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Abstract: An oxidative route for the formation of 7,8-diaza[5]helicene and the corresponding N-oxides in high yields was developed. A mechanism of formation and possible interconversion of these products is put forward. Reduction of the N-oxides provided the title compound in quantitative yield.

Key words: diaza[5]helicenes, oxidation, amines, N-oxides, heterocycles

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In the framework of our research on the azahelicene system, we were interested in obtaining 7,8-diaza[5]helicene (2). The position of the two nitrogen atoms, adjacent and located on the central ring, may arouse interest both from a theoretical standpoint and for practical purposes, with emphasis on the following points: (i) determination of the energy barrier for the interconversion between the P- and M-enantiomers, (ii) the circular dichroism spectra and (iii) the formation of metal complexes and the study of ligand–metal energy transfer, with the purpose of obtaining tunable light emission as a function of the selected metal ion.

A certain number of syntheses of 7,8-diaza[5]helicene are reported in the literature. Some early papers deal with the reduction of 2-nitronaphthalene with different reducing agents.1 Later (1965), phosphine was used as the reducing agent.2 However, at present, 2-nitronaphthalene is expensive and not available on a large scale, possibly because it is toxic and commercially uninteresting. The reduction of 2,2¢-dinitro-1,1¢-binaphthyl with lithium aluminum hydride has also been reported,3 but the starting material is nowadays not readily available. The synthesis of benzoyl[ci]cinnimine, and the corresponding N-oxide, was carried out starting from 2,2¢-dinitro-1,1¢-biphenyl.4 A coupling method starts from 2,2¢-azanaphthalene and aluminum trichloride,5 but once again the starting material is not so easily achievable. The oxidative approach, namely the oxidation of diamino derivatives, was seldom considered promising. Some papers have reported the oxidation of amines to form azoxy or N,N¢-dioxide derivatives, either using hydrogen peroxide and polyoxometalates,6 or with the use of aliphatic peracids.7 The oxidation of 2,2¢-diamino-1,1¢-binaphthyl (1) with sodium perborate was reported by Corbett and Holt to yield only traces of diazene.8 In the present communication, the use of other reagents capable of oxidizing diamine 1 in high yields is explored and discussed. The proposed approach starts from readily available reagents. A convenient route for the preparation of either 7,8-diaza[5]helicene or intermediate products that can be converted into the target helicene is illustrated.

Scheme 1 shows the products detected and isolated via flash chromatography after the oxidation of diamine 1 with m-chloroperoxybenzoic acid (MCPBA). The formation of side products was assessed by HPLC; however, GC/MS analysis did not allow us to identify the impurities, probably due to their thermal instability. It turned out that the formation of side products decreased when there was an increase in the dilution and the dropwise addition rate of the oxidizing agent. The identification of the N-oxides 3 and 4 was achieved by electrospray ionization mass spectrometry (ESI-MS) and NMR spectroscopy.

Scheme 1 Oxidation of 2,2¢-diamino-1,1¢-binaphthyl (1) with MCPBA

The oxidation of amino derivatives has been widely studied for a long time,9 and it is well known that different products are formed depending upon the oxidant and the experimental conditions. One of the steps of the reaction mechanism generally accepted for this oxidation consists of the transformation of the amino group into a nitroso derivative, possibly via a hydroxylamin derivative.4,6 The
dimerization of two nitroso groups to the corresponding \(N,N'-\)dioxide derivative has been studied in depth,\(^6,10\) and was also observed under reductive conditions.\(^7\) The papers mentioned above also reported formation of the \(N,N'-\)dioxide species upon treatment of hydroxylamino derivatives with hydrogen peroxide in chloroform, whilst the azoxy derivative was isolated when water was used as the solvent. The eventual formation of the azo functional group may be explained by the direct condensation of a nitroso derivative with the starting amine.\(^{11}\) An interconversion between the products formed was also hypothesized. In the present work, control experiments were carried out in order to understand if the products formed may interconvert. Indeed, \(2, 3\) and \(4\) were reacted, in separate batches, with MCPBA under our experimental conditions. It was found that \(2\) was partially transformed into its \(N\)-monooxide, \(10\%\) of the \(N\)-monooxide \(3\) was transformed into the corresponding \(N,N'-\)dioxide \(4\), along with more than \(20\%\) mass loss of \(3\), and, finally, only \(10\%\) mass loss was observed when \(4\) was reacted. For a better understanding of the mechanism of this oxidation, two series of reactions were carried out, the first with different amounts of MCPBA at \(50^\circ\)C and the second at three different temperatures while keeping the amine-to-oxidant molar ratio at \(1:3\). The two series of reactions were repeated twice. The quantitation of the reaction products for the first and second reaction series are reported in Figure 1 and Figure 2, respectively. Quantitative analysis was undertaken at three different wavelengths for \(2, 3\) and \(4\), while the amount of diamine \(1\) was determined only at 254 and 350 nm due to its low extinction coefficient at 313 nm.

One would expect that a smaller amount of oxidant should lead to diazene \(2\), while upon increasing the amount of oxidant, the reaction would shift toward the more oxidized products \(3\) and \(4\). On the contrary, even at low oxidant concentration and at low temperature, the amount of diazene \(2\) is very low and nearly independent of an increase in the amount of oxidant or in the temperature. The quantity of diazene \(2\) being essentially constant, independent of the experimental conditions, and so small, means that its possible transformation to one or both of the other two products will result in very little influence on their amounts; for this reason, we will not take this factor into consideration in further discussions. In Scheme 2, a simplified reaction mechanism is drawn.

Figure 2 indicates that the formation of \(N,N'-\)dioxide \(4\) dominates at low temperature. This may be easily explained considering that product \(4\) derives from the dimerization of two nitroso groups, namely two free radicals, and the activation energy for this dimerization should be rather low. In contrast, compound \(3\) is expected to arise from an elimination reaction between one nitroso and one

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**Scheme 2** Outline of the reaction mechanism

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hydroxylamino group. This reaction is slower than the dimerization of two free radicals and, indeed, product 3 becomes the prevailing product at higher temperature. A reasonable explanation of the trend displayed in Figure 1 stems from the following considerations: at low oxidant concentration a partial oxidation to the nitroso–hydroxylamino derivative is likely to occur. The NO and NHOH groups may, in turn, undergo condensation leading to 3. This reaction, however, is still slow. Hence, increasing the amount of the oxidizing agent results in conversion of the hydroxylamino group into a nitroso group, thus increasing the amount of 4. In the same way, the observed low amount of diazene 2 can be rationalized: the rate of condensation is expected to be low enough to be detrimental for the direct formation of the helicene. Considering the trends of the control experiments, we can conclude that the amount of 4 destroyed by the oxidation is counterbalanced by the amount of 3 transformed into 4; on the other hand, part of 3 is directly destroyed and this explains the trends shown in Figure 1.

Interestingly and different from that reported for the oxidation of aromatic amines, N,N′-dioxide 4 could be obtained. By using hydrogen peroxide in the presence of metal complexes as the oxidizing system, 4 was obtained only in chloroform solution. A possible explanation may be based on the fact that in the substrate described in the present work the two naphthyl groups are not coplanar for steric reasons. This allows oxidation of the hydroxylamino group to the corresponding nitroso group and easy cross-coupling of the nitroso radicals leading to the formation of 4.

2,2′-Diamo-1,1′-binaphthyl (1) and m-chloroperoxybenzoic acid (70% w/w) (MCPBA) are commercial products. HPLC analyses were performed on an Agilent 1200 series instrument with an Agilent ZORBAX Eclipse XDB-C18 5 μm, 4.6 × 150 mm column, using MeCN as solvent at a flow rate of 0.5 mL/min. The GC/MS instrument was an Agilent 6890 Network GC system, with an Agilent 7000A spectrophotometer 5973 Mass Select Detector. The ESI-MS apparatus was a Bruker Esquire 3000+ instrument with an electrospray source and a quadrupole ion trap detector. The samples were dissolved in 50:50 MeOH–H2O (containing 1% formic acid) and infused into the ESI source via a microsyringe pump at a rate of 4 μL/min. NMR spectra were recorded either on a Bruker ARX 400 or Bruker Avance 500 spectrometer operating at proton resonance frequencies of 400 and 500 MHz (100 and 125 MHz for 13C NMR, respectively) using CDCl3 as solvent and TMS as internal standard. Ultraviolet/visible absorption spectra were recorded on a Thermo Nicolet Evolution UV/Vis-500 spectrophotometer, with MeCN as solvent and Vision 32 software, using a 1-cm path length cell. FT-IR spectra were recorded on a Thermo Avatar 370 instrument in ATR reflection mode using a zinc selenide crystal. All spectra were recorded at r.t.

Reactions with Different Amounts of Peroxide

The molar ratios and amounts of NaHCO3 and MCPBA are reported in Table 1. Diamine 1 (0.015 g, 0.05 mmol) was dissolved in a mixture of H2O (4.5 mL) and MeCN (4.5 mL). The temperature was raised to 50 °C. Solid NaHCO3 was added and then the soln of MCPBA in MeCN (10 mL) was added dropwise over 30 min; the resulting mixture was stirred further for 1 h. After cooling, sat. aq NaHCO3 (15 mL) was added. A soln of pyrene as internal standard was added and the resulting solution was extracted with CH2Cl2 (3 × 10 mL). The organic layer was dried (Na2SO4) and concentrated under reduced pressure. The residue was dissolved in MeCN and then analyzed by HPLC at three different wavelengths (254, 313 and 350 nm).

Table 1 | Reactions with Different Amounts of Peroxide

<table>
<thead>
<tr>
<th>Molar ratios (1/peroxide/NaHCO3)</th>
<th>70% MCPBA (g/mmol)</th>
<th>NaHCO3 (g/mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:1.5:1.5</td>
<td>0.019 (0.08)</td>
<td>0.006 (0.08)</td>
</tr>
<tr>
<td>1:3</td>
<td>0.039 (0.16)</td>
<td>0.013 (0.16)</td>
</tr>
<tr>
<td>1:5</td>
<td>0.061 (0.25)</td>
<td>0.021 (0.25)</td>
</tr>
<tr>
<td>1:8</td>
<td>0.103 (0.40)</td>
<td>0.034 (0.40)</td>
</tr>
<tr>
<td>1:10:10</td>
<td>0.123 (0.50)</td>
<td>0.042 (0.50)</td>
</tr>
</tbody>
</table>

Reactions at Different Temperatures

The conditions were the same as those reported above, using a molar ratio of 1:3:3 (1/1/1). Workup was the same as above. The temperatures chosen were –2 °C, 20 °C and 50 °C.

Control Experiments

Compound 2 or 3 or 4 (0.048 mmol) and NaHCO3 (0.048 mmol) were dissolved in a mixture of H2O (4.5 mL) and MeCN (4.5 mL). A large amount of MCPBA (0.385 mmol; 8:1 ratio with the selected helicene) in MeCN (10 mL) was added dropwise to the solution during 30 min, and the mixture was left at 50 °C for a further 1 h. After cooling, sat. aq NaHCO3 (15 mL) was added. A soln of pyrene as internal standard was added and the resulting solution was extracted with CH2Cl2 (3 × 10 mL). The organic layer was dried (Na2SO4) and concentrated under reduced pressure. The residue was dissolved in MeCN and then analyzed by HPLC at three different wavelengths (254, 313 and 350 nm).

Preparative Reaction

2,2′-Diamo-1,1′-binaphthyl (1) (0.45 g, 1.6 mmol) was dissolved in a mixture of H2O (100 mL) and MeCN (100 mL) and the temperature was brought to 50 °C. When this temperature was reached, first NaHCO3 (0.67 g, 7.9 mmol) was added and then a solution of 70% MCPBA (1.95 g, 7.9 mmol) in MeCN (200 mL) was added dropwise during 1 h. The resulting mixture was stirred for an additional 1 h. After cooling, H2O (50 mL) and sat. aq NaHCO3 (50 mL) were added and the resulting solution was extracted with CH2Cl2 (3 × 30 mL). The organic layer was dried (Na2SO4) and concentrated under reduced pressure. The residue (0.49 g) was flash-chromatographed on silica gel (EtOAc/hexane, 3:2) giving 1 (0.03 g, 7%), 2 (0.01 g, 2%), 3 (0.16 g, 34%) and 4 (0.25 g, 50%). Under these conditions, other oxidation products or byproducts were not eluted from the column.

7,8-Diaza[5]helicene (2)

Mp 268–269 °C (Lit.2 269–270 °C).

IR: 3058, 2960, 2922, 2850, 1647, 1540, 1505, 1455, 1415, 1337, 1257, 1239, 1162, 1092, 1079, 1035, 957, 878, 845, 821, 810, 783, 775, 757, 748, 651 cm–1.

1H NMR shifts and coupling constants for compounds 2, 3 and 4 are reported in Table 2 (atom numbering is given in Scheme 1).

Synthesis of 7,8-Diaza[5]helicene 415

ESI-MS: \( m/z = 281 \ [M + H]^+ \).

UV/Vis (MeCN): \( \lambda_{\text{max}} (\log e) = 271 (4.24), 305 (4.32), 324s (4.08), 395 (3.35), 417 \) nm (3.33).

7,8-Diaza[5]helicene N-Oxide (3)
Yellow-brown solid; mp 248–251 °C \[\text{Lit.}^8 250–252 \) °C (dec)].
IR: 3062, 2923, 2853, 1613, 1595, 1511, 1448, 1424, 1369, 1335, 1261, 1237, 912, 879, 822, 807, 766, 747, 719, 679, 666, 651 cm\(^{-1}\).

\(^{13}\)C NMR (CDCl\(_3\)): \( \delta = 144.08, 137.22, 134.53, 133.47, 133.19, 132.33, 131.57, 130.19, 129.85, 129.15, 128.47, 128.42, 128.32, 128.13, 126.09, 117.59, 115.43 \).

ESI-MS: \( m/z = 297 \ [M + H]^+ \).

UV/Vis (MeCN): \( \lambda_{\text{max}} (\log e) = 252 (4.14), 281 (4.26), 330 (4.14), 350s (3.96), 417 (3.48), 442 \) nm (5.51).

7,8-Diaza[5]helicene N,N’-Dioxide (4)
Creamy yellow solid; mp 230–232 °C (dec).
IR: 3082, 1610, 1592, 1577, 1507, 1462, 1443, 1427, 1396, 1363, 1325, 1263, 1168, 1144, 1123, 1070, 1048, 1018, 963, 952, 932, 889, 878, 840, 826, 811, 784, 770, 746, 657 cm\(^{-1}\).

\(^{13}\)C NMR (CDCl\(_3\)): \( \delta = 144.08, 137.22, 134.53, 133.47, 133.19, 132.33, 131.57, 130.19, 129.85, 129.15, 128.47, 128.42, 128.32, 128.13, 126.09, 125.88, 123.40, 117.59, 115.43 \).

ESI-MS: \( m/z = 313 \ [M + H]^+ \).

UV/Vis (MeCN): \( \lambda_{\text{max}} (\log e) = 251 (4.17), 282 (4.00), 334 (4.06), 375s \) nm (3.54).

Anal. Calcd for C\(_{20}\)H\(_{12}\)N\(_2\)O\(_2\): C, 76.91; H, 3.87; N, 9.97. Found: C, 76.73; H, 3.89; N, 8.97.

Reduction of the N-Oxides
Either N-oxide 3 (0.15 g, 0.5 mmol) or N,N’-dioxide 4 (0.16 g, 0.5 mmol) was dissolved in anhyd Et\(_2\)O (20 mL) and an excess of LiAlH\(_4\) (0.04 g, 1 mmol) was added. The mixture was heated at reflux (36 °C) for 5 h. After cooling, unreacted LiAlH\(_4\) was destroyed by adding MeOH (10 mL); H\(_2\)O (20 mL) was added and the ether layer, after separation and drying (Na\(_2\)SO\(_4\)), was concentrated to give 7,8-diaza[5]helicene (2) in quantitative yield.

References
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(9) For example, see: Bamberger, E.; Rising, A. Ber. Dtsch. Chem. Ges. 1900, 33, 3623.