PERKIN 2 COMMUNICATION

A tetracyclic benzimidazole derivative of Kemp's triacid

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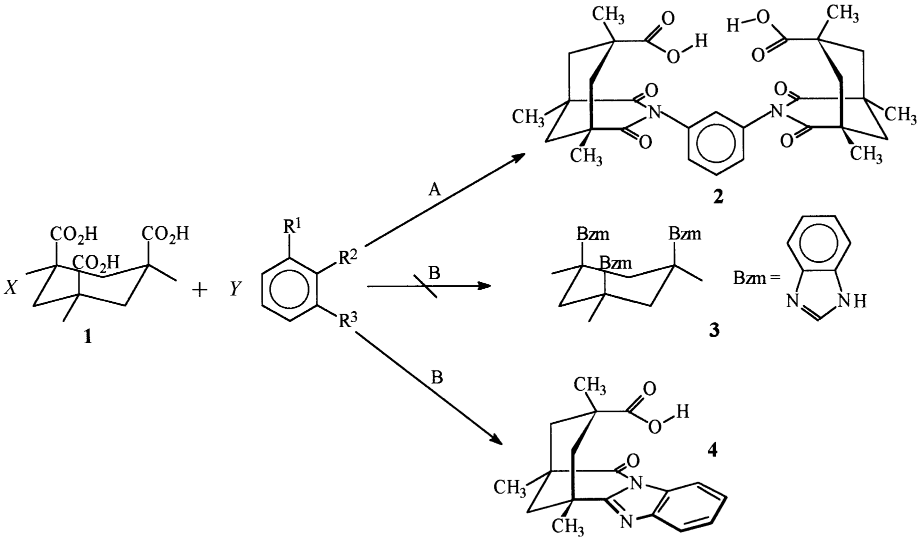
Fusion of Kemp's triacid with *o*-phenylenediamine produced a unique tetracyclic compound, identified structurally by X-ray crystallography and solution NMR spectroscopy, having one of the original carboxylic groups free, one forming a benzimidazole unit, which itself forms an amide with the remaining carboxylic group.

Rebek and co-workers[1] reported a new class of chelating agents derived from 1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid (**1**, Kemp's triacid),[2] of which the first examples were those derived from *m*-phenylenediamine **2** (Scheme 1, A). In view of our interests in polydentate benzimidazoles,[3] we attempted to produce the tris(benzimidazole) chelating ligand **3** which had the potential of providing a rigid NNN coordinating environment towards selected first-row transition elements. Similar chelating ligands based on 1,3,5-triaminocyclohexane have recently[4] been used as a basis for preparing low molecular weight mimics/models of the active sites in metalloenzymes. These small model complexes were specifically designed to promote a secondary coordination sphere consisting of chains of hydrogen-bonded solvent molecules which are believed to be important in the overall catalytic function of certain enzymes.[5]

Instead of **3** the unique tetracyclic product **4** was obtained† on condensing Kemp's triacid **1** with three equivalents of *o*-phenylenediamine in a polyphosphoric acid medium as previously described[6] (see Scheme 1, B). Analysis of the ^1H and ^{13}C NMR spectra indicated that the product apparently had three distinct residual methylene groups and three distinct methyl groups, one benzimidazole moiety and an unreacted carboxylic group. The product was finally characterised *via* X-ray crystallography.‡ Suitable crystals were produced by slow evaporation of a saturated acetonitrile solution. The molecular structure is shown in Fig. 1.§

In the condensation reaction, one carboxylic group provided the C-7 carbon of the benzimidazole, a second forms the amide together with the secondary nitrogen of the benzimidazole and the third is unreacted and remains 'free'. The molecule is extremely rigid. The compound is of interest in relation to the development of new chiral auxiliaries[7] based on Kemp's triacid from a simple 'one pot' synthesis. The remaining 'free' carb-



Scheme 1 *Reagents and conditions:* A: $X = 2$, $Y = 1$, $R^1 = R^3 = NH_2$, $R^2 = H$; direct fusion of the two solids. B: $X = 1$, $Y = 3$, $R^1 = R^2 = NH_2$, $R^3 = H$; (*i*) polyphosphoric acid, heated for 4 h with efficient stirring, 140–160 °C, (*ii*) strong base (pH ~ 9).

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† Compound **4** was obtained as a white powder by the reaction of Kemp's triacid (1.00 g, 3.87 mmol) in polyphosphoric acid (30 cm^3) and *o*-phenylenediamine (1.25 g, 11.56 mmol) as previously described.[6] Yield (0.64 g, 2.05 mmol, 53%), mp >300 °C (Found: C, 67.7; H, 6.7; N, 8.4. Calc. for $C_{18}H_{20}N_2O_3\cdot 0.5CH_3CH_2OH$: C, 68.1; H, 6.9; N, 8.4%). $\delta_H[(CD_3)_2SO$, 200.13 MHz] 1.11 (3 H, s, CH_3), 1.28 (3 H, s, CH_3), 1.47 (3 H, s, CH_3), 2.5, 2.25, 1.64, 1.48, 1.4 (5 × 1 H, d, CH_2), 7.27–7.35 (2 H, m, Ar-2 and -3), 7.59–7.67 (1 H, m, Ar-1) and 8.04–8.13 (1 H, m, Ar-4); $\delta_C[(CD_3)_2SO$, 50.32 MHz] 24.9, 26.1, 30.6, 34.7, 38.7, 41.4, 41.5, 43.7, 45.7, 115.6, 119.5, 124.6, 124.9, 131.3, 143.4, 159.7, 173.6 and 176.6; *m/z* (FABMS) 313 (MH^+, 100%); *m/z* (EIMS) [Found: M^+, 312.1485 (100%). $C_{18}H_{20}N_2O_3$ requires *M*, 312.1474].

‡ Crystal data for **4**: $C_{18}H_{20}N_2O_3$, $M = 312.36$, orthorhombic, space group *Fdd*2, $a = 13.7644(15)$, $b = 43.389(5)$, $c = 10.5161(12)$ Å, $Z = 16$, $D_c = 1.321$ g cm^{-3}, $\mu = 0.09$ mm^{-1} (Mo-Kα, $\lambda = 0.710\,73$ Å), $F(000) = 2656$, $T = 160$ K. 9713 reflections were measured on a Siemens SMART CCD area-detector diffractometer and yielded 3537 unique data ($2\theta \le 57.12°$, $R_{int} = 0.0348$) for structure solution (direct methods) and refinement (on F^2 with statistical weighting scheme, anisotropic displacement parameters, and constrained isotropic H atoms). Final $R' = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{\frac{1}{2}} = 0.0903$ for all data, conventional $R = 0.0389$ on F values of 3298 reflections with $F_o^2 > 2\sigma(F_o^2)$, goodness of fit 1.136 on F^2 for all data and 213 refined parameters. A final difference synthesis showed no features outside ±0.23 e $Å^{-3}$. The absolute structure was indeterminate.[11] Programs used were Siemens SMART (control) and SAINT (integration) software and SHELXTL.[12] Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC).§

§ For details of the CCDC deposition scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 188/65.

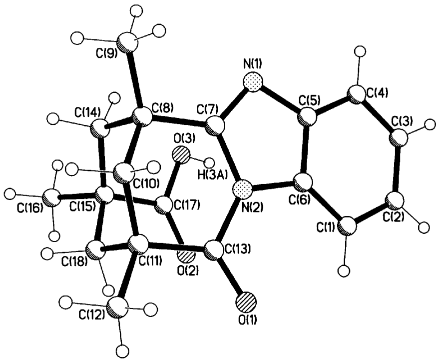

Fig. 1 Molecular structure with atom labelling

oxylic acid residue is intermolecularly hydrogen-bonded to the tertiary nitrogen of the aza-tricycle with an N · · · O distance of 2.690 Å. It is presumably free for further functionalisation with chiral compounds. Although a benzoxazole derivative of the aza-tricycle skeleton is known,[8] the benzoxazole unit is not fused to the system as in **4** but is a simple substituent. Except for a range of ligands similar to **2** and their complexes with several metals, the aza-tricycle skeleton with at least one carbonyl group adjacent to nitrogen was found in only a few structures[9] in the October 1996 release of the Cambridge Structural Database:[10] most of these are dicarboximides and have a variety of substituents at nitrogen and/or at the carbon atom which retains the carboxylic acid function in **4**.

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