SYNTHETIC APPROACHES TO DIAZABIPHENYLENES: STNTHESIS OF THE CARBON-NITROGEN SKELETON OF 1,5- AND 2,6-DIAZABIPHENYLENE.

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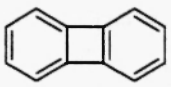
Abstract: The full carbon-nitrogen skeletons of the non-benzenoid heteroaromatic compounds 1,5- and 2,6-diazabiphenylene have been prepared in two steps from *cis, trans, cis*-tricyclo[5.3.0.$0^{2\,6}$]-decane-3,8-dione. Intermediates of higher oxidation state that can serve as precursors to 1,5- and 2,6-diazabiphenylene derivatives have also been prepared.

Introduction: The non-benzeneoid aromatic compound biphenylene 1 was first prepared over 50 years ago and because of its unusual electronic structure has been extensively studied (1). Less work has been carried out on the nitrogen-containing analogues having a nitrogen atom in each of the six-membered rings, and this is probably associated with the fact that they are relatively inaccessible in useful quantities by methods developed so far (2 – 6).



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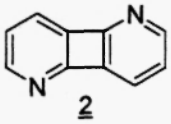

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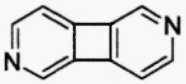

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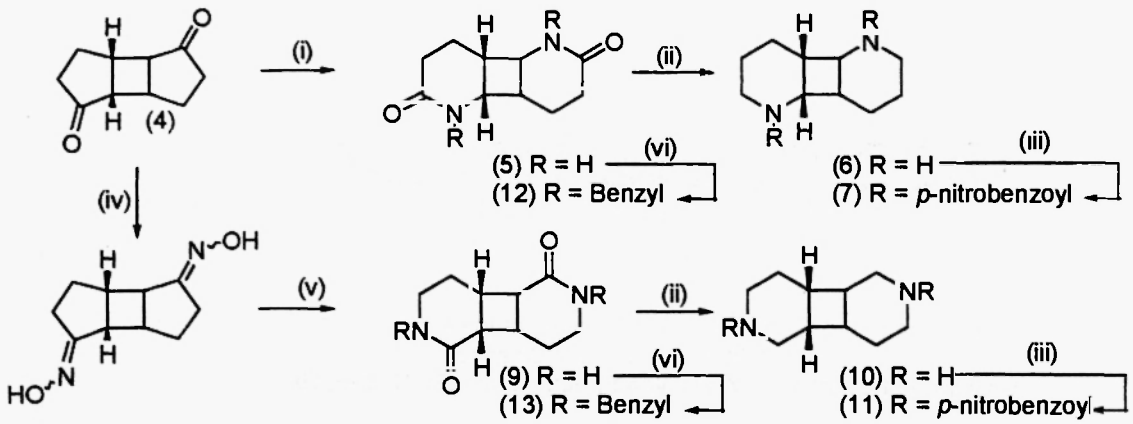
We have been studying the properties and applications of 1,5- and 2,6-diazabiphenylene (2 and 3 respectively), in particular their ability to intercalate with DNA, and sought a simple and flexible synthetic route to these heterocycles that would also allow preparation of more highly substituted diazabiphenylene derivatives. We report here a simple approach to the carbon-nitrogen framework of 1,5- and 2,6-diazabiphenylene, and describe the synthesis of an intermediate of higher oxidation state that can serve as a precursor to 1,5- and 2,6-diazabiphenylene derivatives.

Results and discussion: Our strategy has been to use suitably functionalised cyclobutanes as starting materials which can be elaborated to the diazabiphenylene nucleus by a ring expansion reaction. The tricyclic diketone 4, obtain in 47% yield by the photodimerisation of cyclopentenone in cyclohexane (7), served as the starting point for the synthesis of both the 1,5- and 2,6-diazabiphenylene skeletons (Scheme 1).



Scheme 1. Reagents: (i) NaN_3/conc. HCl, 5-10°C, 30 min. (ii) BH_3/THF, 5°C/20min, then reflux, 30 min (iii) Pyridine/Na_2CO_3/*p*-nitrobenzoyl chloride, reflux, 1hr.
(iv) $NH_2OH.HCl$/2.5M NaOH/EtOH, reflux, 30min, (v) Polyphosphoric acid, 120°C, 10 min. (vi) NaH/DMF, 75°C 1h, then benzyl chloride, 75°C, 4h.

Treatment of 4 with hydrazoic acid generated *in situ* from sodium azide and concentrated hydrochloric acid gave the bislactam 5 in excellent yield (91%, ν_{max} 3060, 1665cm^{-1}), as the product of a Schmidt rearrangement. The formation of this bislactam was predicted on the basis that the group which migrates to the electron deficient nitrogen atom during a Schmidt rearrangement is the one of greater bulk (8). Thus, the bond a-b would be expected to migrate preferentially (Figure 1). This bislactam is the precursor to the 1,5-diazabiphenylene skeleton.

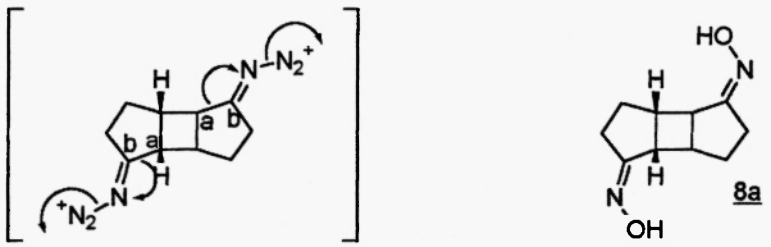


Figure 1

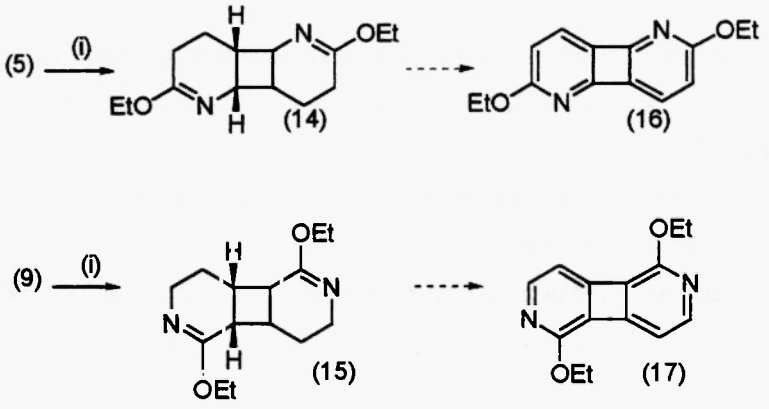
The precursor to the 2,6-diazabiphenylene skeleton is the bislactam 9, which was formed by Beckmann rearrangement of the dioxime 8. This was obtained as a mixture of isomers in 74% yield by treatment of the diketone 4 with hydroxylamine in aqueous ethanolic sodium hydroxide. These were not separated, but were treated with 85% polyphosphoric acid at 120°C for 10 min, to give bislactam 9 in good yield (80%, ν_{max} 3030, 1640cm^{-1}). That the dioxime isomers undergo rearrangement to a single bislactam product indicates that isomerisation to a single preferred isomer occurs prior to bond migration (9). The stereoelectronic control requirements of the Beckmann rearrangement is that the migrating group is anti-periplanar (10) to the N-O bond. This

in turn suggests that isomer 8a is the progenitor of bislactam 9 and is the most thermodynamically favourable isomer that forms under these reaction conditions.

Reduction of 5 with borane/tetrahydrofuran complex at 5°C produced the tricyclic diamine 6, 79%, which possessed the full carbon-nitrogen framework of 1,5-diazabiphenylene. This compound was hygroscopic, and consequently was more conveniently characterised as its bis(N-p-nitrobenzoyl) derivative, 11, 47% from 9.

Initially, the bislactams 5 and 9 were difficult to distinguish spectroscopically, but further confirmatory evidence for their structures came from study of the proton NMR spectra of their bis-N-benzyl derivatives 12 and 13, prepared by treatment with sodium hydride followed by benzyl chloride in DMF. The benzylic protons of 12 appeared as an AB quartet in the 1H NMR spectrum, centered on δ = 4.45ppm, J = 15Hz, which is typical of geminal coupling, whilst those of 13 appeared as a singlet at δ = 4.62ppm. Molecular modelling studies of 12 indicated a restriction of free rotation of each benzyl group by the other lactam ring, so that the benzylic protons were non-equivalent. This feature can only be accommodated by the structure 12 and not by structure 13 in which free rotation of the benzyl groups, and equivalence of the benzyl protons is to be expected.

The bislactams 5 and 9 were converted to the bis-O-ethyl lactim ethers 14 and 15 by treatment with triethyloxonium fluoroborate, in yields of 83% and 62% respectively. These are potential precursors to the diazabiphenylenes 16 and 17 (Scheme 2). It is our intention to carry out conversion 14 and 15 to 16 and 17 by dehydrogenation and we will report on the results of these studies in due course.



Scheme 2. Reagent: (i) $EtO^{+}BF4^{-}/CH_2/Cl_2$, 18h.

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11. Analytical data for compounds 5, 7, 9, 11, 14 and 15.

5 *cis, trans, cis*-3,9-diazatricyclo[6.4.0.0^{2,7}] dodecane-4,10-dione

M.pt. 338°C (sealed tube, decomp.) Found: C 61.97%, H 7.37%, N 14.45%. $C_{10}H_{14}N_2O_2$ requires C 61.83%, H 7.27%, N 14.42%.

7. N,N'-bis(4-nitrobenzoyl)-*cis, trans, cis*-3,9-diazatricyclo[6.4.0.0^{2,7}]dodecane

M.pt. 256-257°C. Found: C 62.39%, H 5.47%, N 12.08%. $C_{24}H_{24}N_4O_6$ requires C 62.07%, H 5.17%, N 12.07%.

9 *cis, trans, cis*-4,10-diazatricyclo[6.4.0.0^{2,7}]dodecane-3,9-dione

M.pt >320°C (decomp.) Found C 61.98%, 7.35%, N 4.17%. $C_{10}H_{14}N_2O_2$ requires C 61.83%, H 7.37%, N 14.42%.

11. N,N'-bis(4-nitrobenzoyl)-*cis, trans, cis*-4,10-diazatricyclo[6.4.0.0^{2,7}]dodecane

M.pt. 242-246°C. (decomp.) Found: C 62.13%, H 5.31%, N 12.00%. $C_{24}H_{24}N_4O_6$ requires C 62.07%, H 5.17%, N 12.07%

14 *cis, trans, cis*-4,10-diethoxy-3,9-diazatricyclo[6.4.0.0^{2,7}]dodeca-3,9-diene

M.pt. 41-43°C. Found: C 66.96%, H 8.78%, N 11.59%. $C_{14}H_{22}N_2O_2$ requires C 67.17%, H 8.86%, N 11.19%. ν_{max} 1660, 1380cm^{-1} δ (90MHz, $CDCl_3$) 1.1-1.5 (6H, t, 7Hz, 2 x CH_3), 1.7-2.6 (10H, m, 1-H, 2x5-H, 2 x 6-H, 2 x 11-H, 2 x 12-H) 3.7-3.9 (2H, m, 2-H, 8-H) 4.0-4.4 (6H, q, 7Hz, 2 x OCH_2) ppm.

15 *cis, trans, cis*-3,9-diethoxy-4,10-diazatricyclo[6.4.0.0^{2,7}]dodeca-3,9-diene

M.pt. 64-65°C. Found: C 67.50%, H 9.03%, N 11.31%. $C_{14}H_{22}N_2O_2$ requires C 67.17%, H 8.86%, N 11.19%. ν_{max} 1660, 1380cm^{-1} δ (90MHz, $CDCl_3$) 1.0-1.5 (6H, t, 7Hz, 2 x CH_3), 1.5-1.8 (4H, m, 1-H, 2-H, 7-H, 8-H) 2.3-2.8 (4H, m, 2 x 6-H, 2 x 12-H) 3.8-4.4 (6H, q, 7Hz, 2 x OCH_2) ppm.

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