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On the Illusive Nature of *o*-Formylazobenzenes: Exploiting the Nucleophilicity of the Azo Group for Cyclization to Indazole Derivatives

Maike V. Peters,[†] Ragnar S. Stoll,[†] Richard Goddard,[†] Gernot Buth,[‡] and Stefan Hecht*[,†]

Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr, Germany, and Forschungszentrum Karlsruhe GmbH, ANKA/ISS, Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany

hecht@mpi-muelheim.mpg.de

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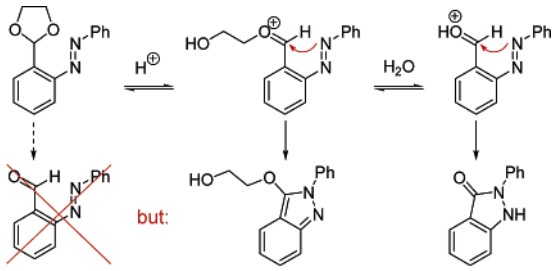

Facile rearrangement of azobenzenes is shown to occur in cases where the azo group is placed in the ortho position to carbonyl electrophiles to furnish the indazole skeleton. While this study demonstrates the illusive nature of *o*-formylazobenzenes, it offers potential for the synthesis of indazoles and related heterocycles.

Introduction

Photochromism allowing for the light-triggered, selective, and reversible transformation between two usually tautomeric or isomeric types of chromophores constitutes a key design principle to be harnessed for the design of future photoswitchable materials and devices.[1] Several photochromic families have been developed, and the chemical and physical differences between the respective switching states have been used to photomodulate properties from the molecular up to the macroscopic scale.[2] While the discovery of photochromism of azobenzenes dates back to 1937,[3] these photochromes continue to be among the most frequently explored mainly due to their ease of preparation and the significantly differing properties of the *E*- and *Z*-isomers.[4] We were aiming to incorporate azobenzene moieties directly into the framework of metalloporphyrins, and by exploiting the large structural reorganization accompanying the *E*−*Z*-photoisomerization we sought to photoswitch accessibility of the porphyrin metal center, thereby potentially enabling photomodulation of catalytic activity.[5]

The target *meso*-[2,6-bis(phenylazo)phenyl]-substituted metalloporphyrins **1** can, in principle, be synthesized from a preformed metalloporphyrin precursor or via acid-catalyzed condensation of pyrrole or dipyrromethanes with the respective aldehydes (Scheme 1).[6] While the postfunctionalization approach employing a versatile transition-metal-catalyzed cross-coupling/oxidation sequence[7] finally proved successful,[5] several important observations have been made during our attempt to prepare

[†] Max-Planck-Institut für Kohlenforschung.
[‡] Forschungszentrum Karlsruhe GmbH.

(1) (a) *Photochromism − Molecules and Systems*; Dürr, H., Bouas-Laurent, H., Eds.; Elsevier: Amsterdam, 2003. (b) *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, 2001. (c) *Organic Photochromic and Thermochromic Compounds*; Crano, J. C., Guglielmetti, R. J., Eds.; Kluwer Academic/Plenum Publisher: New York, 1999. (d) *Organic Photochromes;* El'tsov, A. V., Ed.; Consultants Bureau: New York, 1990. (e) Special Issue: Photochromism: Memories and Switches. Irie, M., Ed. *Chem. Rev.* **2000**, *100*, 1683−1890. (f) Willner, I.; Rubin, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 367−385.

(2) Hecht, S. *Small* **2005**, *1*, 26−29.

(3) Hartley, G. S. *Nature (London)* **1937**, *140*, 281.

(4) (a) Zollinger, H. *Azo and Diazo Chemistry: Aliphatic and Aromatic Compounds*; Interscience Publishers: New York, 1961. For reviews, consult: (b) Rau, H. In *Photochromism − Molecules and Systems;* Dürr, H., Bouas-Laurent, H., Eds.; Elsevier: Amsterdam, 2003; pp 165−192. (c) Fanghänel, D.; Timpe, G.; Orthman, V. In *Organic Photochromes*; El'tsov, A. V., Ed.; Consultants Bureau: New York, 1990; pp 105−177. (d) Griffiths, J. *Chem. Soc. Rev.* **1972**, 481−493.

(5) Peters, M. V.; Goddard, R.; Hecht, S. *J. Org. Chem.* **2006**, *71*, 7846−7849.

(6) For a review, consult: Lindsey, J. S. In *The Porphyrin Handbook*; Kadish, K., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 1999; Vol. 1, pp 45−118.

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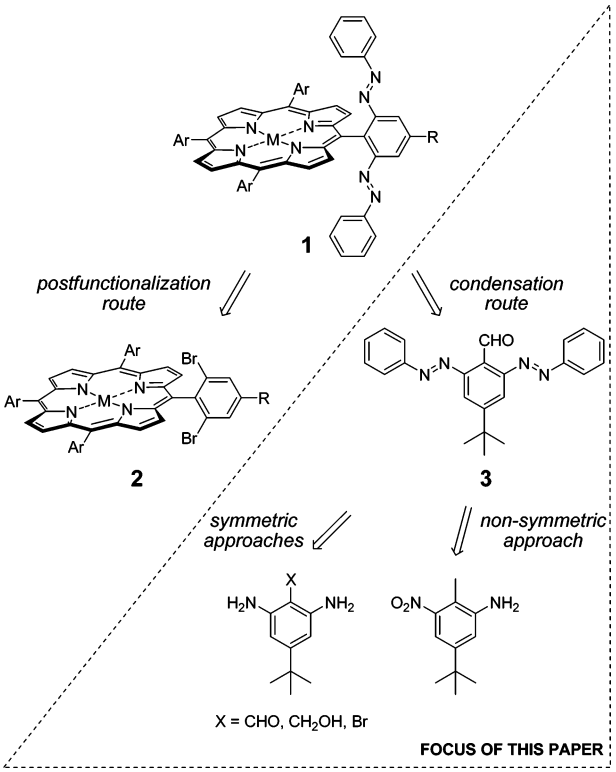
SCHEME 1. Motivation



bisazoaldehyde precursor **3**. Several synthetic routes involving symmetric and nonsymmetric approaches, in which the azobenzene moiety is either simultaneously or stepwise formed via condensation of aniline with nitrosobenzene derivatives, i.e., the so-called Mills reaction,[8] have been explored. In the course of these studies, we realized that *o*-arylazobenzaldehydes are not isolable compounds but rather undergo intramolecular cyclization due to the close proximity of the formyl electrophile and the nucleophilic azo group. Here, we present our synthetic results including the unambiguous characterization of the rearrangement products and propose a mechanism for this potentially practical synthesis of the indazole heterocyclic skeleton.

Results and Discussion

Symmetric Approaches. To establish the 2,6-bis(arylazo)-phenyl substitution pattern, 2,6-diaminobenzenes carrying a substituent in the 1-position that can be transformed into an aldehyde, e.g. alcohol, ester, methyl, or bromide, are needed. To ensure the necessary regiochemistry in the nitration to the dinitro precursors, we chose to introduce a 4-*tert*-butyl group, which sterically shields its ortho positions, i.e., 3- and 5-positions, thereby forcing the incoming nitro groups into the required 2- and 6-positions, i.e., ortho to the latent aldehyde. Several commercially available starting materials, i.e., **4**, **7**, and **11**, were employed (Scheme 2). Two-fold nitration using forcing conditions[9] was achieved in good yields to provide the 2,6-dinitro-derivatives **5**, **8**, and **12**. In particular, the conversion **4** → **5** is noteworthy since it occurs with concomitant chemoselective oxidation of the benzylic alcohol to the corresponding aldehyde and represents the by far most practical route to this common porphyrin precursor.[10] While the nitro functionalities in **5** could unfortunately not be reduced without concurrent reduction of the aldehyde, **8** and **12** were successfully transformed into the corresponding phenylenediamines **9** and **13**. Please note that catalytic hydrogenation over Pd/C could not be employed for the reduction of **8** due to debromination. Protection of the amine functionalities provided **10** in moderate yield; however, formylation by a metalation/DMF-trapping sequence failed. In the final symmetrical attempt, 2-fold Mills coupling[8] of nitrosobenzene to **14**, prepared by reduction of **13**, was not successful. A thorough search of the literature[11] revealed that similar problems had been encountered by Ruggli and co-workers[11b] when trying to perform 2-fold Mills couplings on phenylenediamine.[12] We therefore decided to synthesize the desired *m*-bis(phenylazo)-benzene derivatives by sequential formation of the azo groups.

Nonsymmetric Approach. Stepwise introduction of the azo moieties requires the protection of one aniline terminus, most conveniently as the oxidized nitro group, and involves initial Mills coupling to the nitroaniline followed by reduction of the nitro group and subsequent second Mills coupling.[11] To avoid potential chemoselectivity problems during nitro group reduction, we chose 4-*tert*-butyltoluene **16** as commercially available and inexpensive starting material (Scheme 3). Two-fold nitration gave **17**, which could be reduced to provide **18** in almost quantitative yield. This highly selective and high-yielding monoreduction process could be achieved by using ammonium sulfide in refluxing ethanol and represents the key step in the synthesis.[13,14] Mills reaction afforded **19**, which subsequently was reduced to azoaniline **20** and subjected to another Mills reaction to yield bis(phenylazo) derivative **21**.

Depending on the relative orientation of the trans-configured azo bonds, meta-linked bisazobenzene derivative **21** can adopt three stable conformations, namely anti-anti, syn-anti, or syn-syn conformations (Figure 1a). While H NMR spectroscopy does not allow a distinction of these three conformations, presumably due to a rapid exchange between these energetically rather similar structures, X-ray crystallographic analysis[9] on several crystals showed that **21** adopts the anti-anti conformation in the solid state (Figure 1b). Interestingly, this finding is in contrast to the recently reported example of alternating pyridinedicarboxamide-bis(phenylazo)benzene foldamers,[12] in which the *m*-bisazobenzene segments show a preference for the syn-syn conformation.

(7) (a) Lim, Y.-K.; Lee, K.-S.; Cho, C.-G. *Org. Lett.* **2003**, *5*, 979−982. (b) Lim, Y.-K.; Choi, S.; Park, K. B.; Cho, C.-G. *J. Org. Chem.* **2004**, *69*, 2603−2606.

(8) It should be noted that the formation of azobenzenes from condensation of nitrosobenzenes with anilines in acetic acid, frequently referred to as the Mills reaction: (a) Mills, C. *J. Chem. Soc.* **1895**, *67*, 925−933, was first described by Baeyer: (b) Baeyer, A. *Chem. Ber.* **1874**, *7*, 1638−1640.

(9) See the Supporting Information.

(10) Rose, E.; Kossanyi, A.; Quelquejeu, M.; Soleilhavoup, M.; Duwavran, F.; Bernard, N.; Lecas, A. *J. Am. Chem. Soc.* **1996**, 118, 1567−1568.

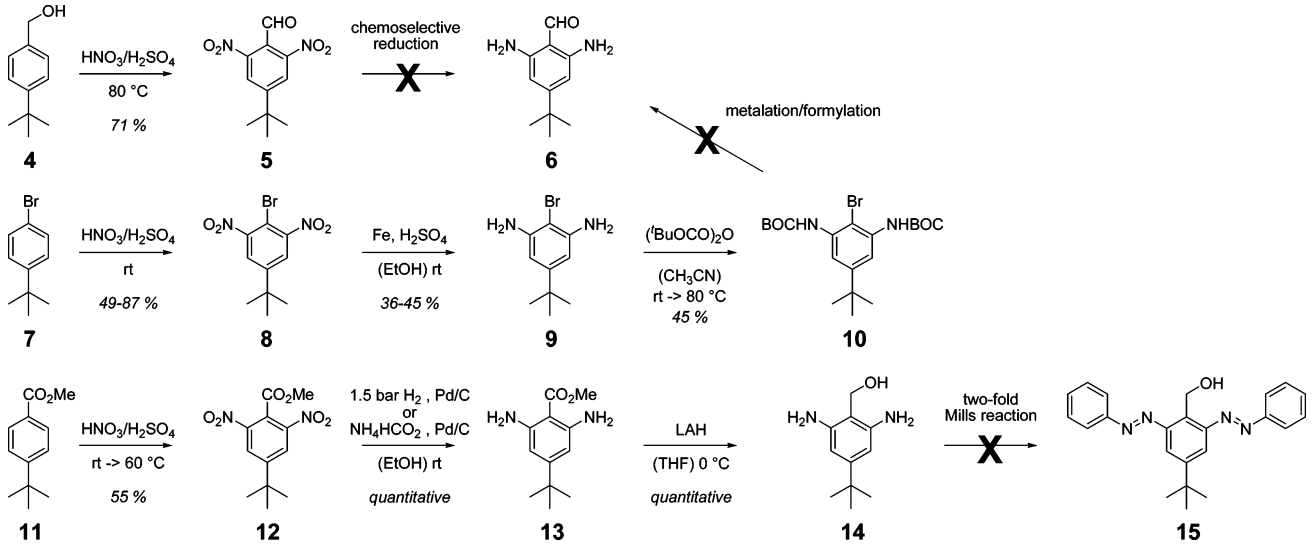
(11) The synthesis of differently connected oligo(azobenzene)s has been been pioneered by Ruggli and co-workers, who exploited iterative Mills coupling and nitro-reduction sequences. For *o*-bis(phenylazo)benzenes, see: (a) Ruggli, P.; Rohner, J. *Helv. Chim. Acta* **1942**, *25*, 1533−1542. For *m*-bis(phenylazo)benzenes, see: (b) Ruggli, P.; Wust, W. *Helv. Chim. Acta* **1945**, *28*, 781−791. For *p*-oligo(phenylazo)benzenes, see: (c) Ruggli, P.; Bartusch, G. *Helv. Chim. Acta* **1944**, *27*, 1371−1384. (d) Ruggli, P.; Iselin, E. *Helv. Chim. Acta* **1947**, *30*, 739−742.

(12) Similar synthetic problems have recently been encountered in the construction of oligomers containing *m*-bis(phenylazo)benzenes: Tie, C.; Gallucci, J. C.; Parquette, J. R. *J. Am. Chem. Soc.* **2006**, *128*, 1162−1171.

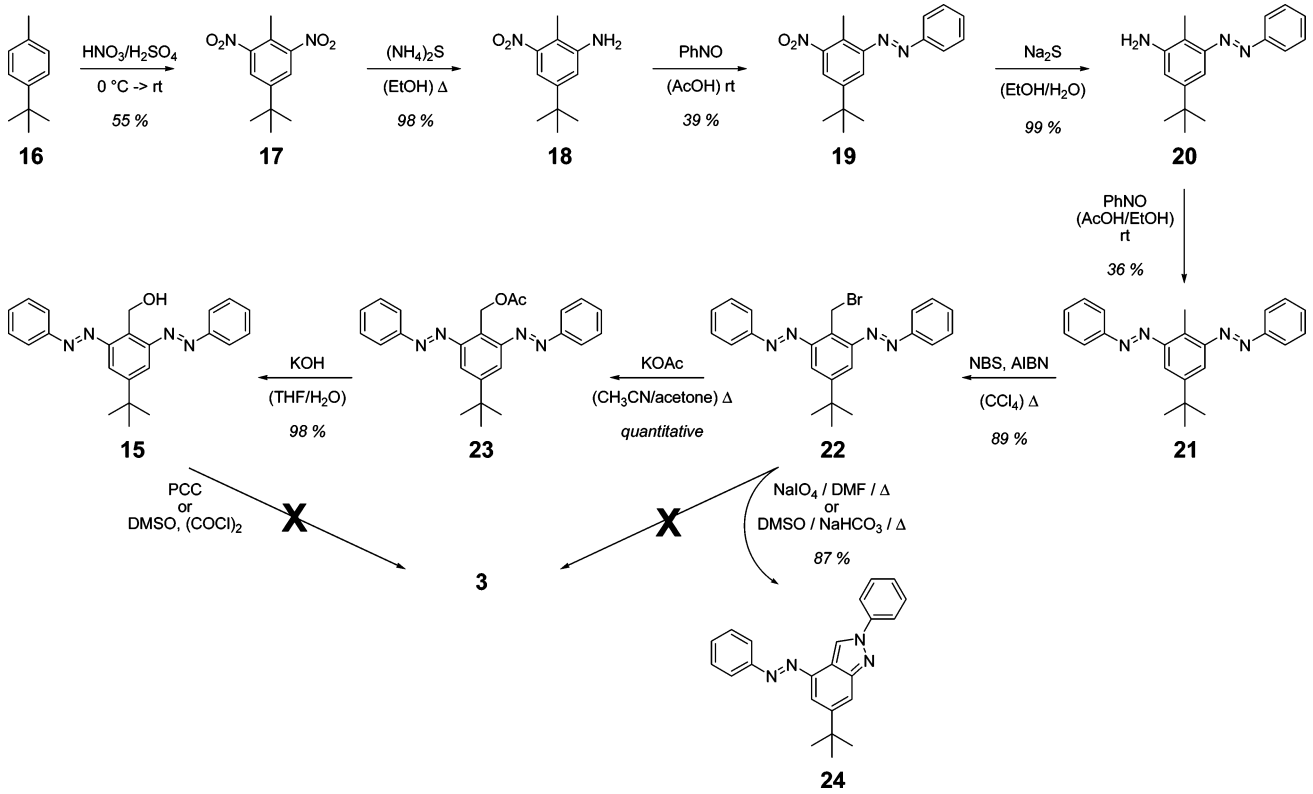
(13) Chemoselective reduction to nitroaniline: (a) Finger, G. C.; Reed, F. H. *J. Am. Chem. Soc.* **1944**, *66*, 1972−1974 using the ammonium sulfide method developed by: (b) Murray, M. J.; Waters, D. E. *J. Am. Chem. Soc.* **1938**, *60,* 2818−2819.

(14) A potential route via nitration of 2-amino-4-*tert*-butyltoluene failed in our hands and gave complex product mixtures, contradictory to literature reports: Rosevear, J.; Wilshire, J. F. K. *Aust. J. Chem.* **1985**, *38*, 723−733.

SCHEME 2. Symmetric Approaches



SCHEME 3. Nonsymmetric Approach



To prepare the desired porphyrin precursor **3**, the benzylic methyl group had to be oxidized to the corresponding benzaldehyde (Scheme 3). Radical bromination provided benzyl bromide **22**, which was converted to the benzyl alcohol **15** via the acetate **23**. Several oxidation procedures including Kornblum oxidation of **22** as well as PCC-mediated and Swern oxidations of **15** were employed; however, no aldehyde product could be obtained. Instead, the main product of the Kornblum oxidation of **22**, also present in the oxidation of **15**, was isolated, and its NMR spectroscopic data indicated the loss of symmetry while UV/vis spectroscopy showed a bathochromic shift of the absorption maximum indicative of an electronic change and/or extension of the chromophore.[9] Finally, the nature of the rearrangement product **24** was unambiguously revealed by a single-crystal X-ray structural analysis[9] (Figure 2).

The unexpected presence of the indazole skeleton shows an involvement of the azo group in the observed rearrangement. Clearly, a reaction of the benzylic substituent with the distant azo nitrogen atom is occurring followed by rearomatization (vide infra). Interestingly, in **24** the reacting azo group is locked in a syn conformation during the course of the reaction, while the remaining azo fragment adopts a syn conformation as well. Since all oxidative attempts to prepare **3** have failed in our hands yet not due to oxidation of the azo group, we were eager to find out if *o*-formylazobenzenes, placing both azo and aldehyde functionalities into close proximity, represent isolable com-

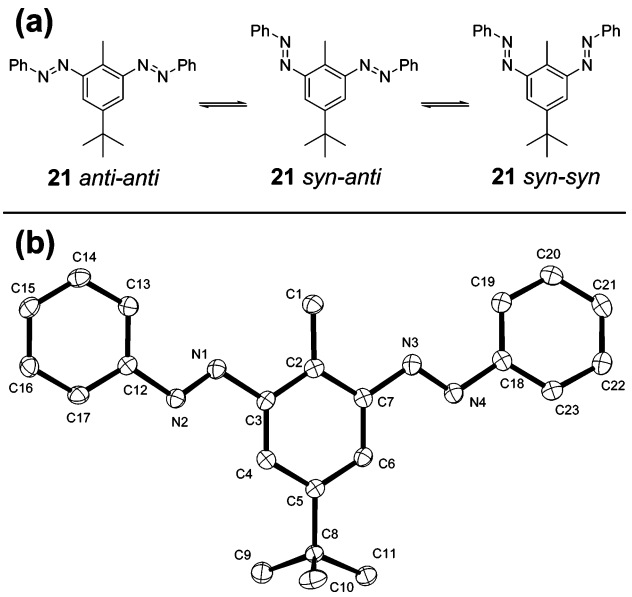


FIGURE 1. Conformational preference of *m*-bis(phenylazo)benzene derivative **21**. (a) Potential minimum conformations. (b) Single-crystal X-ray structural analysis of **21**, showing that the molecule adopts the anti-anti conformation.

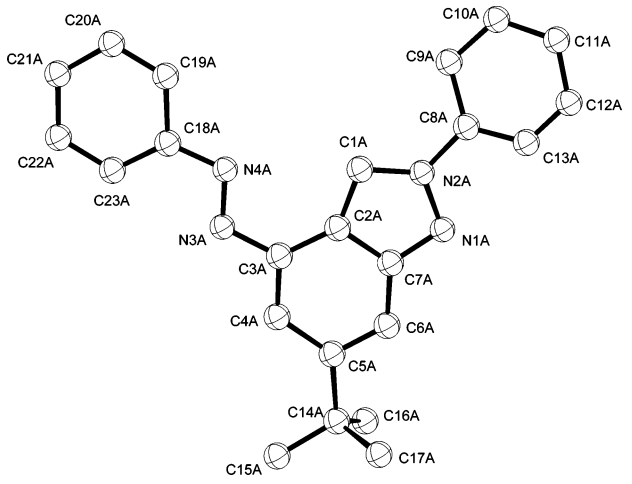
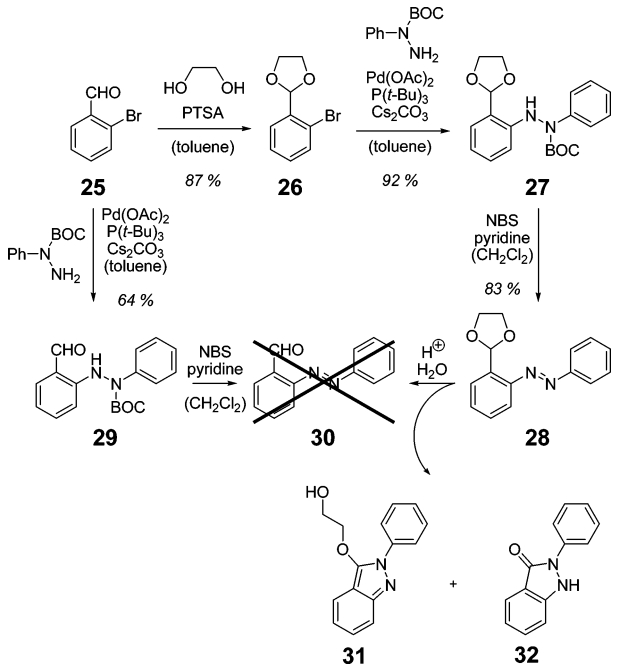


FIGURE 2. Single-crystal X-ray structural analysis of rearrangement product **24**.

pounds or if they undergo such a rearrangement process in general. For the purpose of simplicity, further studies were carried out on a minimalistic model system.

Rearrangement Model Studies. Initially, synthesis of **30** was attempted via NBS-mediated oxidation of **29**, which was readily obtained by N-arylation of **25** (Scheme 4).[7a] However, addition of NBS to **29** led to rapid disappearance of the typical orange color associated with the azo dye. While this finding provided further support that the azo group actively participates in the observed transformation, a more convenient investigation of the rearrangement process was achieved by monitoring the acid-catalyzed hydrolysis of acetal **28**. Azo dye **28** was prepared from acetal **26** by N-arylation followed by NBS-mediated oxidation. The successful oxidation step to furnish the azo chromophore in the presence of the protected aldehyde, i.e., **27** → **28**, furthermore showed that previously the aldehyde moiety was involved in the attempted rearrangement **29** → **30**.

SCHEME 4. Synthesis and Reactivity of Model Compounds



When **28** was treated with dilute acid at room temperature to unmask the aldehyde functionality in the presence of the preinstalled azobenzene moiety, decoloration within few minutes was observed. In analogy to the previous experiments, compound **30** could not be detected. Instead, two colorless products were formed and isolated. Structural identification using NMR spectroscopy, mass spectrometry, and single-crystal X-ray structure analysis (in the case of **32**, see Figure 3) provided clear evidence for the formation of indazoles **31** and **32**.[9] Both compounds belong to the indazole heterocyclic family as already observed in the case of the rearrangement **22** → **24** (vide supra).

Figure 3 shows the structure of **32** obtained by single-crystal X-ray structural determination. The analysis reveals that in the solid the H atom attached to N2 is bent 38° out of the mean plane of the indazolone moiety in order to engage in a favorable H-bonding N−H···O intermolecular interaction with a neighboring molecule in the crystal [N···O distance 2.808(5) Å].[9] A similar pyramidalization of the N atom has been observed in the crystal structures of 2-*N*-acetyl-3-indazolinone[15] and 2-*N*-benzylindazolone.[16]

In view of the observed acid-induced rearrangement of **28** giving rise to formation of **31** and **32**, we propose the following mechanism for this transformation (Scheme 5). Initial protonation and ring opening of the acetal generates the first electrophile, which can be intercepted by intramolecular nucleophilic attack of the azo group to generate product **31** after final deprotonation/rearomatization. Hydrolysis competes with cyclization and generates the protonated aldehyde as another potent electrophile, which can undergo ring closure to yield **32** after deprotonation and tautomerization. It should be pointed out that the employed acidic conditions are needed to initiate the reaction sequence by transforming the acetal to an electrophilic moiety; however, cyclization to the indazole skeleton does not necessarily involve acid catalysis. If an electrophilic group is

(15) Smith, D.; L.; Barrett, E. K. *Acta Crystallogr., Sect B: Struct. Crystallogr. Cryst. Chem.* **1969**, *25*, 2355−2361.

(16) Kurth, M. J.; Olmstead, M. M.; Haddadin, M. J. *J. Org. Chem.* **2005**, *70*, 1060−1062.

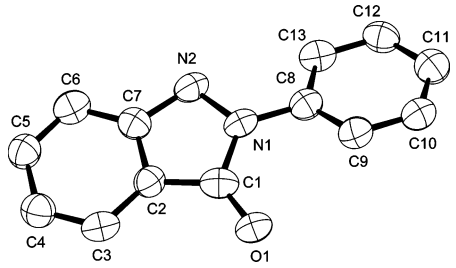
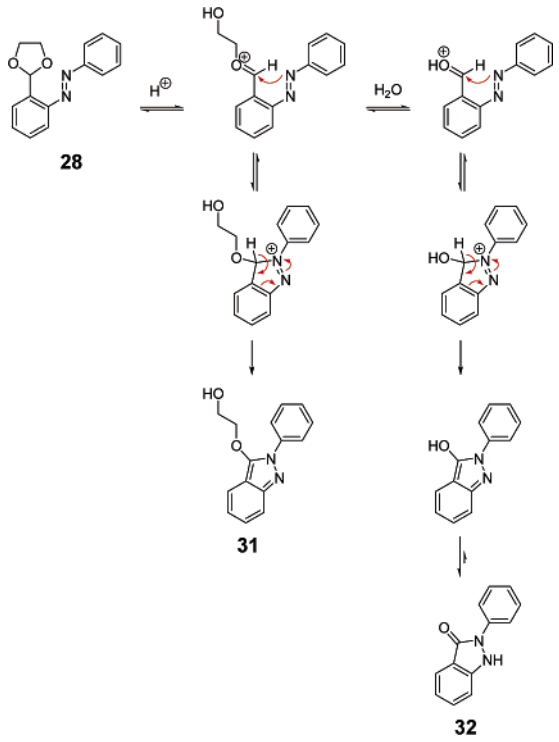


FIGURE 3. Single-crystal X-ray structural analysis of rearrangement product **32**.

SCHEME 5. Proposed Rearrangement Mechanism



generated in the ortho position to the azo moiety, cyclization occurs as indicated by the observed reactivity of **15**, **22**, and **29** under nonacidic conditions.

In control experiments, no equilibration between **31** and **32** under the same acidic conditions was observed; i.e., **31** was not converted to **32**, demonstrating that the final deprotonation step to reestablish aromaticity in the system is essentially irreversible (please note that subsequent tautomerization is not possible in the case of **31**). Therefore, the product distribution **31/32** = 78:17 reflects the competition between intramolecular cyclization and intermolecular hydrolysis. Both ring closures belong to the class of highly favored 5-*exo-trig* cyclization processes,[17] in which the in situ generated, activated carbonyl-based electrophiles are attacked by a considerably nucleophilic, distant N-atom of the azo group.

The basicity of the azo group is well documented in the literature,[4] and the electron-donating capability of the azo group has recently been utilized to achieve photoswitchable azo-heteroatom interactions.[18] However, the azo group's nucleophilicity toward carbon electrophiles as a means to construct nitrogen-containing heterocycles has been poorly explored, except for the early work by Freundler.[19,20] In view of the large variety of azobenzene precursors, which are readily available from different precursors including aniline, nitrobenzene, and halobenzene derivatives, this transformation has considerable potential for indazole heterocycle synthesis. Furthermore, the observed facile rearrangement implies that for a few of the many reported azo dyes carrying *o*-aldehyde substituents reassignments of the respective chemical structures should be seriously considered.[21,22]

(17) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734−736.

Experimental Section

Experimental details of the rearrangement of model compound **28** are given below. For a complete compilation of general methods, crystallographic details, synthetic procedures, and characterization data, see the Supporting Information.

Synthesis of Model Compound 28. *N*-*tert*-Butoxycarbonyl-*N*′-[(1,3-dioxolan-2-yl)phenyl]-*N*-phenylhydrazine 27. In a sealed tube, 0.63 mL (5.0 mmol) of **26**,[23] 1.183 g (5.7 mmol) of *N*-*tert*-butoxycarbonyl-*N*-phenylhydrazine,[24] 58 mg (0.25 mmol) of palladium(II) acetate, 0.062 g (0.3 mmol) of tri-*tert*-butylphosphine, 2.46 g (7.5 mmol) of Cs_2CO_3, and 30 mL of toluene were mixed in a nitrogen atmosphere. The reaction mixture was stirred for 30 min at room temperature and then heated at 110 °C for 14 h. The solid was filtered through Celite, the solvent was evaporated, and the residue was recrystallized from hexane to yield 1.64 g (92% yield) of the product as brown crystals. R_f (Hex/EA, 3/1) = 0.4. ^{1}H NMR (CD_3CN, 400 MHz): δ (ppm) = 7.65 (s, 1H, Ar-*H*), 7.57 (d, 1H, ^3J = 7.7 Hz, Ar-*H*), 7.33 (m, 3H, Ar-*H*), 7.22 (t, 1H, ^3J = 7.8 Hz, ^4J = 1.4 Hz, Ar-*H*), 7.13 (tt, 1H, ^3J = 7.4 Hz, ^4J =

(18) The intramolecular coordination of the *o*-phenylazo group to various heteroatoms has been exploited. For silicon, see: (a) Kano, N.; Komatsu, F.; Kawashima, T. *J. Am. Chem. Soc.* **2001**, *123*, 10778-10779. (b) Kano, N.; Yamamura, M.; Komatsu, F.; Kawashima, T. *J. Organomet. Chem.* **2003**, *686*, 192−197. (c) Kano, N.; Yamamura, M.; Kawashima, T. *J. Am. Chem. Soc.* **2004**, *126*, 6250−6251. (d) Kano, N.; Komatsu, F.; Yamamura, M.; Kawashima, T. *J. Am. Chem. Soc.* **2006**, *128*, 7097−7109. For boron, see: (e) Kano, N.; Yoshino, J.; Kawashima, T. *Org. Lett.* **2005**, *7*, 3909−3911. For phosphorous, see: (f) Yamamura, M.; Kano, N.; Kawashima, T. *J. Am. Chem. Soc.* **2005**, *127*, 11954−11955.

(19) A thorough literature survey reveals that some initial evidence for this type of rearrangement involving azobenzene precursors carrying either *o*-aldehyde or *o*-acetal groups dates back to work by Freundler: (a) Freundler, M. P. *Bull. Soc. Chim. Fr.* **1904**, *31*, 862−867. (b) Freundler, M. P. *Bull. Soc. Chim. Fr.* **1904**, *31*, 868−875.

(20) The formation of 2*H*-indazolone derivatives from azobenzene precursors has been reported in a few cases with the following ortho substituents. For hydroxymethyl groups, see: (a) Freundler, M. P. *Bull. Soc. Chim. Fr.* **1903**, *29*, 742−747. For ketones, see: (b) Alberti, A.; Bedogni, N.; Benaglia, M.; Leardini, R.; Nanni, D.; Pedulli, G. F.; Tundo, A.; Zanardi, G. *J. Org. Chem.* **1992**, *57*, 607−613. For carboxylic acids, see: (c) Freundler, M. P. *Bull. Soc. Chim. Fr.* **1911**, *9*, 735−739.

(21) A search of the Beilstein database reveals more than 23000 entries of different azobenzene derivatives. In the few cases reporting *o*-(arylazo)arylaldehydes, an alternative structural assignment to the respective 2*H*-indazolone derivatives seems plausible: (a) Karamé, I.; Jahjah, M.; Messaoudi, A.; Tommasino, M. L.; Lemaire, M. *Tetrahedron: Asymmetry* **2004**, *15*, 1569−1581. (b) Radbakrishnan, T.; Kolawole, G. A.; Revaprasadu, N.; Nair, P. S.; Sreekala, N. B. *Synth. React. Inorg. Met.-Org. Chem.* **2002**, *32*, 1153−1175. (c) Saleh, A. A.; Aly, F. M.; El-Baradie, K.; El-Dken, A. A. *Egypt. J. Chem.* **1990**, *33*, 255−266. (d) Ifrim, S. *Bulet. Inst. Polit. Iasi* **1973**, *19*, 139−15.

(22) The oldest literature precedent of controversial assignment of an *o*-(arylazo)arylaldehyde is related to the so-called "Azoopiansäure", the product of reducing 2-formyl-5,6-dimethoxy-3-nitrobenzoic acid with zinc under acidic conditions: (a) Prinz, O. *J. Prakt. Chem.* **1881**, *24*, 353−374. (b) Liebermann, C. *Chem. Ber.* **1886**, *19*, 351−354. (c) Grüne, H. *Chem. Ber.* **1886**, *19*, 2299−2305. (d) Claus, A.; Predari, F. *J. Prakt. Chem.* **1897**, *55*, 171−185.

(23) Franz, J. A.; Barrows, R. D.; Camaioni, D. M. *J. Am. Chem. Soc.* **1984**, *106*, 3964−3967.

(24) Wolters, M.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 3803−3805.

1.1 Hz, Ar-*H*), 6.83 (m, 2H, Ar-*H*), 5.79 (s, 1H, C*H*), 4.07 (m, 4H, CH_2CH_2), 1.38 (s, 9H, t-Bu-*H*). ^{13}C NMR (CD_3CN, 100.6 MHz): δ (ppm) = 154.74, 147.54, 143.97, 130.95, 129.31, 128.62, 125.50, 123.34, 122.30, 120.32, 112.67, 103.76, 82.46, 65.76, 28.3. MS (EI, 110 °C): m/z = 356 ([M]$^+$), 300, 255, 93. **2-(2-Phenylazo)-phenyl-1,3-dioxolane 28.** In a nitrogen atmosphere, 47 mg (0.133 mmol) of **27** was dissolved in 2.5 mL dry dichloromethane. Then, a solution of 0.013 mL of pyridine and 28 mg of NBS in 2.5 mL of dichloromethane was added. The color immediately changed to orange. The solution was stirred at room temperature for another 2 h, and the solvent was evaporated. After purification by column chromatography (Hex/EA, 8/1), 43 mg (83%) of an orange oil was isolated. R_f (Hex/EA, 5/1) = 0.3. ^{1}H NMR (CD_3CN, 400 MHz): δ (ppm) = 7.69 (m, 2H, Ar-*H*), 7.56 (dd, 1H, ^3J = 7.6 Hz, ^4J = 1.6 Hz, *Ar*-H), 7.43 (dd, 1H, ^3J = 7.8 Hz, ^4J = 1.4 Hz, Ar-*H*), 7.34 (m, 5H, Ar-*H*), 6.55 (s, 1H, C*H*), 3.85 (m, 4H, CH_2CH_2). ^{13}C NMR (CD_3CN, 100.6 MHz): δ (ppm)= 153.7, 151.1, 137.5, 132.4, 132.2, 130.75, 130.3, 127.8, 123.7, 115.7, 100.0, 66.3. MS (EI, 254 °C) m/z = 254 ([M]$^+$), 181, 105. HRMS (ESI pos): m/z = 277.094773 (calcd 277.094750 for $C_{15}H_{14}N_2O_2Na$). GC: 98.8% peak area.

Hydrolysis of Model Compound 28. In a one-necked flask, 123 mg (0.49 mmol) of **28** was dissolved in 2 mL of acetone, and 0.98 mL of 1 M HCl were added. The solution was stirred at room temperature for 75 min during which time the orange color completely disappeared. The mixture was diluted with ethyl acetate, washed with saturated aqueous $NaHCO_3$ solution, and dried over $MgSO_4$, and the solvent was evaporated. Both products were separated by preparative HPLC (MeOH/H_2O, 55/45) prior to characterization. **2-Phenyl-1,2-dihydroindazol-3-one 31.**[25] 60% isolated yield. R_f (Hex/EA, 1/1) = 0.38. ^{1}H NMR (CD_3CN, 400 MHz): δ (ppm) = 7.91 (m, 2H, Ar-*H*), 7.78 (dt, 1H, ^3J = 7.9 Hz, ^4J = 1.3 Hz, Ar-*H*), 7.61 (t, 1H, ^3J = 7.2 Hz, ^4J = 1.2 Hz, Ar-*H*), 7.49 (m, 2H, Ar-*H*), 7.37 (dt, 1H, ^3J = 8.2 Hz, ^4J = 0.8 Hz, Ar-*H*), 7.25 (m, 2H, Ar-*H*). ^{13}C NMR (CD_3CN, 400 MHz): δ (ppm) =161.9, 148.1, 138.9, 133.5, 130.0, 126.0, 124.4, 123.57, 120.0, 113.8. MS (EI, 130 °C): m/z = 210 ([M]$^+$), 181, 104, 77. IR (KBr): $\tilde{\nu}$ (cm^{-1}) = 676 (arom, m), 747 (arom, s), 1360 (s, C=C), 1501 (s, C=C), 1654 (s, C=O), 3111 (NH, m). HRMS: m/z = 233.068210 (calcd 233.068530 for $C_{13}H_{10}N_2O_1Na$). **2-Phenyl-3-(2′-hydroxyeth-1′-yl)-2H-indazole 32** (14% isolated yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) = 7.78 (d, 2H, ^3J = 7.5 Hz, Ar-*H*), 7.63 (d, 1H, ^3J = 8.5 Hz, Ar-*H*), 7.57 (d, 1H, ^3J = 8.9 Hz, Ar-*H*), 7.45 (m, 2H, Ar-*H*), 7.37 (t, 1H, ^3J = 7.4 Hz, Ar-*H*), 7.23 (t, 1H, ^3J = 6.7 Hz, Ar-*H*), 6.95 (t, 1H, ^3J = 6.7 Hz, Ar-*H*), 4.50 (t, 2H, ^3J = 4.3 Hz, CH_2), 3.88 (t, 2H, ^3J = 4.4 Hz, CH_2). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ (ppm) = 147.8, 145.6, 138.4, 129.1, 128.1, 127.2, 124.1, 120.7, 119.3, 117.9, 108.5, 77.3, 77.0, 76.7, 75.6, 61.3. MS (EI): m/z = 254 ([M]$^+$), 210, 181, 104, 77. HRMS: m/z = 277.094841 (calcd 277.094749 for $C_{15}H_{14}N_2O_2Na$).

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Supporting Information Available: Experimental procedures including general methods, crystallographic details, syntheses, characterization data, and copies of ^{1}H NMR and ^{13}C NMR spectra. Crystallographic information files (CIF) for compounds **21**, **24**, and **32**. This material is available free of charge via the Internet at http://pubs.acs.org.

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