Heterocyclic Compounds with Bridgehead Nitrogen Atoms. Part 8.[1,2] The Synthesis and Properties of Cyclopenta[4,5]azepino[7,1,2-*cd*]-pyrrolizine (Cyclopenta[*h*][2.2.4]cyclazine)

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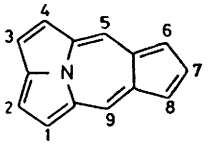
The title compound is obtained (*i*) by the reaction of 5-(*NN*-dimethylaminomethylene)-1-(*NN*-dimethyliminiomethyl)cyclopenta-1,3-diene perchlorate with the conjugate base of 3*H*-pyrrolizine or (*ii*), in better yield, by the reaction of 3,5-bis-(*NN*-dimethylaminomethylene)-3*H*,5*H*-pyrrolizinium perchlorate with the conjugate base of cyclopentadiene. The compound resembles azulene in its visible and near-u.v. spectrum and in the ease of electrophilic attack in the five-membered carbocyclic ring (positions 6 and 8). Products of acylation, nitration, nitrosation, bromination, and *NN*-dimethylaminomethylation are described.

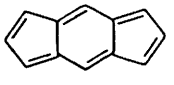
A PRELIMINARY account of our work on the synthesis of cyclazines from 3*H*-pyrrolizine has already been published [2] and full details have been given [1] of that part of the work which is concerned with [2.2.3]cyclazines and their 6-aza-derivatives. The present paper deals with the synthesis of cyclopenta[*h*][2.2.4]cyclazine † (1a) from 3*H*-pyrrolizine and with the properties of this new ring system.

RESULTS AND DISCUSSION

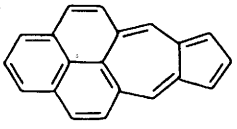
s-Indacene (2) [3] and azuleno[5,6,7-*cd*]phenalene (3) [4] have been synthesised from the cyclopentadiene-iminium salt (5) by reaction with the conjugate bases of cyclopentadiene (pK_a 15) [5] and phenalene (pK_a 19.5),[6] respectively. 3*H*-Pyrrolizine (4) (pK_a 29),[7] though less acidic, is comparable in many ways to these acidic hydrocarbons and its reaction with the perchlorate (5)



(1) a; parent
b; 6,8-D_2
c; 6-CHO
d; 6-COMe
e; 6-NO_2
f; 6-NO
g; 6-NHCOMe
h; 6-Br
i; 6,8-Br_2
j; 6,8-$(CHO)_2$
k; 6,8-$(CH_2NMe_2)_2$
m; 6-Br, 8-NO_2
n; 6-CHO, 8-Br
o; 6-Br, 8-CN
p; 6-Me
q; 6,8-Me_2



(2)



(3)

and sodium hydride, in *NN*-dimethylformamide, gave the cyclopentacyclazine (1a) in 19% yield [Scheme, route (*a*)]. Various attempts to improve this reaction by changing the conditions (see Experimental section) resulted in reduced yields (0—10%) of the cyclazine. Attempts were also made to condense 3*H*-pyrrolizine with the fulvenecarbaldehyde (7) [8] in the presence of (*a*) sodium hydride, (*b*) acetic anhydride, or (*c*) phosphoryl chloride (followed, in the last case, by heating the derived salt with a weak base). Each of these reactions gave a trace of the cyclazine (1a) but none was satisfactory as a preparative method.

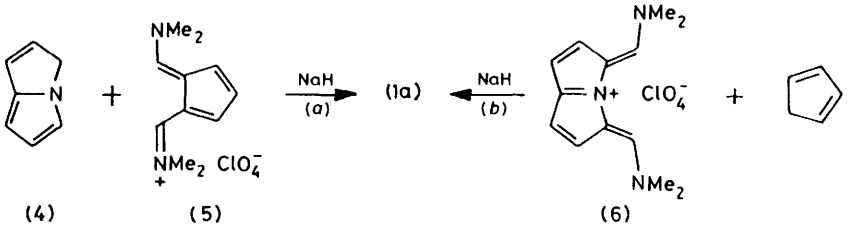
Chemical evidence for the structure of the cyclazine (1a), and improved yields (40—60%), were obtained by a second synthesis in which the bis-(*NN*-dimethylaminomethylene)pyrrolizinium perchlorate (6) [1] and cyclopentadiene were treated with sodium hydride in *NN*-dimethylformamide [Scheme, route (*b*)].

In confirmation of structure (1a), the ^1H n.m.r. spectrum (Table 1) of the cyclazine showed the expected singlet (H-5 and -9) and AB_2 (H-6, -7, and -8) and AB (H-1, -2, -3, and -4) systems. In our preliminary communication,[2] we tentatively assumed, by analogy with [2.2.3]cyclazines, that the low-field doublet of the AB system was due to H-2 and -3, and the high-field doublet to H-1 and -4. We have now shown, however, that these assignments ought to be reversed, since irradiation at the resonance frequency of H-5 and -9 causes a nuclear Overhauser enhancement (23 ± 2%) of the low-field doublet which must, therefore, be due to H-1 and -4, the protons nearer to H-9 and -5. The high-field doublet showed no Overhauser enhancement. Having assigned the ^1H resonances unambiguously, we were then able to identify the corresponding non-quaternary ^{13}C resonances (see Experimental section) of the cyclazine by using the double-resonance technique described by Birdsall and his co-workers.[9]

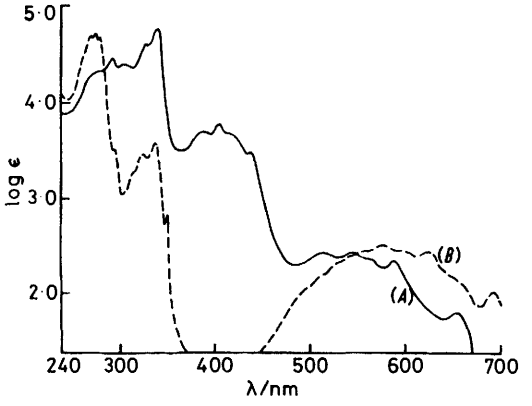
Cyclopenta[*h*][2.2.4]cyclazine, a green crystalline solid, has 14 peripheral π-electrons and is an analogue of azulene. Its visible and near-u.v. spectrum (Figure), like that of azulene, has three main regions of absorption, weak, medium, and strong in intensity, the first being blue-shifted and the other two red-shifted with respect to the corresponding absorptions of azulene. The weak, long-wavelength band (480—680 nm) was suppressed by the addition of a strong acid (Table 2) and the ^1H n.m.r.

† See footnote to Part 7 (preceding paper).

spectrum of the cyclazine, in trifluoroacetic acid, had a two-proton singlet at δ 4.50 (CH_2), showing that a *C*-protonated species was present. The identification of this species as the 6*H*-isomer (8) rests partly on the interpretation (Experimental section) of the remaining ^1H resonances (though this was not strictly definitive owing to the coincidence of certain lines) and partly on the fact that recovery of the cyclazine (1a) from a solution in deuteriotrifluoroacetic acid gave the 6,8-dideuterio-compound (1b). The protonation of the cyclazine at C-6 is analogous to the protonation of azulene at C-1 and is energetically favourable because of the formation of a [2.2.4]cyclazinylium ion, the unknown parent (9) of which may be regarded as a 10π-electron analogue of the tropylium ion.



SCHEME



Electronic spectra of (*A*) cyclopenta[4,5]azepino[7,1,2-*cd*]-pyrrolizine (1a) (——) and (*B*) azulene in ethanol (– – – –)

The resemblance of cyclopenta[*h*][2.2.4]cyclazine to azulene was further shown in various electrophilic substitution reactions which occurred, at the 6- and 8-positions, under mild conditions similar to those used in the azulene series. Monosubstitution was carried out (*a*) by Vilsmeier acylation (Me_2NCOR–$POCl_3$), to give a carbaldehyde and an acetyl derivative, (*b*) by nitration with tetranitromethane, (*c*) by nitrosation with sodium nitrite in acetic acid, and (*d*) by bromination with *N*-bromosuccinimide. The acyl and nitro-derivatives were identified, from their ^1H n.m.r. spectra (Table 1), as the 6-substituted compounds (1c), (1d), and (1e) by the deshielding effects of the carbonyl and nitro-groups on the protons at positions 5 (singlet) and 7 (doublet). The spectrum of the 6-nitroso-compound (1f) showed an even larger deshielding of H-5, but the H-7 resonance was obscured by the multiplet due to H-1, -2, -3, and -4; otherwise the spectrum was very similar to that of the 6-nitro-compound, thus confirming the structure. Reduction of the 6-nitro-compound with zinc–acetic anhydride–acetic acid gave the 6-(*N*-acetylamino)-compound (1g). The 6-bromo-compound (1h) was unstable and its n.m.r. spectrum could not be obtained, but its structure is not in doubt since dibromination of the parent cyclazine (1a) gave the 6,8-dibromo-compound (1i), readily identifiable from its simple n.m.r. spectrum.

Other examples of 6,8-disubstitution were observed when the cyclazine (1a) was formylated with an excess of the Vilsmeier reagent and when the Mannich reaction was carried out with paraformaldehyde and *NNN'N'*-tetramethyldiaminomethane. The 6-bromo-8-nitro-cyclazine (1m) was obtained by bromination of the 6-

TABLE 1

^1H N.m.r. data [a] of cyclopenta[4,5]azepino[7,1,2-*cd*]pyrrolizines (δ/p.p.m. from $SiMe_4$)

Compound	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8	H-9	*J*/Hz
(1a)	7.67	7.44	7.44	7.67	8.76	7.82	7.94	7.82	8.76	$J_{1,2}$ 4.6, $J_{6,7}$ 3.8
(1p)	7.58	7.33	7.33	7.54	8.56	(2.86)	7.76	7.74	8.58	
(1q)	7.52	7.23	7.23	7.52	8.42	(2.82)	7.60	(2.82)	8.42	$J_{1,2}$ 4.6
(1k)	7.67	7.49	7.49	7.67	8.87	(3.11) (2.32)	7.83	(3.11) (2.32)	8.87	$J_{1,2}$ 4.5
(1i)	7.71	7.46	7.46	7.71	8.63		7.81		8.63	$J_{1,2}$ 4.8
(1c)	← 7.24—7.68 →				10.30	(9.79)	8.01	*b*	8.50	$J_{7,8}$ 4.25
(1d)	← 7.45—7.86 →				10.30	(2.76)	8.16	*b*	8.61	
(1e)	← 7.84—8.11 →				10.35		8.51	7.58	8.96	$J_{7,8}$ 4.5
(1f)	← 7.88—8.15 →				10.65		*b*	7.64	8.98	$J_{7,8}$ 4.7
(1j)	8.16	8.04	8.04	8.16	10.51	(10.45)	8.49	(10.45)	10.51	$J_{1,2}$ 5.0
(1m)	← 7.87—8.08 →				9.12		8.54		10.33	
(1n)	← 7.71—8.03 →				10.38	(10.16)	8.20		8.98	

[a] In $CDCl_3$; values in parentheses refer to protons in substituent groups. [b] Signal included in H-1, -2, -3, and -4 multiplet.

nitro-compound and by nitration of the 6-bromo-compound, and the 8-bromo-6-carbaldehyde (1n) by formylation of the bromo-compound. The 6,8-dibromocyclazine gave the 6-bromo-8-cyano-compound (1o) on being heated with copper(I) cyanide in pyridine.

TABLE 2

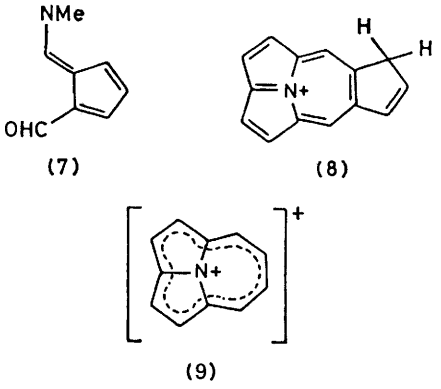
U.v. and visible spectra [a] of cyclopenta[4,5]azepino-[7,1,2-cd]pyrrolizines [$\lambda_{max.}$/nm (log ε)] [b]

Compound			
(1a)	*273* (4.27)	387 (3.68)	516 (2.43)
	294 (4.45)	406 (3.77)	544 (2.42)
	306 (4.38)	*415* (3.67)	*560* (2.39)
	328 (4.60)	438 (3.47)	589 (2.35)
	341 (4.75)		655 (1.82)
(1p)	272 (4.14)	394 (3.57)	*548* (2.13)
	299 (4.42)	422 (3.58)	572 (2.21)
	333 (4.54)	443 (3.52)	621 (2.16)
	344 (4.63)	*452* (3.47)	693 (1.58)
(1q)	275 (4.12)	395 (3.58)	*554* (2.20)
	305 (4.44)	429 (3.62)	602 (2.26)
	335 (4.50)	*450* (3.62)	648 (2.17)
	346 (4.61)	458 (3.66)	>700
(1i)	275 (4.46)	396 (3.85)	576 (2.60)
	295 (4.47)	*405* (3.84)	616 (2.56)
	313 (4.32)	*423* (3.84)	*685* (1.98)
	344 (4.77)	430 (3.87)	
	357 (4.95)	448 (3.90)	
		457 (3.93)	
(1c)	240 (4.38)	462 (4.15)	510 (3.43)
	258 (4.55)		*592* (2.16)
	305 (4.25)		
	313 (4.26)		
	350 (4.70)		
	366 (4.94)		
(1e)	242 (4.07)	474 (4.18)	*520* (3.74)
	271 (4.59)		*558* (3.15)
	305 (4.03)		
	376 (4.62)		
(1j)	273 (4.54)	460 (4.04)	505 (3.71)
	298 (4.50)		
	372 (4.77)		
(1o)	234 (4.25)	413 (3.74)	528 (2.79)
	276 (4.26)	*434* (3.75)	
	292 (4.26)	454 (3.82)	
	318 (4.10)		
	347 (4.58)		
	363 (4.77)		
(1a) [c]	248 (4.19)	398 (3.76)	
	292 (4.73)		
	335 (4.22)		
	348 (4.47)		

[a] In ethanol unless otherwise stated. [b] Italicised values refer to shoulders or inflections. [c] In 1.5M ethanolic perchloric acid.

1,3-Disubstituted azulenes lacking strongly electronegative groups may undergo electrophilic substitution at the 5- or 2-positions.[10] To investigate the possibility of similar reactions in the cyclopenta[2.2.4]-cyclazine series, we chose the 6,8-dibromo-compound for an initial study. Three reactions (formylation, nitration, and bromination) were tried, but no substitution was observed in the cyclazine portion of the molecule. Much decomposition occurred in all cases and small yields of the 8-bromo-6-carbaldehyde (1n) and 6-bromo-8-nitro-compound (1m) were obtained. Thus the only identifiable mode of reaction was electrophilic attack in the carbocyclic ring with displacement of bromine. A similar halogen displacement occurs as a minor reaction pathway in the acetylation of 1,3-dichloroazulene.[10a]

It seemed possible, at this point, that methyl groups might be more effective than bromine atoms in preventing substitution at the 6- and 8-positions. The required 6,8-dimethyl compound (1q) was obtained by reduction of the 6,8-dicarbaldehyde (1j), either by the Huang-Minlon procedure [11] or, in better yield, by reaction with diborane.[12] The 6-methyl compound (1p) was obtained similarly.



An attempted Vilsmeier formylation of the 6,8-dimethylcyclazine (1q) caused much decomposition and three products were obtained in trace amounts. Mass spectrometry showed that two of these (M^+ 247 and 275) were probably formyl and diformyl derivatives, respectively, of the 6,8-dimethylcyclazine. Treatment of the dimethylcyclazine with tetranitromethane gave at least eight products, all in very small yield, two of which (M^+ 264 and 309) were nitro- and dinitro-derivatives, respectively. The positions of substitution were not determined. Another product (M^+ 250) was identified, by its ^{1}H n.m.r. spectrum, as the 6-methyl-8-nitrocyclazine, showing that displacement of a blocking group had again taken place. We conclude from these results that electrophilic substitution reactions are unlikely to be a useful source of cyclopenta[*h*][2.2.4]cyclazines bearing substituents in the cyclazine portion of the molecule.

Cyclopenta[*h*][2.2.4]cyclazines show a further similarity to azulenes [13] in the effect of 6- and 8-substituents (1- and 3-substituents in azulenes) on the electronic absorption spectra (Table 2); acyl and nitro-groups cause a marked hypsochromic shift of the long-wavelength band (which is then partially obscured by the second absorption band) while methyl groups and bromine cause a bathochromic shift.

EXPERIMENTAL

N.m.r. data were obtained at 100 (for ^{1}H) and 25.2 MHz (for ^{13}C) and, unless otherwise stated, refer to solutions in deuteriochloroform with $SiMe_4$ as internal standard. I.r. data refer to Nujol mulls. Alumina for chromatography (Laporte type H) was deactivated, where specified, by treatment with 10% aqueous acetic acid (0.05 or 0.1 cm^3 per g alumina). Silica for t.l.c. and p.l.c. was Merck Kieselgel G. For drying, benzene and ether were kept over sodium, *NN*-dimethylacetamide, pyridine, and diglyme [bis-(2-methoxyethyl) ether] were kept over Linde molecular sieve (type

4A), and *NN*-dimethylformamide (DMF), after being kept over molecular sieve, was distilled from calcium hydride. Light petroleum refers to the fraction of b.p. 60—80 °C. Extracts were dried over magnesium sulphate (unless otherwise stated) and evaporated under reduced pressure.

Cyclopenta[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1a).—(*a*) A solution of freshly distilled 3*H*-pyrrolizine (8.0 g) in dry DMF (500 cm^3) was stirred under nitrogen and 5-(*NN*-dimethylaminomethylene)-1-(*NN*-dimethyliminiomethyl)-cyclopenta-1,3-diene perchlorate [8] (5) (22.1 g) was added in one batch. The resulting suspension was stirred for 5 min and sodium hydride (3.9 g of 50% oil dispersion) was added in small portions during 30 min. After being stirred for a further 15 min at room temperature, the solution was heated at 70 °C for 30 min and under reflux for 18 h. A nitrogen atmosphere was maintained throughout. The solution was then cooled, filtered through Kieselguhr, and evaporated, and the residue was chromatographed twice on deactivated alumina. The first column removed most of the tarry material and the second column separated the mobile material into (*i*) a red-brown band, eluted with benzene–light petroleum (1 : 1), and (*ii*) a brown-orange band eluted with benzene. The material from band (*ii*) was not identified but band (*i*) yielded *cyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (2.73 g, 19%), as green plates, m.p. 198—199 °C (from light petroleum) (Found: C, 88.3; H, 4.5; N, 7.3. $C_{14}H_9N$ requires C, 87.9; H, 4.7; N, 7.3%), forming red (concentrated) or green (dilute) solutions; δ_C 113.56 (C-2 and -3), 120.81 (C-6 and -8), 121.76 (C-5 and -9), 122.54 (C-1 and -4), 131.16 (C-7), and 131.35 (s, C-5a and -8a); C-2a, -4a, and -9a resonances not definitely identified.

The following molecular complexes were prepared in ethanol and recrystallised from the same solvent: the 1,3,5-*trinitrobenzene complex*, m.p. 168—169 °C (Found: C, 58.9; H, 2.8; N, 13.8. $C_{20}H_{12}N_4O_6$ requires C, 59.4; H, 3.0; N, 13.9%); the *picric acid complex*, m.p. 335 °C (Found C, 57.3; H, 2.7; N, 13.2. $C_{20}H_{12}N_4O_7$ requires C, 57.15; H, 2.9; N, 13.3%), and the 2,4,7-*trinitrofluorenone complex*, m.p. 206—207 °C (Found: C, 63.7; H, 2.5; N, 10.85. $C_{27}H_{14}N_4O_7$ requires C, 64.0; H, 2.8; N, 11.1%).

Various attempts were made to improve reaction (*a*): (*i*) by using other solvents (pyridine, dimethyl sulphoxide, tetrahydrofuran, diglyme, or hexamethylphosphoramide); (*ii*) by using butyl-lithium (reaction in tetrahydrofuran) as the base; (*iii*) by adding the sodium hydride before the iminium salt (in DMF); (*iv*) by changing the reaction temperature and/or duration. All these variations gave lower yields (0—10%) than the one described above.

(*b*) A solution of 3,5-bis-(*NN*-dimethylaminomethylene)-3*H*,5*H*-pyrrolizinium perchlorate [1] (6) (0.398 g) and cyclopentadiene (0.170 g), in dry DMF (150 cm^3) was stirred under nitrogen and sodium hydride (0.120 g of 50% oil dispersion) was added, in small portions, during 20 min. After being stirred under nitrogen for 20 h, the solution was filtered through Kieselguhr and evaporated. The residue was chromatographed on deactivated alumina, in benzene–light petroleum (1 : 1), to give the cyclopenta-azepinopyrrolizine (0.108 g; 45%), m.p. 198—199 °C, i.r. and n.m.r. spectra identical with those of the product obtained by method (*a*). Repetition of the reaction on a similar scale gave yields in the range 40—48% but one reaction, on a larger scale, gave an exceptional yield of 61%.

Measurement of Nuclear Overhauser Enhancement (*N.O.E.*).—The procedure used was that of Bell and Saunders.[14] The sample solution of the cyclopenta-azepinopyrrolizine (1a), in deuteriochloroform, was deoxygenated by shaking with aqueous sodium dithionite. The n.o.e. was found by setting the second r.f. field (H_2) at the strength and frequency (121 Hz above the centre of the AB system) required to saturate H-5 and -9, and the intensities of the AB resonances were measured by electronic integration. The intensity of the low-field doublet was greater than that of the high-field doublet. The frequency of H_2 was then moved to a position 121 Hz below the centre of the AB system (where no proton resonance is present) and the AB intensity measurement was repeated to give a standard area. The intensities of the low- and high-field doublets were then equal to each other and to the intensity observed for the high-field doublet when H-5 and -9 were being irradiated. The intensity measurement was repeated ten times for each value of H_2 and the average n.o.e. of the low-field doublet was calculated.

Protonation and Deuteriation of Cyclopenta[4,5]*azepino*-[7,1,2-cd]*pyrrolizine*.—(a) *Protonation*. A solution of the cyclazine (1a), in trifluoroacetic acid, contained the 6*H*-cyclopenta[4,5]azepino[7,1,2-*cd*]pyrrolizinium ion (8), δ 4.50 (2 H, s, 6-CH_2), 7.84 (2 H, s, H-7 and -8), 8.58 (2 H, d, H-2 and -3), 8.68 and 8.72 (2 H, d + d = t, H-1 and -4), 9.38 (1 H, s, H-5), and 9.47 (1 H, s, H-9). (It is possible that the assignments for H-2,-3 and H-1,-4 ought to be interchanged, and similarly for H-5 and H-9.)

(b) *Deuteriation*. The cyclopenta-azepinopyrrolizine (0.072 g) was dissolved in [^{2}H]trifluoroacetic acid (2 cm^3) and the solution was kept at room temperature for 45 min. The product was then recovered by dilution with deuterium oxide, neutralisation with anhydrous potassium carbonate, and extraction with ether. The cycle of operations was then repeated and the final product was recrystallised from light petroleum to give 6,8-dideuteriocyclopenta[4,5]-azepino[7,1,2-*cd*]pyrrolizine (0.056 g) (M^+, 193. $C_{14}H_7D_2N$ requires *M*, 193); δ 7.38 (2 H, d, H-2 and -3), 7.62 (2 H, d, H-1 and -4), 7.89 (1 H, s, H-7), and 8.70 (2 H, s, H-5 and -9).

Cyclopenta[4,5]*azepino*[7,1,2-cd]*pyrrolizine-6-carbaldehyde* (1c).—A solution of the cyclopenta-azepinopyrrolizine (1a) (0.112 g) in dry DMF (5 cm^3) was cooled (ice–sodium chloride) and stirred while phosphoryl chloride (0.190 g) was added dropwise. An orange precipitate appeared and stirring was continued for 30 min at ice–sodium chloride temperature, 30 min at room temperature, and 30 min at 70 °C. Saturated aqueous sodium carbonate (10 cm^3) was added and the solution was heated for 30 min at 70 °C, cooled, and diluted with 2M aqueous sodium hydroxide. Extraction with chloroform, evaporation of the extract, and chromatography of the residue on deactivated alumina, in ether, yielded the *aldehyde* (0.115 g, 89%), copper-red plates, m.p. 135—136 °C (from ethanol) (Found: C, 81.9; H, 4.0; N, 6.1. $C_{15}H_9NO$ requires C, 82.2; H, 4.1; N, 6.4%); $\nu_{max.}$ 1 640 cm^{-1} (C=O).

Cyclopenta[4,5]*azepino*[7,1,2-cd]*pyrrolizine-6,8-dicarbaldehyde* (1j).—The cyclopenta-azepinopyrrolizine (1a) (0.104 g), in dry DMF (10 cm^3), was treated with phosphoryl chloride (0.50 g), as in the procedure for mono-formylation, and the solution was heated at 100 °C for 2 h. Hydrolysis with aqueous sodium carbonate (10 min at 100 °C) and work-up as for the mono-aldehyde yielded, after chromatography on deactivated alumina in chloroform, the orange *dialdehyde* (0.115 g, 85%), m.p. 315—316 °C (decomp.) (from ethanol) (Found: C, 77.45; H, 3.3; N, 5.7. $C_{16}H_9NO_2$ requires C, 77.7; H, 3.7; N, 5.7%); $\nu_{max.}$ 1 650 cm^{-1} (C=O).

6-*Acetylcyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1d).—

The cyclopenta-azepinopyrrolizine (1a) (0.102 g), in dry *NN*-dimethylacetamide (3.5 cm³), was treated with phosphoryl chloride (0.4), as in the procedures for formylation, and the solution was stirred at ice–sodium chloride temperature for 1 h and at 100 °C for 2 h. Hydrolysis with aqueous sodium carbonate, work-up, and chromatography yielded the *acetyl compound* (0.090 g, 76%), orange-red plates, m.p. 144—145 °C (from ethanol) (Found: C, 82.2; H, 4.7; N, 6.3. $C_{16}H_{11}NO$ requires C, 82.4; H, 4.75; N, 6.0%); $\nu_{max.}$ 1 630 cm^{-1} (C=O).

Reaction of the ketone with hydroxylammonium chloride and sodium acetate in 50% aqueous ethanol (75 °C for 3 h) and purification of the product by chromatography gave the *oxime* (82%), brown-yellow needles, m.p. 203—204 °C (from benzene) (Found: C, 77.1; H, 4.7; N, 11.0. $C_{16}H_{12}N_2O$ requires C, 77.4; H, 4.9; N, 11.3%).

6-*Nitrocyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1e).—A solution of the cyclopenta-azepinopyrrolizine (1a) (0.101 g) in dry pyridine (5 cm³) was cooled to 0 °C, stirred under nitrogen, and treated dropwise with tetranitromethane (0.110 g) in dry ethanol (2 cm³). The solution was stirred for 1 h at 0 °C, and then diluted with ice-cold 2M aqueous sodium hydroxide (30 cm³). The solution was extracted repeatedly with chloroform and the extract was washed with 2M aqueous hydrochloric acid (2×), saturated aqueous sodium carbonate (2×), and finally with water before being dried (K_2CO_3) and evaporated. Chromatography of the residue on deactivated alumina, in chloroform, yielded the *nitro-compound* (0.093 g, 75%), red plates, m.p. 249—250 °C (from ethanol) (Found: C, 70.8; H, 3.15; N, 11.8. $C_{14}H_8N_2O_2$ requires C, 71.2; H, 3.4; N, 11.9%); δ [$(CD_3)_2SO$ at 120 °C] 7.70 (1 H, d, H-8), 8.06—8.41 (5 H, m, H-1, -2, -3, -4, and -7), 9.27 (1 H, s, H-9), and 10.13 (1 H, s, H-5).

6-(N-*Acetylamino*)*cyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1g).—A stirred solution of the foregoing nitro-compound (0.111 g) and sodium acetate (0.3 g) in acetic acid (8 cm³) and acetic anhydride (8 cm³) was treated with zinc dust (0.75 g), in small portions, during 5 min. The solution was stirred for 1 h, diluted with water (100 cm³), and extracted with dichloromethane. The extract was washed with aqueous ammonia (2×) and then with water (2×), dried, and evaporated. Chromatography of the residue on deactivated alumina, in chloroform, yielded the dark green N-*acetylamino-compound* (0.091 g, 77%), m.p. 232—233 °C (from ethanol) (Found: C, 77.4; H, 4.6; N, 11.0. $C_{16}H_{12}N_2O$ requires C, 77.4; H, 4.9; N, 11.3%); δ [$(CD_3)_2SO$ at 105 °C] 3.22 (3 H, s, Me), 7.79—8.08 (5 H, m, H-1, -2, -3, -4, and -8), 8.66 (1 H, d, H-7), 9.07 (1 H, s, H-9), 9.28 (1 H, s, H-5), and 10.38 (1 H, s, NH).

6-*Nitrosocyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1f).—A stirred solution of the cyclopenta-azepinopyrrolizine (1a) (0.100 g) in acetic acid (10 cm³) was cooled to 10 °C and a solution of sodium nitrite (0.060 g) in water (3 cm³) was added dropwise. After 15 min, the solution was diluted with water, basified with sodium carbonate, and extracted with chloroform. Evaporation of the dried extract and chromatography of the residue on deactivated alumina, first in ether to remove a trace of pink impurity, and then in chloroform, gave the *nitroso-compound* (0.024 g, 21%), red-brown needles, m.p. 340 °C (from acetone) (Found: C, 76.05; H, 3.55; N, 12.5. $C_{14}H_8N_2O$ requires C, 76.35; H, 3.7; N, 12.7%).

6-*Bromocyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1h).—A solution of the cyclopenta-azepinopyrrolizine (1a) (0.105 g) in dry benzene(5 cm³) was shaken with *N*-bromosuccinimide (0.099 g) until the starch–iodide test showed the absence of active bromine. The solution was chromatographed directly on alumina, in benzene, and the eluate was evaporated at 25 °C to give the green, unstable *bromo-compound* (0.143 g, 98%), m.p. 154—158 °C (decomp.) (Found: M^+, 268.9 841 and 270.9 825. $C_{14}H_8BrN$ requires *M*, 268.9 841 and 270.9 821), which decomposed rapidly in solution, with deposition of black material, and less rapidly in the solid state.

6,8-*Dibromocyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1i).—A solution of the cyclopenta-azepinopyrrolizine (1a) (0.101 g) in dry benzene (15 cm³) was shaken with *N*-bromosuccinimide (0.195 g) and kept for 3 h at room temperature. Chromatography on alumina, in benzene, yielded the *dibromo-compound* (0.120 g, 65%), green needles, m.p. 147—148 °C (from benzene–light petroleum) (Found: C, 48.1; H, 1.7; N, 3.8. $C_{14}H_7Br_2N$ requires C, 48.2; H, 2.0; N, 4.0%).

6,8-*Bis*-(NN-*dimethylaminomethyl*)*cyclopenta*[4,5]*azepino*-[7,1,2-cd]*pyrrolizine* (1k).—A solution of the cyclopenta-azepinopyrrolizine (1a) (0.108 g) in *NNN'N'*-tetramethyldiaminomethane (5 cm³), containing paraformaldehyde (0.074 g), was treated with acetic acid (0.5 cm³), shaken for a short time, and kept at room temperature for 48 h, during which a red oil was deposited. Water and sodium carbonate were added and the product was extracted into ether. The extract was dried and evaporated and the residue was chromatographed on deactivated alumina, first in benzene and then in ether which eluted the green *diamine* (0.149 g, 86%), m.p. 110—111 °C (from benzene) (Found: C, 78.6; H, 7.5; N, 13.5. $C_{20}H_{23}N_3$ requires C, 78.65; H, 7.6; N, 13.8%).

8-*Bromocyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine*-6-*carbaldehyde* (1n).—A stirred solution of the freshly prepared bromo-compound (1h) (0.072 g) in dry DMF (10 cm³) was cooled in ice and phosphoryl chloride (0.050 g) was added dropwise. The solution was stirred for 30 min at 0 °C, for 1.5 h at room temperature, and for 10 min at 70 °C. It was then treated with an excess of 2M aqueous sodium hydroxide and extracted with chloroform. The extract was dried and evaporated, and the residue was chromatographed on deactivated alumina. Elution with light petroleum gave the 6,8-dibromocyclopenta-azepinopyrrolizine (0.011 g), though none was present in the starting material, and elution with ether gave the red-orange *bromoaldehyde* (0.057 g, 72%), decomp. 230—320 °C (Found: C, 60.6; H, 2.5; N, 4.4. $C_{15}H_8BrNO$ requires C, 60.4; H, 2.7; N, 4.7%).

6-*Bromo*-8-*nitrocyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1m).—(*a*) A thoroughly shaken suspension of the 6-nitro-compound (1e) (0.093 g) and *N*-bromosuccinimide (0.069 g) in dry benzene(23 cm³) was kept at room temperature for 20 h, after which the starch–iodide test showed incomplete reaction. The solution was then heated under reflux for 10 min and chromatographed directly on deactivated alumina. Elution with benzene–ether (1 : 1) yielded the red *bromo-nitro-compound* (0.107 g, 80%), m.p. 287—288 °C (from ethanol–chloroform) (Found: C, 54.3; H, 2.0; N, 8.9. $C_{14}H_7BrN_2O_2$ requires C, 54.6; H, 2.2; N, 8.9%).

(*b*) A solution of the freshly prepared bromo-compound (1h) (0.020 g) in dry pyridine (2 cm³) was cooled (ice–sodium chloride) and treated, dropwise, with tetranitromethane (0.020 g) in dry ethanol (2 cm³). The green solution became red and, after 10 min, dark material began to form. The solution was then diluted with ice-cold 2M aqueous sodium hydroxide and extracted with chloroform. The extract was

washed with dilute hydrochloric acid, with aqueous sodium carbonate, and finally with water, dried, and evaporated. Chromatography of the residue on alumina gave, by elution with benzene, the 6,8-dibromocyclopenta-azepinopyrrolizine (0.002 g) and, by elution with chloroform, the bromonitro-compound (0.006 g, 25%), m.p. 287—288 °C, i.r., n.m.r., and mass spectra identical with those of the product obtained by method (*a*).

6-*Bromo*-8-*cyanocyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1o).—A solution of the dibromo-compound (1i) (0.111 g) in pyridine (25 cm^3) was heated under reflux with an excess of copper(I) cyanide and a trace of copper(I) iodide for 24 h. After being cooled, the solution was filtered through Kieselguhr and evaporated, and the residue was chromatographed on alumina, in benzene, to give (*i*) starting material (0.039 g): (*ii*) the *bromocyano-compound* (0.038 g, 41%), brown needles, m.p. 240—242 °C (Found: C, 60.9; H, 2.1; N, 9.2. $C_{15}H_7BrN_2$ requires C, 61.05; H, 2.4; N, 9.5%); $\nu_{max.}$ 2 240 cm^{-1} (C≡N), δ [$(CD_3)_2SO$ at 120 °C] 8.07—8.36 (5 H, m, H-1,-2,-3,-4, and -7), 9.13 (1 H, s, H-5), and 9.21 (1 H, s, H-9): and (*iii*) the orange-yellow 6,8-dicyanocyclopenta[4,5]azepino[7,1,2-*cd*]pyrrolizine (0.002 g, 2.5%), m.p. 270—273 °C; M^+ 241; δ 8.00 (2 H, d, H-2 and -3), 8.18 (2 H, d, H-1 and -4), 8.34 (1 H, s, H-7), and 9.26 (2 H, s, H-5 and -9).

6-*Methylcyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1p).—(*a*) A solution of the aldehyde (1c) (0.059 g) and hydrazine hydrate (2 cm^3) in diethylene glycol (20 cm^3) and ethanol (5 cm^3) was heated on a water-bath for 30 min. Finely powdered potassium hydroxide (1 g) was added, low boiling material was distilled off, and the residual solution was heated under reflux for 3 h. After being cooled, the solution was diluted with water and extracted with ether. The extract was washed with water, dried, and evaporated, and the residue was chromatographed on alumina, in benzene, to give the 6-*methylcyclopenta-azepinopyrrolizine* (0.021 g, 39%) as green plates, m.p. 157—158 °C (from light petroleum) (Found: C, 87.8; H, 5.1; N, 6.7. $C_{15}H_{11}N$ requires C, 87.8; H, 5.4; N, 6.8%).

(*b*) Freshly distilled boron trifluoride–diethyl ether complex (0.59 cm^3) was added, dropwise, to a stirred solution of the aldehyde (1c) (0.051 g) in dry diglyme (25 cm^3) and diethyl ether (10 cm^3). The solution was then added, dropwise, under nitrogen, to a stirred, ice-cooled suspension of sodium borohydride (0.260 g) in dry diglyme (5 cm^3) and the whole was stirred for 30 min at 0 °C and for 1 h at room temperature. The solution was poured into ice-cold 2M aqueous potassium hydroxide and extracted with light petroleum. Evaporation of the washed (water) and dried extract, and chromatography of the residue on alumina, in benzene, yielded the methyl compound (0.031 g, 64%), m.p. 157—158 °C, identical with the specimen prepared by method (*a*).

6,8-*Dimethylcyclopenta*[4,5]*azepino*[7,1,2-cd]*pyrrolizine* (1q).—(*a*) The dialdehyde (1j) (0.052 g) was heated under reflux with hydrazine hydrate (2 cm^3) in ethanol (10 cm^3) for 45 min. The resulting red-brown suspension was added dropwise to diethylene glycol (20 cm^3) containing finely powdered potassium hydroxide (1 g). Low-boiling material was distilled off, and the residual solution was heated under reflux for 3.5 h. Work-up as described for the monomethyl compound gave the 6,8-*dimethylcyclopenta-azepinopyrrolizine* (0.023 g, 50%) as green plates, m.p. 155—156 °C (from light petroleum) (Found: C, 87.7; H, 5.6; N, 6.3. $C_{16}H_{13}N$ requires C, 87.6; H, 6.0; N, 6.4%).

(*b*) The dialdehyde (0.190 g), in diglyme (50 cm^3) and ether (20 cm^3), was treated with boron trifluoride–diethyl ether complex (1.9 cm^3) and the resulting solution was added, during 45 min, to sodium borohydride (0.7 g) in diglyme (40 cm^3). Details were as described for the diborane reduction of the monoaldehyde. After a further 30 min at 0 °C and 1 h at room temperature, the solution was worked up, as described for the monomethyl compound, to yield the dimethyl compound (0.113 g, 67%), m.p. 155—156 °C, identical with the specimen prepared by method (*a*).

Attempted Formylation of 6,8-*Dibromocyclopenta*[4,5]-*azepino*[7,1,2-cd]*pyrrolizine*.—A solution of the dibromo-compound (1i) (0.051 g) in dry DMF (10 cm^3) was cooled to 0 °C and stirred while phosphoryl chloride (0.030 g), in dry DMF (4 cm^3), was added dropwise during 5 min. The solution was stirred for a further 15 min at 0 °C, 30 min at 60 °C, and 30 min under reflux. T.l.c. showed the presence of starting material but, since tarry material was being formed, the solution was cooled, diluted with ice–water, and basified with 2M aqueous sodium hydroxide. Extraction with chloroform, evaporation of the dried extract, and chromatography of the residue on alumina, in light petroleum–benzene (4 : 1), yielded (*i*) starting material (0.014 g) and (*ii*) 8-bromocyclopenta[4,5]azepino[7,1,2-*cd*]pyrrolizine-6-carbaldehyde (0.008 g, 18%), ^1H n.m.r. and mass spectra identical with those of an authentic specimen.

Attempted Nitration of 6,8-*Dibromocyclopenta*[4,5]*azepino*-[7,1,2-cd]*pyrrolizine*.—The dibromo-compound (1i) (0.027 g), in pyridine (10 cm^3) was treated with tetranitromethane (0.015 g) in ethanol (2 cm^3) as described for previous nitrations. After 1.5 h at 0 °C, the solution was worked up and the chloroform-soluble fraction was separated by p.l.c. on silica to yield a green band (probably starting material), a red-brown band (unidentified and very weak), and a red band that yielded 6-bromo-8-nitrocyclopenta[4,5]azepino-[7,1,2-*cd*]pyrrolizine (0.002 g), i.r. and ^1H n.m.r. spectra identical with those of an authentic specimen.

Attempted Formylation of 6,8-*Dimethylcyclopenta*[4,5]-*azepino*-[7,1,2-cd]*pyrrolizine*.—The dimethyl compound (1q) (0.028 g), in dry DMF was treated with a two-fold excess of phosphoryl chloride, as described for the attempted formylation of the dibromo-compound. After 5 min at 0 °C and 5 min at 60 °C, tarry material had been formed and the solution was worked up in the usual way. Chromatography on alumina yielded (*i*) starting material (0.0 035 g): (*ii*) a yellow-green band that yielded a dark powder (0.0 002 g), M^+ 275 (diformyl derivative requires M 275): (*iii*) a green band that yielded a trace of a brown powder, M^+ 247 (monoformyl derivative requires M 247): and (*iv*) an orange band that yielded a trace of sticky brown material, M^+ 278.

Attempted Nitration of 6,8-*Dimethylcyclopenta*[4,5]*azepino*-[7,1,2-cd]*pyrrolizine*.—The dimethyl compound (1q) (0.101 g), in pyridine (100 cm^3), was treated with tetranitromethane (0.100 g) in ethanol (10 cm^3) as described for previous nitrations. The solution was kept at 0 °C for 1 h and worked up in the usual way. Initially, there was little evidence of decomposition but dark, tarry material separated during the washing of the chloroform extract. The chloroform-soluble fraction was separated by p.l.c. on silica, in chloroform–benzene (4 : 1) to give, in order of chromatographic mobility: (*i*) a deep purple product (0.002 g), M^+ 264 (mononitro-derivative requires M 264); (*ii*) a brown product (trace), M^+ 264; (*iii*) 6-methyl-8-nitrocyclopenta[4,5]-azepino[7,1,2-*cd*]pyrrolizine (0.0025 g) as a brick-red powder (Found: M^+, 250 $C_{15}H_{10}N_2O_2$ requires M, 250); δ 2.83

(3 H, s, Me), 7.79—8.11 (4 H, m, H-1, -2, -3 and -4), 8.37 (1 H, s, H-7), 8.01 (1 H, s, H-5), and 10.30 (1 H, s, H-9): (*iv*) a red-purple product (trace), M^+ 309 (dinitro-derivative requires M 309); (*v*) a yellow-brown product (trace), probably 8-methylcyclopenta[4,5]azepino[7,1,2-*cd*]pyrrolizine-6-carbaldehyde (Found: M^+, 233. $C_{16}H_{11}NO$ requires M, 233); δ 2.89 (3 H, s, Me), 7.67—8.11 (4 H, m, H-1, -2, -3, and -4), 8.13 (1 H, s, H-7), 8.89 (1 H, s, H-9), 10.16 (1 H, s, CHO), (1 H, s, H-5); and (*vi*) traces of three other coloured and 10.49 products, M^+ 233, 221, and 277, respectively.*

We thank the S.R.C. for a research studentship (to M. A. J.).

[9/1318 *Received*, 20*th August*, 1979]

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* *Note added in proof.* Since this paper was submitted, syntheses of the [2,2,4]cyclazinylium cation (9) and of 2-chlorocyclopenta[*h*][2,2,4]cyclazine have been reported.[15]

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