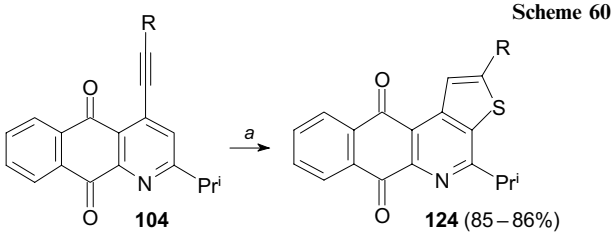
(*a*) $Na_2S \cdot 10\,H_2O$, EtOH, Δ, 0.5 h

Scheme 59



(*a*) S, NaOH, EtOH, Δ, 5 – 100 min; R = Bu^n, CMe_2OH, Ph, 4-$Me_2NC_6H_4$, 4-$MeOC_6H_4$,1-hydroxycyclohexyl, 1-methoxycyclohexyl

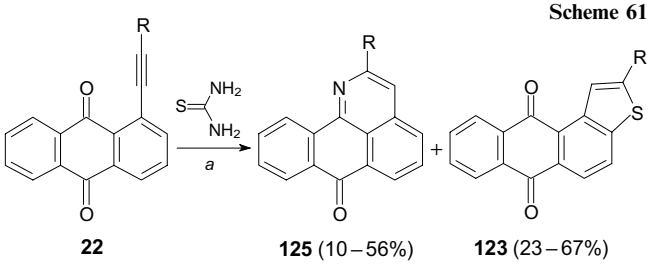
Scheme 60



(*a*) S, NaOH, EtOH, Δ, 5 min; R = Ph, CH(OH)Me, 1-hydroxycyclohexyl

Of particular interest is the evaluation of the reactivity of *peri*-ethynylanthraquinones with reagents containing two different nucleophilic centres (for example, S and N atoms). In this case, the question arises whether the reaction will be chemoselective or two competitive reactions will occur. This issue was addressed using the reaction of *peri*-ethynyl-9,10-anthraquinones **22** with thiourea (Scheme 61).[97] It was found that the reaction of compounds **22** with an excess of thiourea in refluxing pyridine in the presence of sodium ethoxide affords two heterocycles: dibenzo[*de*,*h*]quinolin-7-

Scheme 61



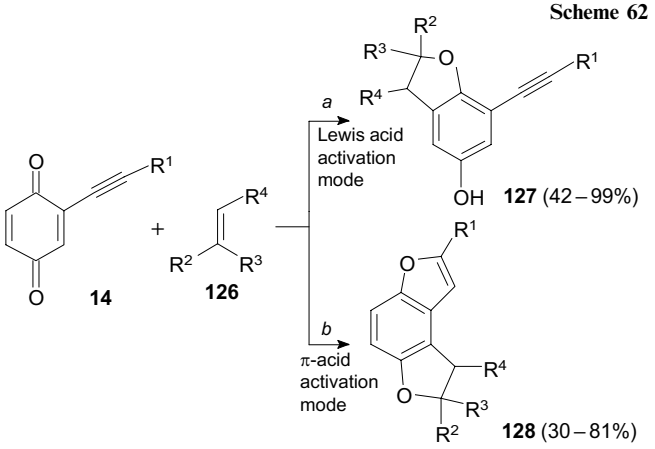
(*a*) EtONa, PyH, 115 °C, 8 – 36 h; R = Bu^n, n-C_5H_{11}, Ph, 4-MeC_6H_4, 4-$Me_2NC_6H_4$, 4-$H_2NC_6H_4$, 1,5-dimethylpyrazol-4-yl

ones **125** and anthra[2,1-*b*]thiophene-6,11-diones **123**, with the latter predominating.

3.2. O-Heterocyclization of *peri*-alkynylquinones involving a carbonyl oxygen atom

Quinones containing fused O-heterocycles are often synthesized by the cyclization involving the carbonyl oxygen atom of *peri*-alkynylbenzo- and alkynylanthraquinones. Thus, the investigation of the intermolecular heterocyclization of 2-alkynyl-1,4-benzoquinones **14** with electron-rich styrenes **126** demonstrated that the reaction can be directed to the formation of either dihydrobenzofuran **127** or dihydrobenzodifuran **128**.[98] The regioselectivity of cycloaddition was found to be a result of different activation modes, which depend on the nature of metal salts. Thus, $Bi(OTf)_3$ acts as a Lewis acid and AuCl as a π-acid (Scheme 62).

Scheme 62



(*a*) $Bi(OTf)_3$, MeCN, 0 °C, 3 – 6 h; (*b*) AuCl, THF, 50 °C, 8 – 12 h; R^1 = H, cyclo-C_3H_5, Bu^n, Bu^t, Ph, 4-MeC_6H_4, 4-ClC_6H_4, 4-FC_6H_4, TMS; R^2 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 2-Th; R^3 = H, Me, Et, 4-$MeOC_6H_4$; R^4 = H, Me

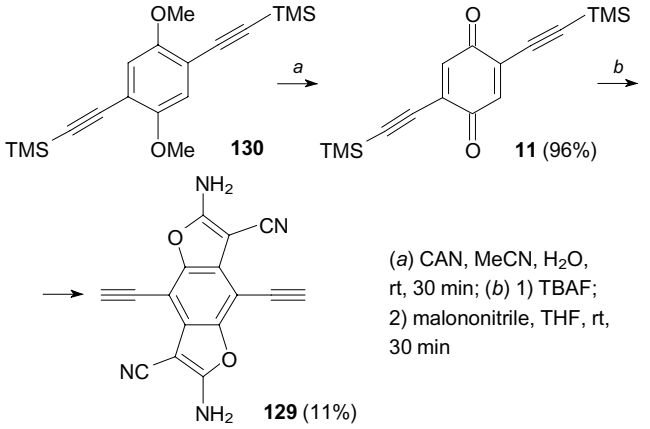
The $Bi(OTf)_3$-catalyzed reactions in acetonitrile at 0 °C for 3 h produce benzofurans **127**. The formation of benzodifuran **128** in the presence of AuCl occurs in THF at a higher temperature (50 °C) and requires a longer time (10 h). Both types of reactions are sensitive to the nature of substituents at the double bond, one of which should necessarily have strong electron-donating properties.

Yi *et al.*[99] reported an original strategy of the synthesis of π-conjugated benzo[1,2-*b*:4,5-*b*]difuran (BDF, **129**). The distinguishing feature of this reaction is that the cyclization involves the carbonyl oxygen atom and the CH-active group of benzoquinone but leaves the triple bond intact (Scheme 63).

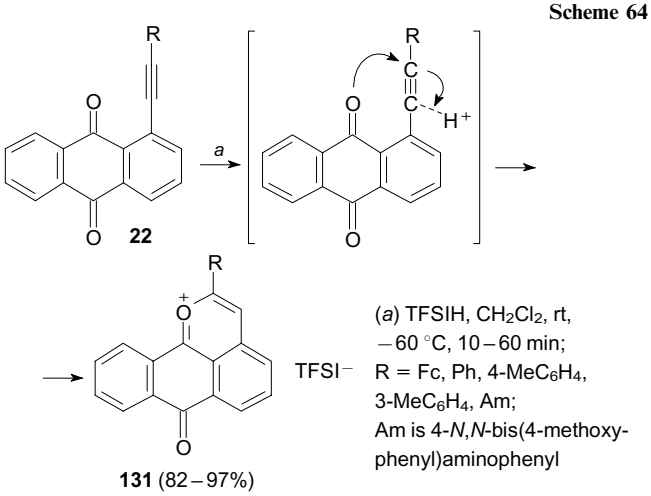
The first step involved the hydrolysis – oxidation of dimethoxybenzene **130** in the presence of CAN to give diethynyl-1,4-benzoquinone **11** in nearly quantitative yield. Then the intermediate was desilylated. The key step was the reaction of the malononitrile carbanion with the appropriate quinone followed by the double intramolecular cyclization to form target product **129**. Compounds of the BDF type may be of interest for the preparation of redox-active chromophores.

Kondo *et al.*[100, 101] discovered the strong acid-promoted cyclocondensation of 1-arylethynyl-9,10-anthraquinones **22** (Scheme 64) having both fundamental and applied importance (for more detail see Section 4). The

Scheme 63



Scheme 64



protonation of compounds **22** with 1.4 – 1.7 equiv. of bis(trifluoromethanesulfonyl)imide (TFSIH) in dichloromethane gave 2-substituted dibenzo[*de*,*h*]chromenylium cations **131**.

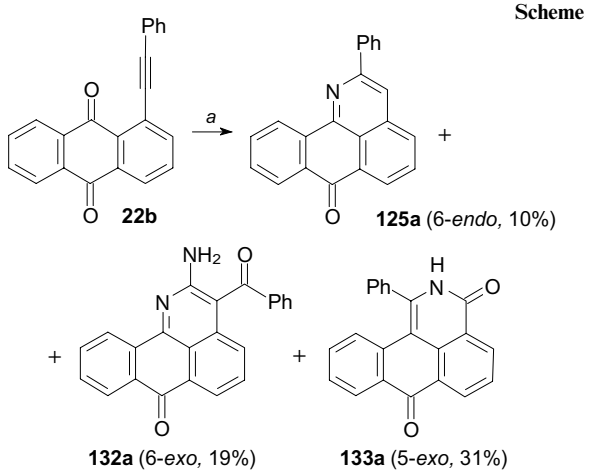
3.3. Cyclization of *peri*-alkynyl-9,10-anthraquinones involving a modified carbonyl group

The ability of the C=O group to be transformed into other functions and its favourable spatial arrangement with respect to the C≡C bond of *peri*-R-ethynyl-9,10-anthraquinones significantly simplify the development of straightforward methods of synthesis. These specific features are often used to prepare new biologically active heterocyclic compounds.

The reactions of 1-alkynyl-9,10-anthraquinones with nitrogen polynucleophiles were systematically addressed in a number of publications (see, for example, the studies [22, 36, 97, 102, 103]). In the first study of this cycle,[102] which described the reaction of guanidine with *peri*-phenylethynyl-9,10-anthraquinone, the authors demonstrated that the process has a complex character and is accompanied by a series of cascade transformations, involving the addition, cyclization, elimination and rearrangements (Scheme 65).

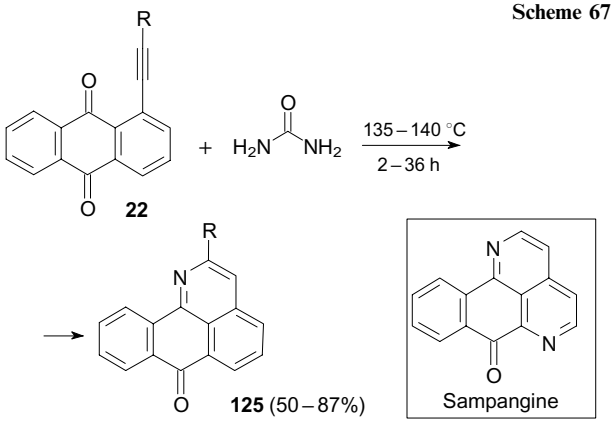
The reaction of guanidine with 1-phenylethynyl-9,10-anthraquinone (**22b**) in refluxing *n*-butanol affords three annulated heterocycles: 2-phenyl-7*H*-dibenzo[*de*,*h*]quinolin-7-one (**125a**), 2-amino-3-benzoyl-7*H*-dibenzo[*de*,*h*]quinolin-7-one (**132a**) and 1-phenyl-7*H*-dibenzo[*de*,*h*]isoquinoline-

Scheme 65



(*a*) guanidine, Bu^{n}OH, Δ, 18 h

Scheme 67



R = Bu^n, n-C_5H_{11}, Ph, 4-$MeOC_6H_4$, 4-$O_2NC_6H_4$, $PhOCH_2$, $Me_2C(OH)$, TMS, Py, 1,5-dimethylpyrazol-4-yl

3,7-dione (**133a**). The mechanisms of formation of compounds **125** and **132** were described in detail in the study.[102]

Scheme 66 shows the most interesting mechanism of the insertion of one nitrogen atom of guanidine between two carbon atoms of the C—C bond, without the cleavage of the molecule, to form an unusual structure — dibenzoisoquinoline **133**. The possible sequence of transformations includes the 5-*exo-dig* cyclization as the first step followed by the fragmentation – recyclization. The reaction is completed with the elimination of formimidine ($NH_2CH{=}NH$). This process can be considered as a competition between three types of alkyne cyclization: the nucleophilic 6-*endo* and 5-*exo* attacks at the electrophilic alkyne moiety and the 6-*exo* cyclization, in which alkyne acts as a nucleophilic agent.

As is seen in Scheme 65, compounds **125** and **132** are analogues of the alkaloid sampangine, which was shown to be active against fungi and mycobacteria.[104] Taking into account the practical significance of these derivatives, the authors searched for an appropriate reagent and optimal conditions for the selective synthesis of 2-R-7*H*-dibenzo[*de,h*]quinolin-7-ones **125** (Scheme 67).

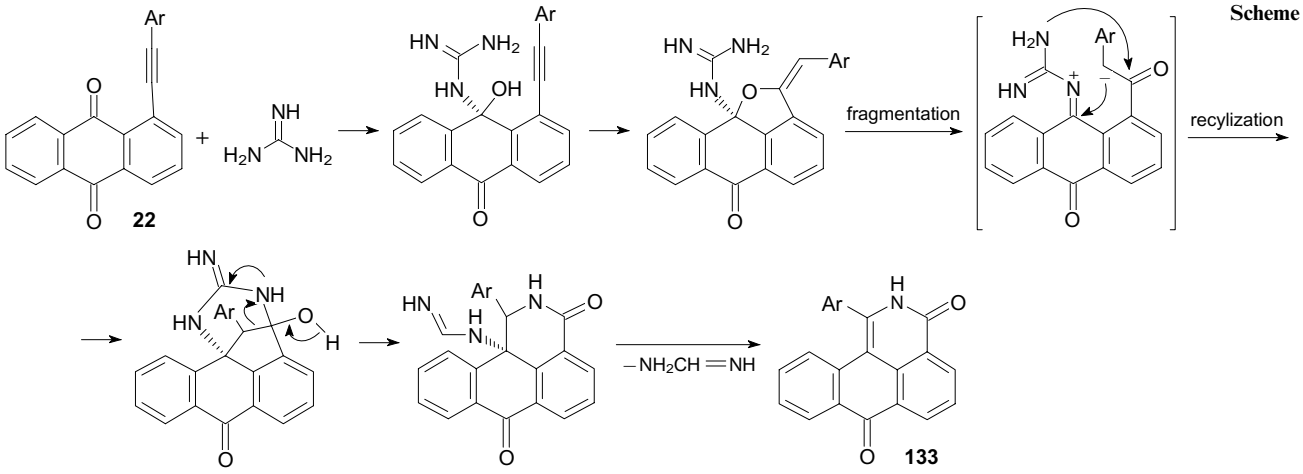
Urea (carbamide) appeared to be the reagent of choice for the regioselective cyclization of 1-alkynylanthraquinones. As opposed to guanidine, the reaction of urea with 1-R-ethynyl-9,10-anthraquinones **22** affords dibenzoquinolin-7-ones **125** as the only products in high yields. Since urea is poorly soluble in most organic solvents, the reaction is performed in a melt. (It is worth noting that urea is the commercially available non-toxic product commonly used as a fertilizer.) The treatment of the reaction mixture involves its dilution with water and the filtration of the precipitated product. Therefore, the conditions of this reaction meet the green chemistry requirements. The mechanism of this transformation was described in the study.[102]

Baranov *et al.*[105] performed the double *peri*-heterocyclization using urea. However, this reaction was less successful. Probably, this is because the cyclization conditions were different from those described above. The previously unknown naphthophenanthrolines **134** were prepared by the reaction of 1,4-diethynyl-9,10-anthraquinones **36e**,**f** with urea in DMF (Scheme 68).

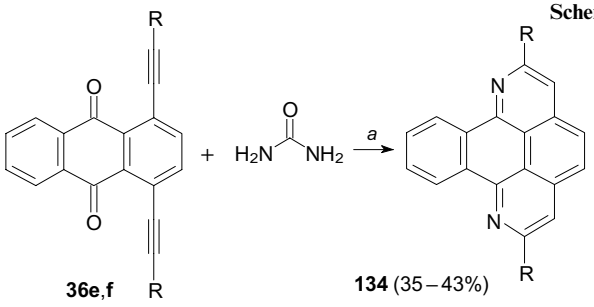
An unusual result was obtained when studying the reactions of guanidine with *peri*-alkynylquinones **22** containing electron-withdrawing substituents (Scheme 69).[37] The reaction of alkynes **22** with guanidine in refluxing n-butanol affords O-5-*exo-dig* cyclization products (**133**) and N-6-*exo-dig* cyclization products (**132**) along with comparable amounts of 9,18-diaryltetrabenzo[*a*,*de*,*j*,*mn*]-tetracene-4,13-diones **135**.[37] The latter compounds are very unusual carbocyclization products. This is a new type of cyclization, the mechanism of which is unknown. However, the authors proposed the possible reaction scheme (Scheme 70).

The putative reaction mechanism involves the addition of a nucleophilic group, which is generated through the

Scheme 66



Scheme 68



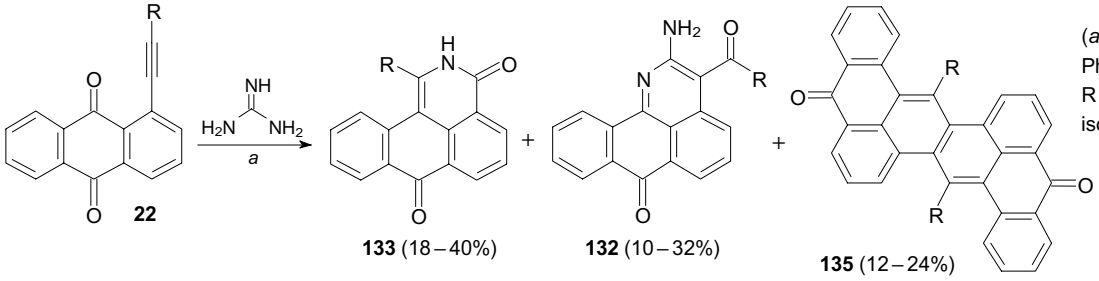
(*a*) DMF, Δ, 0.5–3 h; R = CH_2OPr^i (**e**), n-C_6H_{13} (**f**)

transformation of the alkyl moiety into enol or enamine, to the triple bond followed by the aldol condensation. In this transformation, guanidine plays a dual role. First, it promotes the desired regioselectivity (the formation of enamine). Second, guanidine can act as a reducing agent, which, like hydrazine in the Wolff–Kishner reduction, is involved in the deoxygenation of intermediate **136** apparently along with the final ring formation. The synthetic significance of reductive dimerization of internal acetylenes is that it occurs under very mild conditions, providing a simple route to flexible non-planar polyaromatic products with interesting electrochemical properties.[37]

A different composition and a different product ratio were observed in the reaction of guanidine with *peri*-alkynyl-9,10-anthraquinones **22** containing electron-donating substituents (Scheme 71).[36] In all cases, the cyclization affords quinolin-7-ones **132**, whereas the pyrazole derivative undergoes partial 5-*exo* cyclization to form isoquinoline **133b**.

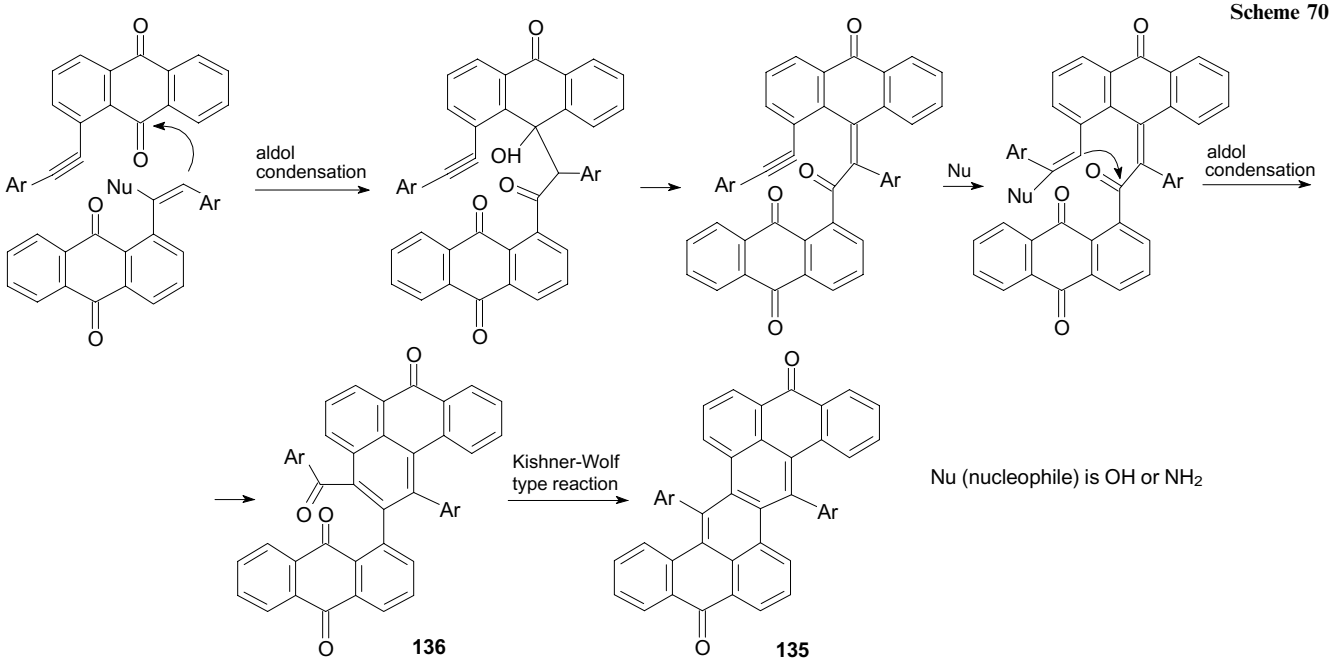
The cyclization of guanidine with 9,10-anthraquinone **22c** containing an alkynol moiety is a more complex process. It produces both linear isoxazole **137** and two fused heterocycles **138** and **139**. In all cases, the ring formation involves the nitrogen atom of the external nucle-

Scheme 69

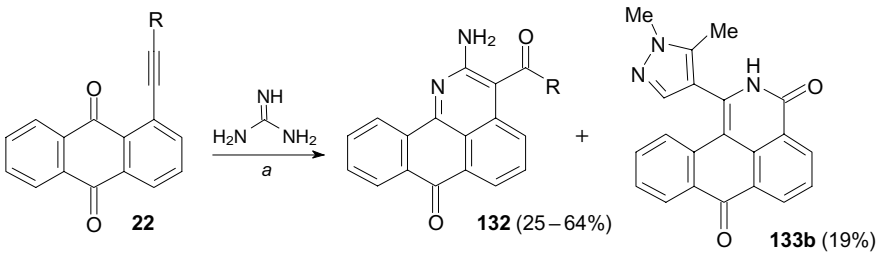


(*a*) MeOH, Bu^nOH, PhMe, Δ, 9–19 h; R = 4-BrC_6H_4, 4-AcC_6H_4, isoquinolin-3-yl

Scheme 70



Scheme 71



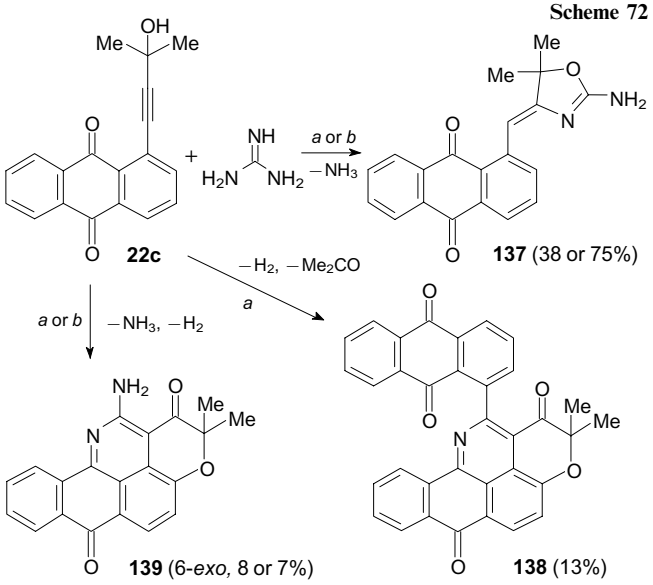
(*a*) MeOH, Bu^nOH, PhMe, Δ, 28 h; R = 4-$Me_2NC_6H_4$, 2,4,6-$Me_3C_6H_2$, 1,5-dimethylpyrazol-4-yl

ophile (guanidine) and the hydroxyl oxygen atom of the substrate (Scheme 72).[103, 106]

Pyridine rings of **138** and **139** are formed through an external nucleophile. Thus, the attack of guanidine on the C=O group is followed by the addition of the nitrogen atom of the resulting hemiaminal moiety at the triple bond. In the subsequent O-cyclization, the acidic CH moiety of the quinone ring is attacked by the hydroxyl group of the substrate.[103] Major linear product **137** is formed through the addition of guanidine at the triple bond followed by the O-cyclization and elimination of an ammonia molecule (Scheme 73).[106]

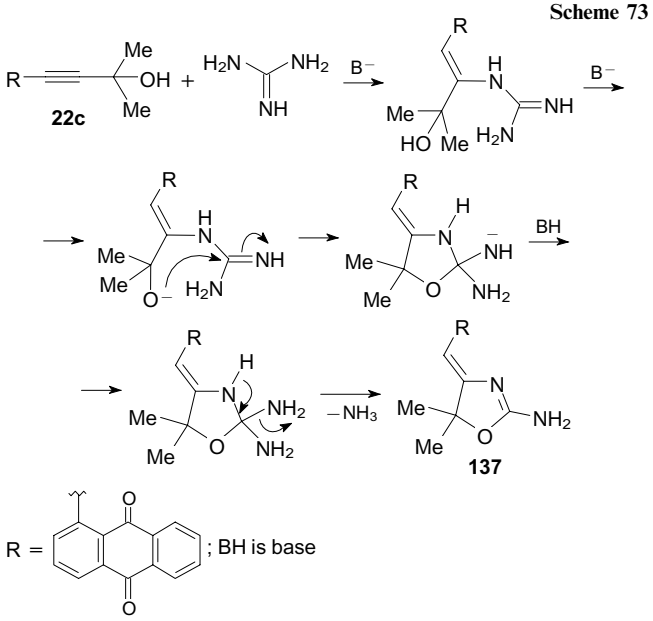
1-Alkynyl- (**22**) and 2-alkynyl-9,10-anthraquinones (**26**) are structural vinylogues of α-acetylene ketones. Therefore, a need arises to compare the reactivity of these compounds. Actually, the complete triple bond cleavage of α-acetylene ketones by the treatment with EDA discovered[13] in 2011 has stimulated the authors to examine the potential of this unusual transformation in a series of 1-alkynyl- and 2-alkynyl-9,10-anthraquinones.[107] Recall that the reaction of diaryl ketoalkynes **140** with EDA in a sealed tube in THF (110–125 °C) leads to the complete cleavage of the triple bond to form derivatives of acetophenone (**141**) and 2-substituted imidazoline (**142**) along with the expected Michael adducts (Scheme 74).[13]

Scheme 72

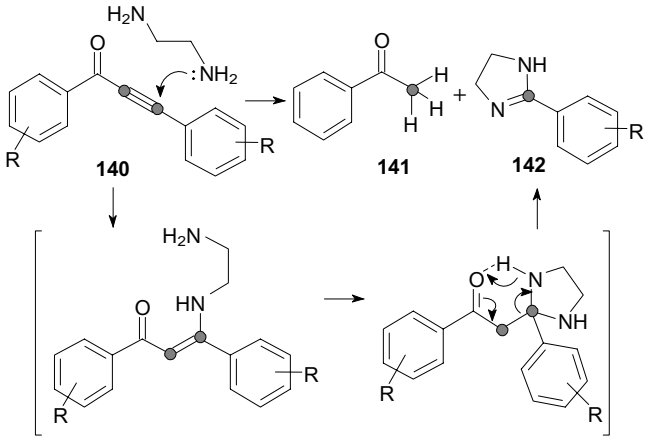


(*a*) MeOH, Bu^{n}OH, PhMe, Δ, 4 h; (*b*) PyH, Δ, 16–60 h

Scheme 73



Scheme 74

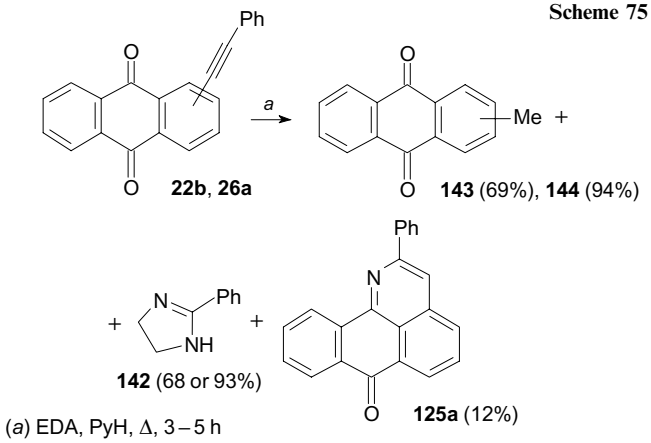


The experimental and theoretical studies allowed the authors to suggest the mechanism of this cascade transformation, in which one alkyne carbon atom is reduced to form three C–H bonds, whereas another carbon atom is oxidized to form three C–N bonds (one π-bond and two σ-bonds). The first, most rapid, step involves the intermolecular Michael addition of the amino group followed by the relatively slow intramolecular addition of the second amino group accompanied by the 5-*exo*-*trig* cyclization. This step and the final fragmentation are concerted reactions.

The investigation of the reactions of 1-phenylethynyl- (**22b**) and 2-phenylethynyl-9,10-anthraquinones (**26a**) with EDA in refluxing pyridine revealed the similarity of these compounds with α-acetylene ketones. It was shown that this reaction leads to the triple bond cleavage giving 2-phenyl-4,5-dihydroimidazole (**142**) and the corresponding 1-methyl- (**143**) and 2-methyl-9,10-anthraquinones (**144**) (Scheme 75).[107]

The fragmentation of isomers **22b** and **26a** most efficiently occurs in refluxing pyridine in the presence of a 50-fold excess of EDA. Both reactions afford compounds **142**–**144** as the decomposition products of alkynes. Besides,

Scheme 75



(*a*) EDA, PyH, Δ, 3–5 h

in the case of alkyne **22b**, dibenzo[*de*,*h*]quinolin-7-one (**125a**) was isolated as the 6-*endo*-*dig* cyclization product. The formation of this product can be described as a sequence of transformations shown in Scheme 76. Experiments demonstrated that the first step, the intermolecular Michael addition of amine, is fast. Meanwhile, the second (intramolecular) addition is slower due to the deactivating effect of the introduced electron-donating amino group on the double bond. The latter fragmentation step can be considered as the retro-Mannich reaction giving acetophenone enol and imine. This final step occurs through the formation of a six-membered transition state as a concerted process. The mechanism of the triple bond cleavage of alkynylquinones apparently involves the stereoelectronic assistance from an electron pair of the nitrogen atom in the step of the C–N bond cleavage (shown in red in Scheme 76).[108, 109]

The mechanism of the triple bond cleavage of 2-phenylethynyl-9,10-anthraquinone (**26a**) is presented in Scheme 77. The intermolecular Michael addition of the amino group through polarization of the triple bond is the first step of the reaction. The intramolecular addition of the second amino group occurs more slowly due to the deactivating effect of the first introduced amino group on the triple bond. The final step is a concerted process resulting in the fragmentation of the 5-*exo*-*trig* intermediate.

Undoubtedly, the discovery of this reaction is of theoretical interest as an example of the complete cleavage of the strong C≡C bond with EDA under mild conditions (in the absence of metal catalysts).[107]

3.4. Chemical transformations of a carbonyl group in alkynylquinones with retention of the triple bond

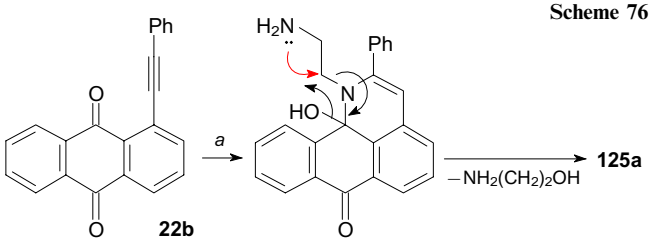
When performing transformations of a carbonyl group in alkynylquinones to prepare compounds with new properties, a need often arises to retain the triple bond. These transformations are addressed in the studies[110–112] (Scheme 78).

The reaction of dialkyne **41b** with 4-substituted anilines in a ratio of 1 : 2 using $TiCl_4$ as the dehydrating agent gave diimines **145**. The removal of the TMS group with K_2CO_3 followed by the reaction with a Pt complex in the presence of CuI afforded oligomers **146** (for derivatives containing 4-nitro or 4-n-butoxy substituents).

Another type of transformations of a carbonyl group into the nitrile group was reported by Glöcklhofer *et al.*[61] The authors developed a method for the synthesis of cyanoacenes. The first attempt to apply this approach to synthesize 2,6-dialkynyl-9,10-dicyanoanthracene **147** from the corresponding dialkyne **41b** was not quite successful, because the authors failed to remove the impurity of the starting compound either by column chromatography or by crystallization (Scheme 79).

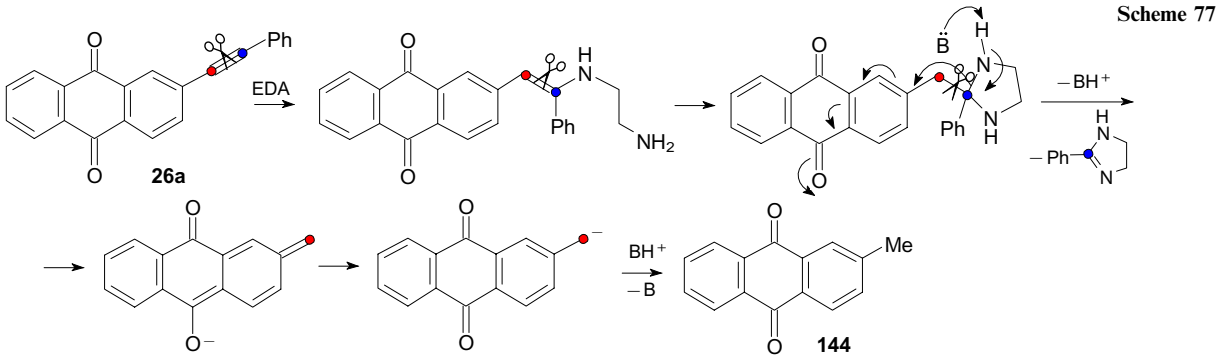
The Sonogashira reaction with dibromide **148** as the substrate, in which the cyano group was introduced in advance, proved to be more successful.[61] This made it possible to develop a reliable procedure for the synthesis

Scheme 76

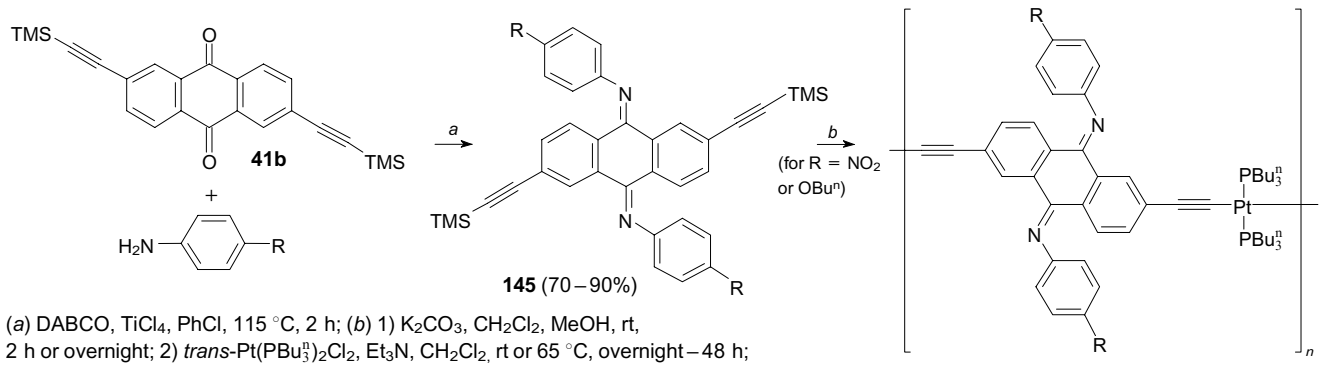


(*a*) EDA, PyH, Δ, 3 h

Scheme 77

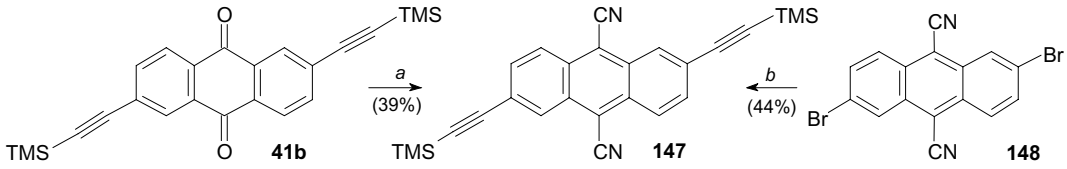


Scheme 78

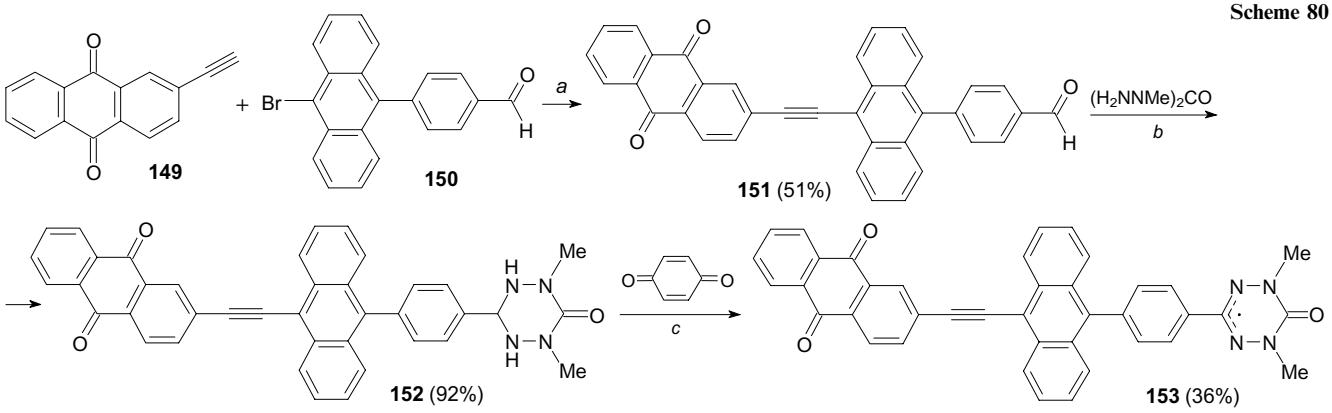


(*a*) DABCO, $TiCl_4$, PhCl, 115 °C, 2 h; (*b*) 1) K_2CO_3, CH_2Cl_2, MeOH, rt, 2 h or overnight; 2) *trans*-Pt(PBu^n_3)$_2Cl_2$, Et_3N, CH_2Cl_2, rt or 65 °C, overnight–48 h; R = H, NO_2, OBu^n, SMe, Br, C≡CTMS

Scheme 79



Scheme 80



of cyanoarenes. The latter compounds are promising for application in organic field-effect transistors (OFET).

To conclude this Section devoted to the chemical properties of alkynylquinones, let us describe the transformation of alkynyl-9,10-anthraquinone giving a stable radical with retention of the triple bond.[113] This paramagnetic molecule was intended to explore the intramolecular energy transfer by fluorescence spectroscopy (Scheme 80). In the first step, the cross-coupling of 2-ethynyl-9,10-anthraquinone (**149**) with bromoanthracene **150** in the presence of $Pd(PPh_3)_4$ in refluxing THF gives intermediate (4-formylphenyl)anthracene **151**. The latter compound reacts with carbonic acid bis(1-methylhydrazide) under reflux in THF to give 1,2,4,5-tetrazinane **152**. In the final step, the oxidation of compound **152** with a one-and-a-half excess of *p*-benzoquinone in refluxing benzene affords target verdasyl radical **153**.

Teki *et al.*[113] did not discuss the factors responsible for a low yield of the target compound (36%) and did report the results of monitoring of the reaction product composition. It can be suggested that the low yield is due to an insufficient excess of the oxidizing agent (50%). During the course of oxidation, benzoquinone is reduced to hydroquinone to form a relatively stable quinone – hydroquinone charge-transfer complex, resulting in that the oxidizing agent is partially removed from the reaction. This is an example of the straightforward rational synthesis of a model compound, in which the acceptor (anthraquinone) is linked to the donor (phenylanthracene and verdasyl radical) through a triple bond.

By analyzing the publications on the chemical properties of alkynylquinones, it can be stated that these properties are in general similar to those of acetylenylarenes. Thus, functionalized vicinal alkynylarenes and alkynylquinones are often utilized to prepare fused systems. In both cases, the reaction pathway and the composition of the reaction products can be controlled using both internal parameters (the structure of substituents in the substrates) and external stimuli (the nature of the reagents, the solvent and the catalyst). Moreover, alkynylquinones exhibit higher reactivity compared to that of alkynylarenes due to the triple bond activation by carbonyl groups.

Besides, *peri*-alkynylquinones have a specific feature associated with the spatial proximity of the C=O group and the triple bond, which offers additional possibilities for various cascade transformations with their participation to form both carbo- and heterocyclic fused systems. This specificity is manifested in the reaction with EDA resulting in the triple bond cleavage of a series of α-acetylene ketones and their vinylogues, 1-acetylenyl- and 2-acetylenyl-9,10-anthraquinones. The reactions with 2-isomers and keto acetylenes follow the same pathway and produce 2-R-substituted imidazolines and the corresponding methylquinones and methylarenes, whereas the reactions of *peri*-alkynylquinones afford, apart from these products, fused heterocycles, dibenzo[*de,h*]quinolin-7-ones.

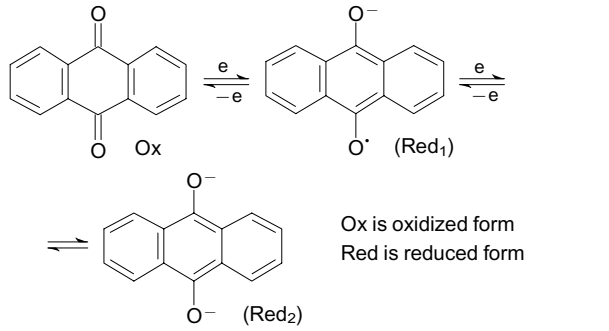
4. Physicochemical properties

In studies of physicochemical properties of quinones containing a triple bond, one of priority areas of research is the characterization of compounds promising as molecular switches. This is associated with reversible redox reactions typical of quinone derivatives (Scheme 81).

Researchers make great efforts to design organic, inorganic and organometallic molecular switches responsive to external stimuli, such as photoirradiation, to external stimuli pH changes or redox transformations. In particular, Norel *et al.*[114] examined the possibility of using the reversibility of the redox process in molecular electronics to construct components of reversible switching systems based on porphyrin derivatives with ruthenium acetylide bridges.

Oyama *et al.*[115] synthesized new dinuclear structures containing $Ru(dppe)_2$ units [dppe is 1,2-bis(diphenylphosphino)ethane] bridged by an ethynyl or butadiynyl group to

Scheme 81

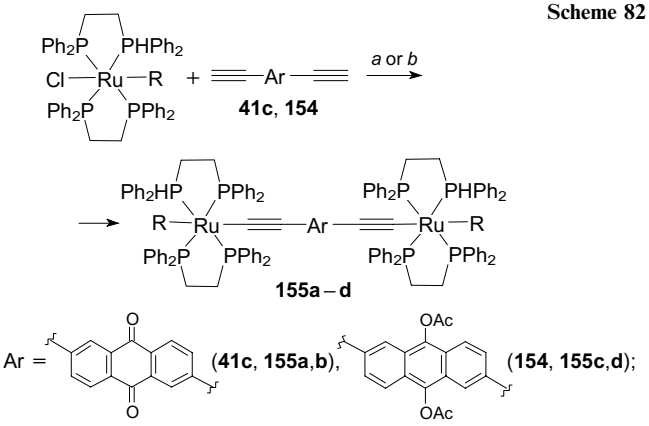


the diacetoxyanthracene (AcAC) or anthraquinone core in order to use them as molecular switches.

Thus, the reaction of 9,10-diacetoxy-2,6-diethynylanthracene (**154**) with *cis*-$RuCl_2(dppe)_2$ in the presence of $NaPF_6$ in CH_2Cl_2 afforded product **155c**. Its anthraquinone analogue **155a** was synthesized under the same conditions using 2,6-diethynyl-9,10-anthraquinone (**41c**) as the starting compound. Butadiynyl derivative **155d** was produced from diethynylanthracene **154** using $KB(C_6F_5)_4$ in Et_3N as the condensing agent. Anthraquinone butadiynyl analogue **155b** was synthesized in a similar fashion (Scheme 82).

The analysis of the UV-Vis-NIR spectra of these compounds demonstrated that complexes **155c**,**d** (AcAC derivatives) are characterized by a stronger electronic interaction between the ruthenium units, whereas metal–AQ–metal interactions were not observed in compounds **155a**,**b**. The difference between the AQ and AcAC derivatives is that cross-conjugated systems containing the AQ moiety exhibit the so-called quantum interference effect,[116] resulting in the blockade of conduction in the metal–molecule–metal system (MMM), as opposed to linear-conjugated 9-10-dihydroxyanthracene (HOA). It should be emphasized that the redox process is reversible. Therefore, these complexes can be considered as potential candidates for the construction of reversible switching systems for molecular electronics (Scheme 83).

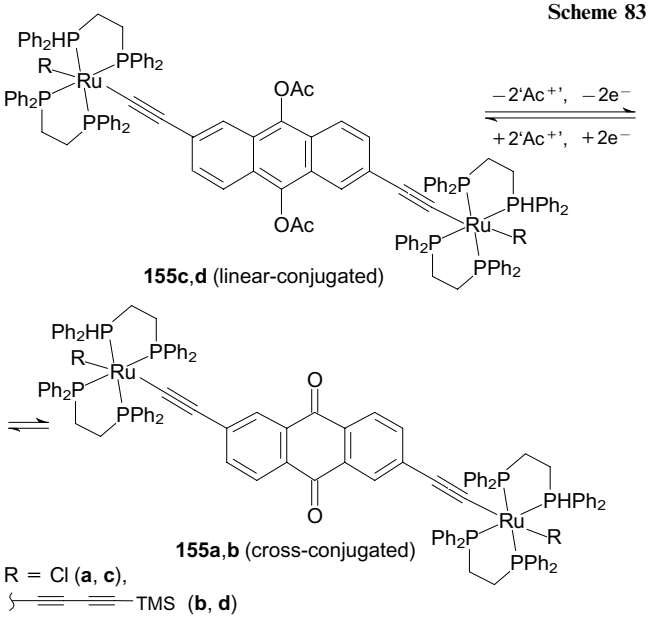
Scheme 82



(*a*) $NaPF_6$, CH_2Cl_2, rt, 21 h; (*b*) $KB(C_6F_5)_4$, Et_3N, rt, −50 °C, 2–22.5 h

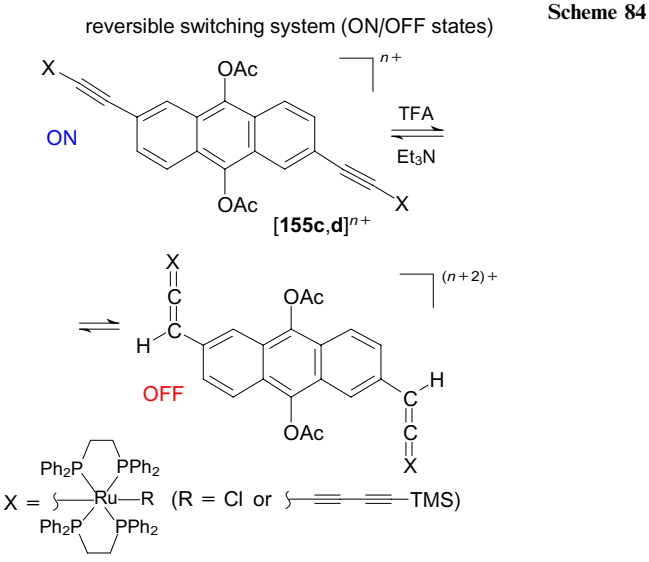
Compound	R	Ar	Conditions	Yield (%)
155a	Cl	AQ	*a*	56
155b	C≡C–C≡CTMS	AQ	*b*	33
155c	Cl	AcAC	*a*	49
155d	C≡C–C≡CTMS	AcAC	*b*	62

Scheme 83



The reversible switching can be achieved not only *via* redox transformations but also through reversible protonation [with trifluoroacetic acid (TFA)]–deprotonation (Et_3N) (Scheme 84).

Scheme 84

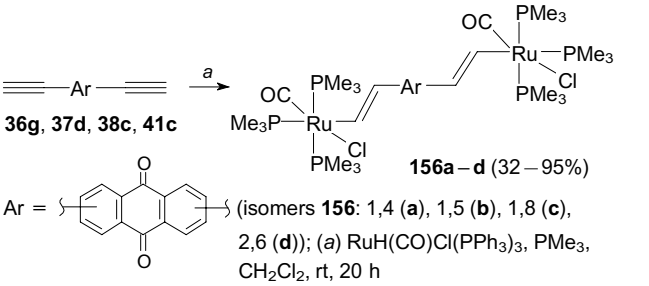


This process can be illustrated by linear-conjugated compounds **155c**,**d** exhibiting significant electronic interaction in the MMM system. The protonation affords the corresponding vinylidene compounds, thereby disturbing the conjugation and hindering the interaction between metal ions. Therefore, compounds **155c**,**d** act as reversible on/off switches with varying pH.

Li *et al.*[117] synthesized and characterized another type of ruthenium complexes derived from isomeric dialkynyl-9,10-anthraquinones. The authors studied four isomeric dinuclear complexes, in which two ruthenium units are attached to the 1,4- (**156a**), 1,5- (**156b**), 1,8- (**156c**) or 2,6-positions (**156d**) of the central anthraquinone moiety (Scheme 85).

The X-ray diffraction study revealed an interesting feature. Thus, the 1,4-anthraquinone moiety of compound

Scheme 85



156a is non-planar, which strongly contrasts to the planar skeleton of 1,5-isomer **156b**. Two phenyl rings in the anthraquinone moiety of compound **156a** form a V shape, with both carbonyl oxygen atoms deviating from the plane of the anthraquinone ring. An important feature of these complexes is that two metal centres in isomers **156a–c** can interact with each other through an anthraquinone bridge, *i.e.*, carbonyl groups do not hinder this interaction despite the cross-conjugated character of this bridge.[117]

To study the electrochemical properties of ethynylanthraquinone systems, Mai *et al.*[77] used another type of complexes incorporating ethynyl bridges that connect the central linear- or cross-conjugated unit to two terminal metalloporphyrin macrocycles. The authors reasonably believed that such conjugated oligoporphyrin systems can be used as switches in electronic devices. They synthesized dimeric nickel-containing porphyrins **78**, **79** and **157** containing the central quinone or benzene ring and acetylene linkers intended for studies of interactions between the porphyrin macrocycles (the synthesis is described in Section 2.3).[77] The authors compared the spectroscopic and electrochemical parameters of two types of dimeric ethynylporphyrins: compounds containing the benzene (conducting) linker (compounds **79** and **157**) and compound containing the cross-conjugated quinone linker (**78**).

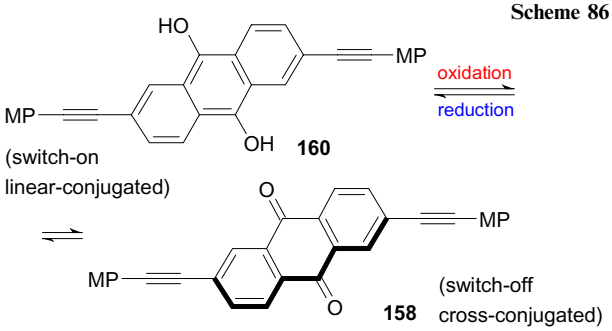
The UV-Vis-NIR spectra and electrochemical data showed that there is a strong electronic coupling between two porphyrin units in compounds **79** and **157**, whereas this coupling is virtually absent in quinone **78**. This can be attributed to the fact that the quinone ring breaks the conjugation, thereby disrupting the electronic coupling between two porphyrin units. In dimer **78**, the quinone linker can be reversibly switched on and switched off by electrochemical or chemical means from cross-conjugated quinone to through-conjugated benzene states.

It can be supposed that these dimeric porphyrins can be used for the construction of redox-driven molecular switches.[77] This research group[76] continued the study of the switching effect in dimeric Ni porphyrin complexes containing the central anthraquinone (**158**) and 9,10-diacetoxy- (**159**) or 9,10-dihydroxyanthracene (**160**) moieties instead of the benzoquinone moiety.

The UV-Vis absorption spectra showed that there is a strong coupling between two porphyrin units in anthracene-bridged porphyrin dimers **159** and **160**, whereas this coupling is absent in dimer **158** with the anthraquinone linker. It is important that the anthraquinone bridge system can be reversibly switched from the cross-conjugated (switching off) to linear-conjugated (switching on) state through two-electron reduction–oxidation reactions (Scheme 86).

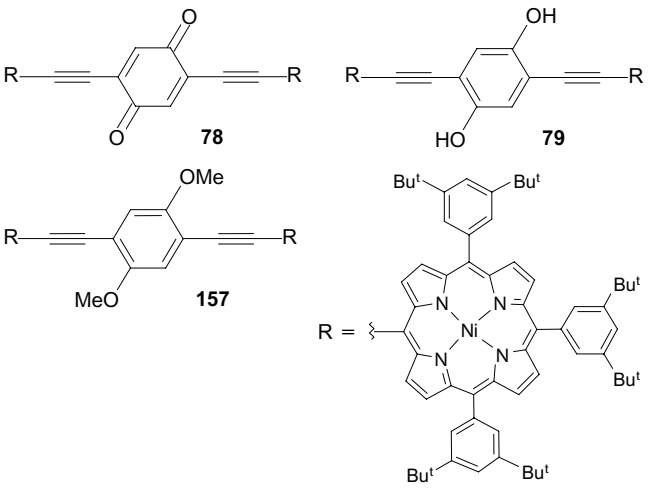
This specific feature suggests that the anthraquinone-based system can be used as a redox potential-driven switch in molecular electronic devices.

Scheme 86

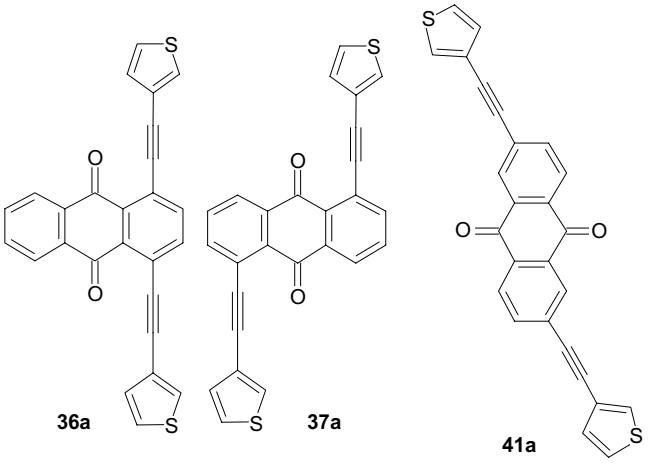


The relevance of research on controlled molecular switches gave impetus to a continuous extension of the range of compounds suitable for their construction. Weber and co-workers[4] systematically characterized a series of new 1,4-, 1,5- and 2,6-diethynyl-9,10-anthraquinones (compounds **36a**, **37a** and **41a**, the synthesis is presented in Scheme 16) containing π-conjugated 3-thienyl side units capable of adhesion to a gold substrate. Such compounds can form monolayers with Au^{III} or semiconductor surfaces, which is a necessary condition for the design of redox-active switches (Scheme 87).

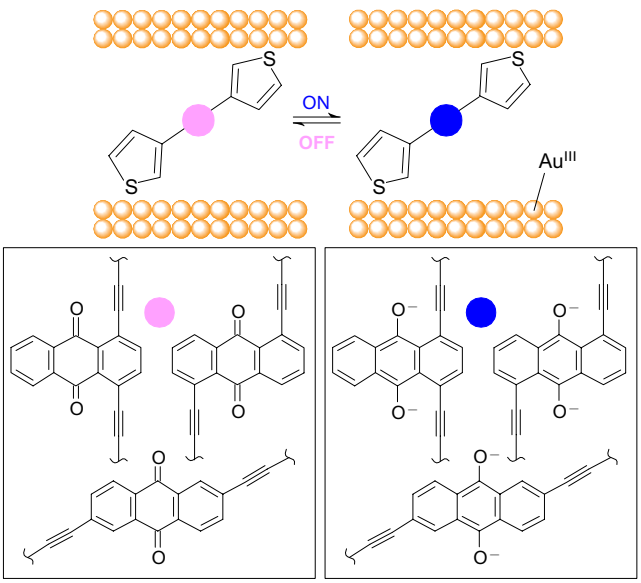
Structures 78, 79, 157



Structures 36a, 37a, 41a



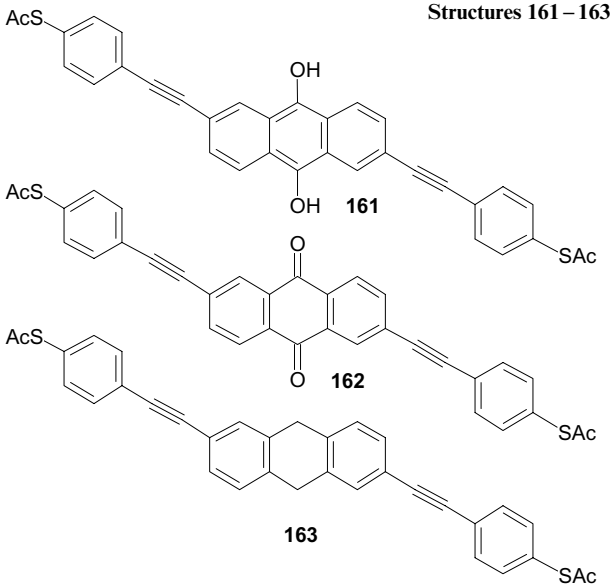
Scheme 87



The investigation of the electronic properties of anthraquinones **36a**, **37a** and **41a** by cyclic voltammetry (CV) showed[4] that these compounds are characterized by a redox potential with a high conductance ratio $G_{on}/G_{off} \sim 4$. This a prerequisite for their application as redox-active switches. In the authors' opinion, for applicability in real-world devices, it is necessary to add functional groups, which are able to form hydrogen bonds with carbonyl groups of anthraquinone, in order to stabilize the radical intermediate.[4]

In recent years, researchers have increasingly attempted to use organic molecules to design electronic devices in view of certain limitations on the application of silicon semiconductors. Unsurprisingly, alkynylquinones have attracted great attention of chemists and physicists due to their specific structures and the possibility of application in molecular electronics.[118] An example of the development of this area of research is a comparative study of the conductance of bis(4-acetylthiophenylethynyl) derivatives of the linear-conjugated system based on 9,10-dihydroxyanthracene (HOA, **161**), cross-conjugated anthraquinone (AQ, **162**) and 9,10-dihydrianthracene (AH, **163**) with a broken conjugation, which are anchored with terminal groups capable of contacting with metal.[118]

Structures 161 – 163



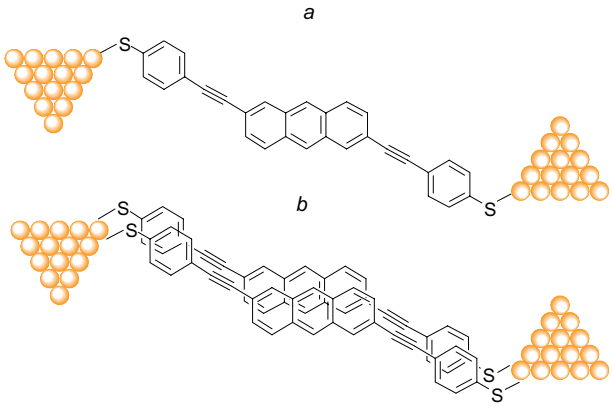


Figure 1. Model of the formation of the Au|AC|Au junction, involving the stacking of a single molecule (*a*) and two molecules of anthracene **164a** (*b*). The Figure was prepared by the authors using the data of the study.[118]

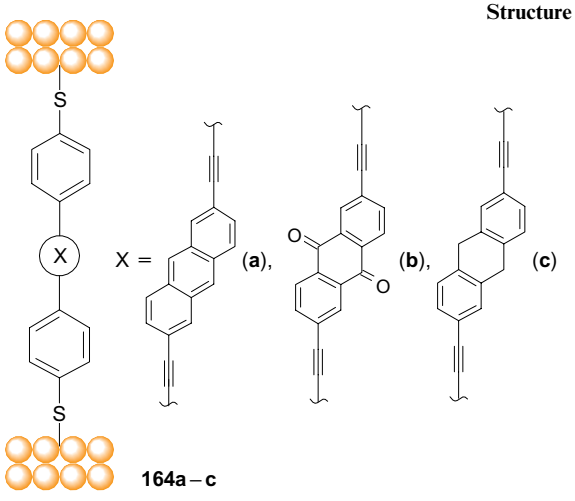
The role of the sulfur atom, as in the previous case, is to bind to the gold surface, thereby providing the electronic coupling Au|AC|Au (AC is anthracene) (Fig. 1).

The experiments demonstrated that the conductance of linear-conjugated molecule **161** is several hundred times higher than that of molecule **163** with a broken π-conjugation, and the conductance of the latter is about five times higher than that of cross-conjugated molecule **162**. This result is attributed to destructive quantum interference present in compound **162**. All dithiolated derivatives are of a similar length (~2.6 nm), but only dihydroxyanthracene **161** is capable of forming a larger number of Au|AC|Au junctions.

The relevance of the research on the conductance of oligo(phenylene ethynylenes) (OPEs), in particular, of anthracenes and anthraquinones **164a – c** bearing terminal dithiol groups attached to two gold electrodes, was confirmed by the study.[119]

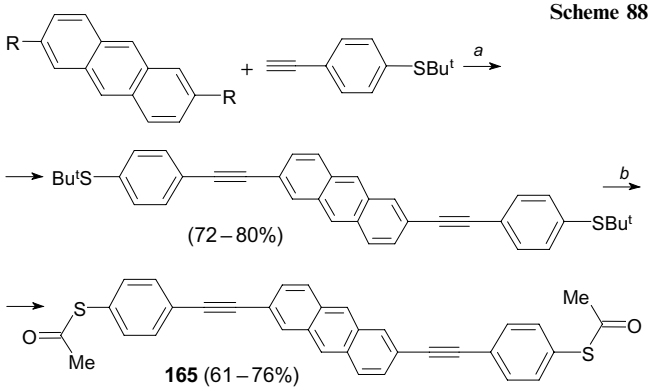
A series of linear- and cross-conjugated OPEs bearing terminal dithiol substituents were synthesized by the Sonogashira cross-coupling followed by the transformation of

Structure 164



164a – c

Scheme 88



(*a*) $Pd(PPh_3)_2Cl_2$, CuI, DIPA, Et_3N, THF, Δ, 11–21 h;
(*b*) AcCl, BBr_3, PhMe, $CHCl_3$, rt, 3.5–5 h; R = I, Br

the *tert*-butyl protecting group to the acetylthiol group. An example of the synthesis of compound **165** is presented in Scheme 88.

It was found that the conductance of linear-conjugated anthracene **165** is higher than that of cross-conjugated anthraquinone **162** or dihydroanthracene **163**. As in the above case, this is attributed to destructive quantum interference in compound **162** and the broken π-conjugation in dihydro derivative **163**. The calculations demonstrated [119] that an increase in the length of the molecule and(or) increase in the energy difference between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are associated with a decrease in the conductance of linear-conjugated anthracenes. The clear correlations between the molecular structure features and the conductance developed by the authors can serve as a guidance for the design of electronic devices.

Guédon *et al.*[120] studied the properties of two types of rigid π-conjugated molecular conductors of the OPE family, which form self-assembled monolayers (SAMs) on thin (200 nm) gold layers deposited onto silicon substrates (Fig. 2). Anthraquinone **164b** is cross-conjugated, whereas anthracene **164a** has a linear-conjugated structure. Both central units contain terminal thiol groups and have a length of 24.5 Å, but their properties are different. The experiments demonstrated that the conductance of compound **164b** is almost two orders of magnitude lower than that of derivative **164a**. According to theoretical calculations and the published data, this fact is associated with

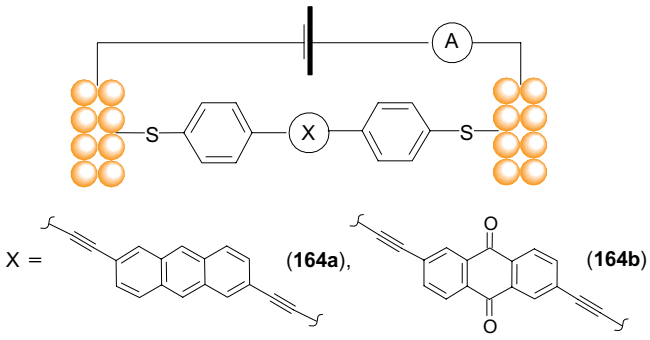


Figure 2. Schematic view of the formation of self-assembled layers of molecules **164a**,**b** on a conducting gold substrate (A is an ammeter). The Figure was prepared by the authors using the data of the study.[120]

quantum interference typical of cross-conjugated anthraquinones. The observation of interference in molecules at room temperature opens up a route to a new type of molecular devices, in particular to controlled molecular switches with a high switching on/off ratio.[120]

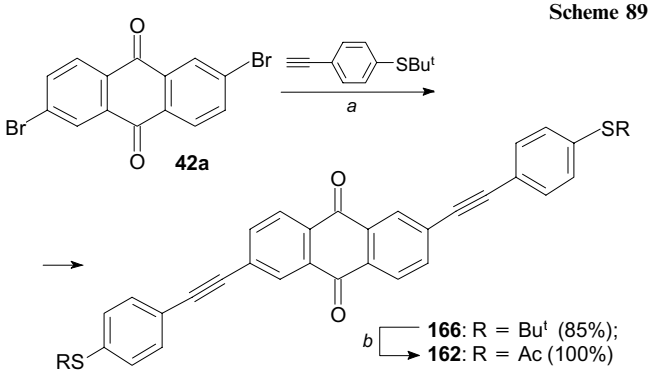
Van Dijk *et al.*[121] performed the optimized synthesis of dialkynylanthraquinones **166** and -anthracenes **167** bearing terminal *tert*-butylthiol groups starting from appropriate dibromides under the standard Sonogashira reaction conditions. Then compounds **166** and **167** were transformed into more labile acetylthiol derivatives **162** and **168**, which can easily bind to the gold electrode (Schemes 89 and 90).

Model butylthioanthraquinone derivative **166** was shown to be transformed from the cross-conjugated to linear-conjugated structure through the two-electron redox reaction. This property can be used to develop redox potential-driven switches for molecular electronic devices.

Devices relying on the reversibility of redox processes can be designed using other structural composites. In particular, tetrathiafulvalenes (TTF) are commonly used for the fabrication of redox sensors for metal ions.[122] Thus, new fluorescence chemosensor **169** (TTFAQ) made up of a biscrown-annulated receptor and two anthracene fluorophores was prepared with the participation of carbonyl groups of alkynylquinone **41b** (Scheme 91).

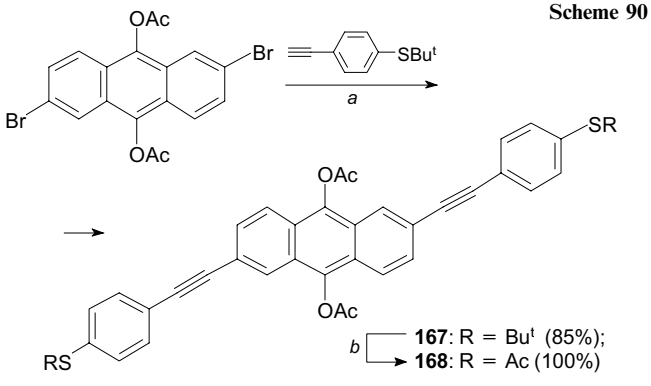
Such systems are attractive for designing redox chemosensors for metal cations. The photoinduced electron transfer (PET) from the donor (TTFAQ moiety) to the acceptor (anthracene) leads to fluorescence quenching. Upon oxidation, the TTFAQ moiety releases two electrons to form a stable dication with a planar anthracene structure, resulting

Scheme 89



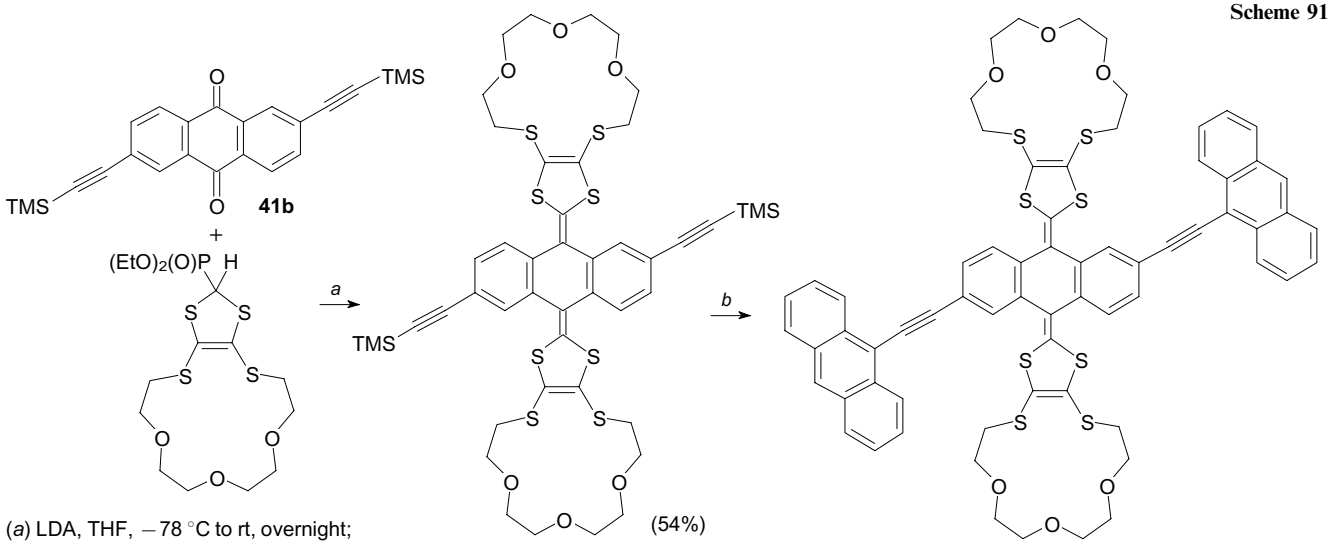
(*a*) $Pd(PPh_3)_2Cl_2$, CuI, DIPA, THF, Δ, 20–24 h;
(*b*) Br_2, AcOH, AcCl, $CHCl_3$, rt, 18 h

Scheme 90



(*a*) $Pd(PPh_3)_2Cl_2$, CuI, DIPA, THF, Δ, 20–24 h;
(*b*) Br_2, AcOH, AcCl, $CHCl_3$, rt, 18 h

Scheme 91



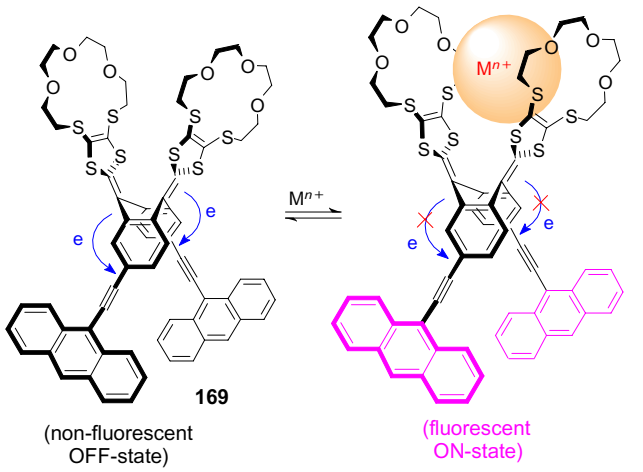
(*a*) LDA, THF, −78 °C to rt, overnight;
(*b*) 1) K_2CO_3, THF, MeOH, rt, 30 min;
2) 9-iodoanthracene, $Pd(PPh_3)_4$, CuI, piperidine, rt, overnight

in the suppression of the PET process and fluorescence enhancement.[122]

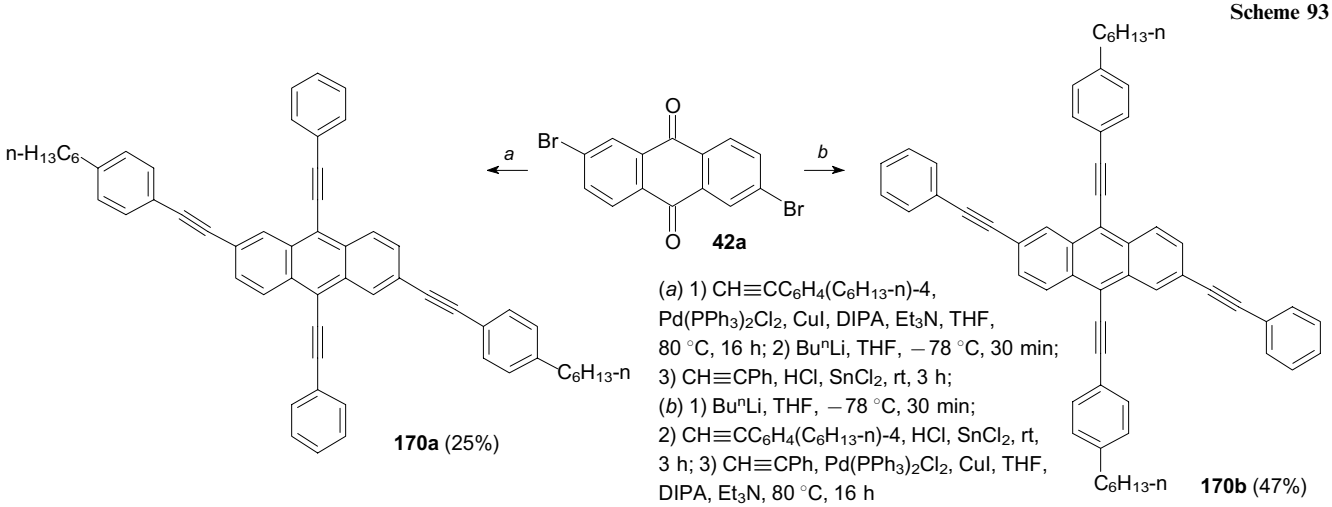
The authors applied this principle to design a sensor employing the complexation of chemosensor **169** with metal ions. The principle of sensor operation is schematically depicted in Scheme 92. Uncomplexed compound **169** shows quenched fluorescence (turn off) and, after complexation with metal cations, the electron-donating ability of the TTFAQ moiety is attenuated. This effect, in turn, suppresses the PET process (turn on). Taking into account this property of the TTFAQ moiety, the latter can be used, when paired with appropriate receptors, as a fluorescence chemosensor for large metal cations, *e.g.* Ba^{2+}.

Recent years have witnessed rapid progress in the design of new anthracene- and pentacene-based organic semiconductors, which are used in highly efficient organic transistors. In order to address this relevant issue, Hur *et al.*[60] applied a combination of the Sonogashira reaction and the transformation of a carbonyl group into an acetylene group. This leads to the transformation of the cross-conjugated structure of 2,6-dibromo-9,10-anthraquinone (**42a**) into the linear-conjugated anthracene structure, which is, as mentioned above, a necessary condition for imparting semiconducting properties to compounds.[60] Scheme 93 illustrates quite simple procedures for the synthesis of two isomeric molecules **170a**,**b**.

Scheme 92

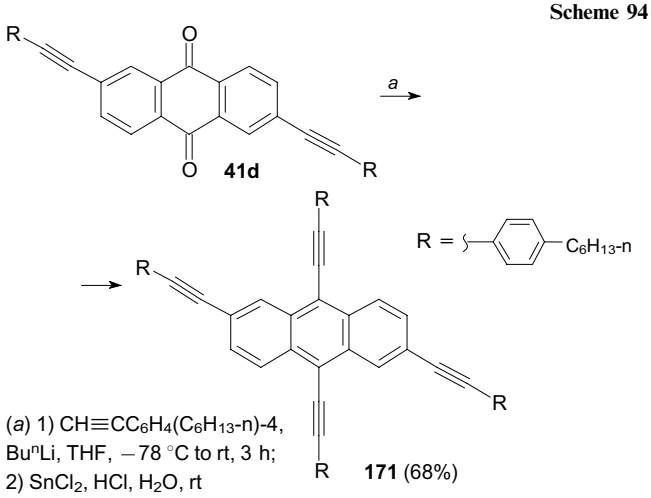


Scheme 93



(*a*) 1) CH≡CC$_6$H$_4$(C$_6$H$_{13}$-n)-4, $Pd(PPh_3)_2Cl_2$, CuI, DIPA, Et_3N, THF, 80 °C, 16 h; 2) Bu^nLi, THF, −78 °C, 30 min; 3) CH≡CPh, HCl, $SnCl_2$, rt, 3 h;
(*b*) 1) Bu^nLi, THF, −78 °C, 30 min; 2) CH≡CC$_6$H$_4$(C$_6$H$_{13}$-n)-4, HCl, $SnCl_2$, rt, 3 h; 3) CH≡CPh, $Pd(PPh_3)_2Cl_2$, CuI, THF, DIPA, Et_3N, 80 °C, 16 h

Scheme 94



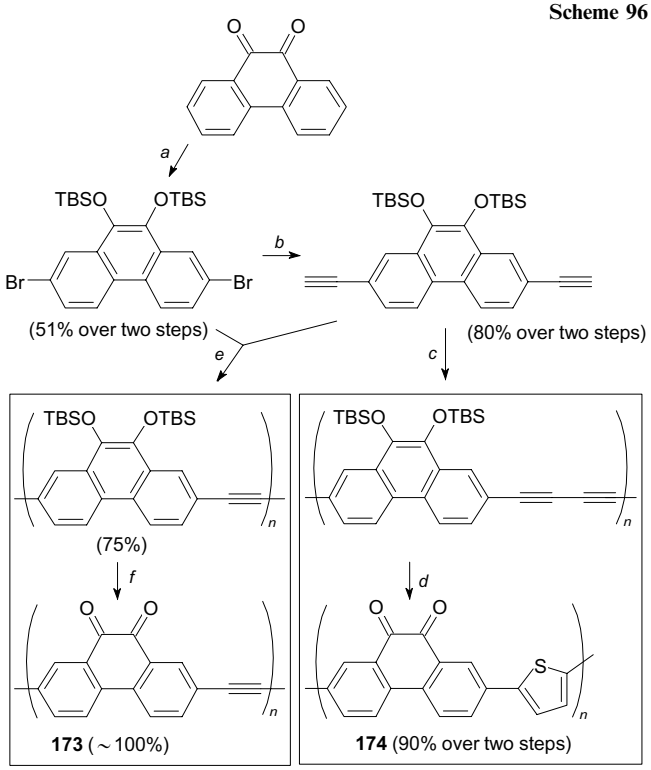
The investigation of the electronic and physical properties of isomeric ethynylanthracenes **170a**,**b** demonstrated that the difference in the position of the 1-ethynyl-4-n-hexylphenyl groups in the anthracene ring has a significant effect on the characteristics of the molecule. In particular, compound **170a** is better soluble in organic solvents. Besides, a stronger intermolecular interaction is observed for isomer **170b** because it has a more compact film morphology, exhibiting higher hole mobility ($\sim$0.27 cm^2 V^{-1} s^{-1}) in thin-film transistor devices.[60]

Taking into account the favourable effect of the introduction of 1-ethynyl-4-n-hexylphenyl groups into the anthracene molecule, this research group[123] synthesized analogue **171** containing four hexylphenylethynyl substituents *via* the modification of 2,6-bis[(4-n-hexylphenyl)ethynyl]-9,10-anthraquinone (**41d**) (Scheme 94). Target tetraalkyne **171** was synthesized by the reaction of n-butyllithium with a solution of anthraquinone **41d** in THF followed by the reduction with $SnCl_2$ in HCl.

The semiconducting properties of this compound were evaluated in an organic thin-film transistor (OTFT) and a single-crystal field-effect transistor (SC-FET). The former transistor exhibited a mobility of about 0.13 cm^2 V^{-1} s^{-1}, whereas the mobility of SC-FET was much higher (1.00 – 1.35 cm^2 V^{-1} s^{-1}). It is of practical importance that the conductance of films can be controlled by varying the nature of alkyl chains.

To further develop this area of research, the authors synthesized hexylthienoanthracenes **172a**,**b** in order to evaluate the possibility of their application in the fabrication of organic field-effect transistors and photoelectronic elements.[58] The 2-ethynylthiophene group was introduced at the 9 and 10 positions of anthraquinone in the presence of Bu^{n}Li followed by the reduction with tin chloride in HCl (Scheme 95).

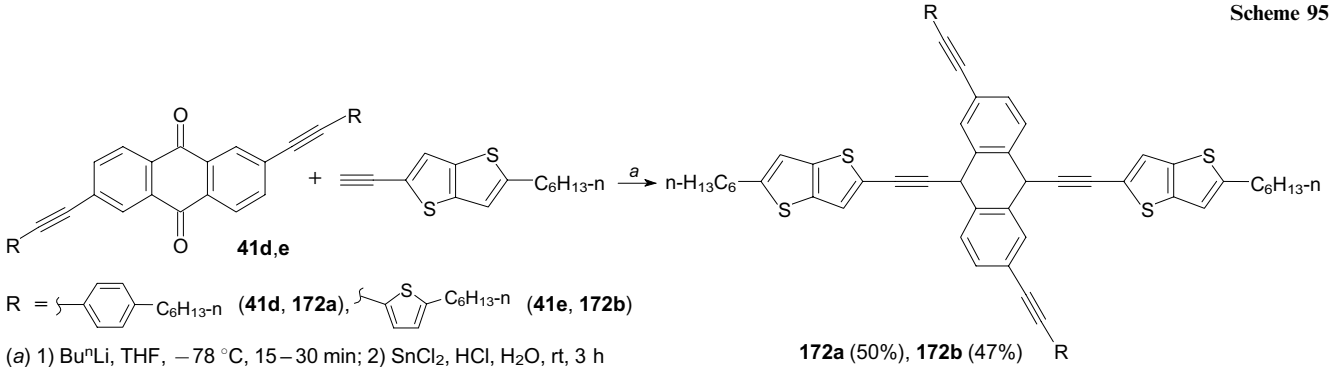
Scheme 96



Such anthracene-based conjugated molecules are characterized by a good processability. For example, they can be used to fabricate thin films on large areas. The carrier mobility in compounds **172a**,**b** was 0.15 and 0.10 cm^2 V^{-1} s^{-1}, respectively; the mobility of single-crystal field-effect transistors was 0.70 and 0.23 cm^2 V^{-1} s^{-1}.[58]

In the past decades, cyanated acenes have attracted attention as promising candidates for the fabrication of oxidation-resistant OFETs because of their high electron affinity.[61] Besides, these compounds were investigated as potential materials for the fabrication of lithium-ion batteries. Guo *et al.*[124] described the synthesis of two new

Scheme 95



linear polymers, poly(2-ethynylphenanthrene-9,10-dione) (PEPQ, **173**) and poly[2-(2-thienyl)phenanthrene-9,10-dione] (PTPQ, **174**) (Scheme 96).

A comparative study of the electrochemical properties of these two polymers showed that the replacement of the ethynyl moiety in PEPQ (**173**) by the thiophene moiety in PTPQ (**174**) endowed the latter with faster redox kinetics and a greater electronic conductivity.[124] Although the electrochemical performance of these materials is far from practical applications, the results of this study may be useful for the development of a rational approach to the construction of eco-friendly organic materials for lithium-ion batteries. As opposed to inorganic cathode materials, organic materials have obvious advantages such as the eco-friendly fabrication, facile processability, easy recyclability and disposability.[124]

Both chemists and physicists have shown keen interest in macrocyclic dehydroannulenes containing a triple bond, which can be considered as precursors of various polymer materials with a high carbon content. Such fundamentally important property of dehydroannulenes as aromaticity of macrocyclic rings is still a subject of much discussion.[75] The physicochemical properties of a series of hexadehydro[18]annulenes **74**–**76** containing different numbers of *p*-benzoquinone moieties (the synthesis is presented in Scheme 35) were investigated. In these annulenes, the diatropicity of the central 18-membered ring was shown to gradually increase with increasing number of *p*-benzoquinone units due to enhancement of the double bond character at the annulation site (see compound **76**). Annulenes **74** and **75** containing both electron-withdrawing and electron-donating groups can be considered as new dehydro[18]annulene-type push–pull π-systems.

The molecular conformation is an important structural characteristic of organic compounds. The conformation not only affects the properties of individual molecules but also plays an important role in intermolecular interactions promoting the formation of well-defined microstructures.

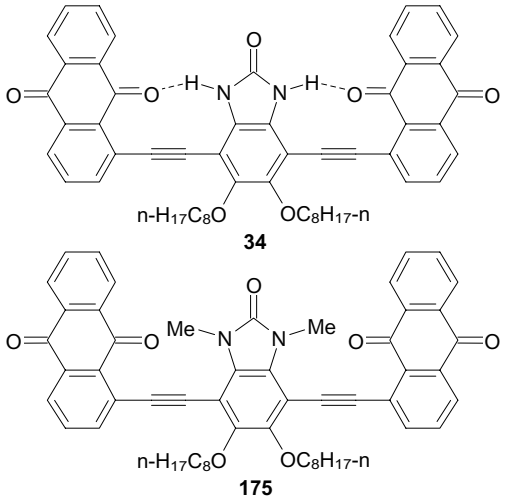
Zhu *et al.*[48] described model compound **34** (the synthesis is presented in Scheme 13) containing two alkynylquinone moieties linked together by intramolecular hydrogen bonds. The latter provide complete coplanarity of this conformation of the π-system and give rise to short π–π stacking contacts promoting molecular self-assembly and the solid-state growth of one-dimensional nano(micro)-fibres.

A comparison of bis(alkynylanthraquinone) **34** and its analogue **175**, which does not contain free NH grou ps, demonstrated that intramolecular hydrogen bonds and the coplanarity of model compound **34** are responsible for its strong intermolecular aggregation in the solid state. The results of the study[48] not only allow the establishment of a fundamental correlation between intramolecular noncovalent bonds and the properties of the molecule but also make it possible to predict the strategies to endow the materials with desired properties.

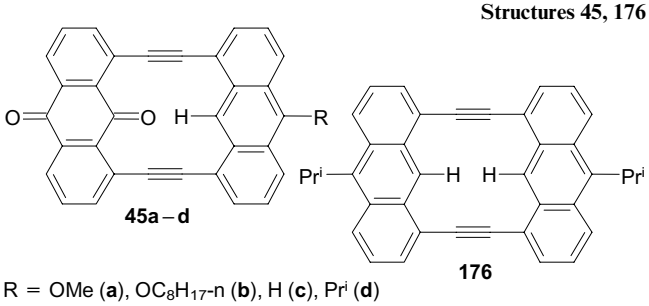
The introduction of a triple bond in an organic molecule often imparts rigidity to the final product, particularly when this bond is involved in the macrocycle. For example, this strategy is applied to prepare cyclic arylene–ethynylene oligomers, which have attracted attention as new π-conjugated compounds in structural and supramolecular chemistry.

The Sonogashira reaction was used to synthesize two types of π-conjugated compounds (see Scheme 18): anthracene–acetylene oligomer **176** and a macrocycle containing anthracene and anthraquinone moieties (compounds **45a**–**d**).[55,56] The X-ray diffraction study demonstrated that anthraquinone oligomers **45a**–**d** are characterized by a nonplanar structure due to steric hindrance caused by the endocyclic carbonyl group. According to the X-ray diffraction data, compounds **45a**,**d** exist as stacked dimeric pairs in single crystals with intramolecular interactions between the anthraquinone and anthracene moieties. Oligomers **45a**–**c** showed self-association in solution. Their association constants for monomer–dimer exchange were determined by variable-concentration ^{1}H NMR measurements in $CDCl_3$. The strongest association was observed for compound **45b** due to the solvophobic effect of the *n*-octyloxy group.

Structures 34, 175



Structures 45, 176



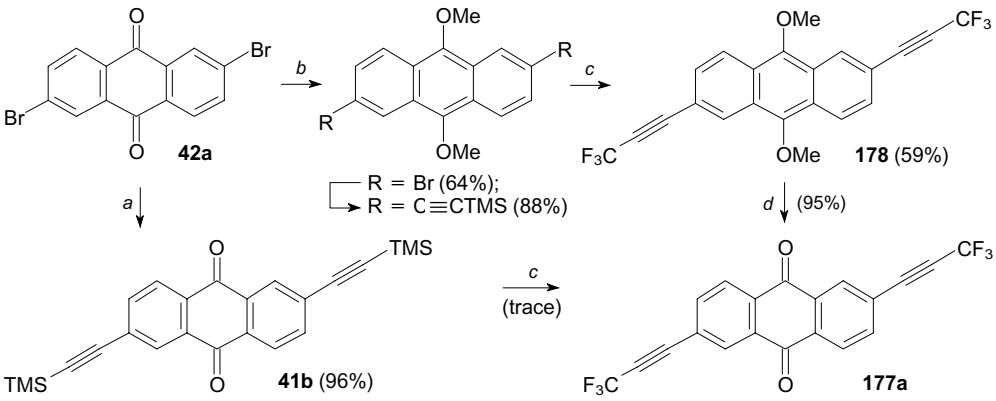
R = OMe (**a**), OC_8H_{17}-n (**b**), H (**c**), Pr^i (**d**)

This strategy of molecular design can be applied to construct different functional π-conjugated anthracene–anthraquinone oligomers.

Organic semiconductors continue to be an attractive area of research in organic chemistry, acetylene compounds often playing a key role in their fabrication. Zhao *et al.*[125] examined the possibility of preparing organic semiconductors based on (trifluoromethyl)ethynyl-containing 9,10-anthraquinone **177a** (Scheme 97). In this reaction, dibromide **42a** served as the starting compound. Despite a large number of steps, the synthesis through the intermediate formation of dimethoxy derivative **178** proved to be favourable because of a higher yield of the target product.

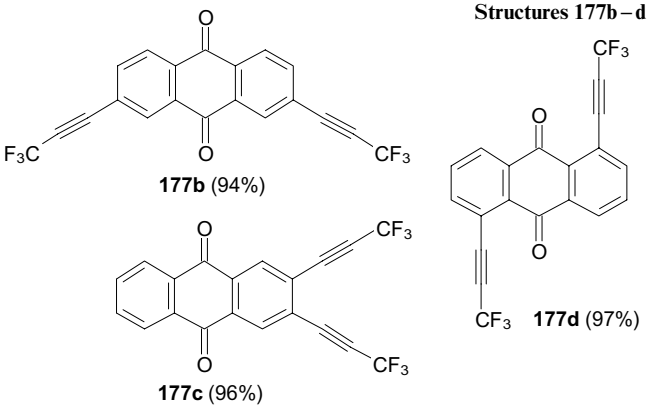
Other electron-deficient alkynylanthraquinones **177b**–**d** were synthesized in a similar fashion from appropriate dihalo-9,10-anthraquinones. It was shown that their π–π

Scheme 97



(*a*) CH≡CTMS, $Pd(PPh_3)_4$, CuI, DIPA, THF, Δ; (*b*) 1) MeI, NaOH, TBAB, $Na_2S_2O_4$, CH_2Cl_2, H_2O, rt, 10 h; 2) CH≡CTMS, $Pd(PPh_3)_4$, CuI, DIPA, THF, 80 °C, overnight; (*c*) [$CuCF_3$], TMEDA, DMF, rt, 18 h; (*d*) NBS, THF, H_2O, rt, 30 min

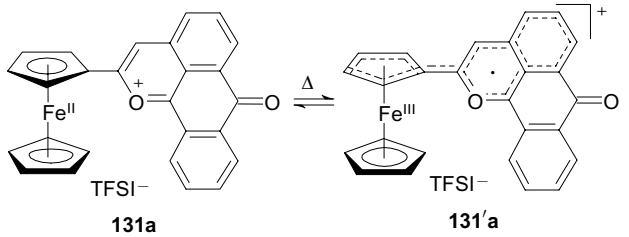
Structures 177b–d



stacking in crystals can be tuned by varying the position of the (trifluoromethyl)ethynyl group in the anthraquinone core. It was found that trifluoromethylanthraquinones act as n-type semiconductors with electron mobility of up to 0.28 $cm^2\ V^{-1}\ s^{-1}$ and they are suitable for the fabrication of organic field-effect transistors.

Functional molecules capable of altering their physical properties upon exposure to external stimuli, such as light, temperature and magnetic field have attracted great attention due to prospects of their application in electronics. Nishihara and co-workers [100, 101] developed an approach to the synthesis of this type of compounds based on alkynyl-9,10-anthraquinones. 9,10-Anthraquinones **22** containing the RC≡C group at the 1 position undergo intramolecular cyclization when treated with TFSIH (see Scheme 64). The fundamentally important results of this cyclization, for example, in the case of the ferrocenyl derivative (R = Fc), are the extension of the π-conjugated system in the chromenilium salts (1-FcPyl]$^+$X$^-$ (**131a**), where Pyl is pyrylium, X = TFSI, TfO, PF_6 and BF_4, and the valence tautomerism between the Fe^{2+} and Fe^{3+} states (Scheme 98).

Scheme 98

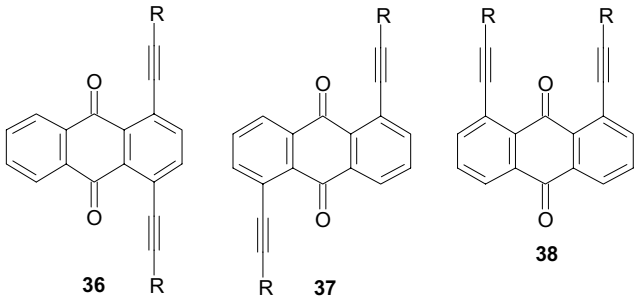


The existence of valence tautomerism was confirmed by ^{57}Fe Mössbauer spectra measured in a wide temperature range (from 12 to 290 K), which showed that the Fe^{2+} ion is in equilibrium with Fe^{3+}. This is attributed to an extension of the π-conjugated system in benzochromenilium salt **131a**, which causes a decrease in the LUMO level of the π* orbital, induces intramolecular electron transfer and gives rise to valence tautomer **131′a** in the solid state.[100, 101]

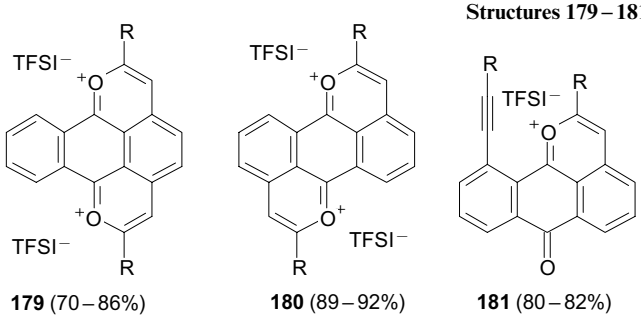
In subsequent studies, Rao *et al.*[50, 126, 127] investigated this reaction in relation to the double proton cyclization of 1,4-, 1,5- and 1,8-diethynylaryl-9,10-anthraquinones (**36**–**38**), which were prepared in a similar way to the synthesis of monoalkynylquinones (see Scheme 64). The intramolecular cyclization of isomers **36** and **37** affords dipyrylium salts **179** and **180** with a pentacyclic skeleton.

The synthesized compounds have unique electrochemical and magnetic properties. This is particularly the case with the dications [1,4(5)-Ar_2Pyl_2]$^{2+}$. These dications are paramagnetic and contain two spins due to valence tautomerism. Such divalent cations can be reduced to the neutral compounds [1,4(5)-Ar_2Pyl_2]^0, which can be considered as

Structures 36–38

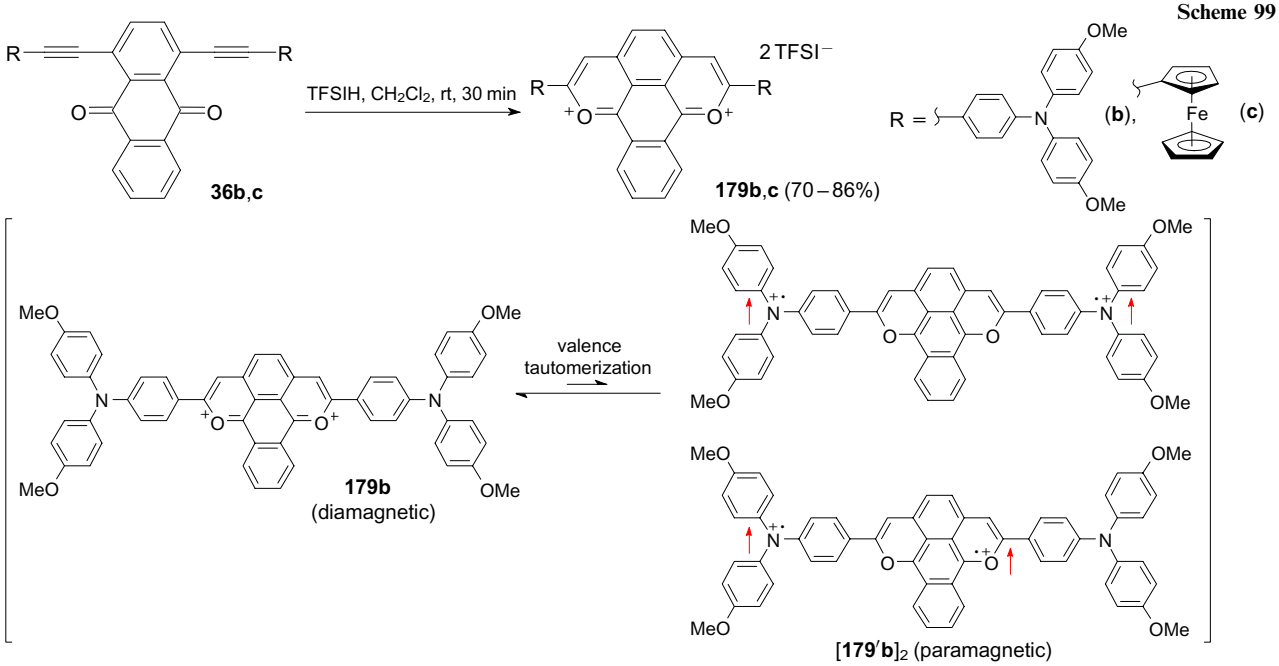


Structures 179–181



R = Fc, Ph, 4-MeC_6H_4, 3-MeC_6H_4, Am

Scheme 99



aromatic systems containing 22 π-electrons ($4n + 2$) and the pentacyclic skeleton (an example of the cyclization for the 1,4-isomer is presented in Scheme 99).[126] Besides, it was shown that these compounds exist as two valence tautomers, the equilibrium between which is shifted mainly to the formation of the diamagnetic state.

Rao *et al.*[127] described the specific features of the cyclization of a series of 1,8-di(arylethynyl)quinones **38**. It was shown that the protonation-induced cyclization of compounds **38** affords the corresponding pyrylium salts [1,8-Ar_2Pyl] (**181**) with a tetracyclic structure and with retention of the triple bond. The formation of pyrylium salts causes extensive donor-acceptor interactions and results in a smaller difference between the HOMO and LUMO (0.50–0.73 V) compared to their 1,4- and 1,5-analogues.[128]

The review [128] summarizes the data on this cyclization of *peri*-alkynyl-9,10-anthraquinones with strong acids. The synthesized compounds have unique electrochemical and magnetic properties because they possess:

— an additionally extended conjugation system,

— strong donor-acceptor interactions,

— a narrow energy gap between the HOMO and LUMO,

— characteristic valence tautomerism.

Besides, the neutral molecules $[1,4\text{-}Am_2Pyl_2]^0$ and $[1,5\text{-}Am_2Pyl_2]^0$ can be considered as aromatic systems with 22 π-electrons ($4n + 2$). These conclusions may be useful in the design of new functional molecular systems.

Dendrimers were chosen as the most promising structures for the construction of efficient light-harvesting antennae for artificial photosynthesis.[129,130] A new type of snowflake-shaped dendrimers **182** with the Zn porphyrin core was synthesized from terminal acetylene **183** under the standard Sonogashira reaction conditions (Scheme 100).[131]

A comparative study of the photoinduced electron transfer (ET) in Zn porphyrin dendrimer **182** and its linear analogue **184** was performed using fluorescence spectroscopy.

Branched Zn porphyrin dendrimer **182** showed a significant increase in the rate of photoinduced ET compared to linear analogue **184** due to dendritic architecture. The enhancement of ET can be attributed to a cooperative effect of conformational changes caused by the hydrophobicity of benzyl ether chains and the π-conjugation of Zn porphyrin with four ethynylanthraquinone groups. This specific feature of snowflake-shaped dendrimers is very important in the design of particular electronic devices.

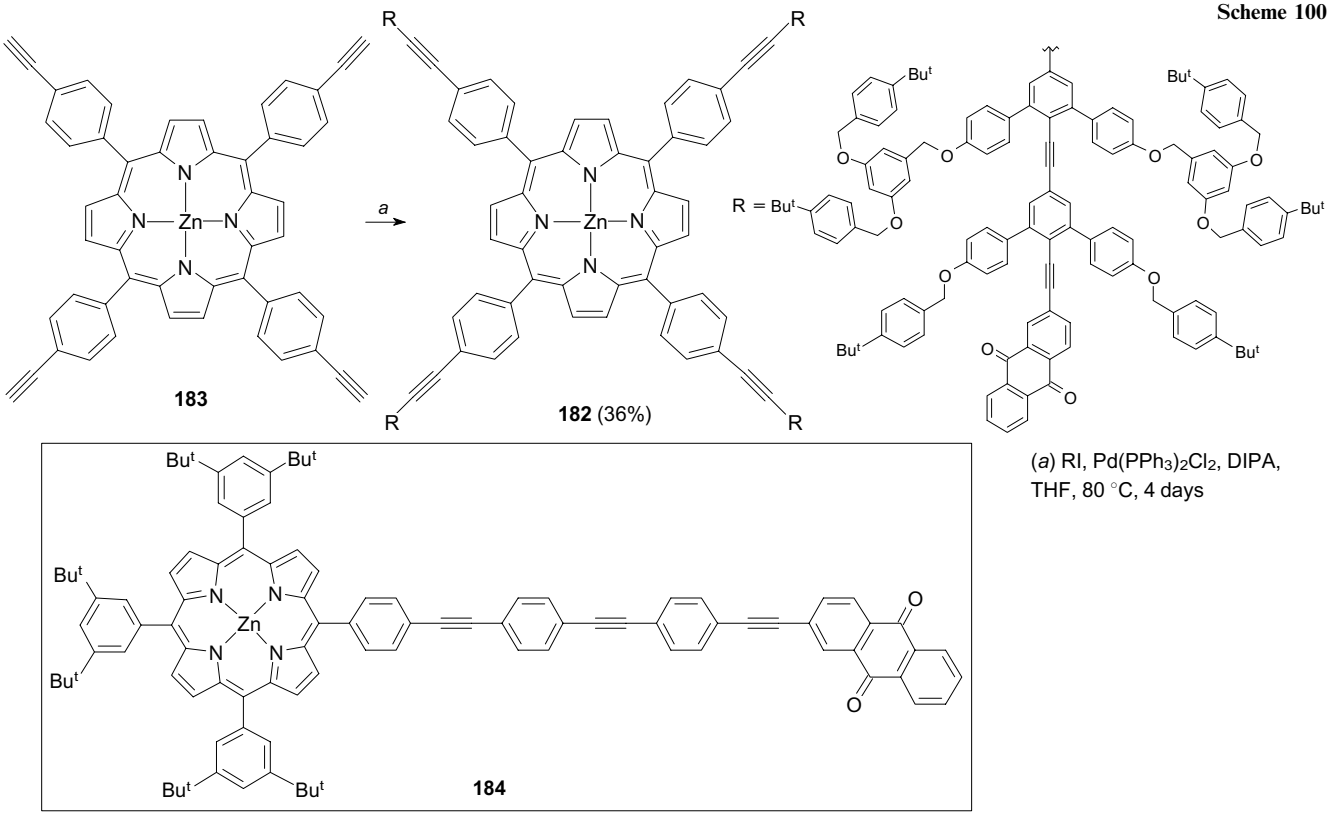
Currently, polymer solar cells attract keen attention of chemists due to their great advantages over the existing inorganic solar cells, such as facile processability, light weight, flexibility and low cost. Li *et al.*[132] synthesized a new class of soluble polymers **185** and **186** by the Sonogashira reaction based on platinum(II) acetylide with the 9,10-anthraquinones spacer, and their photoelectrical properties were studied (Scheme 101).

Polymer platinum compounds are solids, which are stable under thermal and oxidative conditions and are soluble in chlorinated hydrocarbons and toluene. The molecular masses of compounds **185** and **186** calibrated with polystyrene standards were 7270 and 16 250, respectively. Both polymers show good thermal stability; their decomposition starts at 336 (for **185**) and 318 °C (for **186**).

The power conversion efficiency of solar cells fabricated from polymer **185** and the fullerene derivative, [6,6]-phenyl-C_{61}-butyric acid methyl ester (PCBM), is only 0.03%, whereas it increases to 0.35% for the cell fabricated from compound **186** and PCBM. For safety concern, metallopolymer **186** was tested *in vitro* for possible cytotoxicity. This compound showed no toxicity up to a dose of 50 mg mL^{-1} on the HaCaT cell line (human skin keratinocytes). These results provide evidence that Pt^{II} acetylide polymers are safe and can be used to fabricate materials for electronics.

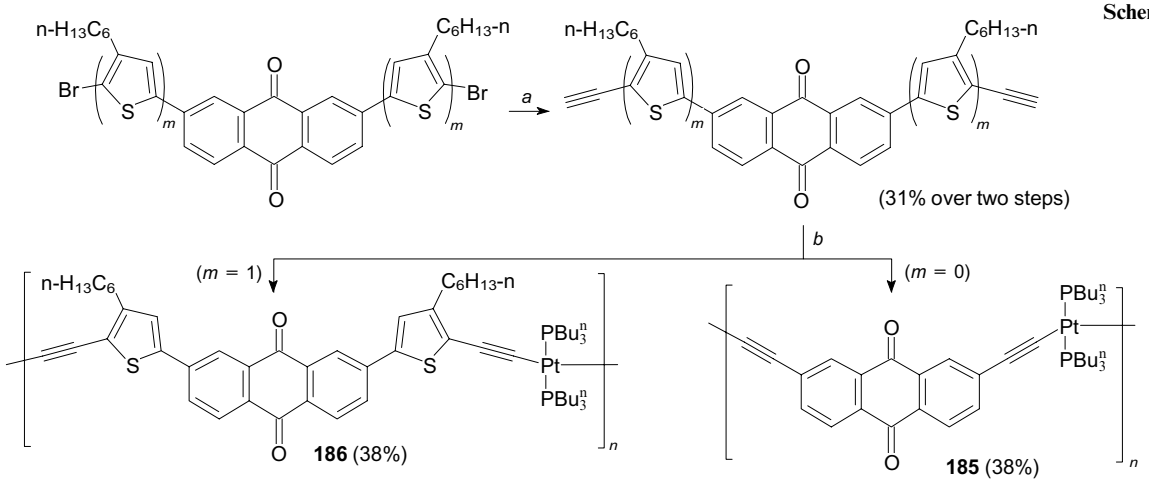
Platinum-containing polymers are also of interest as promising photoactive nanofilms.[110] A comparative study revealed significant differences in the physical properties of quinone polymer **187** and its aza analogues **188** and **189**.[111] Compounds **188** and **189** show intense fluorescence. Only polymer **187**, unlike aza analogues **188** and **189**, exhibits

Scheme 100



(*a*) RI, $Pd(PPh_3)_2Cl_2$, DIPA, THF, 80 °C, 4 days

Scheme 101



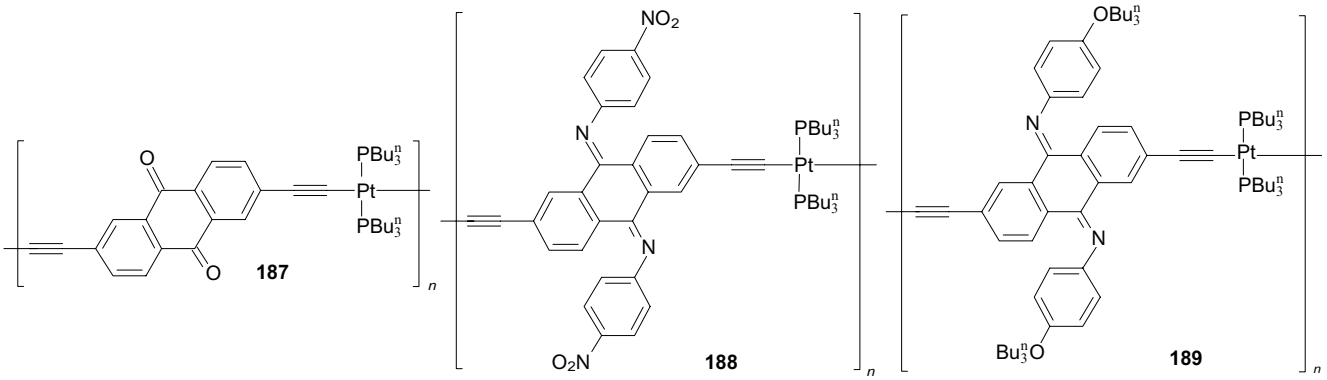
(*a*) 1) CH≡CTMS, $Pd(OAc)_2$, CuI, PPh_3, Et_3N, 50 °C, 24 h; 2) K_2CO_3, MeOH, CH_2Cl_2, rt, overnight; (*b*) *trans*-$[Pt(PBu^n_3)_2Cl_2]$, CuI, Et_3N, CH_2Cl_2, rt, 24 h; *m* = 0, 1

phosphorescence, thereby emphasizing the difference in the electron transfer from the C═O group to the N═C_6H_4X group and also from the NO_2 group to OBu^n. Consequently, such conjugated platinum-containing polymers are promising for the fabrication of photoactive materials.

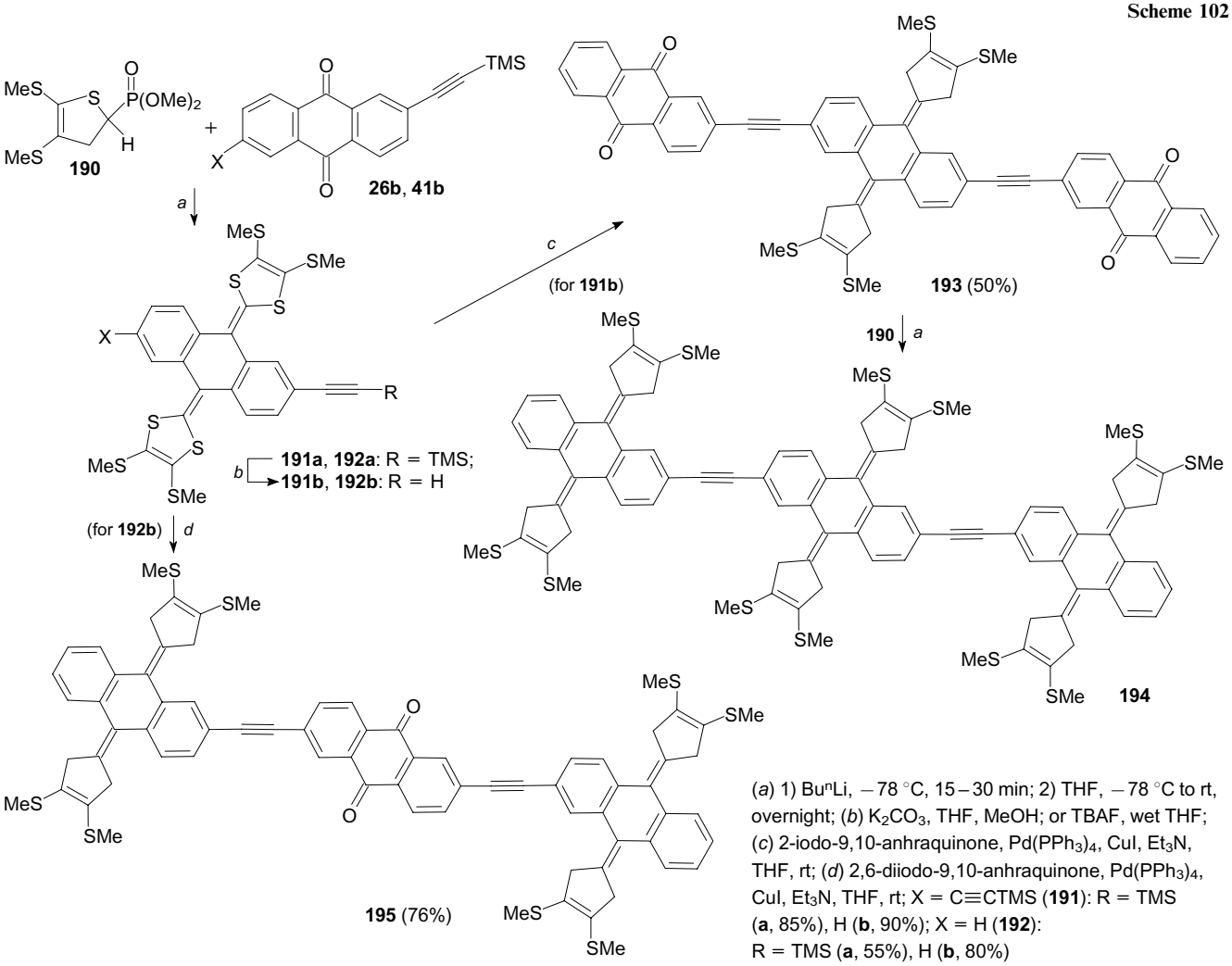
First studies on the characterization of TTF derivatives were published in the 1970s. These compounds have attracted attention as strong π-electron donors capable of forming electrically conducting organic charge-transfer complexes, so-called organic metals. Thus, Yamada and Sugimoto [133] reported the first synthesis of a series of conjugated TTF derivatives based on the Sonogashira and Horner–Wadsworth–Emmons reactions (Scheme 102).[41]

The reactions of mono- (**26b**) and dialkynylquinones (**41b**) with phosphonate **190** in the presence of Bu^nLi at −78 °C afforded 2-ethynylated (**191a**) and 2,6-diethynylated (**192a**) anthraquinone derivatives of tetrathiofulvalene, which can easily be desilylated with K_2CO_3 or TBAF to form corresponding alkynes **191b** and **192b**. The cross-coupling of compound **191b** with 2 equiv. of 2-iodoanthraquinone gave dialkyne **193**, which was then subjected to Horner–Wadsworth–Emmons olefination with phosphonate to form TTFAQ trimer **194**. The cross-coupling of 2,6-diiodoanthraquinone with 2 equiv. of compound **192b** afforded target product **195**. All trimers are moderately soluble in chlorinated organic solvents such as chloroform and dichloromethane. The redox properties of molecular

Structures 187 – 189



Scheme 102

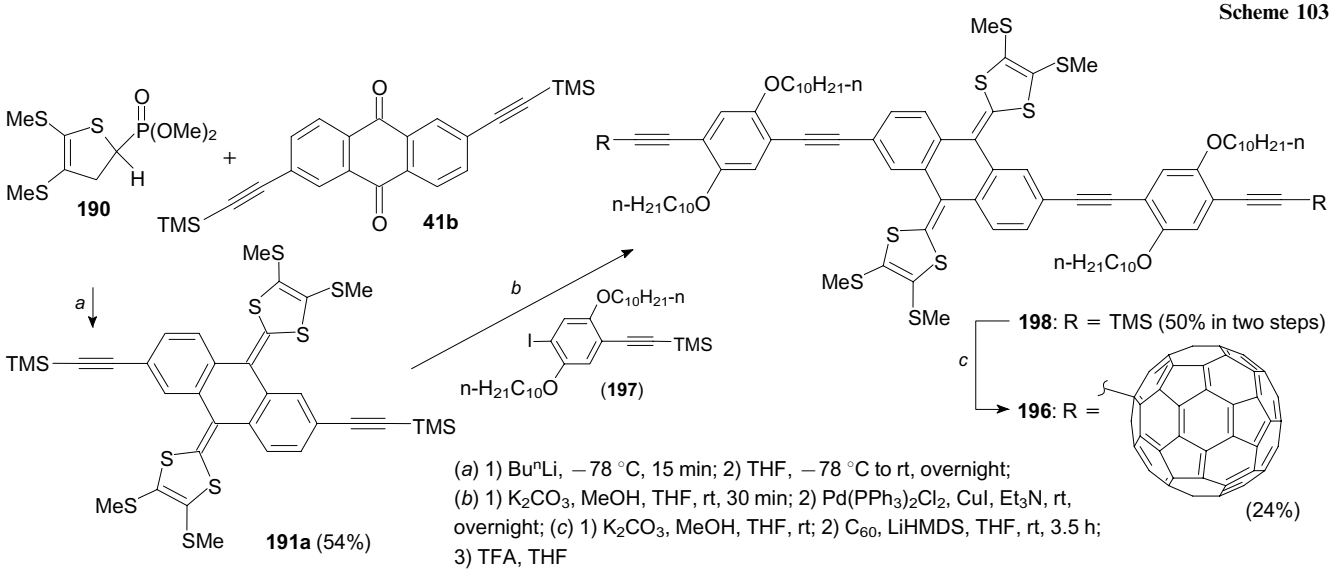


ensembles **193** – **195** were studied. As expected, trimer **194** showed insignificant electronic coupling between TTF moieties, whereas noticeable donor – acceptor (D – A) electronic interactions between electroactive groups were observed in anthraquinone-containing compounds **193** and **195**.

The above TTF derivatives have attracted attention as suitable units for the design of sensing detectors and switches. Yamada and Sugimoto [133] described the synthesis of the TTF derivative of dithioldihydroanthracene **196** belonging to so-called extended π-conjugated molecular structures. According to the published data, these compounds have high electron-donating ability (Scheme 103).

As in the above example, compound **191a** was synthesized by the Wittig – Horner reaction of phosphonate **190** with dialkyne **41b** in the presence of Bu^{n}Li.[62] The desilylation of compound **191a** with potassium carbonate and the subsequent Sonogashira reaction with iodide **197** gave protected dialkyne **198**, which was desilylated with K_2CO_3 in a MeOH – THF mixture (1 : 1) followed by the addition of fullerene C_{60}. The ultrasonic treatment of the resulting reaction mixture in THF followed by the reaction with

Scheme 103

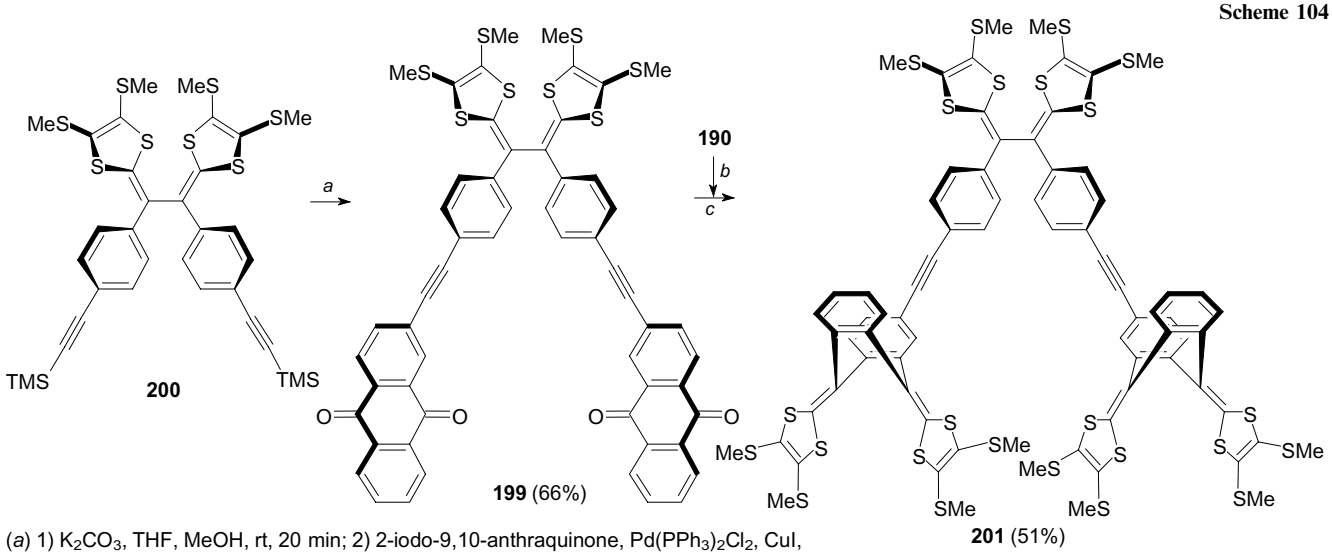


lithium bis(trimethylsilyl)amide (LiHMDS) afforded the C_{60}–TTFAQ–C_{60} triad (**196**). The electronic properties of this compound were characterized by cyclic voltammetry and UV spectroscopy. Electrochemical studies demonstrated that triad **196** is characterized by a narrow HOMO–LUMO gap (1.14 eV). This feature of the macromolecule may be useful in the design of organic semiconductors and nonlinear-optical devices. Being excellent electron donors, such TTFAQ derivatives are widely utilized to fabricate artificial photosynthetic systems, in which fullerene C_{60} generally acts as an electron acceptor.[62]

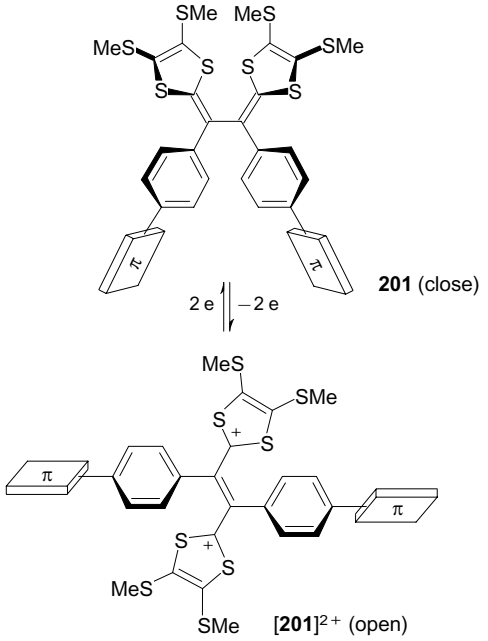
Apart from the traditional use in conducting organic materials, tetrathiafulvalene derivatives have attracted recent attention as potential candidates for the fabrication of redox switches. Among numerous TTF derivatives, diaryl-substituted tetrathiafulvalene vinylogues (TTFV, *e.g.*, compound **199**) demonstrate a unique property as conformational switches related to the simultaneous two-electron redox reaction at the TTFV moiety. Two molecular tweezers containing the TTFV core were synthesized *via* sequential Sonogashira and Horner–Wadsworth–Emmons reactions (Scheme 104).[134]

An acetylenic precursor of TTFV **200** was synthesized by a method described previously. The removal of the trimethylsilyl group in this compound with K_2CO_3 followed by the Sonogashira cross-coupling with 2-iodoanthraquinone afforded molecular tweezer **199**. It is worth noting that the latter compound is the acceptor-donor-acceptor triad AQ–TTFV–AQ. The authors supposed that the target TTFAQ-tipped tweezer can easily be synthesized *via* the double Horner–Wadsworth–Emmons reaction. As shown in Scheme 104, phosphonate **190** was first treated with Bu^nLi at −78 °C followed by the addition of AQ–TTFV–AQ (**199**) to form target molecular tweezer **201**. The electrochemical and spectroscopic methods revealed a significant electronic interaction between the central TTFV moiety and side groups through π-conjugation. In both molecular tweezers, the TTFV hinge undergoes the simultaneous two-electron transfer to form stable dication $[\mathbf{201}]^{2+}$ (Scheme 105).

Scheme 104



Scheme 105

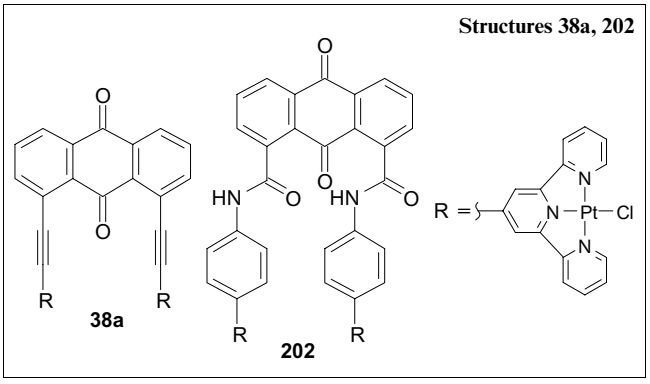


The oxidation of the TTFV scaffold causes a change from the *s-cis* to *trans* configuration of the double bond due to significant electrostatic repulsion between two dithiol moieties. This process is chemically reversible, which is important for the fabrication of redox-switchable devices.[135]

In recent years, emission materials have attracted great attention due to their potential use as luminescent probes and light-emitting diodes.[136, 137] Utsuno *et al.*[54] studied the photochemical properties of dinuclear complexes containing the anthraquinone core bridged *via* an amide linker ($[Pt_2Cl_2$(AQ-amide-tpy$_2$)$](PF_6)_2$, **202**) or an ethynylene linker ($[Pt_2Cl_2$(AQ-eth-tpy$_2$)$](PF_6)_2$, **38a**) (the synthesis of compound **38a** is presented in Scheme 17).

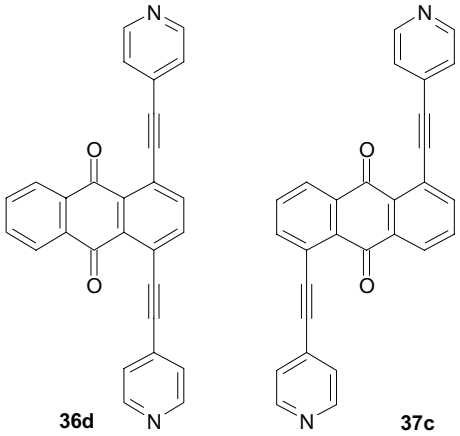
Anthraquinone-1,8-dicarboxylic acid diamide (AQ-amide-tpy$_2$) was synthesized from anthraquinone-1,8-dicarbonyl chloride and 4-([2,2′;6′,2″]-terpyridin-4-yl)aniline in the presence of Et_3N.[54] The investigation of the photochemical properties showed that an intramolecular interaction between two platinum cations in amide-bound dinuclear complex **202** was scarcely observed in the ground state, but this interaction existed in the excited state. On the contrary, an intramolecular interaction in the excited state of dinuclear complex **38a** was weaker. The authors suggested that the restrictions on Pt—Pt distance variations due to the rigidity of the linkage moiety (a triple bond) in structure **38a** prevent the Pt—Pt interaction in the excited state.

Structures 38a, 202



The control of the charge transfer through a single molecule connected to metallic electrodes remains one of fundamental challenges of nanoelectronics. Baghernejad *et al.*[49] synthesized two π-conjugated 1,4- and 1,5-dialkynylanthraquinones (**36d** and **37c**) and evaluated their conductance (the synthesis in presented in Schemes 14 and 15, respectively).

Structures 36d, 37c

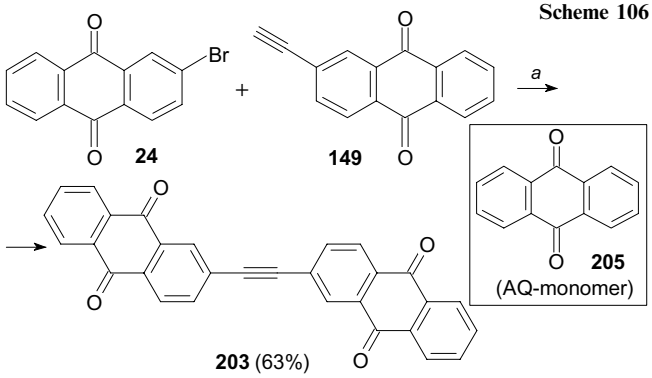


It is worth noting that the conductance of isomer **36d** is significantly different from that of isomer **37c**, which is attributed to the different arrangement of the pyridine units in the linear-conjugated (1,4-AQ) and cross-conjugated (1,5-AQ) molecules. The lower conductance of 1,5-isomer **37c** is consistent with the expected appearance of destructive quantum interference. The experimental data on the conductance are in good agreement with the results of *ab initio* calculations.[49]

An important challenge in the fabrication of efficient lithium-ion batteries is the inclusion of redox-active metal-free organic materials in their composition. Yao *et al.*[65] examined the possibility of application of alkynylanthraquinone-based oligomers as stable organic electrodes for batteries. For this purpose, they synthesized dimer **203** and trimer **204** containing anthraquinone moieties linked by a C≡C bond under the standard Sonogashira reaction conditions (Schemes 106 and 107).

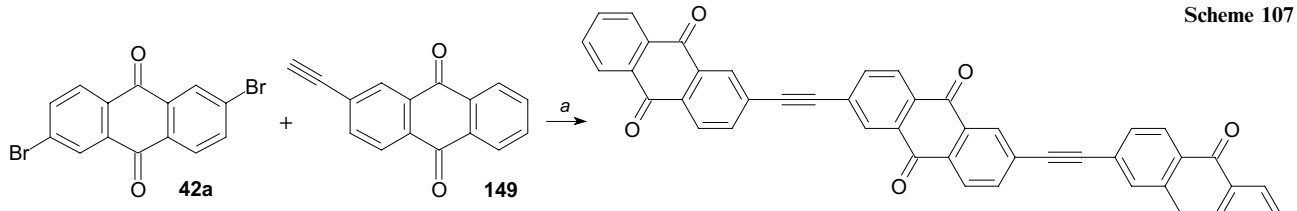
The authors compared the performance of anthraquinone dimer **203** and trimer **204** as batteries with that for 9,10-anthraquinone (**205**). The capacity of monomer **205**

Scheme 106



(*a*) $Pd(PPh_3)_2Cl_2$, CuI, DIPA, THF, Δ, 15 h

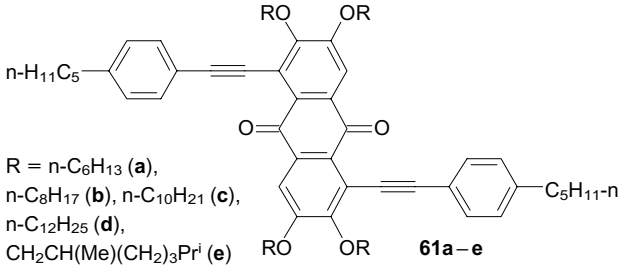
Scheme 107



rapidly decreased, whereas trimer **204** retained constant capacity over hundred cycles. Quantum chemical calculations demonstrated that the oligomerization can lead to a significant increase in the number of intermolecular $\pi-\pi$ interactions. Apparently, the results of these studies can serve as a guidance for the development of new organic oligomers for batteries with good cycling performance and high capacity.

In recent years, extensive research has focused on the synthesis of functional materials with desired properties, among which liquid crystals composed of self-assembled elongated molecules hold a special place. These crystals can be used as anisotropic materials, the processing of which does not require sophisticated technologies.[53] Five new liquid-crystalline alkoxy derivatives of 1,5-dialkynyl-9,10-anthraquinone **61a–e** were synthesized by the Sonogashira cross-coupling (the synthesis is presented in Scheme 29) and their phase transitions were studied.[53]

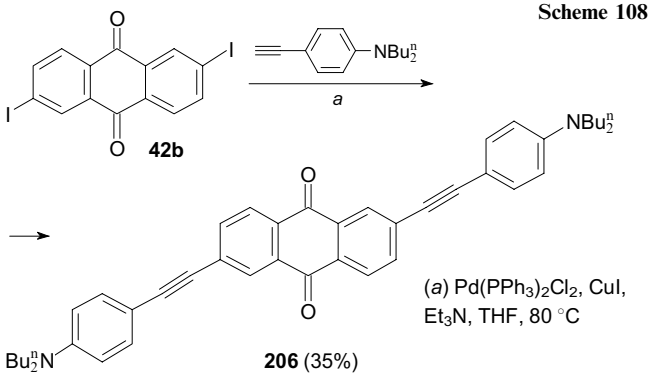
Structures 61a–e



In order to determine the exact nature of mesophases, the authors obtained electron density maps using small-angle and wide-angle X-ray scattering (SAXS and WAXS) methods. A comparison of compounds **61** containing different substituents demonstrated that the crystal columnar rectangular (Crcolrec) phase was stable at a lower temperature for derivative **61a** with the shortest peripheral alkoxy group (R = n-C_6H_{13}). For compounds **61a**,**b**,**e**, the electrical conductance in the columnar hexagonal (Colh) phase was 6.16×10^{-8}, 1.78×10^{-8} and 2.04×10^{-8} S m^{-1}, respectively. It was found that the electrical conductance in the Colh mesophase is almost 10 times higher than that of the corresponding Crcolrec phase. The band gap width (the difference between the HOMO and LUMO) for these dialkynylquinones is in the range from 2.79 to 2.82 eV, making it possible to use these compounds in electronic devices.

The two-photon photopolymerization is of particular interest because this process is demanded in the fabrication of miniature elements for nanotechnology and other fields requiring high precision. This unique process allows the production of complex 3D structures with a spatial resolution of ~120 nm.[138] New two-photon initiator **206** containing a triple bond was synthesized under the standard Sonogashira cross-coupling conditions (Scheme 108).

Scheme 108



Branched alkyl chains were introduced at the terminal electron-donating groups in order to enhance the solubility of the monomer. New initiator **206** has high reactivity in the two-photon induced photopolymerization at a low concentration (0.1 mass %). It is worth noting that it shows high reactivity in the two-photon induced microfabrication.[138]

5. Biological activity of alkynylquinones and their modification products

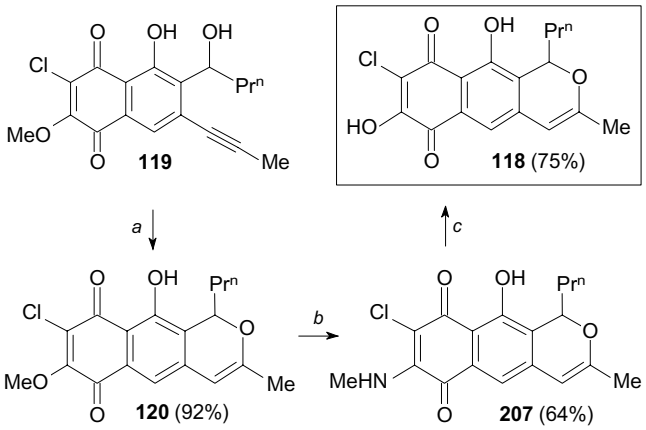
The development of rational and technology-based methods for the synthesis of biologically active compounds as drug candidates takes on particular importance at the present time. There are challenges in both designing total synthesis of natural compounds, which have already been used in medical practice, and developing procedures for the preparation of their synthetic analogues.

An example of the former line of research is the development of the total synthesis of natural chloroquinocin (**118**) (Scheme 109).[74] The starting propynyl-1,4-naphthoquinone **119** was cyclized in the presence of $PdCl_2$ to form pyranoquinone **120**, which was treated with $MeNH_2$ followed by acid hydrolysis of amino derivative **207** giving target chloroquinocin (**118**). Since chloroquinocin is active against Gram-positive bacteria, in particular against methicillin-resistant *Staphylococcus aureus*, one may agree with the authors that the rational approach to the synthesis of this unique pyranonaphthoquinone provides a route to new chemotherapeutic agents.

With the goal of searching for anticancer agents, a series of functional 2,3-dialkynyl-1,4-naphthoquinone derivatives **15** were synthesized from dibromide **13** by the Sonogashira and Castro reactions (the synthesis is presented in Scheme 4).[27,28]

Dyines **15** were evaluated as potential cytotoxic agents against three cancer cell lines: human ovarian adenocarcinoma (OVCAR-8), human metastatic prostate cancer

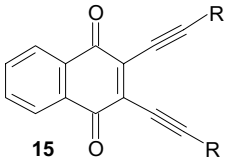
Scheme 109



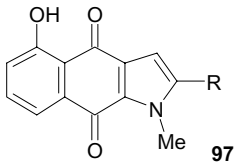
(*a*) $Pd(MeCN)_2Cl_2$, CH_2Cl_2; (*b*) $MeNH_2$, THF, rt; (*c*) HCl, MeOH, 55 °C

(PC-3M) and human bronchoalveolar lung carcinoma (NCI-H358M). All compounds exhibited strong cytotoxic activity on these three cancer cell lines. Thus, the half-maximal inhibitory concentrations (IC_{50}) were not higher than 10 μM. Yamashita *et al.*[86] evaluated benzo[*f*]indole-4,9-diones **97** (the synthesis is presented in Scheme 46) for the ability to suppress the growth of human tumour cell lines, including the A549 (lung cancer) and MCF-7 (breast cancer) cell lines. Compound **97** (R = CH(OH)Me) exhibited a moderate antiproliferative effect against both cell lines with IC_{50} = 41.5 and 56.1 μM, respectively.[86]

Structures 15, 97



R = Ph, 4-$O_2NC_6H_4$, 4-$MeOC_6H_4$, $C(OH)Me_2$, $C(OMe)Me_2$, $(CH_2)_3OH$, Bu^n, n-C_6H_{13}, n-C_8H_{17}, 1-hydroxycyclohexyl



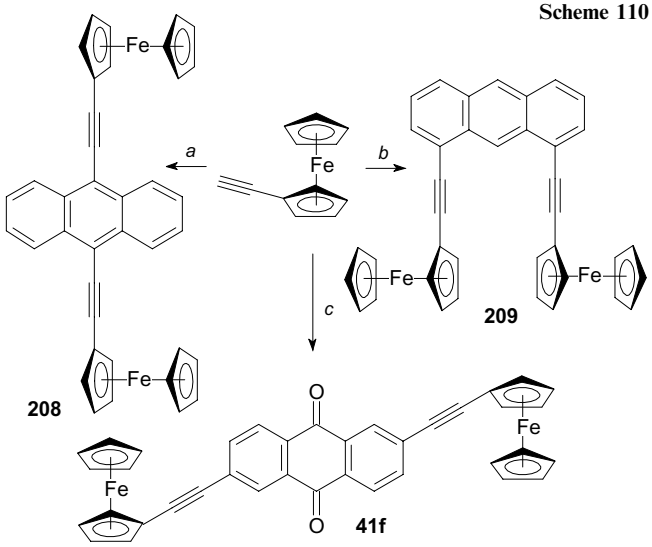
R = Ph, CH(OH)Me, $(CH_2)_2Ph$

An important area of medicinal chemistry is the design of so-called hybrid molecules combining two or more pharmacophore moieties. In this regard, acetylene derivatives of anthraquinones are promising bioconjugates. Some compounds with a triple bond exhibit significant anticancer activity [17] and they are sometimes used in medical practice. On the other hand, anthraquinone derivatives can intercalate into duplex DNA,[18] and many natural anthraquinones exhibit high biological activity.

Singh *et al.*[59] discussed the potential use of ferrocene-substituted bis(ethynyl)anthracene and -anthraquinone derivatives as anticancer agents (Scheme 110).

The reaction of 2,6-diiodo-9,10-anthraquinone (**42b**) with ethynylferrocene in the presence of $Pd(PPh_3)_2Cl_2$ as the catalyst afforded 2,6-bis(ferrocenylethynyl)anthraquinone (**41f**). Two isomeric bis(ferrocenylethynyl)anthracene derivatives **208** and **209** were synthesized in a similar fashion from 9,10- and 1,8-dibromoanthracenes, respectively. The biological activity of compounds **41f**, **208** and **209** was evaluated by molecular docking into various cancerous proteins. Derivative **209** displayed the best interaction with

Scheme 110



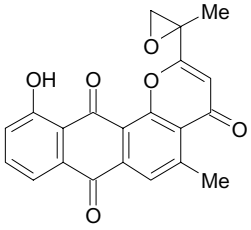
(*a*) 9,10-dibromoanthracene, $Pd(PPh_3)_2Cl_2$, Et_3N, THF, 75 °C, 15 h; (*b*) 1,8-dibromoanthracene, $Pd(PPh_3)_2Cl_2$, Et_3N, PhMe, 90 °C, 15 h; (*c*) 2,6-diiodo-9,10-anthraquinone (**42b**), $Pd(PPh_3)_2Cl_2$, Et_3N, PhMe, 90 °C, 15 h

the cancer-related Aurora A protein, a well-known target for cancer therapy (the binding energy is 10.61 kcal mol^{-1}).

Anthrapyranones exhibit various biological activities. Most often these compounds are used as antibacterial or anticancer agents. For example, the compound BE26554A (**210**), structurally related to the antibiotic saptomycin E, was isolated from the actinobacteria *Streptomyces* A26554 in 1994.[4, 5] Anthrapyran-4-one **210** and its functionalized analogues showed IC_{50} in the range of 0.017 – 0.0007 μM on the P388 leukemia cells. Taking into account the properties of compound **210** and its derivatives, the authors have focused their efforts on the development of a rational method for their synthesis. As a result, they prepared a wide range of compounds **211** (major product) and **212** (minor product) for the further evaluation of their biological activity.[139] An elegant synthesis of anthrapyran-2-ones **211** and **212** *via* a domino reaction, involving the ethynylation, carbonylation and O-cyclization, is presented in Scheme 111.

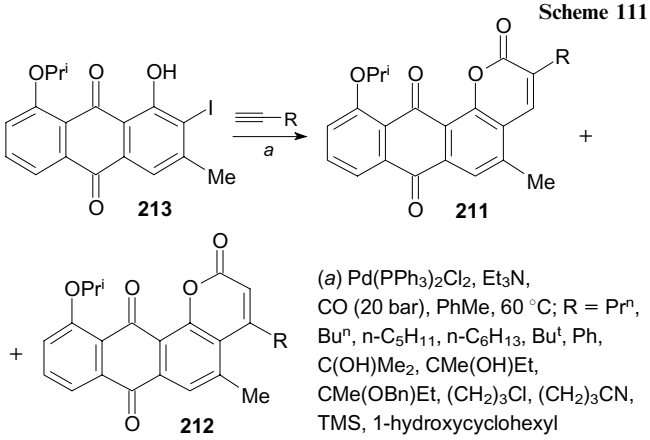
Aryl iodide **213** was used as the starting compound. This transformation successfully combines the Sonogashira reaction with the simultaneous carbonylation in a one-pot fashion giving target products in yields from 26 to 94% and a ratio of **211** – **212** from 1 : 0 to 2 : 1. The simplicity of this approach to the synthesis of anthrapyran-2-ones allows the synthetic chemists to use this method to prepare other analogues of the anticancer agent BE-26554A with improved biological activity.

Structure 210



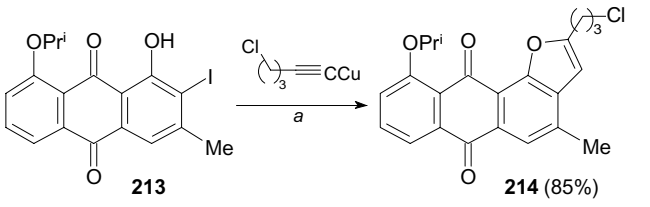
210 (BE-26554A)

Scheme 111



This line of research was further pursued by Rixson *et al.*,[139] who developed, in addition to the above method for the preparation of anthrapyranones, an efficient procedure for the synthesis of anthrafuran derivative **214** (Scheme 112). Anthrafuran **214** was produced by the Castro reaction of aryl iodide **213** with appropriate copper acetylide in high yield.

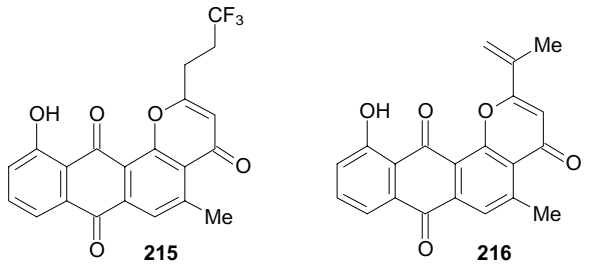
Scheme 112



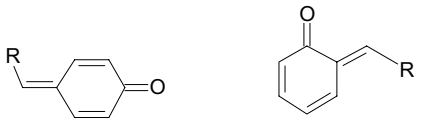
Apart from anthracenefuran **214**, chromones **215** and **216** were found to be the most efficient growth inhibitors of a number of human cancer cell lines. Thus, trifluoromethyl-substituted chromone **215** and anthracenefuran **214** inhibited *in vitro* the growth of the BE2-C neuroblastoma cell line with IC_{50} = 0.20 and 0.38 μM, respectively.†

Low-molecular-mass compounds, which are capable of binding to DNA to form highly stable secondary structures, are often employed to develop anticancer agents. The G-quadruplexes (G4), guanine-rich nucleic acid sequences folded into four-stranded helices (noncanonical DNA motifs), are among the targets for these compounds. As opposed to the majority of G4 ligands, anthraquinone derivatives have suitable redox properties because these compounds easily produce radical anions and dianions upon reduction. In turn, the formation of stable radical anions can be used to design alkylating agents, *e.g.*, quinone methides (QM) from *para*- or *ortho*-benzyl-substituted phenols.

Structures 215, 216

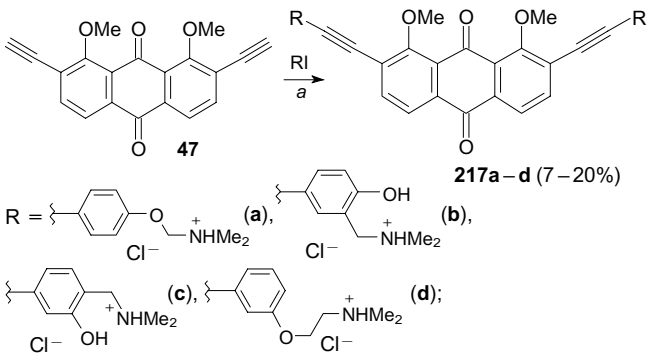


Structures of quinone methides



Percivalle *et al.*[57] anticipated that phenol-containing quinones can *in situ* generate QM at the G4 sites in a similar fashion. G-Quadruplex ligands **217a–c** were synthesized by the Sonogashira reaction (Scheme 113). They selectively inhibit the growth of cancer cells. (The synthesis of starting compound **47** is presented in Scheme 19.)

Scheme 113



Compound **217b** proved to be the most efficient quadruplex ligand. By changing the relative position of substituents in the benzene ring (from *para* to *ortho*), the authors obtained compound **217c** with quite different G4-binding and stabilization properties. This study also demonstrated that the presence of Mannich bases in the molecule is crucial for the efficiency of the G4 ligand.

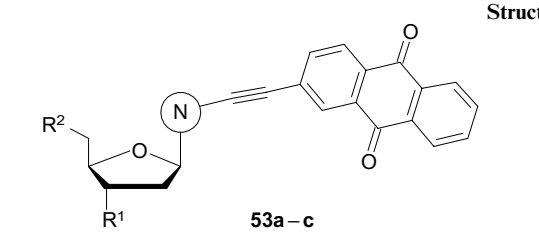
A challenge in biochemistry is to synthesize water-soluble bioconjugates with short linkers required for studies of the propagation of photoinduced holes (cation transport in DNA) by kinetic laser flash photolysis. The synthesis of conjugates **53a–c** (see Scheme 25) was described in the studies.[66, 67, 140] These conjugates include an anthraquinone moiety attached to pyrimidine, pyrrolopyrimidine and purine moieties through an acetylene linker. The structure of conjugates **53a–c** is favourable for electron transfer, and these compounds can be used to study the oxidation of adenosine in DNA.[66, 67]

The rigid C≡C linkers in conjugates **218a–c** enable regiocontrol within the DNA duplex structure.[140]

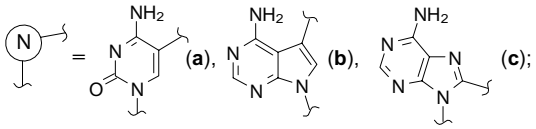
Electrochemical measurements showed that ethynyl linkers enhance the reduction potential of compounds **218a–c** by 125–150 mV compared to that of analogue **219** with an ethyl linker.

† J.E.Rixson, J.R.Abraham, Y.Egoshi, B.W.Skelton, K.Young, J.Gilbert, J.A.Sakoff, K.M.Gericke, A.McCluskey, S.G.Stewart. *Bioorg. Med. Chem.* **23**, 3552 (2015); https://doi.org/10.1016/j.bmc.2015.04.032

Structures 53a – c



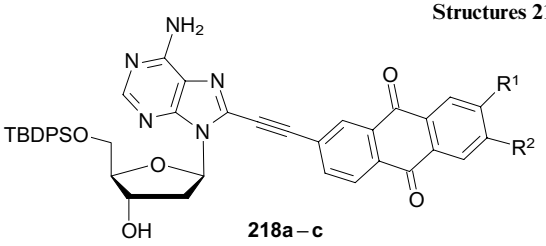
53a – c



(**a**), (**b**), (**c**);

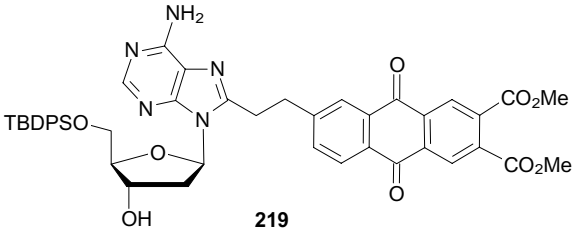
R^1 = OH, $OP(O)(OBn)_2$; R^2 = OH, ODMTr

Structures 218, 219



218a – c

R^1 = H: R^2 = CHO (**a**), $C(O)CF_3$ (**b**); R^1 = R^2 = CO_2Me (**c**);
TBDPS is *tert*-butyldiphenylsilyl



219

6. Conclusion

The review summarizes the data on the synthesis and the chemical, physicochemical and biological properties of acetylene derivatives of quinones published over a period from 2005 to 2020. The current state of the art of the chemistry of alkynylquinones can be estimated as extensively developing, which is clearly seen from a comparison of the data presented in this review and the previous review covering the period of up to 2004. In the previous review,[20] the data on biological activity and physicochemical properties of alkynylquinones, as well as examples of their applications in new technologies, were absent. We not only considered the original synthetic strategies and nontrivial transformations but also discussed the results of the use of unique physicochemical properties of acetylene derivatives of quinones in electronics, optics, sensing devices and medicinal chemistry.

Meanwhile, methods for the introduction of a triple bond in the quinoid ring of benzo- and naphthoquinones are insufficiently well-developed in the chemistry of alkynylquinones. There are scarce studies addressing methods for the synthesis and the properties of acetylene derivatives of *ortho*-quinones.

In order to give an insight into the modern trends in this field of research, let us briefly summarize the most significant advances. Although the Sonogashira reaction remains the most facile method for the synthesis of alkynylquinones, efforts are made to develop new more environmentally benign and cost-effective procedures for the introduction of a triple bond in the quinone core. Mention may be made of the study,[85] described in Section 2.4, in which an elegant procedure was developed for the introduction of a triple bond in *ortho*-quinones. This method combines the electrochemical and chemical oxidation of diols followed by alkynylation of the quinone. It does not require a halogen component and occurs in the absence of an expensive palladium catalyst, a base and a copper salt under mild green chemistry conditions.[85]

Particular attention is paid to the specific features of alkynylquinones associated with the conjugation of the C=O group with the C≡C bond. This conjugation causes significant activation of the triple bond, thereby enhancing its response to external and internal stimuli. It is worth noting that quinones easily undergo reversible redox transformations. A combination of two chemically different moieties in the molecule endows alkynylquinones with unusual properties, making it possible to use these compounds in specific fields. These compounds are successfully applied to fabricate model samples of redox-responsive switches in molecular devices, in which the triple bond provides the conjunction, while the quinone moiety is involved in the redox process.

The successful use of the *peri* position of the C=O group and C≡C bond in 1,5-bis(arylethynyl)anthraquinones is worthy of mention. This structure makes it possible to perform the double intramolecular electrophilic cyclization important from the theoretical point of view. The resulting dipyrylium salts have unique electrochemical and magnetic properties. This is the first example of polycyclic aromatic hydrocarbons with 22 ($4n + 2$) π electrons containing an oxygen atom and having a pentacyclic skeleton (see structures **179** and **180**).

The discovery of the reaction involving *peri*-alkynyl-9,10-anthraquinones, the acetylene moiety of which contains electron-withdrawing groups, is of great importance. The reaction of these compounds with strong bases (KOH or guanidine) affords 9,18-diaryltetrabenzo[*a,de,j,mn*]tetracene-4,13-diones as products of an unusual reductive dimerization of internal alkynes (see Scheme 70). This is a new page in acetylene chemistry, highlighted by Synfacts,[141] which selects the most significant current results in synthetic organic chemistry from the primary literature, enriched with personal comments by experts.

Modern science faces a lot of increasing challenges, which underscores the relevance of both the development of new methods for the synthesis of multifunctional compounds and their application in advanced technologies. Acetylene derivatives of quinones fully comply with these requirements. Based on the available data in this field, it can be expected that in near future synthetic chemists will focus their efforts on searching for rational methods for the synthesis of quinones containing groups with a triple bond and also on examining the fields of their practical application, primarily in medicinal chemistry and fabrication of new advanced materials.

A short list of the most significant results provides evidence that alkynylquinones can be considered as privileged structures, the fundamental and applied potential of which is far from being exhausted. It is possible that in the future, we will witness bright and amazing discoveries in the versatile acetylene chemistry.

We hope that this review will contribute to the knowledge of readers about the reactivity of this class of compounds and will be useful for experts in acetylene and quinone chemistry and also for researches in related fields of organic and medicinal chemistry.

7. List of abbreviations and designations

AC — anthracene,
AcAC — diacetoxyanthracene,
acac — acetylacetonate,
AH — dihydroanthracene,
Am — 4-*N*,*N*-bis(4-methoxyphenyl)aminophenyl,
AQ — anthraquinone,
BDF — benzo[1,2-*b*:4,5-*b*]difuran,
BH — base,
CAN — cerium(IV) ammonium nitrate,
Cp* — pentamethylcyclopentadienyl,
CV — cyclic voltammetry,
DABCO — 1,4-diazabicyclo[2.2.2]octane,
DCB — *o*-dichlorobenzene,
DCC — 1,3-dicyclohexylcarbodiimide,
DCE — 1,2-dichloroethane,
DDQ — 2,3-dichloro-5,6-dicyano-1,4-benzoquinone,
DIPA — diisopropylamine,
DIPEA — diisopropylethylamine,
DHA — *N*,*N*-di-n-hexylamine,
DMA — *N*,*N*-dimethylaniline,
DMAP — 4-dimethylaminopyridine,
DME — dimethoxyethane,
DMTr — 4,4′-dimethoxytrityl,
dppe — 1,2-bis(diphenylphosphino)ethane,
EDA — ethylenediamine,
EnT — energy transfer,
ET — electron transfer,
Fc — ferrocenyl,
FET — transistor
HMDS — bis(trimethylsilyl)amide,
HMPA — hexamethylphosphoramide,
HOA — dihydroxyanthracene,
HOMO — highest occupied molecular orbital,
IC_{50} — half-maximal inhibitory concentration,
IVCT —intervalence charge transfer,
LDA — lithium diisopropylamide,
LUMO — lowest unoccupied molecular orbital,
MOM — methoxymethyl,
MP — metalloporphyrin,
MS — molecular sieves,
MW — microwave irradiation,
NBS — *N*-bromosuccinimide,
Nu — nucleophile,
OFET — organic field-effect transistors,
OPE — oligo(phenylene ethynylenes),
OTFT — organic thin-film transistor,
Ox — oxidized form,
PCBM — [6,6]-phenyl-C_{61}-butyric acid methyl ester,
PEPQ — poly(2-ethynylphenanthrene-9,10-dione),
Piv — pivaloyl,
PTPQ — poly[2-(2-thienyl)phenanthrene-9,10-dione],
Py — pyridyl,
Pyl — pyrylium,
QM — quinone methide,
Red — reduced form,
rt — room temperature,
SC-FET — single-crystal field-effect transistor,
TBAB — tetra(n-butyl)ammonium bromide,
TBAF — tetra(n-butyl)ammonium fluoride,
TBDPS — *tert*-butyldiphenylsilyl,
TBS — *tert*-butyldimethylsilyl,
TCNQ — tetracyanoquinodimethane,
TES — triethylsilyl,
Tf — trifluoromethanesulfonyl (triflyl),
TFA — trifluoroacetic acid,
TFSIH — bis(trifluoromethanesulfonyl)imide,
TFT — thin-film transistor,
Th — thienyl,
TIPS — triisopropylsilyl,
TMEDA — tetramethylethylenediamine,
TMS — trimethylsilyl,
TPH — tetrahydropyran-2-yl,
TTF — tetrathiafulvalene,
TTFV — tetrathiafulvalene vinylogues,
UV, Vis, NIR — UV, Visible and near-IR spectral ranges.

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