Synthesis of Cycl[3,2,2]azines, 6-Azacycl[3,2,2]azines, and Cyclopenta[*h*]cycl[4,2,2]azines from 3*H*-Pyrrolizine

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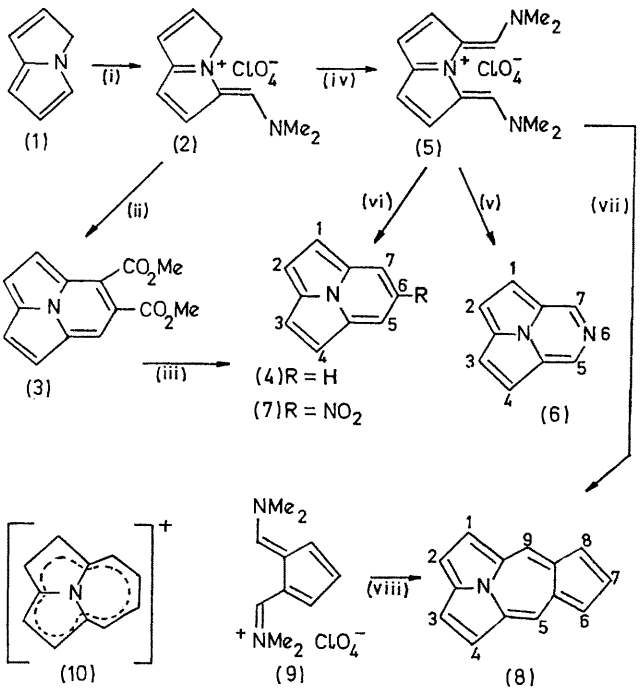
Summary 3*H*-Pyrrolizine has been converted into dimethyl cycl[3,2,2]azine-5,6-dicarboxylate, 6-azacycl-[3,2,2]azine, 6-nitrocycl[3,2,2]azine, and cyclopenta[*h*]-cycl[4,2,2]azine: the last compound is a 14 π-analogue of azulene.

PREVIOUS approaches to the synthesis of cyclazines have started from indolizines[1] or quinolizines;[2] routes starting from pyrrolizines, while clearly possible in principle, seemed less attractive because the synthesis and chemistry of pyrrolizine remained unexplored. Recently, however, 3*H*-pyrrolizine (**1**) has become available by two different routes[3] and its conjugate base has been shown[4] to react with carbonyl compounds at C-3. Our present investigations were inspired by the work of Hafner[5] and of Jutz[6] on the synthesis of conjugated cyclic systems from cyclopentadiene, a compound that resembles pyrrolizine in many ways.

3*H*-Pyrrolizine reacted with *NN*-dimethylformamide–phosphoryl chloride, at low temperature, to give a salt (isolated as the perchlorate) which was assumed to be the 5-dimethylaminomethylene compound (**2**). The conjugate base of this compound was unstable but treatment of the salt with sodium hydride, in the presence of dimethyl acetylenedicarboxylate, gave the cycl[3,2,2]azine derivative (**3**) which was converted, by standard procedures, into cycl[3,2,2]azine (**4**) (m.p. and n.m.r. and u.v. spectra identical with those reported previously [1a,7]). This result confirmed our initial assumption that the reaction of the Vilsmeier reagent with 3*H*-pyrrolizine had taken place at the 5-position.



Reagents: (i) Me_2N·CHO–$POCl_3$–THF; (ii) MeO_2C·C:C·CO_2Me–NaH–DMF; (iii) (a) KOH, (b) $CuCr_2O_4$–quinoline; (iv) Me_2N·-CHS–Ac_2O; (v) NH_3; (vi) $MeNO_2$–KOBu^t; (vii) cyclopentadiene–NaH–DMF; (viii) pyrrolizine–NaH–DMF.

^{1}H *N.m.r. absorptions*[a] (*τ-values*) *of compounds* (**5**), (**7**), *and* (**8**)

(5)			(7)			(8)		
H-1, 4[b]	2·56d	AB (*J* 4·5 Hz)	2·45d	AB (*J* 4·5 Hz)		H-1, 4[c]	2·56d	AB (*J* 4·6 Hz)
H-2, 3[b]	2·36d		2·25d			H-2, 3[c]	2·33d	
H-5, 7	0·79s		1·14s			H-5, 9	1·24s	
						H-6, 8	2·18	AB_2 (*J* 3·8 Hz)
						H-7	2·06	

[a] In $CDCl_3$. [b] The higher-field doublet is assigned to H-1 and H-4 by analogy with cycl[3,2,2]azine. [c] These assignments should possibly be reversed.

The salt (**2**) reacted with *NN*-dimethylthioformamide in acetic anhydride[8]† to give a bis(dimethylaminomethylene)-pyrrolizinium salt, the n.m.r. spectrum of which suggested the presence of more than one isomer. In view of the success of subsequent reactions, however, the mixture must have contained a substantial proportion of the 3,5-isomer

† The more classical Vilsmeier procedures, using *NN*-dimethylformamide, failed to give more than a trace of disubstituted material.

(**5**). Thus treatment of the salt (Scheme) gave 6-azacycl-[3,2,2]azine (**6**), 6-nitrocycl[3,2,2]azine (**7**), and cyclopenta-[*h*]cycl[4,2,2]azine (**8**), the structures of which follow from their n.m.r. spectra (Table). Compound (**8**) was also synthesised (lower yield) from the fulvene derivative (**9**)[9] and pyrrolizine.

Compound (**8**), green plates, m.p. 193—194°, has 14 peripheral π-electrons and incorporates the previously unknown cycl[4,2,2]azine ring-system which might be expected to form an aromatic cation (**10**) with 10 peripheral π-electrons. The ion (**10**) is related to cycl[3,2,2]azine as the tropylium ion is related to benzene and, consequently, compound (**8**) is an analogue of azulene. Its electronic absorption spectrum is similar to that of azulene and electrophilic substitutions (deuteriation, nitration, nitrosation, acylation, bromination, Mannich reaction) occur very readily in the 6- and 8- positions.

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