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Azobenzenes—synthesis and carbohydrate applications

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Contents

1. Introduction

Advances in molecular and supramolecular organization are a major challenge in organic chemistry. The control of molecular and supramolecular assembly may be obtained under ambient conditions by external inputs such as electricity, pH, redox potential, magnetic fields, and light. Various photochemical reactions are described in the literature: *E*/*Z* isomerization, tautomerization, electrocyclic reactions, heterolytic cleavage, and homolytic cleavage. The use of light-powered reactions is the most reliable strategy to convert photochemical energy into reversible physical motion without waste (Fig. 1).

Azobenzene derivatives have been used as photoresponsive functional devices utilized as smart polymers,[1] liquid crystals,[2] molecular switches,[3] and machines.[4] Azobenzene derivatives have received considerable experimental and theoretical attention. Azobenzene exists as two isomers: the isomer *E* (or trans) and the isomer *Z* (or cis) (Fig. 2). The *E* isomer is 50 kJ mol^{-1} more stable thermodynamically than the *Z* form. Consequently, the different spatial arrangements lead to different physical and chemical properties. The *E* to *Z*-photoisomerization of azobenzene induces a change of the dipole moment (μ *E*-azobenzene=0.5 D vs μ

Abbreviations: Ac, acetyl; BBCP, bis(2,2′-bipyridyl)copper(II) permanganate; Boc, *tert*-butoxycarbonyl; *s*-Bu, *sec*-Butyl; *t*-Bu, *tert*-butyl; Bz, benzoyl; CAN, cerium ammonium nitrate; CD, cyclodextrin; DCC, dicyclohexylcarbodiimide; DIB, diacetoxyiodobenzene; DMF, dimethylformamide; DTBB, 4,4′-di-*tert*-butylbiphenyl; Et, ethyl; Fmoc, fluorenylmethyloxycarbonyl; HABA, 4-hydroxyazobenzene-2-carboxylic acid; HOBt, 1-hydroxybenzotriazole; Me, methyl; *i*-Pr, *iso*-Propyl; PTSA, *para*-toluenesulfonic acid; THF, tetrahydrofuran; *p*-Tol, *para*-tolyl; Tf, triflate; Ts, tosyl.

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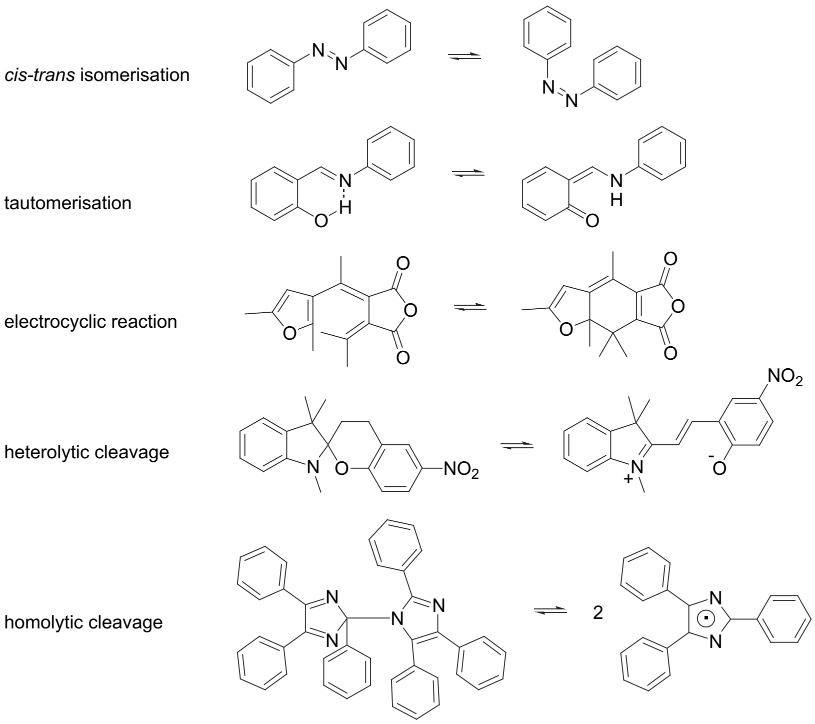
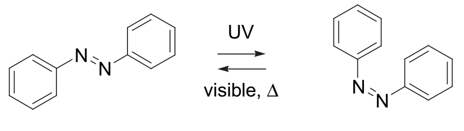


Figure 1. Typical photo-sensor molecules and their photochromic reactions.



(*E*)-1 **(*Z*)-1**

Figure 2. Reversible photoisomerization of azobenzene moieties upon UV–vis irradiation.

Z-azobenzene=3.1 D), which in turn determines the hydrophobic and hydrophilic nature of the *E* and *Z* isomers.

The structure of *E*-azobenzene is not planar; the dihedral angle N,N,C,C is around 17.5°, whereas one of the benzene rings of the *Z*-isomer occupies a plane tilted by 56° from the plane of the other ring. Thus, the distances between the two carbon atoms in the 4- and 4′- positions are 9.0 and 5.0 Å for the *E*- and *Z*-isomer, respectively (Fig. 3).

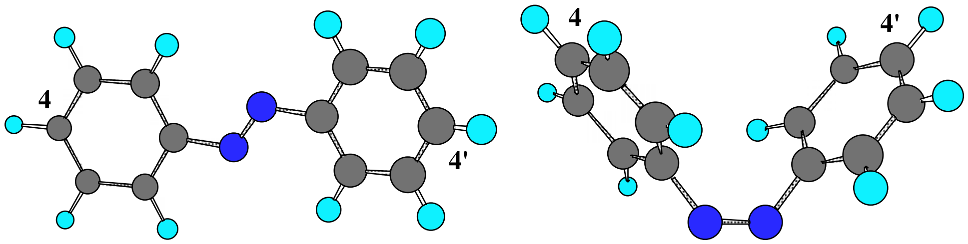


Figure 3. Geometrical structures of *E*- and *Z*-azobenzene.

The UV–visible absorption spectra of *E*-azobenzene is characterized by three major bands: (i) a band at 228 nm originates from π–π* transitions localized on the phenyl groups; (ii) a band at 318 nm originates from symmetry-allowed π–π* transitions, which are delocalized through the molecule including the two nitrogen atoms; and (iii) a band at 440 nm originates from symmetry-forbidden n–π* transitions occurring at the central nitrogen atoms (Fig. 4). It is notable that the UV–visible absorption spectrum of the *Z*-isomer is quite different from that of the *E*-isomer, with a band at 260 nm originating from symmetry-allowed π–π* transitions (318 nm for the *E*-isomer).

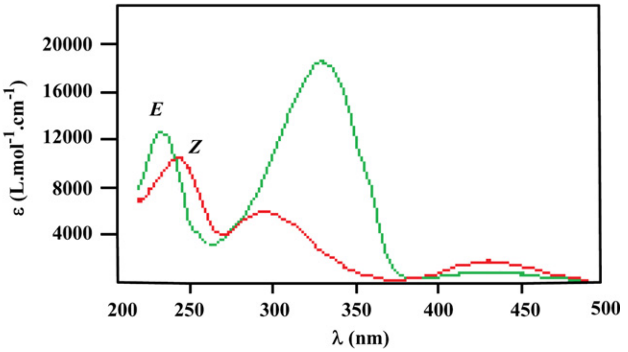
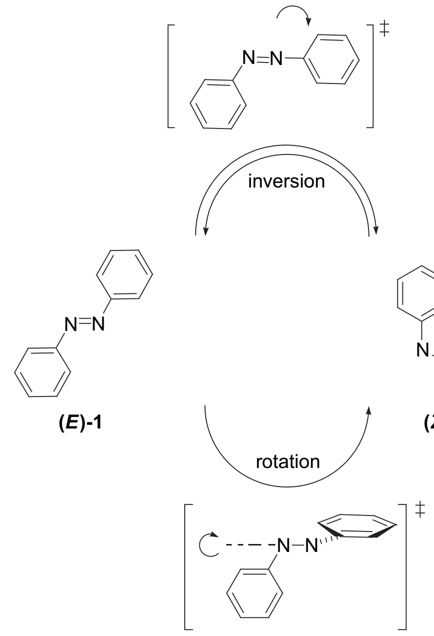


Figure 4. UV–vis absorption spectra of *E*- and *Z*-azobenzene in ethanol.

The mechanism of photoisomerization of azobenzene has been a fundamental subject and two pathways have been described. It is accepted that the photoirradiation step from *E* to *Z* has a rotational pathway and/or an inversion pathway, whereas the heating step from *Z* to *E* has an inversion pathway (Scheme 1).[5]

The Rau classification of azobenzene distinguishes three families of compounds: (i) the azobenzene derivative **1**; (ii) the aminoazobenzene derivative **2**; and (iii) the push–pull azobenzene



Scheme 1. Isomerization pathway from *E*- to *Z*-azobenzene **1** and vice versa.

derivative **3** (Fig. 5). Depending up on the nature of the substituents on the aromatic groups, the equilibria between the (*E*) and (*Z*) compounds are variable.

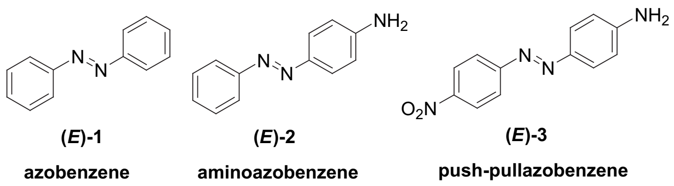


Figure 5. Rau classification of azobenzenes.

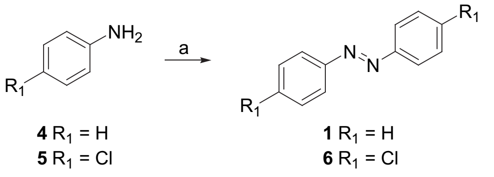
The purpose of the present review is not to list all of the azobenzene syntheses that have been described in the literature, but to provide a comprehensive overview of the recent investigations and the applications in carbohydrate chemistry. Azobenzenes can be obtained by: (i) oxidation of aromatic primary amines; (ii) reduction of aromatic compounds having a nitro group; (iii) coupling of primary arylamines with nitroso compounds (Mills reaction); (iv) electrophilic reactions of diazonium salts; (v) oxidation of hydrazo derivatives; (vi) reduction of azoxybenzene derivatives; and (vii) other methods. It is important to remember that the data to be presented and discussed here has come from different sources using experimental conditions that are not uniform. It is therefore very difficult and often misleading to form general conclusions and establish trends merely on the basis of comparing these data, because each laboratory employs its own experimental conditions and standards. For the sake of clarity, this review has been arranged to describe the synthesis of azobenzene derivatives and of azo-linked carbohydrate moieties in the period from 1998 to 2008.

2. Synthesis of azobenzene derivatives

2.1. Oxidation reactions of aromatic primary amines

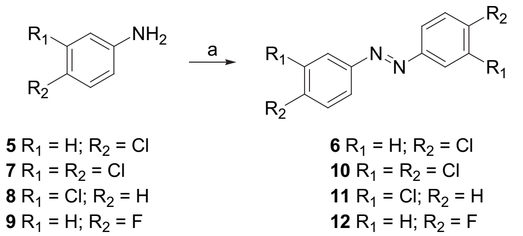
The synthesis of symmetrical azobenzene derivatives has been reported via the oxidation of primary aromatic amines with MnO_2, $KMnO_4$, H_3BO_3, and Hg/I_2. Other metal oxides such as Ag_2CO_3,[6] Ag_2O,[7] $AgMnO_4$,[8] Ni peroxide,[9] $Pb(OAc)_4$,[10] $Ce(OH_3)O_2H$,[11] BBCP,[12] or KO_2,[13] hypervalent iodides such as $PhI(OAc)_2$,[14] and aerial oxidants such as O_2-*t*-BuOK,[15] O_2-Cu_2Cl_2-pyridine,[16] O_2-Co_3O_4,[17] or peroxidase-H_2O_2[18] have permitted the preparation of azobenzene from aniline derivatives, but these reagents have not been used recently.

The use of manganese dioxide (MnO_2) for the oxidation of aniline derivatives **4** and **5** in refluxing hexane was realized to furnish the corresponding azobenzene analogues **1** and **6** in 69 and 61% yields, respectively (Scheme 2).[19]



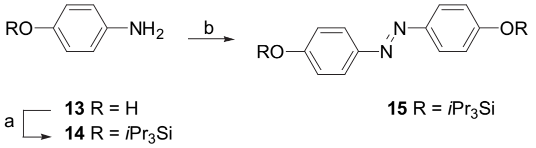
Scheme 2. Reagents and conditions: (a) MnO_2, molecular sieves, hexane, reflux (for **1**: 69%, for **6**: 61%).

More recently, Gilbert et al. reported the dimerization of 4-chloroaniline (**5**) via oxidation with MnO_2 in refluxing toluene to afford the corresponding azo compound **6** in a lower yield (49 vs 61%).[20] Starting from the aniline derivatives **7**–**9** having halogen atoms in the *meta* or *para* position, application of this procedure permitted the formation of the corresponding azobenzene analogues **10**–**12** in 89, 88, and 79% yields, respectively (Scheme 3).



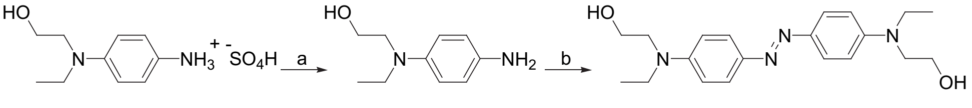
Scheme 3. Reagents and conditions: (a) MnO_2, toluene, 110 °C (for **6**: 49%, for **10**: 89%, for **11**: 88%, for **12**: 79%).

The synthesis of azobenzene derivatives having a protected hydroxyl group in the *para* position of the aromatic ring has been described.[21] The protection of the aromatic hydroxyl group was realized by treatment of 4-aminophenol (**13**) with triisopropylsilyl chloride. The silylated derivative **14** in the presence of MnO_2 in refluxing benzene furnished the azobenzene derivative **15** in 34% overall yield (two steps) (Scheme 4).



Scheme 4. Reagents and conditions: (a) NaH, *i*-Pr_3SiCl, THF; (b) MnO_2, benzene, reflux (34% for two steps).

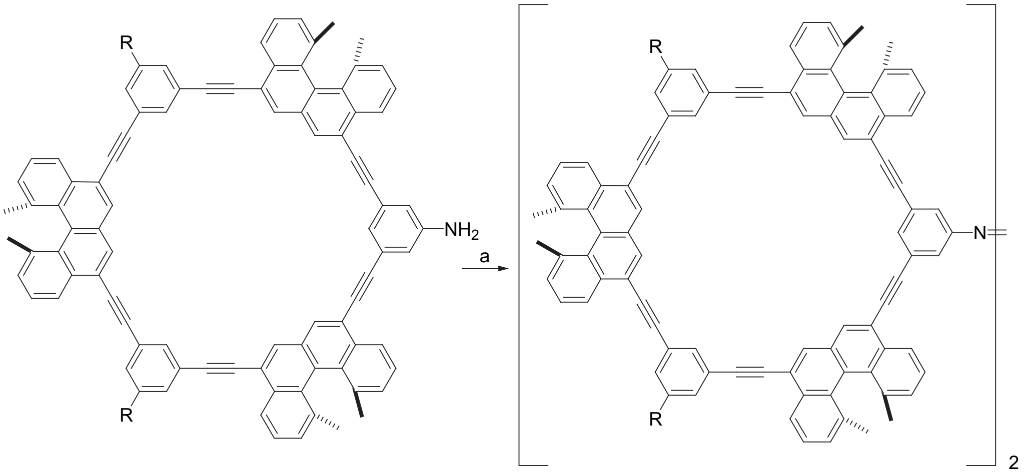
Woolley et al. described the synthesis of the azobenzene derivative **18** with an ethyl(2-hydroxyethyl)amino substituent in the *para* position starting from the commercial benzeneaminium hydrogenosulfate **16** (Scheme 5). Treatment of the salt **16** with sodium bicarbonate generated the amine **17** in 62% yield. Then, oxidation of **17** with MnO_2 gave the azobenzene derivative **18** in 29% yield.[22] It was notable that the primary hydroxyl group was not protected during the oxidation step.



16 **17** **18**

Scheme 5. Reagents and conditions: (a) $NaHCO_3$, ethyl acetate, H_2O (62%); (b) MnO_2, benzene, reflux (62%).

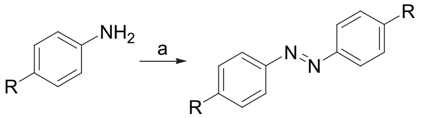
Recently, the synthesis of azobenzene derivatives with steric hindrance has been described. Yamaguchi et al. reported the synthesis of a cycloalkyne dimer **20** linked by an azo group. Oxidative coupling of **19** with MnO_2 in benzene generated the azobenzene **20** in 64% yield (Scheme 6).[23]



19 $R = CO_2n\text{-}C_{10}H_{21}$ **20** $R = CO_2n\text{-}C_{10}H_{21}$

Scheme 6. Reagents and conditions: (a) MnO_2, toluene, 110 °C (64%).

The use of potassium permanganate absorbed onto copper(II) sulfate pentahydrate was studied. This oxidizing reagent offered several practical advantages, namely better yields, a simpler experimental procedure, and utilization of a commercially available oxidant that is safe to handle. Starting from the aniline derivatives **4**, **21**, and **22**, Noureldin et al. reported the synthesis of azobenzenes **1**, **23**, and **24** using the supported permanganate in 77–87% yield (Scheme 7).[24]

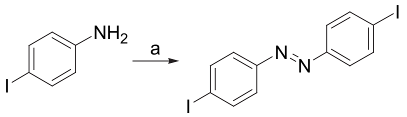


4 R = H
21 R = *sec*Bu
22 R = I

1 R = H
23 R = *sec*Bu
24 R = I

Scheme 7. Reagents and conditions: (a) $KMnO_4$, $CuSO_4\cdot5H_2O$, CH_2Cl_2 (for **1**: 78%; for **23**: 77%; for **24**: 87%).

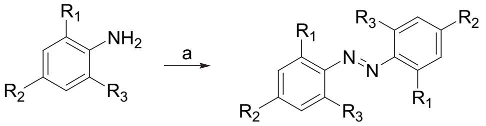
A few years later, Flatt et al. described the synthesis of compound **24** in 15% yield using $CHCl_3$ instead of CH_2Cl_2 (Scheme 8).[25]



22 **24**

Scheme 8. Reagents and conditions: (a) $KMnO_4$, $CuSO_4\cdot5H_2O$, $CHCl_3$ (15%).

In order to limit the use of solvents and to have applications in combinatorial chemistry and in green chemistry, the synthesis of azobenzene derivatives by solvent-free permanganate oxidation was developed.[26] Treatment of the primary aromatic amines **4**, **5**, and **25** with $KMnO_4$, Al_2O_3, and $CuSO_4\cdot5H_2O$ afforded the corresponding azobenzene derivatives **1**, **6**, and **26** in 75, 80, and 70% yields, respectively (Scheme 9).

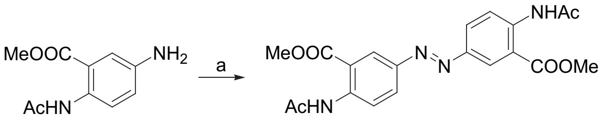


4 $R_1 = R_2 = R_3 = H$
5 $R_1 = R_3 = H$; $R_2 = Cl$
25 $R_1 = R_3 = R_2 = Me$

1 $R_1 = R_2 = R_3 = H$
6 $R_1 = R_3 = H$; $R_2 = Cl$
26 $R_1 = R_3 = R_2 = Me$

Scheme 9. Reagents and conditions: (a) $KMnO_4$, Al_2O_3, $CuSO_4\cdot5H_2O$ (for **1**: 75%, for **6**: 80%, for **26**: 70%).

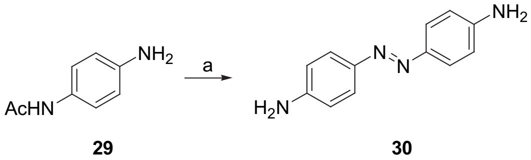
The use of sodium perborate for the oxidation of aromatic amines has been reported. Abelt et al. reported the oxidation of aniline derivative **27** with sodium perborate tetrahydrate in the presence of boric acid in acetic acid to give the azobenzene **28** in 64% yield (Scheme 10) and various amounts of the azoxy compound.[27] It was notable that the amino group and the carboxy group, respectively, in the *para* and *meta* positions of the aromatic ring, were protected.



27 **28**

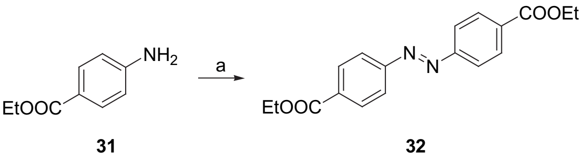
Scheme 10. Reagents and conditions: (a) $NaBO_3\cdot4H_2O$, $B(OH)_3$, AcOH (64%).

Recently, Naeimi et al. reported the synthesis of 4,4′-diaminoazobenzene (**30**)[28] as described by Stubbings et al. (Scheme 11).[29] Starting from the *p*-aminoacetanilide (**29**), treatment with sodium perborate tetrahydrate and boric acid in glacial acetic acid followed by treatment with HCl in methanol furnished the azo compound **30** in 52% overall yield (two steps).



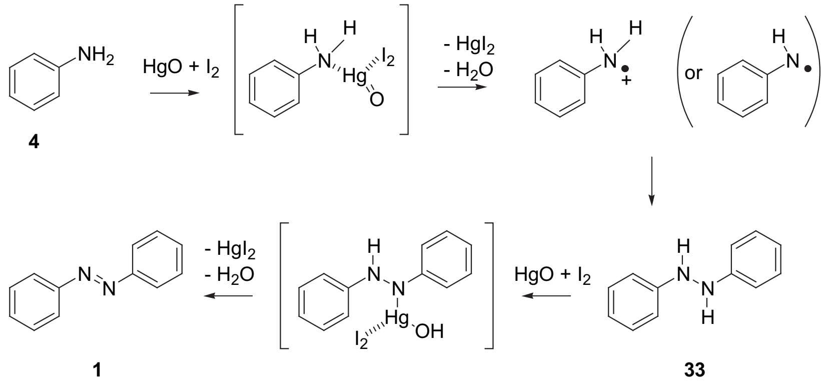
Scheme 11. Reagents and conditions: (a) $NaBO_3 \cdot 4H_2O$, $B(OH)_3$, AcOH then HCl, MeOH (52%).

The synthesis of azobenzenes was described by oxidation with a mercury(II) oxide/iodine reagent. Orito et al. reported the synthesis of azobenzene derivatives **32** by dimerization of aniline derivatives **31** in 87% yield (Scheme 12).[30] As described above, the protection of the carboxy group of the compounds was established before the oxidation reaction.



Scheme 12. Reagents and conditions: (a) HgO, I_2, CH_2Cl_2 (87%).

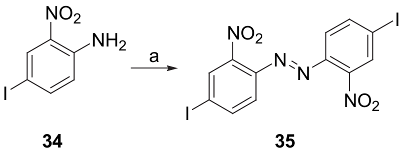
The authors proposed a plausible mechanism involving a nitrogen–nitrogen coupling of an initially formed cation radical (or aminyl radical), which is probably produced by a one-electron transfer, followed by a two-electron oxidation of the resultant hydrazobenzene **33** (Scheme 13).[30]



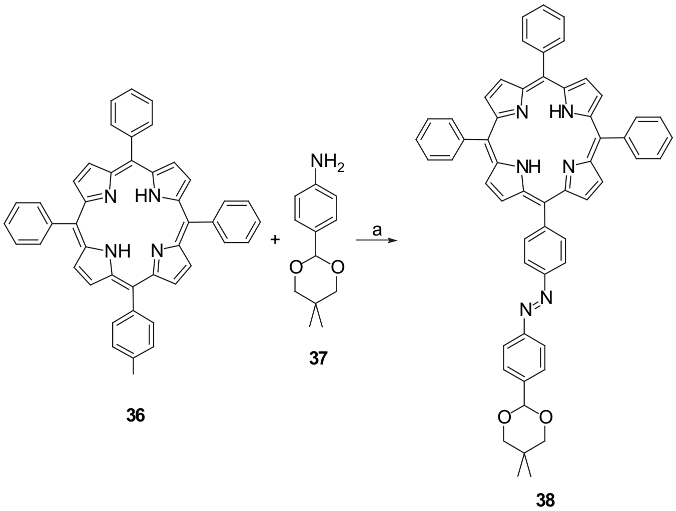
Scheme 13. Mechanism of oxidation of aniline (**4**) with HgO and I_2.

Flatt et al. described the synthesis of azobenzene **35** from 2-nitro-4-iodoaniline (**34**) by oxidation using mercury(II) oxide and iodine (Scheme 14).[25] The poor yield (4%) was presumably due to the low reactivity of the electron-deficient aniline and the sterically hindered azo product.

As described in this section, the oxidative coupling of amines was used for the synthesis of symmetrical azobenzene. One example was reported in the literature concerning the oxidation of the primary aromatic amines for the preparation of dissymmetrical azobenzenes. Oxidative hetero-coupling of free base aminoporphyrin **36** and aminoacetal **37** using MnO_2 as the oxidant was utilized to furnish the dissymmetrical azobenzene **38** in 50% yield (Scheme 15).[31]



Scheme 14. Reagents and conditions: (a) HgO, I_2, CH_2Cl_2 (4%).

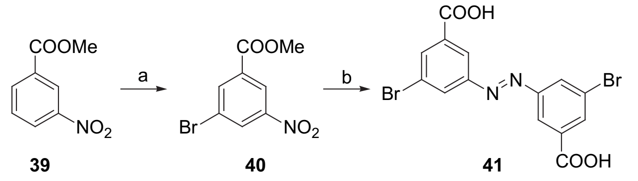


Scheme 15. Reagents and conditions: (a) MnO_2, toluene, 110 °C (50%).

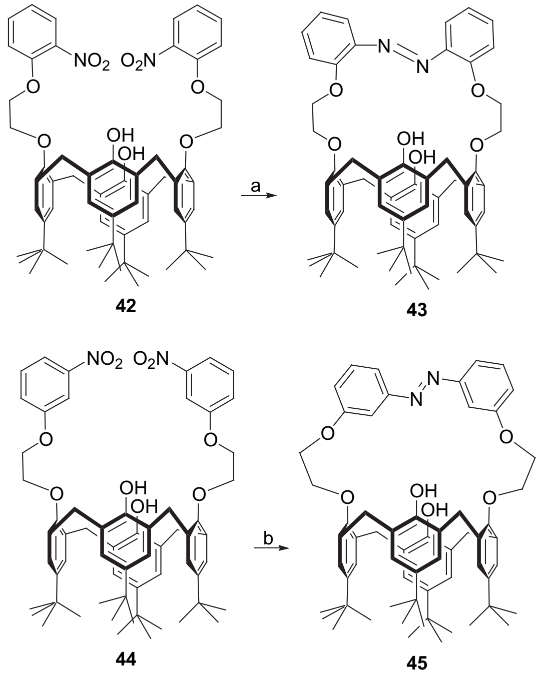
2.2. Reduction reactions of aromatic compounds having nitro groups

The synthesis of azobenzene derivatives has been reported via the reduction of nitro compounds using zinc in a basic medium, via catalytic transfer hydrogenation using HCO_2H, NEt_3/Pb, and via reduction using glucose in a basic medium. Hecht et al. reported the synthesis of azobenzene-core amphiphilic oligo(*meta*-phenylene ethynylene)s.[32] After bromination of methyl 3-nitrobenzoate (**39**), treatment of **40** with zinc under basic conditions yielded the desired azobenzene bis-acid **41** in 63% yield (two steps) (Scheme 16).

Cyclic azobenzenes were prepared by reduction reaction using Zn. Sukwattanasinitt et al. reported the synthesis of azobenzene derivative-bridged crown ether *p*-*tert*-butylcalix[4]arenes.[33] Reductive coupling of *p*-*tert*-butylcalix[4]arene derivative **42** with zinc in the presence of NaOH in isopropanol and water furnished the azobenzene **43** in 8% yield (Scheme 17). Starting from the isomer **44**, application of this strategy using high-pressure method (3 atm nitrogen) gave the azo compound **45** in 59% yield (Scheme 17). It was notable that the 4,4′-derivative was unstable and none of the desired product could be isolated.

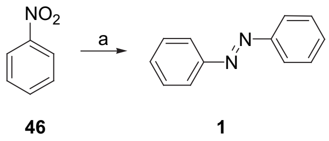


Scheme 16. Reagents and conditions: (a) DIB, H_2SO_4 (90%); (b) Zn, NaOH, EtOH (70%).

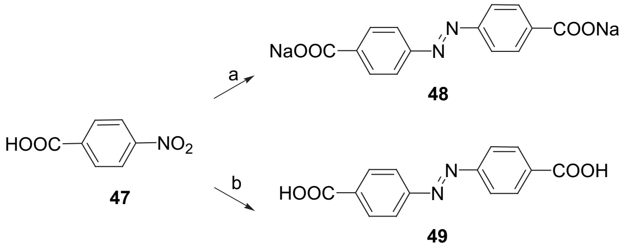


Scheme 17. Reagents and conditions: (a) *i*-PrOH, Zn, H_2O (8%); (b) *i*-PrOH, Zn, H_2O, 3 atm N_2 (59%).

The synthesis of azo compounds by catalytic transfer hydrogenation of nitroarenes has been studied in order to limit the use of flammable hydrogen gas and pressure equipment. Nitrobenzene (**46**) and lead powder in methanol in the presence of triethylammonium formate furnished the azobenzene (**1**) in 92% yield (Scheme 18).[34] Gowda et al. proposed[34] that the initial reduction of the nitro compound furnished a hydroxylamine as a reaction intermediate.



Scheme 18. Reagents and conditions: (a) HCOOH, NEt_3, Pb, MeOH (92%).

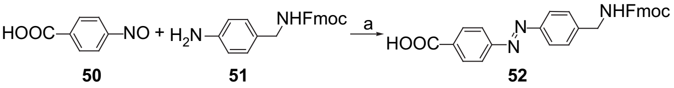


Scheme 19. Reagents and conditions: (a) NaOH, H_2O, glucose (76%); (b) 1. NaOH, H_2O, glucose; 2. AcOH (44%).

The synthesis of azobenzene derivatives having an unprotected carboxy group in the aromatic ring could be effected using glucose as a carbohydrate reducing agent.[35] Starting from 4-nitrobenzoic acid (**47**) in an aqueous solution of NaOH, treatment with an aqueous solution of glucose gave the corresponding azo compound **48** in 76% yield (Scheme 19). Recently, different teams have applied the above synthesis for the preparation of 4,4′-azodibenzoic acid (**49**) in 44% yield.[36]

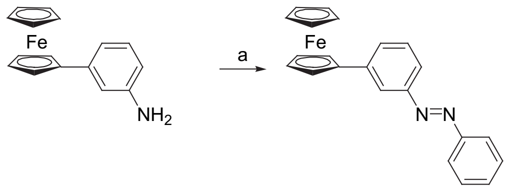
2.3. Coupling of primary arylamines with nitroso compounds (Mills reaction)

The synthesis of dissymmetrical azobenzene derivatives has been reported by treatment of aromatic nitroso compounds and primary arylamines via Mills reactions.[37–52] Compound **52** was obtained starting from the nitroso compound **50** and the aniline derivative **51** in acetic acid at 60 °C in quantitative yield (Scheme 20).[51] It was notable that, using the Mills reaction, different electron-withdrawing and -donating groups could be present in the *ortho*-, *meta*-, and *para*-positions of both the aromatic nitroso compounds and the aromatic amines.



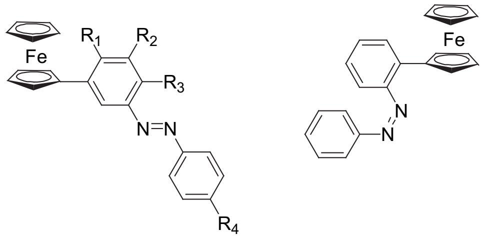
Scheme 20. Reagents and conditions: (a) AcOH (quant).

Nishihara et al. have described the synthesis of ferrocenylazobenzenes.[53] 3-Ferrocenylazobenzene (**54**) was prepared by the reaction of 3-ferrocenylaniline (**53**) and nitrosobenzene (**50**) in acetic acid in 24% yield (Scheme 21). Application of this strategy permitted different ferrocenylazobenzenes **55**–**60** to be obtained (Fig. 6). It was notable that the azobenzene **60** was obtained in the *Z* configuration.



53 **54**

Scheme 21. Reagents and conditions: (a) nitrosobenzene (**50**), AcOH, rt (24%).



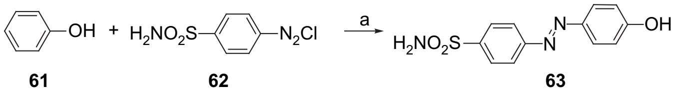
55 $R_1 = R_2 = R_4 = H$; $R_3 = Cl$
56 $R_1 = Cl$; $R_2 = R_3 = R_4 = H$
57 $R_1 = R_2 = R_4 = H$; $R_3 = Me$
58 $R_1 = R_2 = R_4 = H$; $R_3 = OH$
59 $R_1 = OH$; $R_2 = R_3 = R_4 = H$

60

Figure 6. 3-Ferrocenylazobenzene derivatives **55**–**60**.

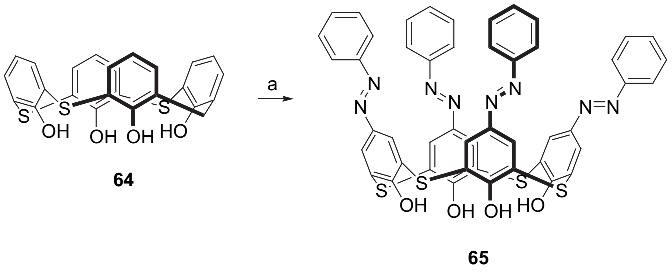
2.4. Diazo-coupling via diazonium salts

The synthesis of dissymmetrical azobenzene derivatives has been reported by the coupling of diazo compounds and diazonium salts in an acidic or basic medium.[54–62] Due to the size of the attacking species, substitution is mostly *para* to the activating group. When the *para* position is already occupied, *ortho* substitution takes place. The pH of the solution was important both for the amine and phenol. In general, the use of an aromatic amine needed a mildly acidic or neutral solution. If the solution was too acidic, the reaction did not occur because the concentration of free amine became too small. Phenol was not active enough for the reaction, but, in slightly alkaline solution, the more reactive phenoxide ion afforded the target azobenzene. Neither amines nor phenols, however reacted in moderately alkaline solution because the diazonium ion was converted into the corresponding diazo hydroxide. Yang et al. reported the formation of the azobenzene derivative **63** by the reaction of phenol (**61**) and diazo compound **62** in AcONa at 0 °C (Scheme 22).[59a]



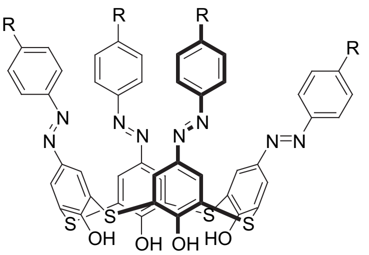
Scheme 22. Reagents and conditions: (a) AcONa (nd).

Contemporary calixarene chemistry has involved the synthesis and development of biologically active compounds. The structures of calixarenes are convenient for performing diazonium coupling. Parola et al. described the diazo-coupling reaction of thiacalix[4]arenes.[63] Starting from thiacalixarene **64**, the synthesis of the tetrakis(phenylazo) derivative **65** was realized by treatment with the corresponding diazonium salt in pyridine and THF in 71% yield (Scheme 23).



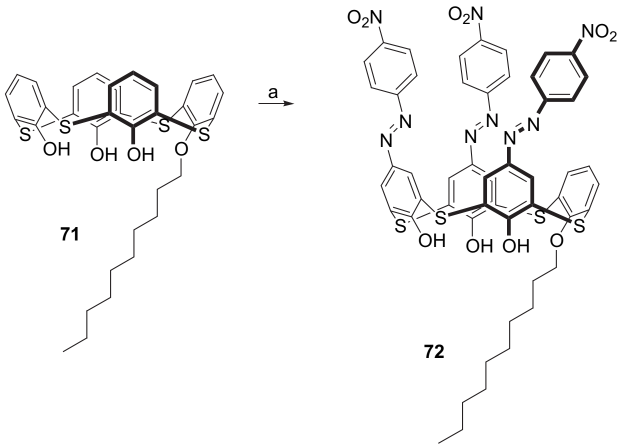
Scheme 23. Reagents and conditions: (a) $C_6H_4N_2BF_4$, THF, pyridine (71%).

Using a similar procedure, Parola et al. and Lhotak et al. reported the synthesis of the tetraazo compounds **66–70** (Fig. 7).[63,64] Bolte et al. reported the synthesis of an azobenzene derivative of thiacalix[4]arene **72** by coupling the monoalkylated thiacalix[4]arene **71** with *p*-nitrophenyldiazonium tetrafluoroborate in 84% yield (Scheme 24).[65] It was notable that the coupling reaction was carried out on the aromatic ring having a free hydroxyl group in the phenol ring.



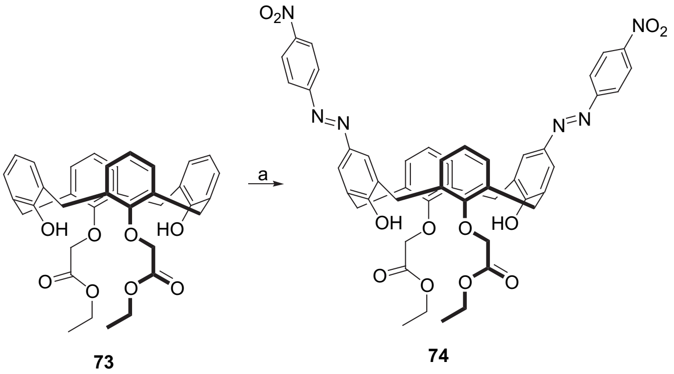
66 R = NO_2
67 R = Me
68 R = OMe
69 R = Br
70 R = COOH

Figure 7. Tetrakis(phenylazo) derivatives **66–70**.



Scheme 24. Reagents and conditions: (a) $p\text{-}NO_2C_6H_4N_2BF_4$, pyridine (84%).

Kim et al. reported the diazo-coupling reaction of calix[4]arene **73** with *p*-nitrobenzenediazonium tetraborate in the presence of pyridine and THF to give the bis-azobenzene derivative **74** in 42% yield (Scheme 25).[66] Application of the above methodology permitted the preparation of calix[4]arene derivatives **75** and **76** with two propyl groups and a monocrown-6 moiety, respectively (Fig. 8).[67]



Scheme 25. Reagents and conditions: (a) $p\text{-}NO_2C_6H_4N_2BF_4$, THF, pyridine, rt (42%).

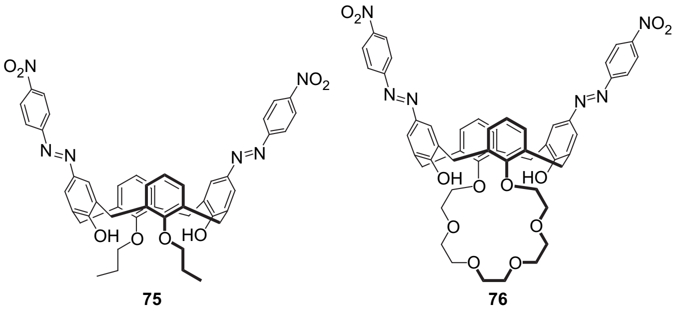
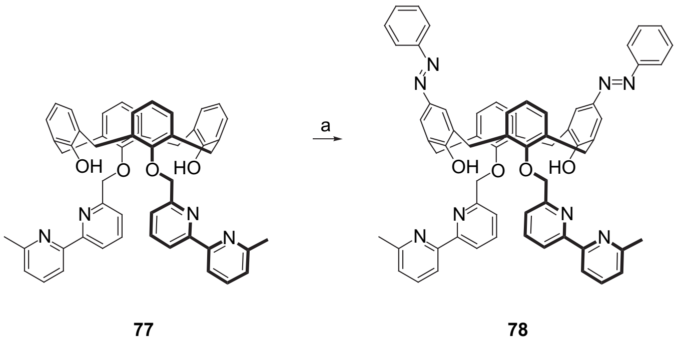


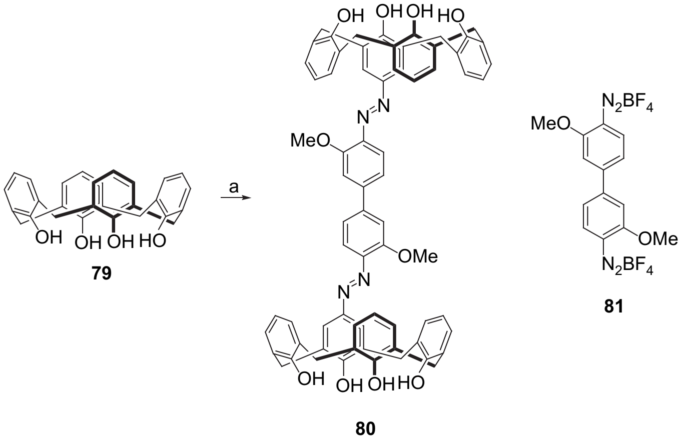
Figure 8. Calix[4]arene derivatives **75** and **76**.

Dumazet-Bonnamour et al. described the synthesis of azocalix[4]arenes containing bipyridyl subunits.[68] A diazo-coupling reaction of calix[4]arene **77** with the diazonium salt led to the corresponding azobenzene derivative **78** in 66% yield (Scheme 26).

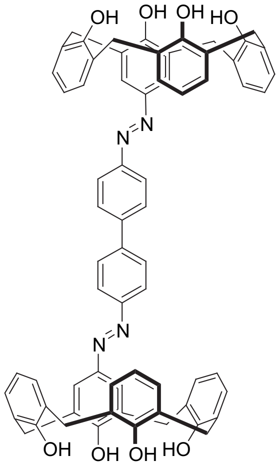


Scheme 26. Reagents and conditions: (a) $C_6H_5N_2BF_4$, THF (66%).

In 2000, Lamartine et al. reported the selective synthesis of new phenylazocalixarenes.[69] A coupling reaction between the tetrazonium salt **81** and calix[4]arene **79** in pyridine and THF gave the azo dimer **80** in 15% yield (Scheme 27). Using the same procedure, compound **82** was also synthesized (Fig. 9).



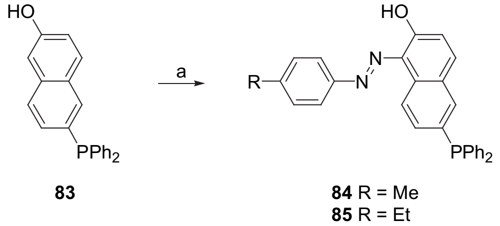
Scheme 27. Reagents and conditions: (a) compound **81**, THF (15%).



82

Figure 9. Calix[4]arene derivative **82**.

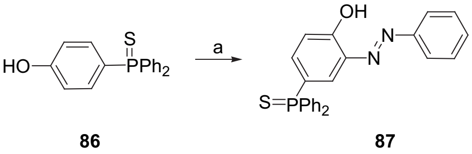
Pritchard et al. reported the first synthesis and structural characterization of a tertiary phosphine containing an azo linkage.[70] After treatment of the phosphine **83** with NaOH in ethanol, the arenediazonium tetrafluoroborate salt in MeCN was added to furnish the azo compounds **84** and **85** in 70% yield (Scheme 28).



Scheme 28. Reagents and conditions: (a) for **84**: 4-$MeC_6H_4N_2BF_4$, AcOH, rt (70%); for **85**: 4-$EtC_6H_4N_2BF_4$, AcOH, rt (70%).

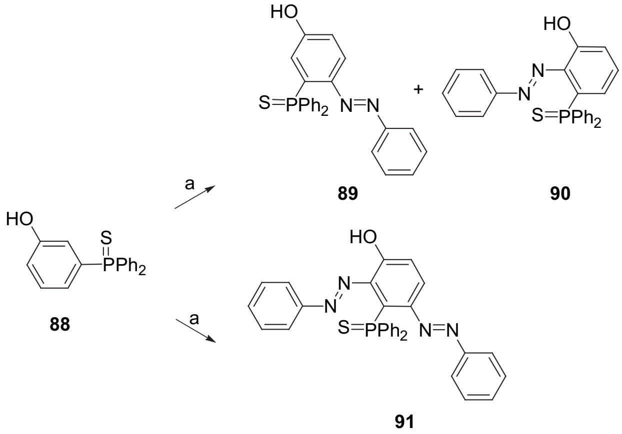
Isolation of arenediazonium salt was essential before addition to the anion of the tertiary phosphine in order to prevent undesirable reactions such as oxidation at the phosphorus atom or decomposition of the diazonium salt by quaternization.

Three years later, Pritchard et al. described the synthesis of some azo-containing phosphine chalcogenides.[71] Treatment of the phenoxide anion of the phosphine derivative with benzenediazonium tetrafluoroborate did not lead to the azo compound but only the diphenylphosphine oxide was isolated. In order to obtain the target azobenzene derivative, the phosphorus atom was protected and the derivative **86** gave the corresponding azobenzene **87** in 60% yield (Scheme 29).



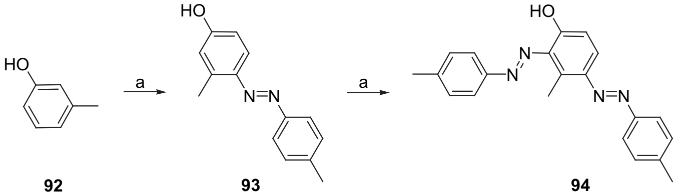
Scheme 29. Reagents and conditions: (a) 1. NaH, THF; 2. $C_6H_5N_2BF_4$, MeCN (60%).

Having established that *p*-hydroxyphenyl(diphenyl)phosphine chalcogenides underwent azo-coupling reactions, Pritchard et al. then investigated the coupling reaction with a *m*-hydroxy analogue **88** (Scheme 30).[71] Using the same procedure, the coupling reaction of **88** with the diazonium salt furnished a mixture of two azo compounds **89** and **90**. The coupling reaction occurred at the expected *ortho*-positions to the *meta*-directing Ph_2PS group. Using the non-selectivity of this coupling reaction, the authors described the synthesis of the bis-azobenzene derivative **91** in 58% yield.



Scheme 30. Reagents and conditions: (a) 1. NaH, THF; 2. $C_6H_5N_2BF_4$, MeCN (58%).

Replacing the Ph_2PS moiety with a formally *ortho*/*para*-directing methyl group was also studied by Pritchard et al.[71] In contrast to compound **88**, treatment of compound **92** with the diazonium salt gave selective coupling to afford the azobenzene derivative **93** in 56% yield. Starting from the azo compound **93**, a second coupling gave the bisazobenzene **94** in 40% yield (Scheme 31).



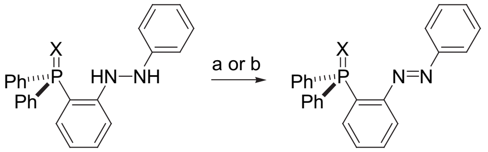
92 **93** **94**

Scheme 31. Reagents and conditions: (a) 1. NaH, THF; 2. p-$MeC_6H_4N_2BF_4$, MeCN (for **93**: 56%; for **94**: 40%).

2.5. Oxidation of hydrazo derivatives

The preparation of azobenzene derivatives has been reported by a *stoichiometric oxidation* process of hydrazo compounds using H_2O_2,[72] O_2,[73] MnO_2,[19] sodium hydroxide,[74] triarylphenol/potassium ferricyanide/sodium hydroxide,[75] iron chloride,[76] periodate resin,[77] $Pb(MeCO_2)_4$,[78] HgO,[79] $(NH_4)_2S_2O_8$,[80] *N*-bromosuccinimide in pyridine,[81] tetrabutylammonium cerium(IV) nitrate[82] and arylsulfonyl peroxide reagents,[83] $NaNO_2$ in acetic anhydride,[84] polyethylene glycol/nitrogen dioxide,[85] and $NaNO_2/NaHSO_4$ on silica support.[86]

The oxidation of hydrazine derivatives using H_2O_2 as oxidant was studied.[87] Oxidation of hydrazobenzenes **95**–**97** with pyridinium tribromide gave the corresponding azobenzenes **98**–**100** in 100, 89, and 26% yields, respectively (Scheme 32). Similarly, the use of *t*-BuOCl as oxidant furnished the azobenzenes **98** and **99** in 61 and 45% yields. It was notable that hydrazobenzene **97** bearing a phosphine selenide moiety was not oxidized by *t*-BuOCl.

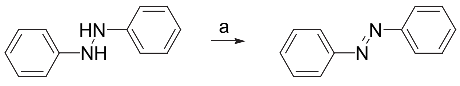


95 X = O
96 X = S
97 X = Se

98 X = O
99 X = S
100 X = Se

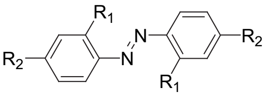
Scheme 32. Reagents and conditions: (a) $pyH^+ Br_3^-$, $CHCl_3$ (for **98**: 100%; for **99**: 89%, for **100**: 26%); (b) t–BuOCl, toluene (for **98**: 61%; for **99**: 45%).

The oxidation of hydrazines using iron chloride was reported by Wang et al.[76] Treatment of hydrazobenzene **33** with $FeCl_3$ as dehydrogenating agent in acetone furnished azobenzene (**1**) in 90% yield (Scheme 33). Application of this methodology permitted the preparation of the azo compounds **6** and **101**–**104** in 81–99% yields (Fig. 10).



33 **1**

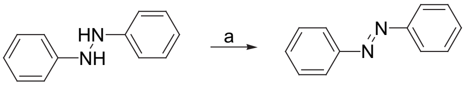
Scheme 33. Reagents and conditions: (a) $FeCl_3{\cdot}H_2O$, acetone (90%).



6 R_1 = H; R_2 = Cl
101 R_1 = H; R_2 = Me
102 R_1 = Cl; R_2 = H
103 R_1 = Me; R_2 = H
104 R_1 = Br; R_2 = H

Figure 10. For **6**: 87%, for **101**: 79%, for **102**: 99%, for **103**: 88%, for **104**: 92%.

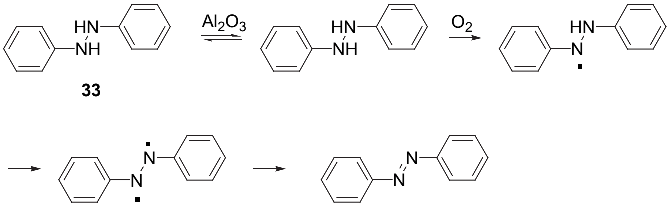
Much effort has been directed toward the development of sustainable chemistry by reduction of the solvent or the use of the resin. Recently, Mihara et al. reported the synthesis of azobenzene derivatives by dehydrogenation of hydrazo compounds using solvent-free conditions.[73a] Commercially available KF/alumina and hydrazobenzene (**33**) furnished the corresponding azobenzene (**1**) in 85% yield (Scheme 34).



33 **1**

Scheme 34. Reagents and conditions: (a) KF/Al_2O_3, O_2 (85%).

The authors proposed a plausible mechanism for the oxidation of the hydrazobenzene via radical species generated on the alumina (Scheme 35).

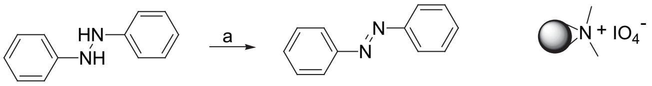


33

1

Scheme 35. Reagents and conditions: (a) KF/Al_2O_3, O_2 (85%).

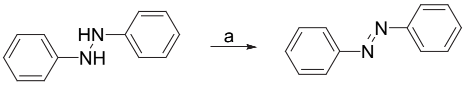
Oxidation of hydrazobenzene was realized using a periodate resin by Rademann et al.[77] The authors reported the synthesis of azobenzene (**1**) (88% yield) starting from hydrazobenzene (**33**) by treatment with the oxidizing periodate resin **105** (Scheme 36).



33 **1** **105**

Scheme 36. Reagents and conditions: (a) resin **105**, MeOH (88%).

In parallel work, it was notable that *catalytic oxidation* of hydrazo compounds was described using oxygen or H_2O_2 as oxidant, NH_4VO_3,[88] $CuCl_2$,[89] Co(II) complexes,[90] and $FeSO_4/KClO_3/H_2SO_4$.[91] Recently, Gozin et al. reported the synthesis of azobenzene (**1**) by treatment of hydrazo compound **33** in the presence of $TiCl_3$ and HBr (Scheme 37).[72] Application of the aforementioned strategy permitted the synthesis of azobenzene derivatives **106**–**109** in 85–95% yields. It was notable that this methodology allowed the preparation of the bisazobenzene compound **109** (Fig. 11).

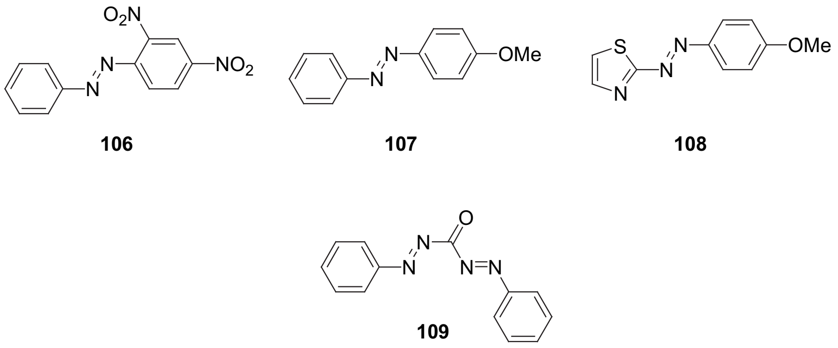


33 **1**

Scheme 37. Reagents and conditions: (a) $TiCl_3$ solution (15% in HCl aqueous solution, 0.2–0.25 mol %), HBr, H_2O_2 (96%).

2.6. Reduction of azoxybenzene derivatives

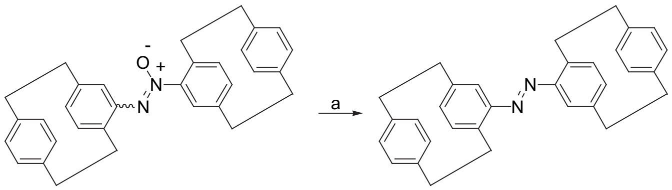
Selective deoxygenation of organic *N*-oxides is a subject of considerable interest in heterocyclic chemistry. In particular,



106 **107** **108** **109**

Figure 11. Azobenzene derivatives **106–109**.

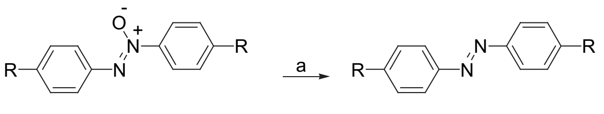
azoxybenzene derivatives were reduced with various reducing agents and with sulfuric acid via a Wallach rearrangement. Aly reported the synthesis of *trans*-azobenzene **111** by the reduction of a mixture of the *E* and *Z* azoxy compounds **110** with $LiAlH_4$ in 82% yield (Scheme 38).[92]



110 **111**

Scheme 38. Reagents and conditions: (a) $LiAlH_4$, THF (82%).

Sanz et al. described the chemoselective deoxygenation of *N*-oxides **112** and **113** under mild conditions with common phosphines in the presence of dichlorodioxomolybdenum(VI) to furnish the corresponding azo compounds **1** and **114** in 97 and 96% yields, respectively (Scheme 39).[93]

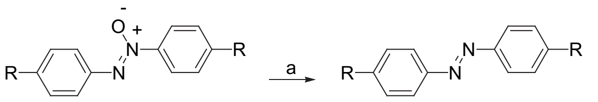


112 R = H
113 R = OMe

1 R = H
114 R = OMe

Scheme 39. Reagents and conditions: (a) $MoO_2Cl_2(dmf)_2$ 5%, PPh_3, THF (for **1**: 97%; for **114**: 96%).

Various metals were used to deoxygenate azoxybenzene derivatives. These methods were efficient, simple, and selective. Yus et al. reported the reduction of azoxy compounds using combinations of $NiCl_2$/Li/DTBB as reducing agents.[94] Starting from the azoxybenzenes **112** and **113**, the corresponding azobenzenes **1** and **114** were obtained in 83 and 79% yields, respectively (Scheme 40). It was notable that the final products depend upon the reaction conditions used: for a short reaction time (1 h), the target compounds were isolated, whereas a longer reaction time (10 h) led to full reduction to the corresponding primary amines.

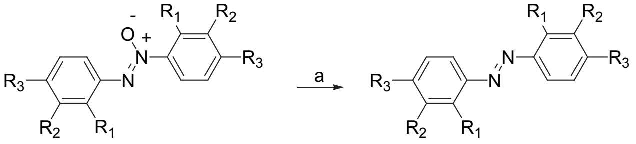


112 R = H
113 R = OMe

1 R = H
114 R = OMe

Scheme 40. Reagents and conditions: (a) $NiCl_2{\cdot}2H_2O$, Li, DTBB, THF (for **1**: 83%; for **114**: 79%).

Konwar et al. described an efficient general system for the deoxygenation of azoxybenzene derivatives in aqueous media.[95] Starting from the azoxybenzenes **112**, **115**, and **116**, treatment with $AlCl_3{\cdot}6H_2O$/KI in acetonitrile and water led to the azobenzenes **1**, **11**, and **103** in 71–75% yields (Scheme 41).

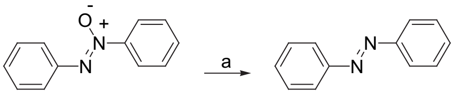


112 $R_1 = R_2 = R_3 = H$
115 $R_1 = R_3 = H$; $R_2 = Cl$
116 $R_1 = Me$; $R_2 = R_3 = H$

1 $R_1 = R_2 = R_3 = H$
11 $R_1 = R_3 = H$; $R_2 = Cl$
103 $R_1 = Me$; $R_2 = R_3 = H$

Scheme 41. Reagents and conditions: (a) $AlCl_3{\cdot}6H_2O$/KI, MeCN, H_2O (for **1**: 71%; for **11**: 75%; for **103**: 72%).

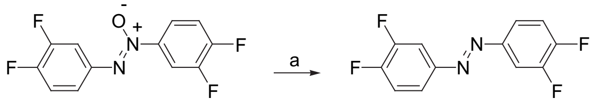
Reduction of azoxybenzene (**112**) using ruthenium(III) chloride in acetonitrile was described by Sandhu et al. to furnish the deoxygenated compound **1** in 82% yield (Scheme 42).[96]



112 **1**

Scheme 42. Reagents and conditions: (a) $RuCl_3$, MeCN (82%).

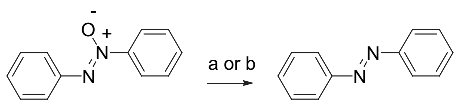
A mild and efficient deoxygenation of azoxybenzene **117** was reported by Singh et al. using CuI and Zn powder in ethanol to give the azo compound **118** in 95% yield (Scheme 43).[97]



117 **118**

Scheme 43. Reagents and conditions: (a) CuI/Zn, EtOH (95%).

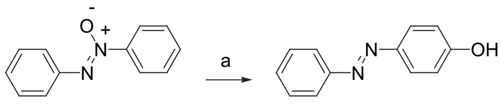
With an increasing focus on green methodologies, Sandhu et al. reported a safe and environmentally friendly procedure for the deoxygenation of azoxybenzene **112** using $Zn(OTf)_2$ to give the corresponding azobenzene (**1**) in 70% yield. In this works, the use of $Cu(OTf)_2$ instead of $Zn(OTf)_2$ furnished compound **1** in 75% yield (Scheme 44).[98]



112 **1**

Scheme 44. Reagents and conditions: (a) $Zn(OTf)_2$, MeCN (70%); (b) $Cu(OTf)_2$, MeCN (75%).

It was notable that the Wallach rearrangement using sulfuric acid induced the direct conversion of azoxybenzene **112** into the corresponding 4-hydroxyazobenzene (**119**) (Scheme 45).[99]

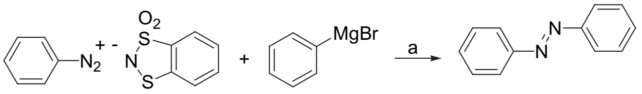


112 **119**

Scheme 45. Reagents and conditions: (a) H_2SO_4.

2.7. Other methods

Different methods to obtain azobenzenes were reported using isocyanates or aryldiazonium salts and metal reagents or aryl hydrazines and quinones. Recently, only the last two methods were studied. In 1998, Fochi et al. developed the synthesis of azobenzene by an electrophilic coupling reaction of arenediazonium salts with Grignard reagents.[100] Thus, treatment of the arenediazonium o-benzenedisulfonimide **120** with a solution of phenylmagnesium bromide (**121**) afforded azobenzene (**1**) in 71% yield (Scheme 46).

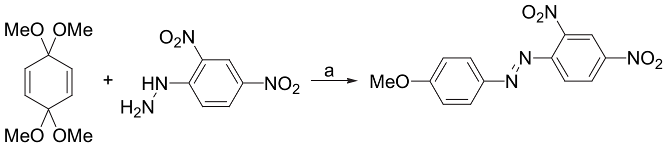


120 **121** **1**

Scheme 46. Reagents and conditions: (a) THF (71%).

In order to find new organometallic compounds useful in organic synthesis, Dughera et al. studied the aforementioned strategy by replacing the Grignard reagent with a triorganoindium compound.[101]

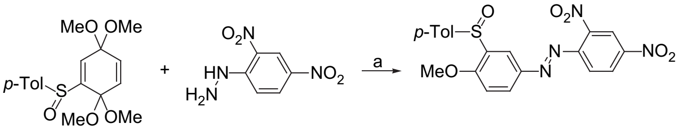
Quinone chemistry is well documented, but only a few studies have been described for the synthesis of azobenzene starting from benzoquinone.[102] Starting from the commercial bis-dimethyl acetal of p-benzoquinone (**122**), the direct reaction of arylhydrazine **123** afforded the azobenzene **124** in 99% yield (Scheme 47).



122 **123** **124**

Scheme 47. Reagents and conditions: (a) MeCN (99%).

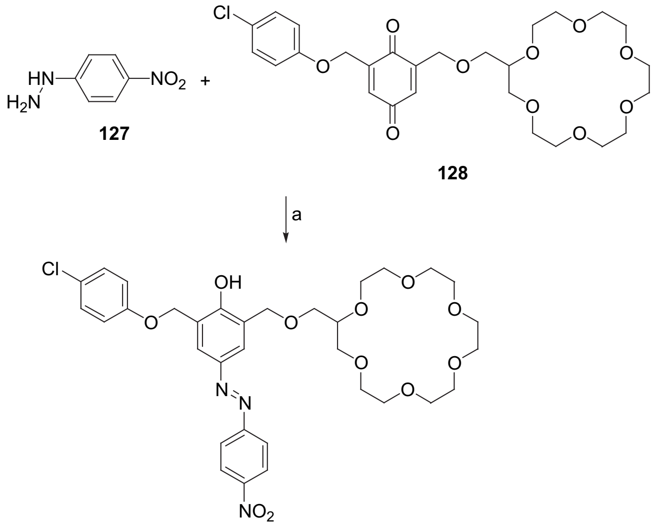
In order to enhance the yield of the azobenzene derivatives, the presence of a one-electron oxidant such as a CAN reagent gave a remarkable increase in the reaction rate and yield. Tobe et al. reported the synthesis of azobenzene (**126**), which was prepared by the reaction of 2-p-tolylsufinyl-1,1,4,4-tetramethoxy-2,5-cyclohexadiene (**125**) and the hydrazine **123** in the presence of CAN in acetonitrile in 85% yield (Scheme 48).[102]



125 **123** **126**

Scheme 48. Reagents and conditions: (a) CAN, MeCN (85%).

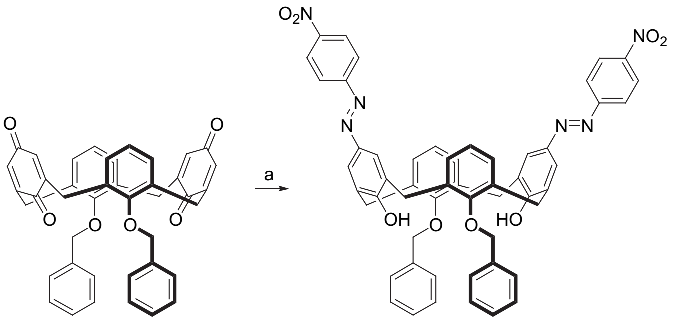
Recently, Kaneda et al. reported the treatment of p-nitrophenylhydrazine (**127**) with benzoquinone **128** having an 18-crown-6 moiety to furnish the azobenzene **129** in 25% yield (Scheme 49).[103]



127 **128** **129**

Scheme 49. Reagents and conditions: (a) EtOH (25%).

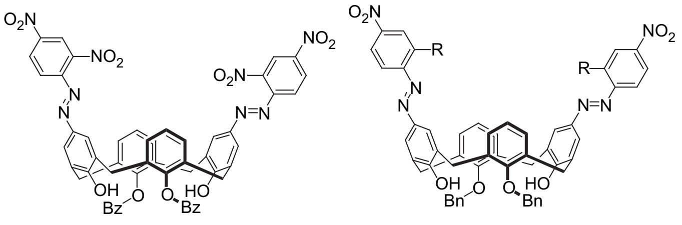
In 2006, azocalix[4]arene having azobenzene **131** has been synthesized by Chawda et al.[104] A non-diazo-coupling route was also used to synthesize azocalix[4]arene derivatives containing two free phenolic groups. Treatment of dibenzoylated calix[4]arene diquinone **130** with 4-nitrophenylhydrazine in the presence of sulfuric acid furnished the bis(nitrophenylazophenol) derivative **131** in 78% yield (Scheme 50).



130 **131**

Scheme 50. Reagents and conditions: (a) $p\text{-}NO_2C_6H_4NHNH_2$, H_2SO_4, EtOH, $CHCl_3$ (78%).

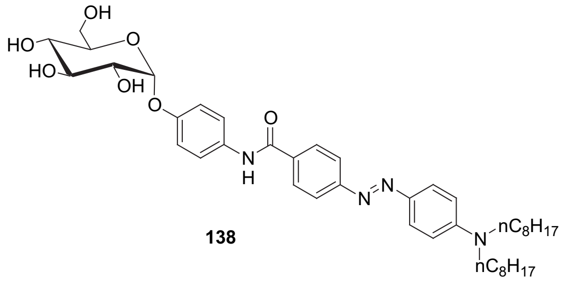
Application of this strategy permitted the synthesis of the corresponding azobenzenes **132**–**134** in 78–84% yields (Fig. 12).



132

133 R=H
134 R=NO_2

Figure 12. Azocalix[4]arene derivatives **132–134**.



138

Figure 13. Azobenzene having D-galactosyl moiety **138**.

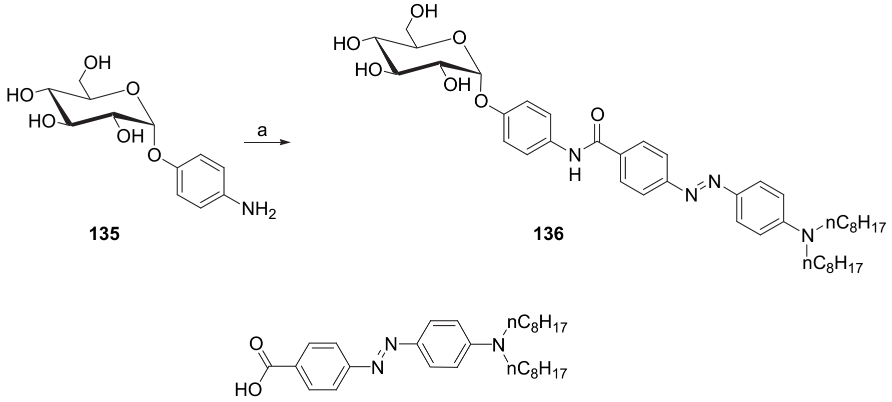
3. Synthesis of azobenzene carbohydrates

Although many glycosides and azobenzene compounds have been studied over the past century, a surprisingly small number of reports regarding azobenzene derivatives having a glycone moiety are available. The different structures described in the literature associate an azobenzenyl group with one or several glycone moieties with or without a linker. The following two routes have been reported in the literature: (i) an azobenzene derivative was directly bound to the glycone part; and (ii) the azobenzene was prepared using standard methods starting from the glycosyl part bearing an aromatic substituent. The carbohydrate moiety comprises modified or natural pentoses, hexoses or cyclodextrins.

3.1. Carbohydrate derivatives having one azobenzene moiety

In order to control the color of dye aggregates, a novel azobenzene glycopyranoside **136** was reported starting from *p*-aminophenyl-α-D-glucopyranoside (**135**).[105] This compound was an amphiphilic glycopyranoside containing an azobenzene chromophore and an amide-benzene auxochrome. Treatment of the azobenzene derivative **137** with oxalyl chloride and addition of the glycoside **135** furnished the target compound **136** in 35% yield (Scheme 51). It was notable that the carbohydrate derivative was used without protection. Compound **138** was obtained according to a similar method (Fig. 13).

Boullanger and Goodby have described the synthesis of amphiphilic azobenzene glycosides and a study of their liquid crystal properties.[106] The authors described the synthesis of the

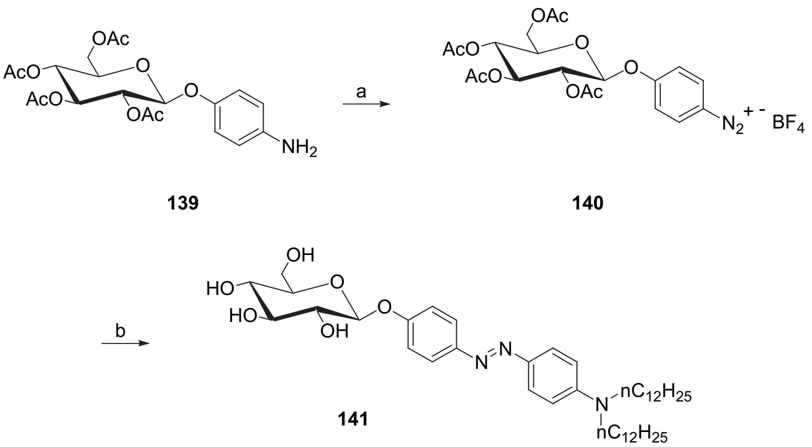


135

136

137

Scheme 51. Reagents and conditions: (a) 4-[(4-di-*n*-octylamino)phenylazo]benzoic acid (**137**), oxalyl chloride, CH_2Cl_2 (35%).



139

140

141

Scheme 52. Reagents and conditions: (a) $BF_3.OEt_2$ then *t*-$BuNO_2$ (quant); (b) picric acid, *N*,*N*-didodecylaniline, Na_2CO_3, $C_2H_4Cl_2$, H_2O (63%); (c) NaOMe, MeOH (91%).

azobenzene moiety using the diazonium strategy in the area of carbohydrate chemistry. Starting from the per-*O*-acetylated 4-aminophenyl glycoside **139**, formation of the corresponding phenyldiazonium tetrafluoroborate **140** was obtained in quantitative yield. Then, the salt **140** was condensed with *N*,*N*-didodecylaniline under phase-transfer conditions and the per-*O*-acetylated compound was fully de-*O*-acetylated by the Zemplen method to furnish the azobenzene **141** in 57% yield (two steps) (Scheme 52). Application of this methodology permitted the synthesis of the phenylazophenyl glycosides **142**–**145** (Fig. 14).

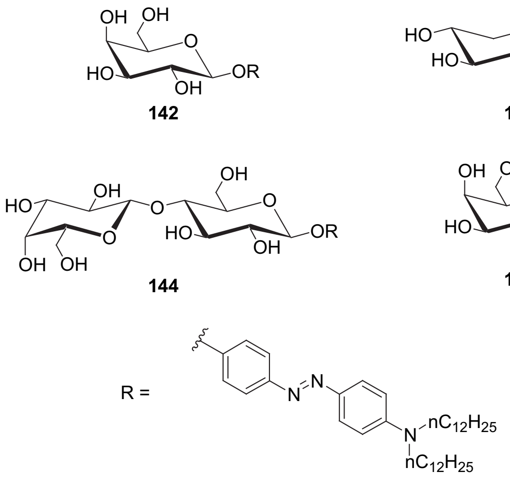
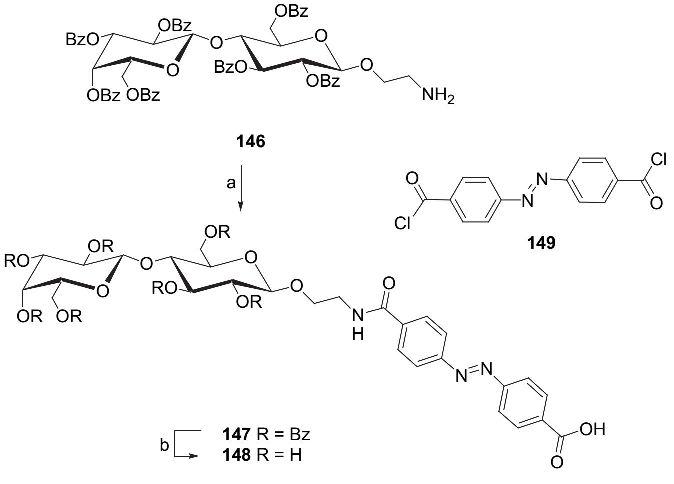


Figure 14. Azobenzene derivatives **142**–**145**.

The synthesis of azobenzene-containing multivalent ligands has been described. Selective amide bond formation between an amine-tethered mannopyranoside derivative **146** and 4,4′-azobenzene dicarbonyl chloride (**149**) was performed in the presence of triethylamine to obtain the dissymmetrical compound **147** in 76% yield (Scheme 53).[107] Classical deprotection of the glycone moiety furnished the targeted azobenzene **148** in quantitative yield.

Development of this methodology led to the isolation of the monoamide **150** (Fig. 15).



Scheme 53. Reagents and conditions: (a) 4,4′-azobenzene dicarbonyl chloride (**149**), NEt_3, THF (76%); (b) NaOMe, MeOH (quant).

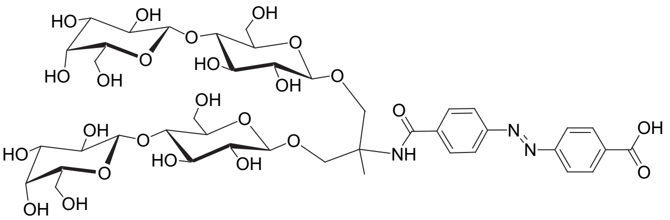
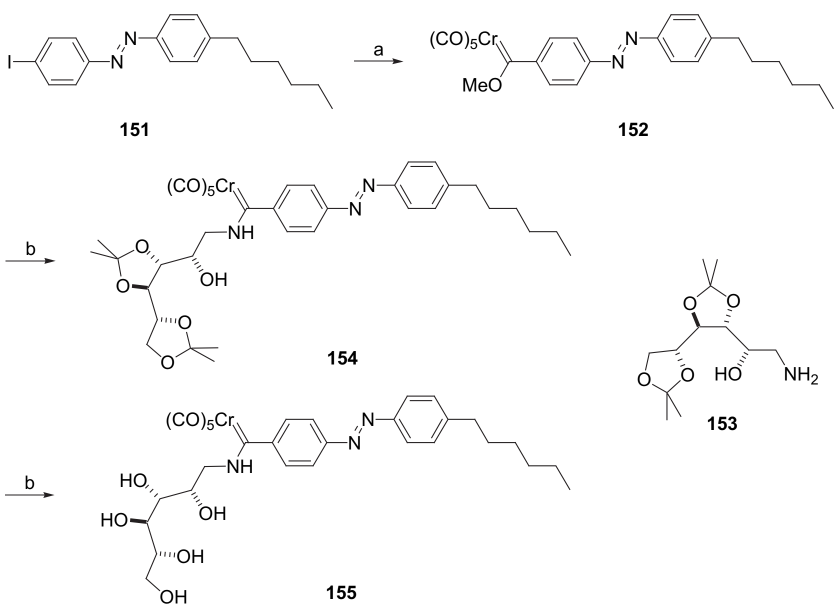


Figure 15. Amine-tethered mannopyranoside derivative **150** having azobenzene moiety.

In 2007, Dotz et al. described the synthesis of amphiphilic carbohydrate-functionalized Fischer carbene complexes having an azobenzene moiety as the hydrophobic part of the molecule.[108] Starting from the azobenzene **151**, the iodine/lithium exchange in diethyl ether followed by transmetallation to zinc, addition of hexacarbonylchromium and O-alkylation afforded the azobenzenechromium carbene **152** in 36% yield. Aminolysis of the methoxycarbene complexe **152** with the glucamine derivative **153** furnished the protected itol **154** in 28% yield. Classical deprotection of the hydroxyl groups of compound **154** afforded the targeted azobenzene derivative **155** in 30% yield (Scheme 54).



Scheme 54. Reagents and conditions: (a) *n*-BuLi, Et_2O, −100 °C then $ZnBr_2$, then $Cr(CO)_6$, −70 to −40 °C (36%); (b) compound **153**, CH_2Cl_2 (34%); (c) PTSA, MeOH, ethyleneglycol (30%).

Using the same methodology, Dotz et al. reported the synthesis of the amphiphilic azobenzene metal carbene **156** (Fig. 16).[108]

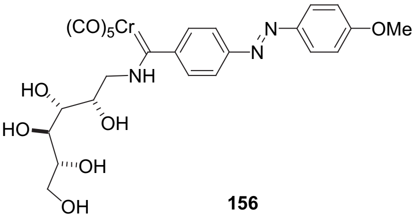
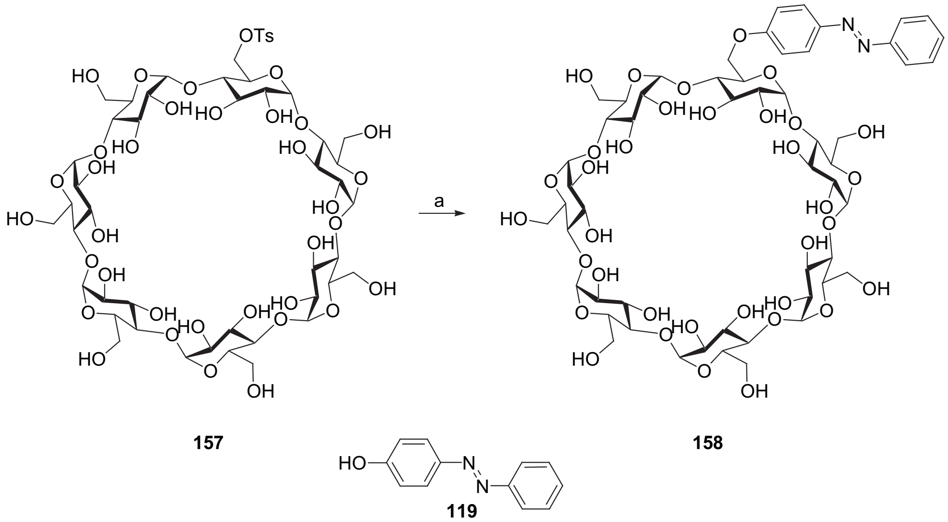


Figure 16. Amphiphilic azobenzene metal carbene **156** having azobenzene moiety.

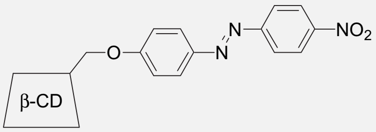
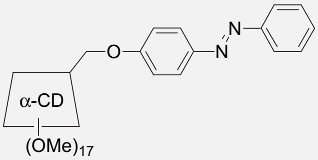
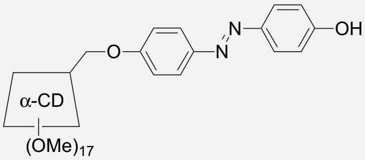
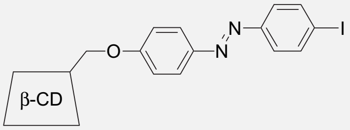
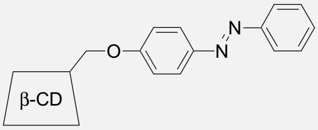
Novel cyclodextrins bearing azobenzene functional groups were reported in the literature. These structures associate the cyclodextrin moiety with the azobenzene via either *O*-ether, amido functions or via different links. Liu et al. reported the synthesis of novel cyclodextrins possessing an azobenzene functional group having an *O*-ether bond.[109] Starting from the *O*-tosylate **157**, etherification with alcohol **119** gave the corresponding ether **158** in 78% yield (Scheme 55).

Similar etherifications were reported in the literature starting from α- and β-cyclodextrins optionally methylated for the synthesis of the azobenzene derivatives **159–163** in 40–74% yield (Table 1).

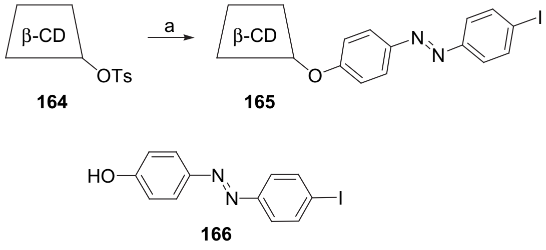


Scheme 55. Reagents and conditions: (a) 4-phenylazophenol (**119**), DMF (78%).

Table 1
Synthesis of azobenzenes **159–163** starting from corresponding *O*-tosylate

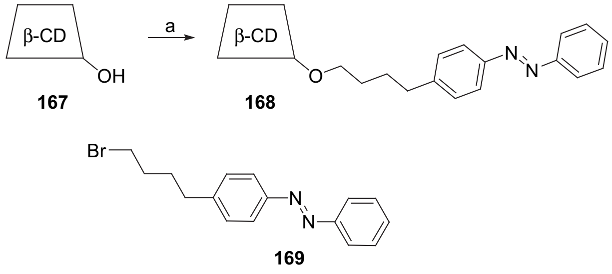
Entry		Product	Yield (%)	Ref.
1	**159**		74	109
2	**160**		76	110
3	**161**		40	110
4	**162**		nd	111
5	**163**		38 39	112 112

Tian et al. reported the synthesis of azobenzene-modified β-cyclodextrin at the 2-position (**165**) starting from the corresponding 2-*O*-tosylate **164** by the addition of the azobenzene derivative **166** (Scheme 56).[111]



Scheme 56. Reagents and conditions: (a) 4-iodophenylazophenol (**166**), K_2CO_3, DMF (nd).

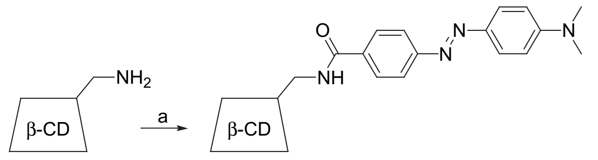
In 2008, Gin et al. described the synthesis of a novel azobenzene-modified β-cyclodextrin **168** in order to prepare a light-gated synthetic ion channel.[113] Compound **168** had a butyl link



Scheme 57. Reagents and conditions: (a) 4-bromobutylazobenzene (**169**), K_2CO_3, DMF (7%).

between the arene moiety and the CD derivative. The attachment of the tether at the secondary face of the β-cyclodextrin (**167**) was effected by deprotonation with sodium hydride and addition of the bromobutylazobenzene (**169**) to give the target modified ß-cyclodextrin **168** in modest yield (7%) (Scheme 57).

Kuwabara et al. reported similar work for the synthesis of azobenzene-modified cyclodextrins with various lengths of spacer between the cyclodextrin and the azobenzene.[114] Starting from the 6-deoxy-6-amino-β-CD **170**, treatment of a dimethylacetamide of 4-hydroxyazobenzene-2-carboxylic acid, dicyclohexylcarbodiimide, and 1-hydroxybenzotriazole furnished the corresponding azobenzene **171** (Scheme 58).

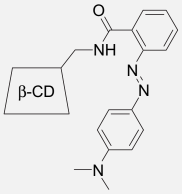
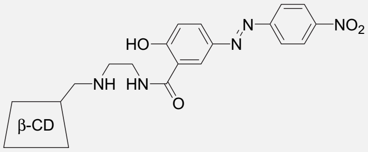
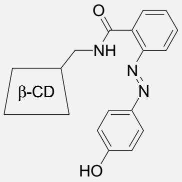
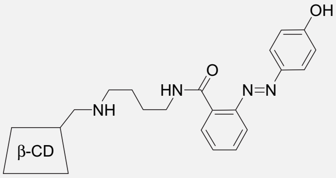
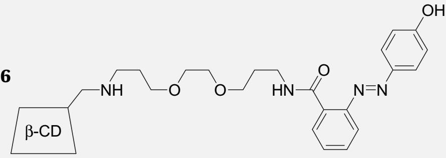


170 **171**

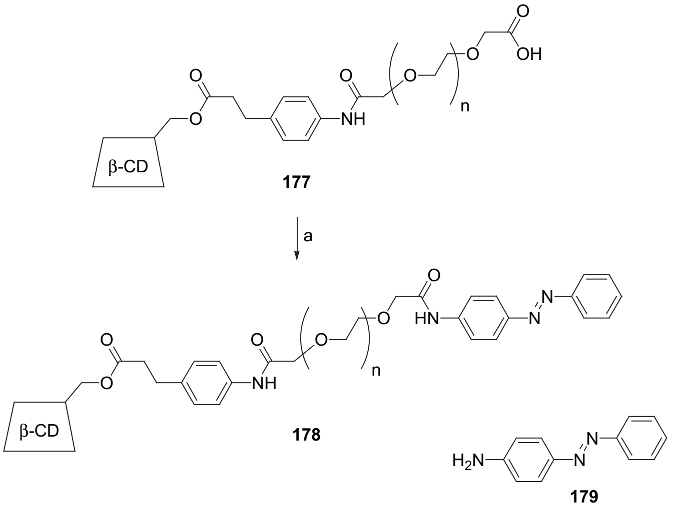
Scheme 58. Reagents and conditions: (a) HABA, DCC, HOBt (nd).

Application of this strategy also permitted the synthesis of the corresponding azobenzene-modified cyclodextrins **172–176** (Table 2).

Table 2
Synthesis of azobenzenes **172**–**176** starting from corresponding amine **170**

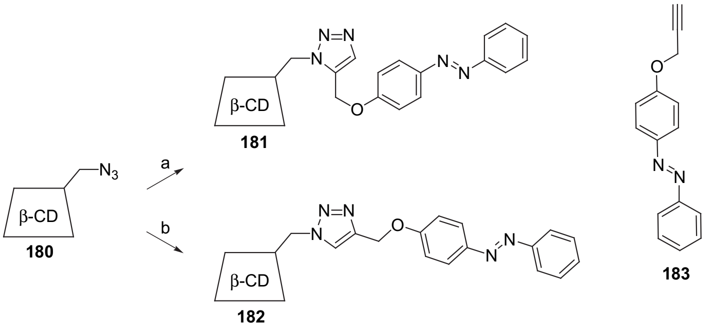
Entry		Product	Yield (%)	Ref.
1	**172**		nd	114
2	**173**		nd	114a
3	**174**		1	114b
4	**175**		15	114b
5	**176**		23	114b

Harada et al. described the synthesis of poly(ethylene glycol)-substituted with an azobenzene group at the chain end.[115] Starting from the poly(ethylene glycol) derivative **177**, amidation using *p*-aminoazobenzene (**179**) in water and DMF gave the corresponding modified cyclodextrin **178** in 15% yield (Scheme 59).



Scheme 59. Reagents and conditions: (a) compound **179**, H$_2$O, DMF (15%).

The click chemistry[116] was applied to the synthesis of an azobenzene-modified cyclodextrin starting from the azido compound **180**.[117] Using 4-propargylazobenzene (**183**), Huisgen 1,3-dipolar cycloaddition was applied in hydrothermal conditions to give the analogue **181** in 69% yield (Scheme 60). The isomer **182** was obtained using a Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition in 71% yield. It was notable that Vargas-Berenguel et al. reported the synthesis of the modified cyclodextrin **181** in 74% yield using a similar method.[112]



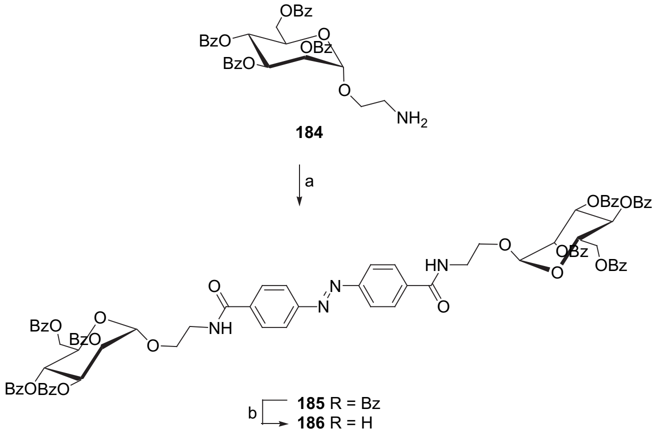
Scheme 60. Reagents and conditions: (a) compound **183**, EtOH, H$_2$O, 85 °C (69%); (b) compound **183**, CuSO$_4$·5H$_2$O, sodium ascorbate, EtOH, H$_2$O (71%).

3.2. Dimers and polymers linked with one azobenzene moiety

The synthesis of azobenzene-containing multivalent ligands has been described. Amide bond formation between an amine-tethered mannopyranoside derivative **184** and 4,4′-azobenzene dicarbonyl chloride **149** was performed in the presence of triethylamine to obtain the symmetrical diamide **185** in 89% yield.[107] Classical deprotection of the glycone moiety furnished the targeted azobenzene **186** in quantitative yield (Scheme 61).

The same strategy was applied to extend the series of compounds to include the mannopyranoside and lactoside derivatives **187–189** (Fig. 17).[107]

Similarly, azobenzene 3,3′,5,5′-tetracarbonyl chloride (**190**) led to the azobenzene derivatives **191–193** (Fig. 18).[107]



Scheme 61. Reagents and conditions: (a) 4,4′-azobenzene dicarbonyl chloride (**149**), NEt_3, THF (89%); (b) NaOMe, MeOH (quant).

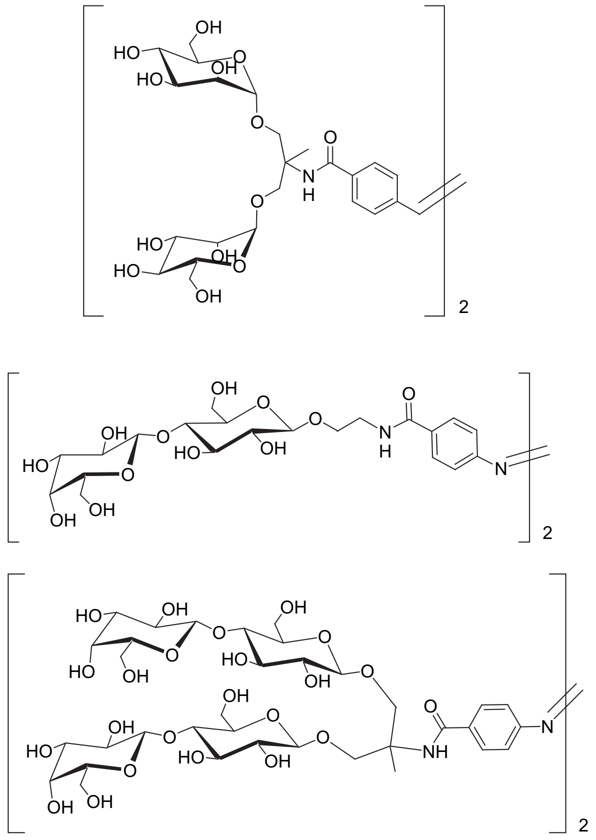


Figure 17. Azobenzene derivatives **187–189** having glycone part.

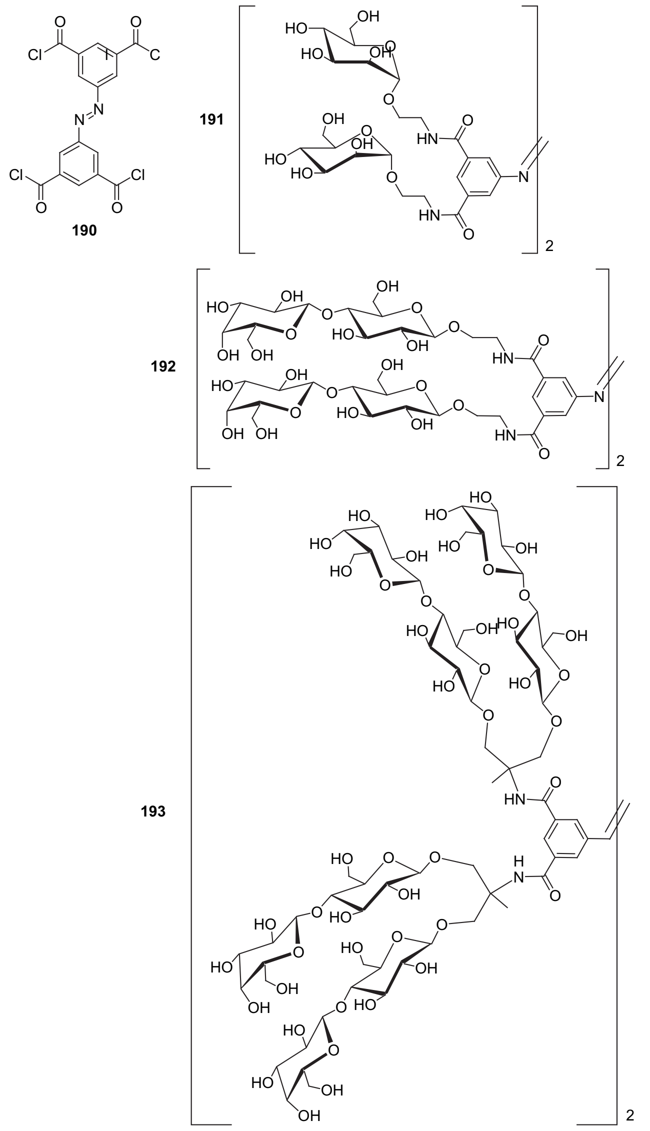
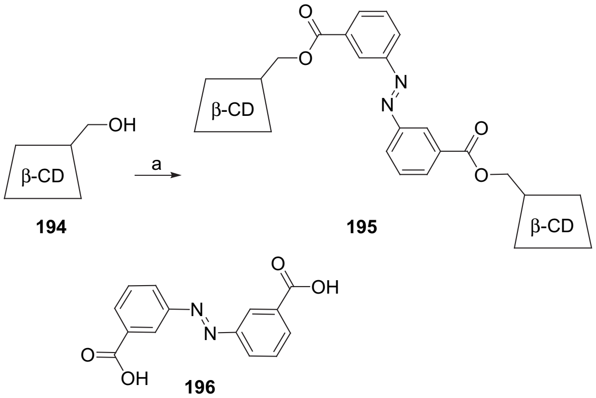


Figure 18. Azobenzene 3,3′,5,5′-tetracarbonyl chloride (**190**) and derivatives **191–193** having glycone part.

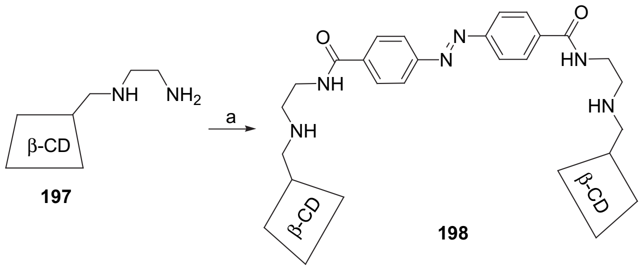
Recently, dimers of cyclodextrin linked by an azobenzene moiety were reported in the literature. Liu et al. described the synthesis of bridged bis(ß-cyclodextrin) with an azobenzene dicarboxylate linker starting from native β-cyclodextrin **194**.[118] Treatment of β-cyclodextrin **194** with 3,3′-azodibenzoic acid (**196**) in presence of



Scheme 62. Reagents and conditions: (a) 3,3′-azodibenzoic acid (**196**), DCC, molecular sieves, DMF (25%).

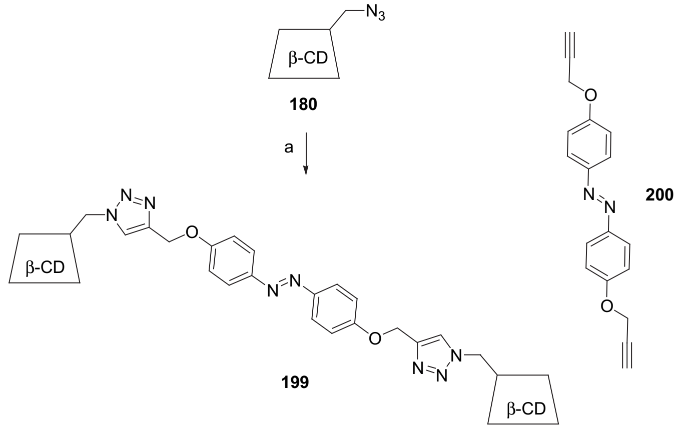
DCC and molecular sieves afforded the corresponding dimer **195** in 25% yield (Scheme 62).

In order to obtain a bisdansyl-modified β-cyclodextrin dimer linked by azobenzene, Hamada et al. reported the synthesis of dimer **198**.[119] Starting from 4,4′-azodibenzoic acid (**49**) in the presence of DCC and HOBt, addition of the modified cyclodextrin **197** furnished the dimer **198** in 32% yield (Scheme 63).



Scheme 63. Reagents and conditions: (a) 4,4′-azodibenzoic acid (**49**), DCC, HOBt, DMF (32%).

In 2008, Vargas-Berenguel et al. reported the synthesis of dimer **199** via the click chemistry strategy.[112] A β-cyclodextrin moiety was bound to the azobenzene moiety by the reaction of 6-deoxy-6-azido-β-cyclodextrin (**180**) with 4,4′-dipropargyloxyazobenzene (**200**) in the presence of $(EtO)_3P \cdot CuI$ in DMF to afford the corresponding 1,2,3-triazole-linked azobenzene-cyclodextrin derivative **199** in 72% yield (Scheme 64).



Scheme 64. Reagents and conditions: (a) 4,4′-dipropargyloxyazobenzene (**200**), $(EtO)_3P \cdot CuI$, DMF (72%).

4. Conclusions

Azobenzenes and carbohydrates are two families of organic compounds widely developed but few studies have associated them. This review updates the major preparations of azobenzene derivatives and the association of a phenylazophenyl group with a glycone moiety such as monosaccharides, itols, and cyclodextrins covering the literature from 1998 to 2009. Although a lot of effort has been devoted to the development of azobenzenes, no general reaction was obtained. Two methods of choice for the synthesis of azobenzenes were developed: (i) creation of the azo bond by coupling two identical or non-identical aromatic compounds;[19–71] and (ii) creation of the azo bond by oxidation of hydrazo compounds[72,73,76,77,87] or by reduction of azoxybenzene derivatives.[92–99] Between the two methods described above, two classes of derivatives can be obtained: the symmetrical and the dissymmetrical azobenzenes. The synthesis of symmetrical azobenzene derivatives was effected by: (i) oxidation reactions of aromatic primary amines; [19–30] (ii) reduction reactions of aromatic compound having nitro groups; [32–36] (iii) diazo-coupling via diazonium salts; [54–71] and (iv) coupling reactions with arenediazonium salts.[100,101] The synthesis of dissymmetrical azobenzene derivatives was effected by: (i) oxidation reactions of aromatic primary amines; [31] (ii) coupling of primary arylamines with nitroso compounds (Mills reaction);[37–53] and (iii) coupling reactions with arenediazonium salts.[100,101] Starting from hydrazo compounds, the oxidation furnished symmetrical azobenzenes[72,73,76,77] and dissymmetrical azobenzenes.[72,73,76,87] Starting from azoxybenzene compounds, the reduction furnished symmetrical azobenzenes[92–99] and dissymmetrical azobenzenes.[99]

The association between a glycone moiety (e.g., monosaccharides, itols, and cyclodextrins) and a phenylazophenyl group with or without a linker was described, furnishing photomodulable structures. Two target families were reported having either one glycone moiety and one phenylazophenyl group[105–115,117] or two glycone parts and one phenylazophenyl group.[107,112,118,119] All of these syntheses were effected by coupling between azobenzene derivatives and carbohydrate derivatives,[105–115,117–119] except one, which described the formation of an azobenzene using a diazonium strategy starting from an aminophenylglycoside.[106]

Acknowledgements

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Biographical sketch

Florian Hamon received his engineering masters degree in chemistry in 2004 from the National Graduate School of Chemistry in Montpellier (ENSCM) and from the Royal Institute of Technology in Stockholm (KTH). In 2008, he obtained his Ph.D. from the University of Poitiers under the supervision of Professor Len and Professor Djédaïni-Pilard. His work was focused on building new supramolecular assemblies associating cyclodextrins, azobenzenes and nucleic acids. Recently, he joined the Gesson-Papot group at the University of Poitiers to work on prodrugs as a postdoctoral fellow.

Francis Barbot was born in Saint-Front (France) in 1946. He received his Ph.D. (1972) and his 'Doctorat-ès-Sciences Physiques' (1980) from the University of Poitiers (France) under the supervision of Professor Ph. Miginiac in the field of organometallic chemistry. Since 1974, he has been a chemist ingenior (C.N.R.S.). Up to 2000, he worked on the reactivity of α-unsaturated organometallic compounds with carbonyl derivatives with particular attention to organoaluminum compounds. Since 2000, he joined UMR 6514 and worked first on dipolar cycloaddition reactions with Professor G. Bashiardes, then on the synthesis of azobenzene derivatives with Professor Ch. Len using, whenever possible, microwave-assisted synthesis. He has 42 publications in international journals.

Florence Djedaini-Pilard was born in Nancy (France) in 1965. She received her undergraduate education at the University of Rennes in 1988 and her Ph.D. degree from the University of Paris XI in Orsay (France) under the supervision of Dr. B. Perly for studies of inclusion complexes of cyclodextrins by NMR. As researcher at Commissariat à l'Energie Atomique (CEA) at Saclay (1990–2000), she developed the chemistry of modified cyclodextrins. In 2000, she moved to the University of Picardie Jules Verne, Amiens, where she rose to the rank of Professor of Chemistry and became the Director of the 'Laboratoire des Glucides', UMR6219. She continues to work on molecular recognition and self-assembly in the carbohydrate field.

Christophe Len was born in L'Isle Adam (France) in 1966. He received his Ph.D. from the University of Picardie Jules Verne (UPJV) in Amiens (France) under the supervision of Professor P. Villa in the field of carbohydrate chemistry. In 1996, he joined Dr. G. Mackenzie's group at the University of Hull (UK) as a postdoctoral fellow to work on the synthesis of nucleoside analogues. In 1997, he became Maître de Conférences at UPJV and worked on the chemistry of antiviral nucleoside analogues, specializing in those with novel glycone systems. In 2003, he received his habilitation and was promoted to full Professor in 2004 at the University of Poitiers (France). For 2008, he had a secondment to the University of Compiègne (France) to develop green chemistry. His current main research interests are in the total synthesis of natural products and bioactive molecules, which include carbohydrates, and green chemistry.