Formation of cyclopropylazoarenes in the azo coupling reactions of the cyclopropanediazonium ion with active aromatic compounds

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10.1070/MC2002v012n03ABEH001595

The decomposition of *N*-cyclopropyl-*N*-nitrosourea with K_2CO_3 generates a cyclopropyldiazonium intermediate, which is trapped *in situ* with 1- and 2-naphthols, 2,7-dihydroxynaphthalene or 8-hydroxyquinoline to afford azo coupling products.

For aromatic diazo compounds, an azo coupling reaction is the most typical chemical transformation occurring with the retention of nitrogen atoms.[1,2] Aliphatic diazonium ions, which were postulated as intermediates in the diazotization of primary amines and the protonation of diazo compounds, usually cannot be trapped by an azo coupling reaction; however, they undergo rapid nitrogen elimination to give carbocation intermediates.[2,3] Nevertheless, it has been found that in some alkanediazonium ions an azo coupling reaction successfully competes with nitrogen elimination. The reported examples involve cyclopropanediazonium ions and bridgehead diazonium ions, in which a loss of nitrogen would lead to a very unstable carbocation.[4] For example, the cyclopropanediazonium ion generated from *N*-cyclopropyl-*N*-nitrosourea **1** gave azo coupling products (cyclopropyltriazenes) with dimethylamine and ethylamine.[5] Azo coupling has been definitely established in the reaction of **1** with lithium azide by the ^{15}N labeling of the α-nitrogen atom; the contribution of a pentazene to the coupling pathway was ~40%.[6] Previously,[7] we found that the alkaline decomposition of nitrosourea **1** in the presence of 3-cyano- or 3-methoxycarbonylspiro[2-pyrazoline-5,1′-cyclopropane] gave rise to corresponding 3-(cyclopropylazo)-1-pyrazolines, the formation of which also involves the generation of the cyclopropanediazonium ion. The reaction of a more complicated tricyclo[2.2.1.0^{2,6}]-heptane-1-diazonium ion (generated from the corresponding *N*-nitrosocarbamate) with 1- and 2-naphthols, which resulted in the formation of 'classic' azo coupling products was reported.[8]

In this study, we trapped the unsubstituted cyclopropanediazonium ion in azo coupling reactions with several active aromatic compounds, predominantly naphthalene derivatives, which are typical substrates for analogous reactions with aromatic diazo compounds. Cyclopropanediazonium intermediates were generated at 0–10 °C by the interaction of compound **1** with K_2CO_3 in the presence of an appropriate aromatic substrate (the molar ratio between reactants was about 1.2:2.5:1) and CH_2Cl_2 as a solvent. In order to accelerate the decomposition of **1**, it is necessary to use moist K_2CO_3 (the reaction time was 1–1.5 h).

The azo coupling reaction easily proceeds with 2-naphthol to form 1-(cyclopropylazo)-2-naphthol **2**† in 90% isolated yield. The structure of this compound was found from the ^1H NMR spectrum, which shows two doublets (*J* 8.8 Hz) for *ortho* protons in a substituted ring and a signal system typical of an unsubstituted naphthalene ring. The attribution of signals due to CH groups in the ^{13}C NMR spectrum was made using the {C,H}-correlation. Azo coupling at the 1-position of 2-naphthol is consistent with analogous reactions of other diazonium intermediates.[1,8,9]

The reaction of the cyclopropyldiazonium ion generated *in situ* proceeds with 1-naphthol in a more complicated manner. When nitrosourea **1** and 1-naphthol were taken in a ratio of 1.2:1, a considerable amount of bisadduct, 2,4-di(cyclopropylazo)-1-naphthol **5**, was obtained together with isomeric 2- and 4-(cyclopropylazo)-1-naphthols **3** and **4**. The molar ratio between the unreacted naphthol and azo compounds **3**–**5** was 1:1:1.9:1.1, respectively (Scheme 1). When nitrosourea **1** and 1-naphthol were taken in a ratio of about 2.2:1, bis-azo derivative **5** was the main reaction product formed in 77% yield. At the same time, among the remainder of monoadducts, compound **3** was the main isomer (ratio **3**:**4** ≈ 6:1); this is evidence for its lower reactivity in the repeated azo coupling step in comparison with isomer **4**. Bis-azo adduct **5** was isolated as red-orange crystals from a hexane solution; compounds **3**‡ and **4** were isolated by TLC (SiO_2, benzene–diethyl ether, 5:1). The structures of the compounds were confirmed by ^1H and ^{13}C NMR spectroscopy and mass spectrometry.† It follows from the ^1H NMR spectra of compounds **2**–**5** that a proton of the *peri*-position to the cyclopropylazo group is downfield shifted with respect to the corresponding proton at the *ortho*-position (Δδ 0.9–1.2 ppm).

† For **2**: mp 40–41 °C (hexane, –20 °C), ^1H NMR (300 MHz, $CDCl_3$) δ: 13.5 (s, OH), 8.72 (br. d, H-8, *J* 8.1 Hz), 7.78 (d, H-4, *J* 8.8 Hz), 7.72 (br. d, H-5, *J* 8.3 Hz), 7.56 (ddd, H-7, *J* 8.1 Hz, *J* 6.6 Hz, *J* 1.9 Hz), 7.38 (ddd, H-6, *J* 8.3 Hz, *J* 6.6 Hz, *J* 1.9 Hz), 7.11 (d, H-3, *J* 8.8 Hz), 3.88 (tt, CH, *J* 7.4 Hz, *J* 3.6 Hz), 1.48 and 1.32 (2m, CH_2CH_2). ^{13}C NMR (50.32 MHz, $CDCl_3$) δ: 152.4 (C-2), 133.7 (C-4), 132.5, 128.2 and 128.1 (C-1, C-4a, C-8a), 128.0 (C-5), 127.6 (C-7), 124.1 (C-6), 121.6 (C-8), 120.0 (C-3), 48.1 (CH), 10.9 (CH_2CH_2). MS, *m*/*z*: 212 (100) $[M]^+$, 184 (56), 169 (32), 156 (40), 143 (18), 129 (30), 115 (39) *et al*.

For **3**:‡ (TLC, SiO_2, benzene–diethyl ether, 5:1, R_f 0.7). ^1H NMR (300 MHz, $CDCl_3$) δ: 13.4 (br. s, OH), 8.36 (br. dd, H-8, *J* 8.1 Hz, *J* 1.6 Hz), 7.72 (br. dd, H-5, *J* 8.0 Hz, *J* 1.6 Hz), 7.70 (d, H-3, *J* 8.5 Hz), 7.55 and 7.48 (2ddd, H-6, H-7, *J* 8.0 Hz, *J* 6.9 Hz, *J* 1.6 Hz), 7.34 (br. d, H-4, *J* 8.5 Hz), 3.73 (tt, 2CH, *J* 7.3 Hz, *J* 3.3 Hz), 1.50 and 1.31 (2m, CH_2CH_2).

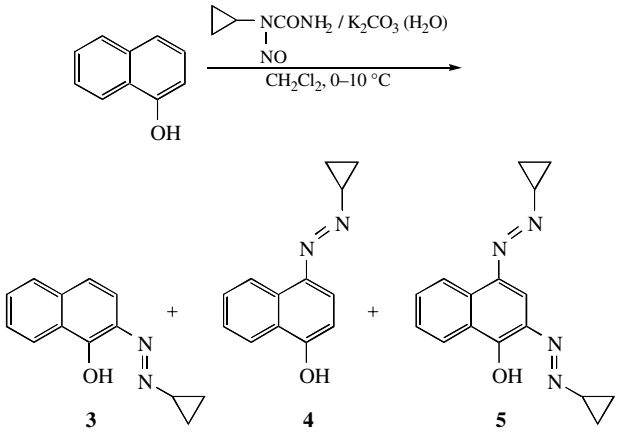
For **4**: mp 134–136 °C (TLC, SiO_2, benzene–diethyl ether, 5:1, R_f 0.60). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.76 (br. d, H-5, *J* 8.9 Hz), 8.22 (br. d, H-8, *J* 8.8 Hz), 7.63 (ddd, H-6, *J* 8.3 Hz, *J* 6.8 Hz, *J* 1.6 Hz), 7.54 (ddd, H-7, *J* 8.3 Hz, *J* 6.8 Hz, *J* 1.6 Hz), 7.38 (br. d, H-3, *J* 8.5 Hz), 6.73 (d, H-2, *J* 8.5 Hz), 6.5 (br. s, OH), 3.89 (tt, CH, *J* 7.2 Hz, *J* 3.7 Hz), 1.56 and 1.28 (2m, CH_2CH_2). ^{13}C NMR (50.32 MHz, CD_3OD) δ: 157.0 (C-1), 141.4 (C-4), 132.9 (C-4a), 127.8 (C-6), 126.0 (C-7 and C-8a), 123.6 (C-5) 123.3 (C-8), 114.2 (C-3), 108.4 (C-2), 51.4 (CH), 9.7 (CH_2CH_2). MS, *m*/*z* 212 (85) $[M]^+$, 184 (32), 157 (32), 144 (30), 143 (38), 115 (100) *et al*.

For **5**: mp 107–109 °C (hexane). ^1H NMR (300 MHz, $CDCl_3$) δ: 13.5 (s, OH), 8.72 (br. d, H-5, *J* 8.2 Hz), 8.40 (br. d, H-8, *J* 8.2 Hz), 7.82 (s, H-3), 7.68 and 7.54 (2ddd, H-6, H-7, *J* 8.2 Hz, *J* 7.0 Hz, *J* 1.9 Hz), 3.92 and 3.74 (2tt, 2CH, *J* 7.3 Hz, *J* 3.4 Hz), 1.58, 1.46 and 1.32 (3m, 2H, 2H and 4H, $2CH_2CH_2$). ^{13}C NMR (50.32 MHz, $CDCl_3$) δ: 153.4 (C-1), 140.6 and 132.5 (C-2, C-4), 130.5 and 126.3 (C-4a, C-8a), 129.6 (C-7), 126.3, 124.4 and 123.4 (C-5, C-6, C-8), 113.7 (C-3), 51.4 and 48.0 (2CH), 11.0 and 10.1 ($2CH_2CH_2$). MS, *m*/*z*: 280 (12) $[M]^+$, 253 (21), 226 (14), 225 (14), 212 (88), 198 (22), 184 (41), 170 (53), 115 (100) *et al.*

For **6**: mp 144–146 °C (MeOH, –20 °C). ^1H NMR (200 MHz, $CDCl_3$) δ: 13.7 (s, OH), 7.66 (d, H-4, H-5, *J* 8.7 Hz), 6.96 (d, H-3, H-6, *J* 8.7 Hz), 3.74 (tt, 2CH, *J* 7.2 Hz, *J* 3.6 Hz), 1.46 and 1.27 (2m, $2CH_2CH_2$). ^{13}C NMR (50.32 MHz, $CDCl_3$) δ: 154.9 (C-2, C-7), 133.7 (C-4, C-5), 133.6 (C-1, C-8), 129.4 (C-4a), 123.3 (C-8a), 117.6 (C-3, C-6), 46.5 (CH), 10.3 (CH_2CH_2). MS, *m*/*z*: 296 (56) $[M]^+$, 268 (16), 241 (52), 240 (78), 213 (72), 199 (100) *et al*.

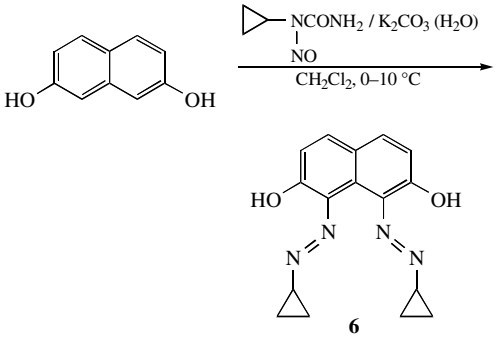
For **7**: mp 116–118 °C (diethyl ether, –20 °C). ^1H NMR (300 MHz, $CDCl_3$) δ: 9.14 (dd, H-4, *J* 8.5 Hz, *J* 1.9 Hz), 8.84 (dd, H-2, *J* 4.2 Hz, *J* 1.9 Hz), 8.2 (br. s, OH), 7.63 (d, H-6, *J* 8.1 Hz), 7.55 (dd, H-3, *J* 4.2 Hz, *J* 8.5 Hz), 7.16 (d, H-7, *J* 8.1 Hz), 3.86 (tt, CH, *J* 7.4 Hz, *J* 3.5 Hz), 1.58 and 1.29 (2m, CH_2CH_2). ^{13}C NMR (50.32 MHz, $CDCl_3$) δ: 154.1 (C-8), 148.3 (C-2), 139.3 (C-8a), 137.6 (C-5), 132.8 (C-4), 126.0 (C-4a), 122.5 (C-3), 114.9 (C-6), 109.8 (C-7), 51.1 (CH), 9.9 (CH_2CH_2). MS, *m*/*z*: 213 (94) $[M]^+$, 186 (63), 185 (100), 171 (55), 158 (57), 144 (24) *et al*.

‡ This sample contained **3** and **5** in a ratio of ~8:1.



Scheme 1

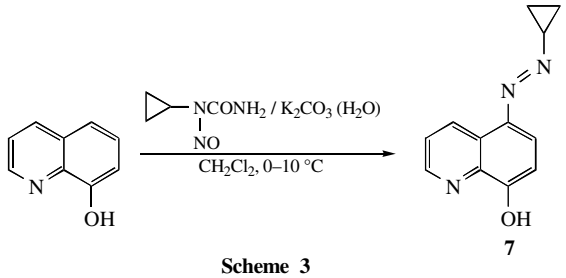
Interestingly, the generation of a cyclopropyldiazonium intermediate in the presence of 2,7-dihydroxynaphthalene under the same conditions gives rise to a double azo coupling adduct, 1,8-di(cyclopropylazo)-2,7-dihydroxynaphthalene **6**, which was obtained with high selectivity in 63% yield on the expectation of nitrosourea **1** (Scheme 2). The preferred formation of bis-adduct **6** is obviously determined by a low solubility of starting dihydroxynaphthalene and high reactivity of initially formed 1-(cyclopropylazo)-2,7-dihydroxynaphthalene. Compound **6**† has an intense molecular-ion peak in the mass spectrum (EI, 70 eV) and a simple ^{1}H NMR spectrum, in which only two doublets (J 8.8 Hz) of protons from the naphthalene fragment and typical signals of two equivalent cyclopropane rings are present.



Scheme 2

The azo coupling reaction of a cyclopropyldiazonium intermediate also proceeds with 8-hydroxyquinoline to give a single isomer; according to the NMR data it corresponds to 5-(cyclopropylazo)-8-hydroxyquinoline **7**.† The product was isolated from diethyl ether at 5 °C as yellow crystals in 52% yield.

Contrary to the hydroxynaphthalenes, phenol reacts with the cyclopropyldiazonium ion to give a complicated mixture of both diazo coupling products and products of O-alkylation of phenol with cyclopropyl and allyl cations.



Scheme 3

The results suggest that the decomposition of *N*-cyclopropyl-*N*-nitrosourea with K_2CO_3 generates an unstable cyclopropyldiazonium intermediate, which can be trapped by hydroxynaphthalenes or 8-hydroxyquinoline as azo coupling products. Corresponding cyclopropylazo compounds are formed in 50–90% yields using only a small excess of starting *N*-cyclopropyl-*N*-nitrosourea. Note that the experimental conditions were identical to those[10] used for the generation and trapping of diazocyclopropane with olefins by the reaction of 1,3-dipolar addition. Apparently, the cyclopropyldiazonium cation and diazocyclopropane can be equiprobable reaction intermediates and react along one or another pathway depending on the nature of substrate.

This work was supported by the Russian Foundation for Basic Research (grant nos. 02-03-33365 and 00-15-97387) and the Research Program of the Russian Academy of Sciences (grant no. 1.15).

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Received: 23rd April 2002; Com. 02/1921