Mechanism of Nucleophilic Solvolysis of 1,2-Dibromo-1,2-dihydrocyclobuta[*b*]pyridine; X-Ray Crystal Structure Analysis of 1,2-Dihydro-1-methoxycyclobuta[*b*]pyridine Methiodide

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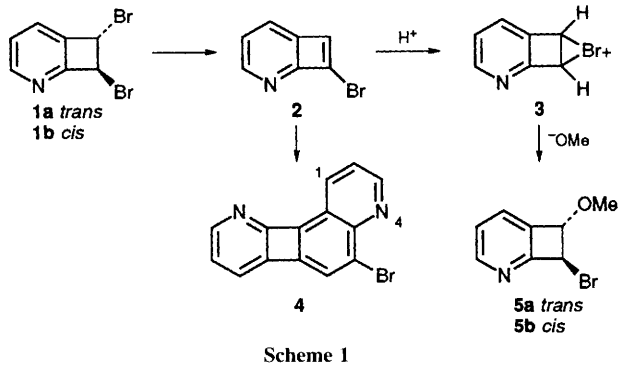
trans-1,2-Dibromo-1,2-dihydrocyclobuta[*b*]pyridine **1a** undergoes nucleophilic methanolysis with retention of configuration *via* 2-bromocyclobuta[*b*]pyridine **2**; the crystal structure of 1,2-dihydro-1-methoxycyclobuta[*b*]pyridine methiodide is described.

1,2-Dibromo-1,2-dihydrocyclobutabenzene is resistant to nucleophilic substitution, as a consequence of the strained ring imposing a relatively high degree of s-character on the carbon–bromine bonds. In contrast, we have found that *trans*-1,2-dibromo-1,2-dihydrocyclobuta[*b*]pyridine **1a**[1] reacts with sodium methoxide in methanol to give predominantly (80%) the *trans*-1-substitution product **5a**,† the ^{1}H NMR spectrum showing singlets for the cyclobutene protons at δ



Scheme 1

4.96 (1-H) and 5.27 (2-H).‡ This was accompanied by traces (*ca.* 5% each) of the corresponding *cis*-isomer **5b**, characterised by doublets in the ^{1}H NMR spectrum for the cyclobutene protons, and the quinoline derivative **4**. A similar ratio of products **4** and **5a, b** was obtained under the same conditions from the *cis*-dibromide **1b**. Preferential displacement of the 1-bromo-substituent in **1**, expected from the relative electron densities at C(1) and C(2), was confirmed by catalytic hydrogenation of **5a** to 1,2-dihydro-1-methoxycyclobuta[*b*]pyridine, followed by an X-ray crystal structure analysis§ of the corresponding methiodide salt (Fig. 1). The internal angles of the pyridine ring differ significantly from 120°, with the largest deviation for C(5)–C(6)–C(6a) of 109.4(7)°. This contrasts with 1,8-diazabiphenylene[2] and 1,2-dihydrocyclobuta[*b*]quinoline,[3] in which the most acute angles in the six-membered rings (at *ca.* 112°) are those subtended at the heteroatom; the analogous angle C(4)–N(3)–C(2a) in Fig. 1 is considerably larger, at 116.7(6)°.

The unexpected observation that substitution of **1a** proceeds with retention of the *trans*-configuration at C(1)–C(2) leads us to propose an elimination–addition pathway involving 2-bromocyclobuta[*b*]pyridine **2** (Scheme 1). While well-documented for aromatic and vinylic substitutions, this type of mechanism is unusual in aliphatic systems,[4] the more so in this case owing to the predicted high energy of the cyclobutadienoid intermediate **2**.[5] However, this pathway is consistent with the formation of the byproduct **4**, one of four possible 'angular' dimeric products of **2**. The structure **4** was established by comparison with substituted benzocyclobutene dimerisations[6] and by ^{1}H NMR spectroscopy, 7-H showing an NOE on irradiation of 6-H. The dimer **4** is the major product (88%) in Et_2O solvent along with **5a** (6%); the *cis*-isomer **5b** could not be detected.

Further support for this mechanism was obtained from an analogous solvolysis of **1a** in CH_3OD, which resulted in deuterium incorporation at C(2) in the product. Neither **1a** nor **5a** underwent H–D exchange under identical conditions (as determined by NMR monitoring). The elimination step is therefore essentially irreversible, E_{1cb} deprotonation at C(2) being facilitated by the β-nitrogen. The addition step appears to proceed *via* reprotonation of **2** followed by *anti*-attack on the resulting bromonium ion **3**; the alternative sequence of nucleophilic addition of methoxide anion to **2** followed by protonation should be less stereospecific.

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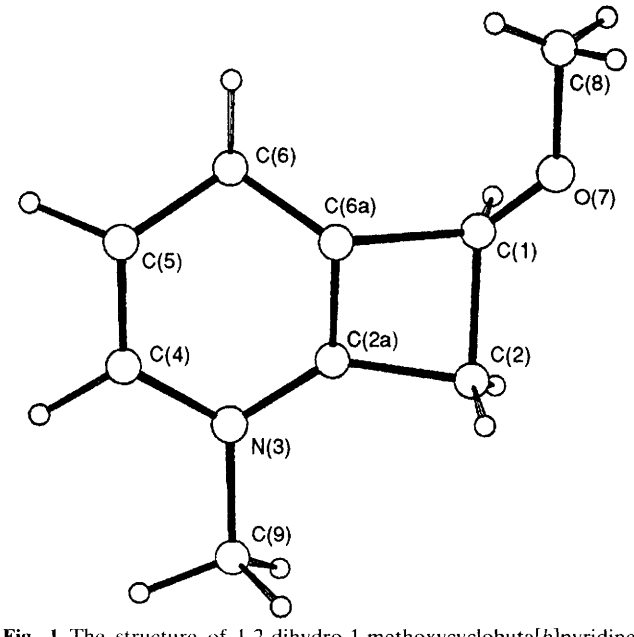

Fig. 1 The structure of 1,2-dihydro-1-methoxycyclobuta[*b*]pyridine methiodide. Selected bond distances (Å) and angles (°): C(1)–C(2) 1.599(12), C(1)–C(6a) 1.649(13), C(1)–O(7) 1.061(13), C(2)–C(2a) 1.528(11), C(2a)–N(3) 1.324(10), C(2a)–C(6a) 1.421(10), N(3)–C(4) 1.355(10), N(3)–C(9) 1.482(9), C(4)–C(5) 1.381(11), C(5)–C(6) 1.436(14), C(6)–C(6a) 1.429(11), O(7)–C(8) 1.449(11), C(6a)–C(1)–C(2) 85.6(7), O(7)–C(1)–C(2) 129.3(9), O(7)–C(1)–C(6a) 136.0(9), C(2a)–C(2)–C(1) 84.0(6), N(3)–C(2a)–C(2) 139.6(6), C(6a)–C(2a)–C(2) 96.9(6), C(6a)–C(2a)–N(3) 122.5(7), C(4)–N(3)–C(2a) 116.7(6), C(9)–N(3)–C(2a) 120.0(6), C(9)–N(3)–C(4) 122.6(7), C(5)–C(4)–N(3) 122.2(8), C(6)–C(5)–C(4) 118.8(7), C(6a)–C(6)–C(5) 109.4(7), C(2a)–C(6a)–C(1) 85.6(6), C(6)–C(6a)–C(1) 130.6(8), C(6)–C(6a)–C(2a) 113.4(8), C(8)–O(7)–C(1) 128.7(8).

Footnotes

† New compounds gave satisfactory microanalytical and mass spectroscopic data.

‡ ^{1}H NMR data ($CDCl_3$, 250 MHz): **4**: δ 6.44 (1H, t, 8-H), 6.68 (1H, dd, 7-H), 7.30 (1H, dd, 2-H), 7.52 (1H, dd, 9-H), 7.66 (1H, s, 6-H), 8.05 (1H, dd, 1-H), 8.83 (1H, dd, 3-H); **5a**: δ 3.61 (3H, s, OMe), 4.96 (1H, s, 1-H), 5.27 (1H, s, 2-H), 7.29 (1H, dd, 5-H), 7.60 (1H, dd, 6-H), 8.65 (1H, dd, 4-H); **5b**: 3.62 (3H, s, OMe), 5.04 (1H, d, 1-H), 5.81 (1H, d, 2-H), 7.29 (1H, dd, 5-H), 7.58 (1H, dd, 6-H), 8.62 (1H, dd, 4-H); 1,2-dihydro-1-methoxycyclobuta[*b*]pyridine: δ 3.36 (1H,

dd, 2-H), 3.58 (3H, s, OMe), 3.66 (1H, dd, 2′-H), 4.98 (1H, dd, 1-H), 7.13 (1H, dd, 5-H), 7.49 (1H, dd, 6-H), 8.48 (1H, dd, 4-H).

§ *Crystal data* for $C_9H_{12}NOI$, M = 277.02, monoclinic, space group $P2_1$, a = 9.871(2), b = 7.316(1), c = 7.732(1) Å, β = 105.11(3)°, U = 539.07 Å^3, $F(000)$ = 268, μ(Mo-Kα) = 27.24 cm^{-1}, Z = 2, D_c = 1.71 g cm^{-3}. Data were collected on a Philips PW 1100 diffractometer in the θ range 3–26° with a scan width of 0.90°. Equivalent reflections were merged to give 986 absorption-corrected data with weights of $I/\sigma(I) > 3.0$. R = 0.0352, R_w = 0.0388 with weights of $w = 1/\sigma^2F_o$ assigned to the individual reflections. Atomic coordinates, bond distances and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

References

1 M. K. Shepherd, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1495.
2 B. R. Deroski, J. S. Ricci, J. A. H. MacBride and J. H. Markgraf, *Can. J. Chem.*, 1984, **62**, 2235.
3 B. R. Deroski, J. H. Markgraf and J. S. Ricci, *J. Heterocycl. Chem.*, 1983, **20**, 1155.
4 A. F. Popov, Z. Piskunova and V. N. Matvienko, *Zh. Org. Khim.*, 1986, **22**, 1299.
5 M. D. Gheorghiu and P. Filip, *Rev. Roum. Chim.*, 1974, **19**, 859.
6 M. K. Shepherd, *Cyclobutarenes. The Chemistry of Benzocyclobutene, Biphenylene, and Related Compounds*, Studies in Organic Chemistry 44, Elsevier, Amsterdam, 1991.