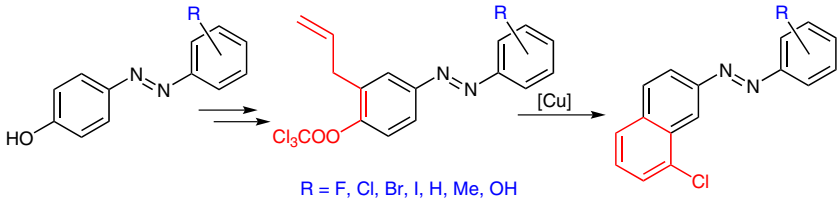
Synlett O. K. Rasheed et al. Cluster

A New Benzannulation Reaction of Azoaromatics

Omer K. Rasheed
James Raftery
Peter Quayle*

School of Chemistry, University of Manchester, Oxford Road, Manchester M13 9PL, UK
peter.quayle@manchester.ac.uk

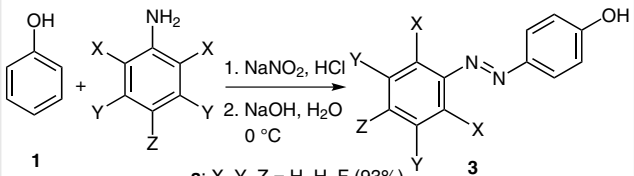


Received: 04.04.2015
Accepted after revision: 26.05.2015
Published online: 10.07.2015
DOI: 10.1055/s-0034-1380450; Art ID: st-2015-s0240-c

Abstract The BHQ benzannulation reaction of azo-substituted (2-allylaryl)trichloracetates, leading to azo-naphthalenes, is described. The scope and limitations of this new synthesis of azoaromatics is discussed.

Key words benzannulation, ATRC, azo, cyclisation, copper, carbene, radical

During a programme of research concerned with the development of functionalised molecular sensors for the detection of metal ions in biological systems we had occasion to prepare azo dyes which incorporated extended naphthalene π-systems.[1] Although there is an extensive literature concerning the preparation of azo dyes – most notably via the one-step diazo coupling chemistry as adumbrated by Griess[2] – downstream transformation of phenols **3**, the usual products of these azo coupling reactions, by way of carbon–carbon bond formation has not been extensively investigated (Scheme 1).

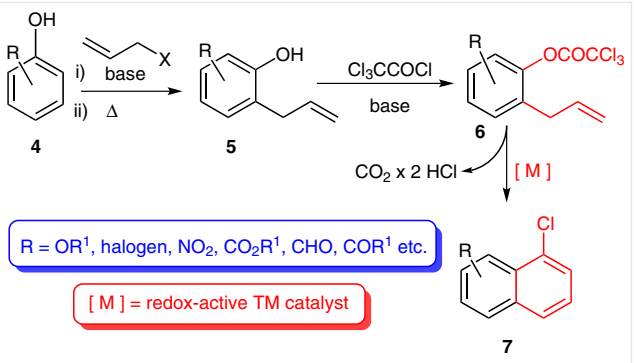


Scheme 1 Azo-coupling reactions

Specifically, the elaboration of triflate derivatives of phenols **3**, using palladium-catalysed cross-coupling reactions, has little precedent.[3a–f] More generally, the Stille- and Suzuki-type coupling of the analogous halo, tin, and boron derivatives of azo-substituted aromatics is at an embryonic stage of development.[3g,h] In addition, although the ability of the azo group to facilitate C–H activation was realized some time ago,[4] it is only recently that synthetic applications have emerged.[5] Likewise, the generation of organolithium reagents derived from azo-functionalised aromatics either by well-established halogen–metal exchange[6a,b] or Snieckus DoG-lithiation[6c] is also underrepresented. The application of dearomatisation strategies, which again utilises the reaction between electropositive organometallics (organolitiums/Grignard reagents) with an electron-deficient azoaromatic has also met with limited application, presumably because of the intervention of competing chemistry at the azo-group.[6c,7a,b,] This aberrant reactivity reflects the tendency of the azo group to undergo electron-transfer reactions with organometallics derived from the more electropositive metals.[7b]

Recently, we disclosed a new, transition-metal-catalysed benzannulation reaction in which (*ortho*-allyl)aryl trihaloacetates were found to participate in a radical cascade sequence which ultimately results in the formation of 1-halo-naphthalene derivatives (the Bull–Hutchings–Quayle or 'BHQ reaction').[8a] This transformation is quite general in scope and proceeds well with substrates possessing one or more of the more common organic functional groups (aldehyde, nitro, ester etc., Scheme 2).

With this development in mind we wondered whether the BHQ reaction could be applied to the synthesis of benzannulated azo compounds.[8f] We presumed that the requisite *ortho*-allyl phenols for the intended BHQ sequence would be available by classical *ortho*-Claisen rearrangement chemistry,[9] a process which does not require

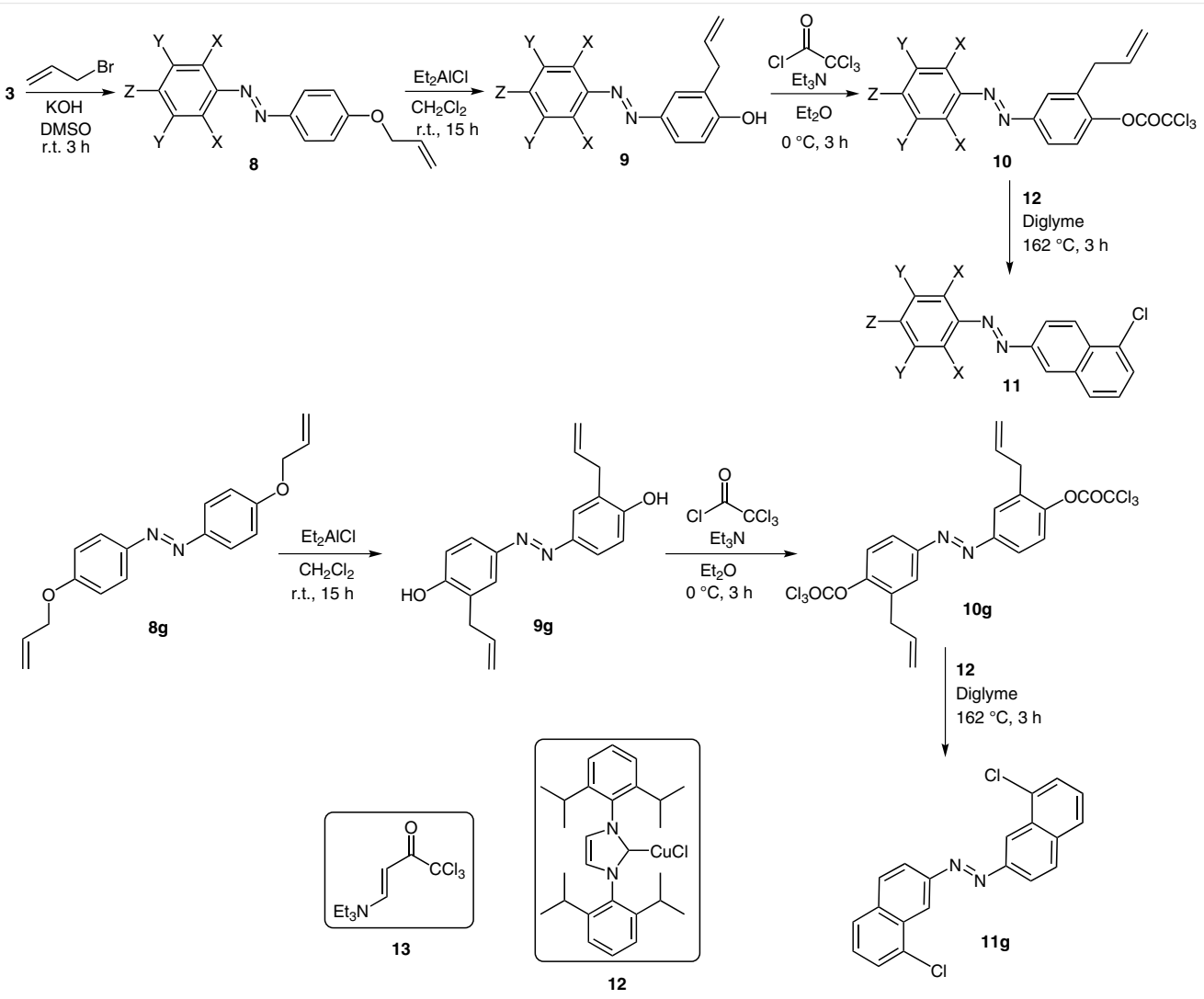


Scheme 2 The 'BHQ' benzannulation sequence

the intervention of highly polarized organometallic intermediates (Scheme 3). In the event of allylation of the readily available azo dyes **3**, which were prepared via standard diazo coupling reactions,[10] was best accomplished, DMSO using KOH as base,[15] in quantitative yields (Scheme 3,Table 1).

Somewhat surprisingly there is little literature precedent[11] for the *ortho*-Claisen rearrangement of azoaromatics and attempted thermolysis of ethers **8** in *N,N*-diethylaniline, as usually prescribed for this type of rearrangement, merely afforded a complex mixture of products or starting material depending upon the exact reaction conditions employed.

Conversion of ethers **8** into phenols[16] **9** was, however, observed in good isolated yields (79–97%) when the rearrangement was conducted in the presence of Et_2AlCl (2.2 equiv) in CH_2Cl_2 at 20 °C for 15 hours.[12] These reactions



Scheme 3 Benzannulation reaction leading to azo-aromatics

were not optimized as they provided material in sufficient quantity and purity for the pivotal BHQ benzannulation reaction.

Table 1 Yields for Claisen-BHQ Sequences

Entry	X	Y	Z	Yield of **8** (%)	Yield of **9** (%)	Yield of **10** (%)	Yield of **11** (%)
1	H	H	H	94	83	81	78
2	H	Me	H	93	84	81	77
3	H	H	Cl	92	87	83	80
4	H	H	F	94	91	89	87
5	H	H	Br	88	81	80	80
6	H	H	I	88	83	81	77
7	H	H	OH	88	79	80	72
8	*i*-Pr	H	H	92	87	82	–
9	H	H	NO_2	81	–	–	–

Having established the feasibility of performing the *ortho*-Claisen rearrangement on a range of azo compounds the utility of the substituted phenols **9** in the BHQ reaction was next examined. Conversion of the phenols **9** into their respective trichloroacetates **10**[17] was readily achieved [Et_3N (1.2 equiv); Cl_3CCOCl (1.2 equiv), Et_2O, 0 °C] in good yields (80–90%). Fortunately, the crude products from the acylation reactions were again of sufficient purity to be used in the pivotal benzannulation reaction as attempted chromatography can lead to deacylation. In passing, it should be noted that the use of an excess of triethylamine/trichloroacetyl chloride should be avoided in the acylation reaction as oxidation of the amine, generating the vinylogous amide **13**, is relatively facile.[13]

Conversion of the trichloroacetates **10** into the benzannulated products **11** proved to be generally uneventful and proceeded to completion over a period of three hours when heated in the presence of the preformed catalyst **12**[8b] (5 mol%) at 162 °C in anhydrous diglyme.[18] The overall regiochemical outcome of the *ortho*-Claisen–BHQ benzannulation sequence was also confirmed in the case of **11a** by way of single-crystal X-ray structure determination (Figure 1).

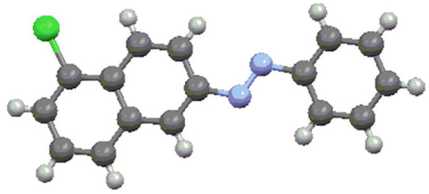
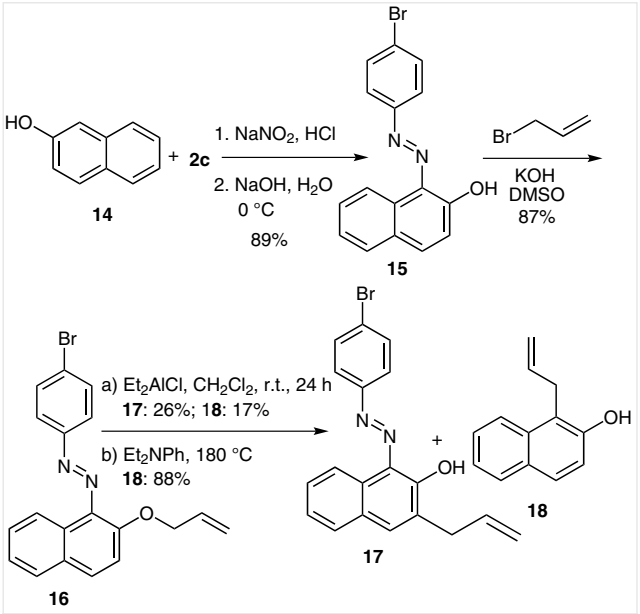


Figure 1 Single-crystal X-ray structure of **11a**

Noteworthy is the observation that the bisallyl ether **8g** was utilized effectively in a 'two-directional' BHQ benzannulation reaction. Here, a double *ortho*-Claisen rearrangement of **8g** afforded the diol **9g**, which ultimately resulted in the isolation of the azo compound **11g** after benzannulation (72% yield for the benzannulation step). This outcome is to be compared with that from the nitro-substituted substrate **8i**, which proved to be wholly resistant towards benzannulation.

Unfortunately, attempted extension of this methodology to the rearrangement of the naphthol derivative **16** proved to be highly capricious. In this case thermolysis of **16** in *N*,*N*-diethylaniline (180 °C, 15 h) merely afforded the phenol **18** in excellent yield (88%),[13] while the use of Et_2AlCl (2.2 equiv, CH_2Cl_2, 0–20 °C) as promotor resulted in the formation of the desired rearranged product **17** (26% isolated yield), together with minor quantities (17% isolated yield) of the phenol **18** (Scheme 4).



Scheme 4 Synthesis of rearranged azo-naphthol derivative via Claisen rearrangement

It should be noted that possible limitation of this chemistry is evident in that attempted rearrangement of the naphthol derivative **17**, where the presence of a proximal azo functional group inhibited the trichloroacetylation step.

In conclusion we have demonstrated that an *ortho*-Claisen–BHQ benzannulation sequence can be applied to the synthesis of benzofused azoaromatics. In most cases the benzannulation proceeds in high yields, complements existing methodology,[14] and enables the synthesis of functionalised azoaromatics. Application to the synthesis of bespoke azonaphthalenes is now in progress.

Acknowledgment

Financial support from the University of Manchester is gratefully acknowledged. The UoM thanks the EPSRC (grant number EP/K039547/1) for the provision of Bruker NMR spectrometers and an Agilent SuperNova X-ray diffractometer.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1380450. Experimental procedures for all new compounds are included, as well as a cif file for compound **11a** (CCDC 1048487).

References and Notes

(1) For applications of related compounds, see: Quandt, G.; Höner, G.; Pabel, J.; Dine, J.; Eder, M.; Wanner, K. T. *J. Med. Chem.* **2014**, *57*, 6809.

(2) (a) Griess, P. *Justus Liebigs Ann. Chem.* **1866**, *137*, 39. (b) Maerino, E. *Chem. Soc. Rev.* **2011**, *40*, 3835. (c) Zollinger, H. *Azo Coupling Reactions*, In *Diazo Chemistry I*; VCH: Weinheim, **1994**, 305.

(3) (a) Gøgsig, T. M.; Kleimark, J.; Nilsson, L.; Korsager, S.; Lindhardt, A. T.; Norrby, P.-O.; Skrydstrup, T. *J. Am. Chem. Soc.* **2012**, *134*, 443. (b) Casa-Solvas, J. M.; Vargas-Berenguel, A. *Tetrahedron Lett.* **2008**, *49*, 6778. (c) Ma, X.; Wang, Q.; Tian, H. *Tetrahedron Lett.* **2007**, *48*, 7112. (d) Harvey, J. H.; Butler, B. K.; Trauner, D. *Tetrahedron Lett.* **2007**, *48*, 1661. (e) Okanao, K.; Tsutsumi, O.; Shishido, A.; Ikeda, T. *J. Am. Chem. Soc.* **2006**, *128*, 15368. (f) Liao, L.-X.; Stellacci, F.; McGrath, D. V. *J. Am. Chem. Soc.* **2004**, *126*, 2181. For a representative example, see: (g) Strueben, J.; Gates, P. J.; Staubitz, A. *J. Org. Chem.* **2014**, *79*, 1719. (h) Pérez-Miqueto, J.; Telleria, A.; Muñoz-Olasagasti, M.; Altube, A.; Garcia-Lecina, E.; de Cózar, A.; Freixa, Z. *Dalton Trans.* **2015**, 2075.

(4) (a) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 313. (b) Cope, A. C. *J. Am. Chem. Soc.* **1965**, *87*, 3272. (c) Kleiman, J. P.; Dubeck, M. *J. Am. Chem. Soc.* **1963**, *85*, 1544. (d) Bagga, M. M.; Flannigan, W. T.; Knox, G. R.; Pauson, P. L. *J. Chem. Soc. C* **1969**, 1534.

(5) (a) Majhi, B.; Kundu, D.; Ahammaed, S.; Ranu, B. C. *Chem. Eur. J.* **2014**, *20*, 9862. (b) Qian, C.; Lin, D.; Deng, Y.; Zhang, X-Q.; Jiang, H.; Miao, G.; Tang, X.; Zeng, Y. *Org. Biomol. Chem.* **2014**, *12*, 5866. (c) Lian, Y.; Bergman, R. G.; Lavis, L. D.; Ellman, J. A. *J. Am. Chem. Soc.* **2013**, *135*, 7122; and references cited therein.

(6) (a) Koźlecki, T.; Syper, L.; Wilk, K. A. *Synthesis* **1997**, 681. (b) Kano, N.; Komatsu, F.; Yamamura, M.; Kawashima, T. *J. Am. Chem. Soc.* **2006**, *128*, 7097. The direct lithiation of azobenzene derivatives has recently been reported, see: (c) Nguyen, T. T. T.; Boussonnière, A.; Banaszak, E.; Castanet, A.-S.; Nguyen, K. P. P.; Mortier, J. *J. Org. Chem.* **2014**, *79*, 2775.

(7) (a) Colonna, M.; Risalti, A. *Gazz. Chim. Ital.* **1956**, *86*, 698. (b) Risaliti, A.; Bozzini, S. *Ann. Chim.* **1964**, *54*, 685. (c) Holm, T. *Acta Chem. Scand. B* **1983**, *37*, 567.

(8) (a) Bull, J. A.; Hutchings, M. G.; Quayle, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 1869. (b) Bull, J. A.; Hutchings, M. G.; Lujan, C.; Quayle, P. *Tetrahedron Lett.* **2008**, *49*, 1352. (c) Bull, J. A.; Hutchings, M. G.; Lujan, C.; Quayle, P. *Tetrahedron Lett.* **2009**, *50*, 3617. (d) Little, M.; Lan, H.; Raftery, J.; Morrison, J. J.; McDouall, J. J. W.; Yeates, S. G.; Quayle, P. *Eur. J. Org. Chem.* **2013**, 6038. (e) Heard, K. W. J.; Morrison, J. J.; Weston, L.; Lo, C. H.; Pirvu, L.; Raftery, J.; Little, M. S.; McDouall, J. J. W.; Yeates, S. G.; Quayle, P. *Chem. Commun.* **2015**, *51*, 6115. ATRP reactions of azo-containing substrates is documented: (f) Fang, L.; Chen, S.; Guo, X.; Zhang, Y.; Zhang, H. *Langmuir* **2012**, *28*, 9767.

(9) (a) Majumdar, K. C.; Nandi, R. K. *Tetrahedron* **2013**, *69*, 6921. (b) Ichikawa, H.; Maruoka, K. *Aliphatic and Aromatic Claisen Rearrangement*, In *The Claisen Rearrangement*; Hiesermann, M.; Nubbermeyer, U., Eds.; Wiley-VCH: Weinheim, **2007**, Chap. 3, 45.

(10) (a) Florea, S.; Rudolf, W. D.; Chivu, M. *Anal. Univ. Craiova, Ser. Chim.* **2005**, *34*, 1; *Chem. Abstr.* **2005**, *146*, 379752. For alternative approaches to related substrates, see: (b) Odabaşoğlu, M.; Turgut, G.; Karadayi, N.; Büyükgüngör, O. *Dyes and Pigments* **2005**, *64*, 271.

(11) Bender, D. R.; Kanne, D.; Frazier, J. D.; Rapoport, H. *J. Org. Chem.* **1983**, *48*, 2709.

(12) Giger, R.; Allain, R.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta* **1970**, *53*, 120.

(13) For a related *ipso*-substitution reaction during a Claisen rearrangement, see: Anjaneyulu, A. S. R.; Isaa, B. M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 993.

(14) Hegele, P.; Santhamma, B.; Schnakenburg, G.; Fröhlich, R.; Kateava, O.; Nieger, M.; Kotsis, K.; Neese, F.; Dötz, K. H. *Organometallics* **2010**, *29*, 672.

(15) **General Method for the Preparation of Allylated Ethers 8**
To a stirred mixture of powdered KOH (5 equiv) in DMSO was added the diazo compound (1 equiv). Allyl bromide (2 equiv) was then added to the mixture. The reaction mixture was stirred for 3 h at r.t. and then poured into H_2O. The organic material was extracted into CH_2Cl_2 (50 mL), and the organic layer was washed with brine (2 × 20 mL), H_2O (1 × 20 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by flash chromatography to give products **8a**–**i**
Synthesis of (*E*)-1-[2-(Allyloxy)phenyl]-2-phenyldiazene (8a)
Yield 94%; mp 70–72 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.64 (2 H, dt, *J* = 5, 1 Hz), 5.34 (1 H, dq, *J* = 10, 1 Hz), 5.47 (1 H, dq, *J* = 17, 2 Hz), 5.95–6.23 (1 H, m) 6.97–7.14 (2 H, m), 7.40–7.58 (3 H, m), 7.81–8.01 (4 H, m) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 69.1, 114.9, 118.1, 122.5, 124.6, 128.9, 130.3, 132.7, 147.1, 152.7, 161.1 ppm. MS (ES$^+$): *m/z* = 239 [M + Na]$^+$. HRMS (ES$^+$): *m/z* calcd for [$C_{15}H_{14}N_2O$ + H]: 239.1179; found: 239.1182. IR (ATR): ν_{max} = 1496, 1579, 1598, 3023 cm^{-1}.

(16) **General Procedure for the Preparation of *o*-Claisen-Rearranged Phenols 9**
To a stirred solution of the allyl ether (1 mmol) in dry CH_2Cl_2 (10 mL) was added Et_2AlCl (2 equiv) at 0 °C under an atmosphere of dry nitrogen. The reaction mixture was stirred at r.t. for 15 h and then quenched by the careful addition of a sat. solution of Na/K tartrate tetrahydrate (10 mL). The organic layer was separated and the aqueous phase extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed (brine, 3 × 20 mL), then H_2O (3 × 20 mL), and dried over $MgSO_4$. The crude mixture was purified by column chromatography (40% CH_2Cl_2 in hexane) to give the products **9a**–**h**.
(*E*)-2-Allyl-4-(phenyldiazenyl)phenol (9a)
Yield 83%; crystalline; mp 91.7–93.0 °C (lit. 89–90 °C) was obtained by column chromatography (40% CH_2Cl_2 in hexane). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.52 (2 H, d, *J* = 6 Hz), 5.21 (1 H, t, *J* = 1 Hz), 5.26 (1 H, dd, *J* = 8, 1 Hz), 6.09 (1 H, ddt, *J* =16, 10, 6 Hz), 6.94 (1 H, dd, *J* = 9, 3 Hz, CH, ArH), 7.44–7.56 (3 H, m, CH, ArH), 7.76–7.82 (2 H, m, CH, ArH), 7.89 (2 H, dd, *J* = 8, 2 Hz, CH, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.1, 116.2, 117.1, 122.5, 123.5, 125.1, 129.1, 130.3, 135.7, 126.1, 147.1, 152.7, 156.9

ppm. MS (ES^+): *m/z* = 239 $[M + H]^+$. MS (ES^-): *m/z* = 237 $[M - H]^+$. HRMS (ES^-): *m/z* calcd for $[C_{15}H_{14}N_2O - H]$: 237.1025; found: 237.1033. IR (ATR): ν_{max} = 1339, 1444, 1465, 1502, 1592, 1737, 3068 cm^{-1}.

(17) **General Procedure for Trichloroacylation (10)**

To the stirred solution of **9** (1 equiv) and Et_3N (1.2 equiv) in dry Et_2O was added dropwise trichloroacetyl chloride (1.2 equiv) at 0 °C. After 3 h at this temperature the reaction mixture was quenched by the addition of H_2O (20 mL). The quenched reaction mixture was extracted with Et_2O (50 mL), and the organic layer was separated, washed [$NaHCO_3$; 3 × 20 mL of a sat. solution), brine (3 × 20 mL), and H_2O (3 × 20 mL)], dried ($MgSO_4$), and concentrated in vacuo to afford the crude products **10a**–**h**, which were of sufficient purity to be used in the next step.

(*E*)-2-Allyl-4-(phenyldiazenyl)phenyl 2,2,2-Trichloroacetate (10a)

Brownish oil; 81% yield. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.50 (2 H, dd, *J* = 6, 1 Hz), 5.15 (1 H, dq, *J* = 8, 1 Hz), 5.19 (1 H, m), 5.92–6.07 (1 H, m), 7.35 (1 H, dd, *J* = 7, 2 Hz), 7.51–7.55 (3 H, m, CH), 7.87–7.97 (4 H, m, CH, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.1, 117.3, 121.8, 122, 122.9, 125.4, 129.1, 131.3, 134.7, 132.9, 151.2, 150.2, 152.5, 160.2 ppm. IR (ATR): ν_{max} = 1351, 1459, 1487, 1541, 1584, 1401, 1799, 2984 cm^{-1}.

(18) **General Procedure for Benzannulation Reactions (11)**

The trichloroacetate (0.5 mmol, 1 equiv) was heated with the catalyst **12** (5 mol%) in diglyme (0.5 mL) at 162 °C for 3 h under an atmosphere of dry nitrogen. The reaction mixture was allowed to cool to r.t. and then purified directly by flash column chromatography (100% PE) to give the products **11a**–**g**.

(*E*)-1-(5-Chloronaphthalen-2-yl)-2-phenyldiazene (11a)

Yield 78%; orange crystals; mp 113–114 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.59 (4 H, m, CH, ArH), 7.66 (1 H, dd, *J* = 7, 1 Hz, CH, ArH), 7.89–8.04 (3 H, m, CH, ArH), 8.18 (1 H, dd, *J* = 9, 2 Hz, CH, ArH), 8.38 (1 H, d, *J* = 9 Hz, CH, ArH), 8.48 (1 H, d, *J* = 2 Hz, CH, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 118.6, 122.9, 125.7, 126.7, 127.2, 127.6, 128.5, 129.2, 131.2, 131.9, 132.1, 132.8, 150.6, 152.6 ppm. MS (ES^+): *m/z* = 267 $[M + H]^+$. HRMS (ES^+): *m/z* calcd for $[C_{16}H_{11}N_2Cl + H]$: 267.0684; found: 267.0674. Anal. Calcd (%) for $C_{16}H_{11}N_2Cl$: C, 72.0; H, 4.1; N, 10.5. Found: C, 71.8; H, 4.0; N, 10.3%. IR (ATR): ν_{max} = 1286, 1334, 1415, 1457, 1570, 3011 cm^{-1}.