Pyrazino[2,1,6-*cd*:5,4,3-*c'd'*]dipyrrolizine: a Doubly Bridged [14]Annulene of Cyclazine Type

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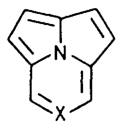
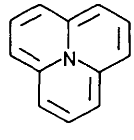
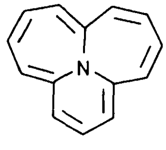
The title compound (**5a**), synthesised in five steps from pyrazino[2,1,6-*cd*]pyrrolizine (**1b**) (6-aza[2.2.3]cyclazine) is stable and diatropic.



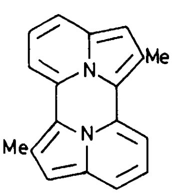
(1)
a; X = CH
b; X = N



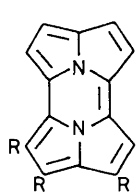
(2)



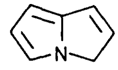
(3)



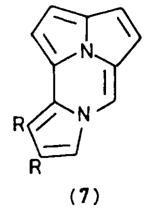
(4)



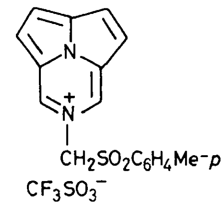
(5)
a; R = H
b; R = CO_2Me



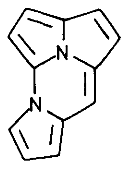
(6)



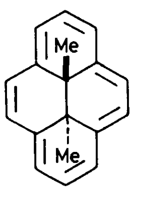
(7)
a; R = H
b; R = CO_2Me



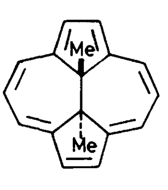
(8)



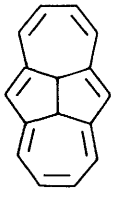
(9)



(10)



(11)



(12)

Of the three uncharged cyclazines originally postulated by Boekelheide,[1a] only [2.2.3]cyclazine (**1a**)[1] (a bridged [10]annulene) and [3.3.3]cyclazine (**2**)[2] (a bridged [12] annulene) have yet been synthesised. [3.4.4]Cyclazine (**3**), a bridged [14]annulene, presents a much more difficult synthetic problem but we have shown[3] that the cyclazine concept can be more easily extended to higher bridged annulene systems by incorporating two separate internal nitrogen atoms, as in the pyrazino[2,1,6-*cd*:5,4,3-*c'd'*]di-indolizine (**4**). We now report the synthesis of pyrazino[2,1,6-*cd*:5,4,3-*c'd'*]dipyrrolizine (**5a**), a doubly bridged [14] annulene.

Our starting point for the synthesis of (**5a**) was 3*H*-pyrrolizine (**6**)[4] which was converted, as previously reported,[5] into 6-aza[2.2.3]cyclazine (**1b**) and thence into the pyrrolocyclazine (**7b**) by a method originally designed[6] for the conversion of pyridines into indolizines. Thus the azacyclazine (**1b**) was quaternised with *p*-tosylmethyl trifluoromethanesulphonate and the resulting salt (**8**)† was treated with dimethyl acetylenedicarboxylate (DMAD), in the presence of triethylamine, to yield (65%) the bright yellow diester (**7b**). The ring system (**7**) is itself new but attempts to obtain the parent compound (**7a**) by hydrolysis and decarboxylation of (**7b**) failed. It seems possible that (**7a**), like its isomer (**9**),[7] is a labile compound and was unable to survive the somewhat severe conditions required for decarboxylation.

Fortunately, the diester (**7b**) was sufficiently reactive, despite its electron-withdrawing substituents, to be converted (61%) into the pyrazinodipyrrolizine tetraester (**5b**) by further reaction with DMAD in the presence of a palladium–charcoal catalyst.[1b] Alkaline hydrolysis of (**5b**) and copper(I)-catalysed decarboxylation[8] in boiling *N,N*-dimethylacetamide[9] yielded the pyrazinodipyrrolizine (**5a**) (34%) as air-stable, cherry-red plates, m.p. 201—203 °C; $\lambda_{max.}$ (EtOH) 252sh, 273, 294, 347, 511, 522, 537, 550, and 565sh nm (log ε 4.30, 4.84, 3.59, 4.28, 3.49, 3.58, 3.87, 4.11, and 2.91); δ_H (360 MHz; $CDCl_3$) 7.86 and 7.93 (J_{AB} 4.5 Hz); δ_C (90.6 MHz; $CDCl_3$) 107.3 (CH), 117.4 (CH), 120.1, and 125.6.

The non-quaternary ^{13}C chemical shifts of (**5a**) are comparable with those of pyrrole (δ_C 107.7 and 118.0) and other electron-rich aromatic compounds, thus providing evidence of strong electron release from the nitrogen atoms. Despite the high π-electron density, however, the protons of (**5a**) are deshielded and the compound must be regarded as diatropic. Of the possible reference compounds, the dihydropyrene (**10**)[10] is probably the best available approximation to a fully aromatic, planar [14]annulene[11] and here the δ_H values for the outer protons are in the range 8.1—8.7 p.p.m. With respect to these values, the protons of (**5a**) are shielded but, since the extent of shielding (taken as 0.8 p.p.m.) does not exceed that of benzenoid protons *ortho* to amino-substituents, this may be attributed entirely to conjugative electron release from the nitrogen atoms. We conclude, therefore, that compound (**5a**) supports a peripheral diamagnetic ring current of about the same magnitude as that in the dihydropyrene (**10**) and the dihydroazupyrene (**11**)[12] (δ_H 8.0—8.8) but larger than that in the 1,6:8,13-bridged [14]annulenes[13] [*e.g.* (**12**); δ_H 7.8—8.2],[14] the π-systems of which are appreciably distorted from planarity.

The δ_H values of (**5a**) contrast sharply with those of the pyrazinodi-indolizine (**4**) (δ_H 5.1—5.9) and reinforce our earlier conclusion[3] that the latter compound, a doubly bridged [16]annulene, has a significant paramagnetic contribution to its ring current despite the fact that, formally, it contains two linked aromatic (indolizine) nuclei.

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† All new compounds gave satisfactory microanalytical results and spectroscopic data consistent with the assigned structures.

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