Azonia-azulene Salts. Part 5.[1] Synthesis of 5*H*-Pyrrolo[1,2-*a*]azepine and of 7*H*-Pyrrolo[1,2-*a*]azepin-7-one

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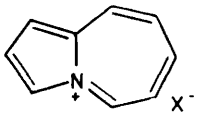
The synthesis of (*Z*)- and (*E*)-1-azido-1,4-diphenylbut-1-ene (6a and b) is described, and their thermal decomposition. The synthesis of 5*H*-pyrrolo[1,2-*a*]azepine (2) and of 7*H*-pyrrolo[1,2-*a*]azepin-7-one (3) *via* the common dihydroazepinone intermediate (11) is also described.

For some years we have been seeking a route to unsubstituted pyrrolo[1,2-*a*]azepinium salts (1), in view of the potential importance of the 10π aromatic system.[1-4] More recently we, and Flitsch,[5,6] have been attempting to prepare pyrrolo[1,2-*a*]azepinones. We report here the synthesis of 5*H*-pyrrolo[1,2-*a*]azepine (2), the simplest such compound yet produced, and of 7*H*-pyrrolo[1,2-*a*]-azepin-7-one (3), the third of the aza-annulenones to be obtained.



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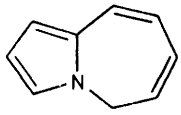

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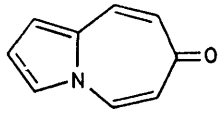
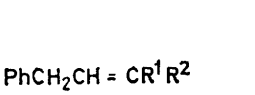
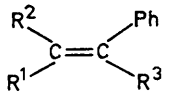


(3)

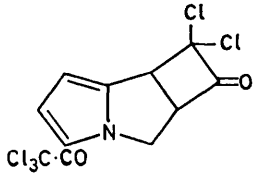
We have made indolo[1,2-*a*]azepines by nitrene insertion, from *o*-azido-diphenylmethanes.[3,4,7,8] An attractive route to pyrrolo[1,2-*a*]azepines would involve thermolysis of a *Z*-azidobenzylalkene of general formula (4). We aimed for the *Z*-alkene, although recent work has shown that this stereochemistry may not be necessary.[9] One simple route to such azidoalkenes would comprise condensation of phenylacetaldehyde with an azidoacetate after the method of Hemetsberger,[10] but all attempts to achieve this condensation have failed. Another well documented route to vinyl azides is that due to Hassner,[11,12] in which iodine azide is added to the appropriate alkene, and hydrogen iodide is subsequently eliminated. For our purposes there are two inherent difficulties in this route, those of regio- and stereoselectivity. We sought to obtain the desired regioselectivity by using 1,3-diphenylpropene (5), and indeed the phenyl group ensured the correct mode of addition of iodine azide to give, after subsequent elimination of hydrogen iodide, only 1-azido-1,3-diphenylpropene (6). To ensure the correct stereochemical result we needed to start with the *Z*-isomer (5a), which is the minor isomer from most preparative procedures. A Wittig synthesis from benzaldehyde and phenylethylidenetriphenylphosphorane, using ether as solvent, gave only the *E*-alkene. In benzene the yield was poor (22%), but the *Z* : *E* ratio [(5a) to (5b)] was 49 : 51. Preparation of the phosphorane in ether with subsequent replacement of the solvent by benzene for the condensation gave an improved yield (32%), but, more important, a *Z* : *E* ratio of 78 : 22. The purified *Z*-isomer (5a) and the pure *E*-isomer (5b) were separately converted into the iodoazides, and hence into the azidoalkenes (6a) and (6b). Pyrolysis of the azidoalkenes gave mixtures of many products, and no n.m.r. signals characteristic of pyrroloazepines were observed. The dibenzylalkene (7) was also prepared, but gave no better results on pyrolysis.



(4) $R^1 = N_3$
(5) $R^1 = N_3$, $R^2 = Ph$



(5) a; $R^1 = R^3 = H$, $R^2 = CH_2Ph$
b; $R^1 = CH_2Ph$, $R^2 = R^3 = H$
(6) b; $R^1 = H$, $R^2 = CH_2Ph$, $R^3 = N_3$
a; $R^1 = CH_2Ph$, $R^2 = H$, $R^3 = N_3$
(7) $R^1 = R^2 = CH_2Ph$, $R^3 = N_3$

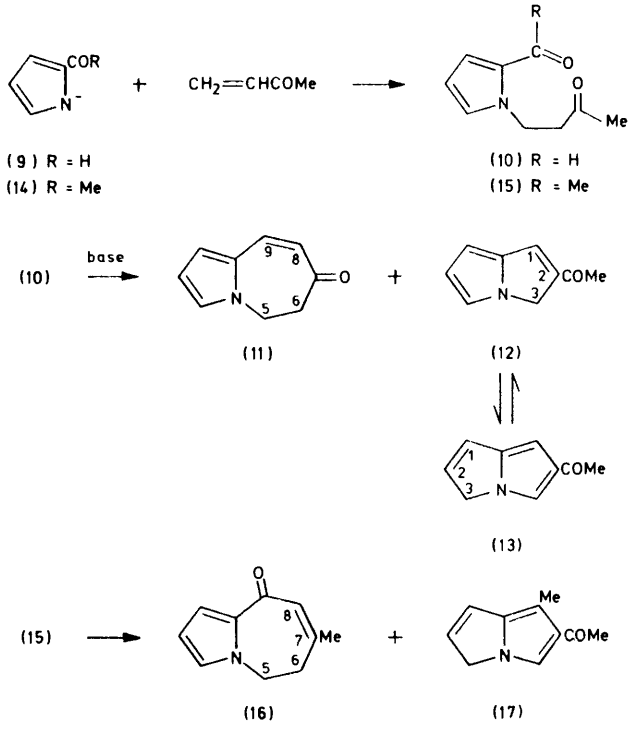


(8)

Our second approach to the pyrroloazepinone (3) started from 3*H*-pyrrolizine, *via* a $[_\pi 2 + _\pi 2]$ cycloaddition with dichloroketen. For reasons reported elsewhere,[13] we obtained the substituted tricyclic compound (8). An attempt to cause ring enlargement to the pyrroloazepinone by treatment with lithium tetramethylpiperidide was unsuccessful. Attempts to add 1-(diethylamino)prop-1-yne to 3*H*-pyrrolizine were similarly unsuccessful.

The anion from 2-formylpyrrole is known to add to electron-deficient double bonds; such an addition is a crucial stage in the synthesis of 3*H*-pyrrolizine. Leaver has informed us that the anion (9) reacts with but-3-en-2-one, and we have improved the addition to give the

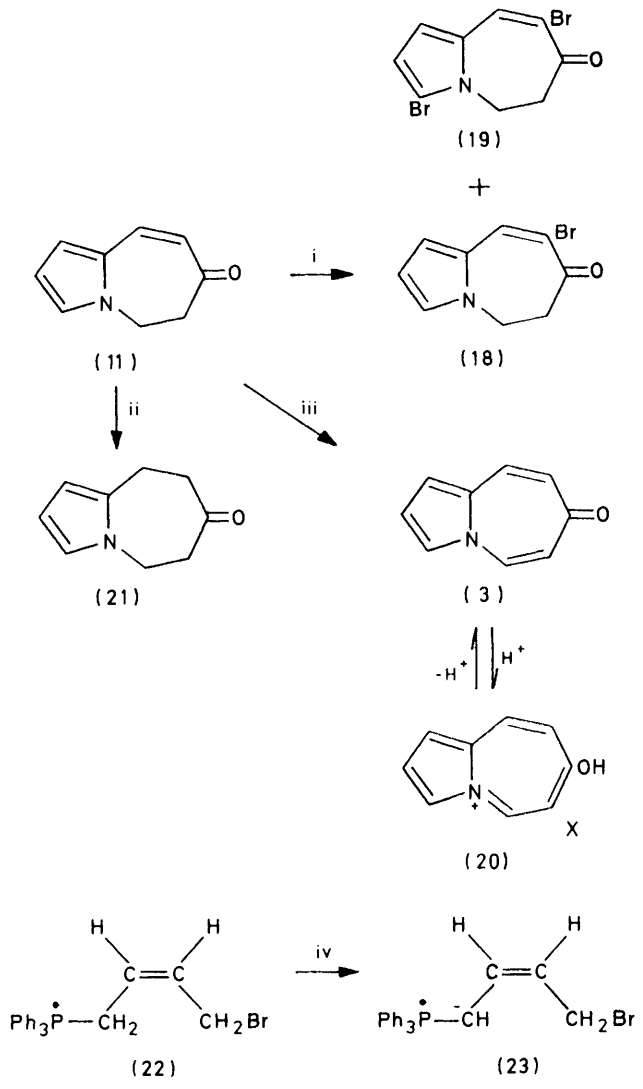
pyrrol-1-ylethyl ketone (10) in 68% yield. An intramolecular aldol reaction of the ketone (10) could conceivably give the dihydropyrrolo[1,2-*a*]azepinone (11) or the acetyl-3*H*-pyrrolizine (12) [or its tautomer (13)]. The oxo-aldehyde (10) was cyclized by sodium ethoxide in boiling ethanol (equilibrating conditions) to give a mixture of two compounds. The first of these, obtained in 40% yield, was the dihydropyrroloazepinone (11). The ^{1}H n.m.r. spectrum showed two multiplets (each 2 H) at δ 2.85 and 4.05 (H-6 and H-5), a widely separated pair of doublets (*J* 11 Hz) at δ 5.9 and 7.05 (H-8 and H-9), and three pyrrole protons. The second compound was 6-acetyl-3*H*-pyrrolizine (13) (31%); the characteristic signals due to unsubstituted ring *A*, and the presence of two singlets, at δ 6.28 and 7.5, one of them broadened, establish the position of the substituent. Under conditions of kinetic control, using lithium di-isopropylamide at −78 °C, two products were again obtained. The yield of pyrroloazepinone (11) was much poorer (16%), and the second product was a different acetylpyrrolizine (12) (27%). It is to be expected that this first-formed product would tautomerize under equilibrium conditions to the more stable 3*H*-pyrrolizine in which the electron-withdrawing substituent is on the



aromatic ring. In an attempt to prepare a methyl-substituted pyrroloazepinone, but-3-en-2-one was added to the anion (14) from 2-acetylpyrrole. The diketone (15), identified by its spectra, was immediately cyclized by sodium ethoxide in ethanol, to give, in very poor yield, two compounds. One was 7-methyl-5,6-dihydropyrrolo[1,2-*a*]azepin-9-one (16), and the second 6-acetyl-7-methyl-3*H*-pyrrolizine (17).

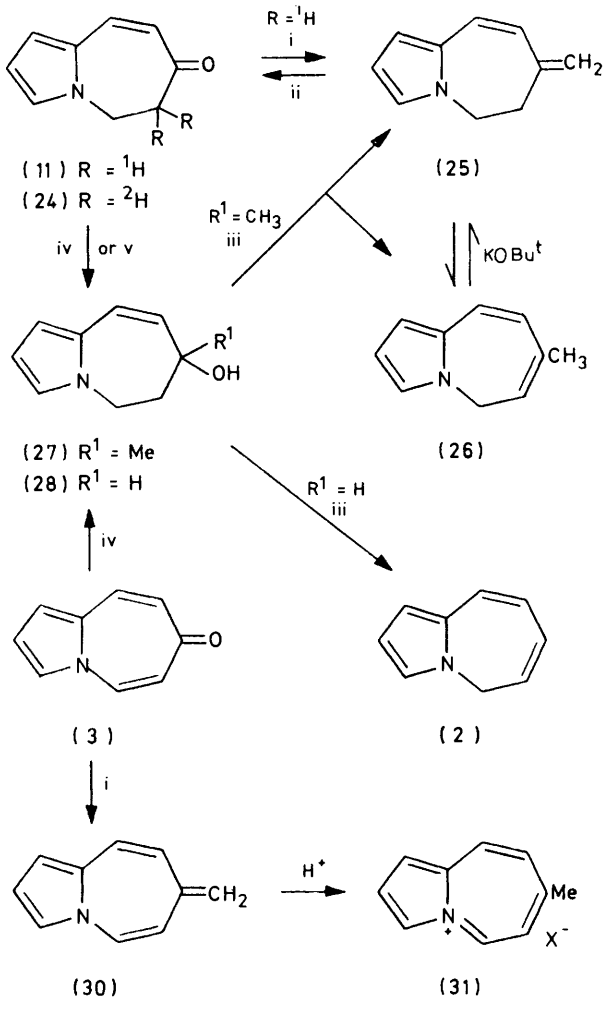
With a route established to the dihydro-derivative (11), a method of dehydrogenation was sought. Bromination–dehydrobromination sequences have proved very successful with similar systems,[2] the reagent of choice being phenyltrimethylammonium tribromide. With this reagent, the ketone (11) gave a poor yield of a monobromo-derivative, but the ^{1}H n.m.r. spectrum (2 H multiplets at δ 3.0 and 4.15, three pyrrole protons at δ 6.1, 6.4, and 6.8 p.p.m., and a singlet at δ 7.6) indicates that substitution has occurred, the shift of the remaining alkene proton at δ 7.5 showing that the compound is the 8-bromo-derivative (18). The same compound was obtained from the ketone (11) and bromine in carbon tetrachloride, in rather better yield, and a second product, a dibromo-ketone, was shown to be the 3,8-dibromopyrroloazepinone (19). The failure of the bromination to proceed *via* the enol, to give the 6-bromo-derivative, is further discussed below. Direct dehydrogenation by dichlorodicyanobenzoquinone (DDQ) has been used on a closely related azepinoindolone.[4] Treatment of the dihydropyrroloazepinone (11) with DDQ in boiling benzene gave, in poor yield, a yellow solid, shown by its spectra to be the pyrroloazepinone (3). Better yields (up to 43% but variable) were obtained by using palladium–charcoal in heterogeneous dehydrogenation at 170 °C. The ^{1}H n.m.r. spectrum of compound (3) showed signals for H-1, H-2, and H-3 at δ 6.7, 6.5, and 7.2, two doublets at δ 7.15 and 7.4 (*J* 12 and 4, and 10.4 Hz, respectively) due to H-9 and H-5, and two quartets at δ 5.9 and 6.25 due to H-6 and H-8 ($J_{5,6}$ 10.4, $J_{8,9}$ 12.4, and $J_{6,8}$ 2.4 Hz). The W-coupling of H-6 and H-8 is similar to that observed with the closely similar azepinoindole.[4] The ^{1}H n.m.r. spectrum in strongly protonating solvents shows the changes characteristic of the formation of 7-hydroxypyrrolo[1,2-*a*]azepinium salts (20); these are discussed in detail later. Solutions of the ketone (3) in trifluoroacetic acid or sulphuric acid were deep red, with an electronic absorption maximum at 455 nm. When the dihydro-derivative (11) with palladium–charcoal was heated in boiling decalin, the tetrahydro-derivative (21) was obtained.

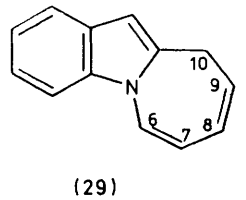
To reach the second objective, the production of an unsubstituted pyrrolo[1,2-*a*]azepine, we have tried direct synthesis and also modification of the ketone (11). We reasoned that formylpyrrole could react with the phosphorane (23) to form 1-bromo-5-pyrrol-2-ylpenta-2,4-diene; the phosphorane (23) was therefore prepared. Addition of 2-formylpyrrole discharged the colour of the solution, but no product was isolated. It seems probable therefore that 2-formylpyrrole is sufficiently strong as an acid to protonate the phosphorane. An attempt to alkylate the anion (9) with the phosphonium salt (22) was similarly unsuccessful. A number of attempts were made to generate, and trap, the enolate from the ketone (11). When the ketone was treated with 1 equiv. of lithium di-isopropylamide in 1,2-dimethoxyethane at −70 °C, and the reaction was quenched with D_2O, a mixture of deuteriated ketones was obtained. With an excess of lithium deuteroxide in deuterium oxide the



Reagents: i, $PhMe_3N^+Br_3^-$ + THF or Br_2 + CCl_4; ii, Pd–C, decalin; iii DDQ or Pd–C; iv Bu^nLi, THF

dideuterio-derivative (24) was obtained. In spite of this apparent formation of the enolate, attempts to trap it with methyl iodide, acetyl chloride, or trimethylsilyl chloride were unsuccessful, nor could enol ester or ethers be prepared by acid-catalysed procedures. The ketone (11) also did not form an enamine, nor a *p*-tolylsulphonylhydrazone, thus precluding a Bamford–Stevens rearrangement. However, triphenylmethylenephosphorane reacted with the ketone (11) to give the exocyclic methylene derivative (25), showing no i.r. carbonyl absorption. The exocyclic methylene protons absorbed as a broad singlet at δ 4.7. An attempt to dehydrogenate compound (25) using DDQ gave the ketone (11). An attempt to isomerize the compound (25) using potassium t-butoxide in dimethyl sulphoxide gave a mixture, identified spectroscopically as exocyclic and endocylic double bond derivatives (25) and (26) in the ratio 60 : 40. A mixture of roughly equal amounts of compounds (25) and (26) was obtained by dehydration with acid of the alcohol (27), obtained from the ketone (11) and methyl-lithium.





Reagents: i, $Ph_3P^+CH_2^-$; ii, DDQ; iii, TsOH; iv, $NaBH_4$; v MeLi

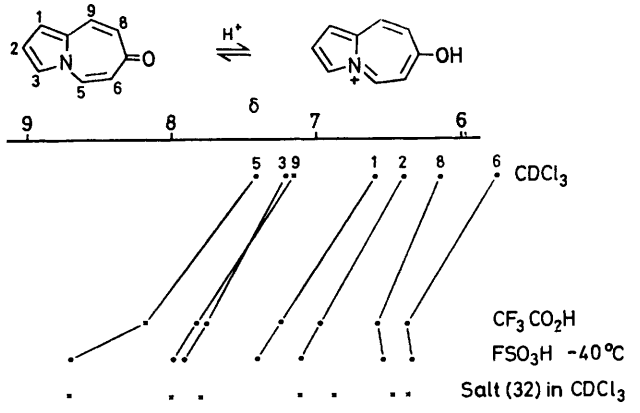
Attempted reduction of ketone (11) by 9-borabicyclo-[3.3.1]nonane failed, but reduction by borohydride gave, in 31% yield, the alcohol (28). Dehydration of the alcohol (28), using toluene-*p*-sulphonic acid in boiling benzene, gave 5*H*-pyrrolo[1,2-*a*]azepine (2), the first unsubstituted pyrroloazepine to be prepared. The ^1H n.m.r. spectrum is complex in the region δ 5—6, but the general pattern closely resembles that of the corresponding area in the spectrum of the 10*H*-azepinoindole (29).

The chemical shift of the methylene doublet in compound (26) is δ 4.5, to be compared with δ 3.5 in compound (29), the extra deshielding being due to the proximity of the nitrogen atom in the former. A few experiments have been done to establish the reactivity of the carbonyl group in the pyrroloazepinone (3). Reduction by sodium borohydride gave the alcohol (28); similar results were obtained in attempts to reduce azepinoindolones.[2,4] Triphenylmethylenephosphorane reacted with the pyrroloazepinone (3) to give the exocyclic methylene derivative (30). Protonating solvents produced a red colour with compound (30), presumably indicating the presence of 7-methylpyrrolo[1,2-*a*]azepinium salts (31), but these could not be isolated, nor could satisfactory n.m.r. spectra be obtained.

Chemical shifts [a] and coupling constants of 7*H*-pyrrolo[1,2-*a*]azepin-7-one (3) in various solvents

	Solvent					
Proton	$CDCl_3$	CD_3COCD_3	CF_3CO_2H	FSO_3H [b]	Δδ [c]	Compound (32) in $CDCl_3$
1	6.7_2	6.8_5	7.2_2	7.9_3	1.2_1	7.6_6
2	6.5_2	6.5_5	7.4_4	7.6_2	1.1	7.4_3
3	7.2	7.5_5	8.2_2	8.4_5	1.2_5	8.5_3
5	7.3_9	7.7_9	8.6_5	9.2_1	1.8_2	9.2
6	5.9_3	5.8_1	6.8_7	6.8_9	0.9_6	6.9_6
7	6.2_5	6.1	7.0_9	7.0_8	0.8_3	7.0_5
8	7.1_5	7.3_4	8.3	8.5_2	1.2	8.3_5
^3J Values (Hz)					ΔJ [d]	
1,2	3.7_6	3.8_2	4.4_7	4.5_5	0.7_9	4.5_5
2,3	2.8_5	2.8_9	2.9_3	3.0_5	0.2	3.1_7
5,6	10.3_9	10.3_7	9.5_1	9.2_6	-1.1_3	9.5_6
8,9	12.3_8	12.3_3	11.2_3	11.0_4	-1.3_4	11.8_4

[a] δ Values (Me_4Si standard). [b] At −40 °C. [c] δ (FSO_3H) − δ ($CDCl_3$). [d] ^3J (FSO_3H) − ^3J ($CDCl_3$).



N.m.r. shifts of the pyrroloazepinones (3) in solvents of various acidities, and of the salt (32)

^{1}H *N.m.r. spectra of* 7H-*Pyrrolo*[1,2-a]*azepin-7-one* (3).—In protonating solvents the pyrroloazepinone (3) must exist in equilibrium with the hydroxypyrrolo[1,2-*a*]-azepinium salt (20); when the protonation is incomplete the signals in the ^{1}H n.m.r. spectrum represent a weighted average of the two forms. We have examined the ^{1}H n.m.r. spectra of solutions in $CDCl_3$, CF_3CO_2H, and fluorosulphonic acid (at −40 °C), and compared them with that of 7-ethoxypyrroloazepinium tetrafluoroborate (32), in which the fully aromatic pyrroloazepinium system must be present. The chemical shifts and coupling constants are recorded in the Table, and plotted in the Figure with an arbitrary acidity scale.

Some observations can be made which indicate the presence of a ring current in the protonated form. All signals show a downfield shift, the largest for position 5, and the smallest for positions 6 and 8, adjacent to the oxygen function. The presence of a downfield shift may be associated with a ring current, though the presence of a positive charge would in any case cause a similar shift. More conclusive is the change in vicinal coupling constants for the seven-membered ring, both showing a reduction of *ca.* 1 Hz to bring them closer to the constants for azulenes.[14] It can be seen that the pyrroloazepinone (3) is fully protonated in fluorosulphonic acid, since the shifts and coupling constants are almost identical with those of the salt (32). Our results agree well with those of Flitsch, Kappenberg, and Schmidt,[6] on the isomeric pyrroloazepin-5- and -7-ones. The changes in chemical shift on going from a non-polar solvent to fluorosulphonic acid are similar, showing that there is approximately the same degree of conjugation between nitrogen and the carbonyl group in all three pyrroloazepinone neutral molecules.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Chromatography was performed on alumina (Woelm; activity shown in parentheses), or silica PF_{254} (for p.l.c.). U.v. spectra were determined for solutions in 95% EtOH, and n.m.r. spectra for solutions in $CDCl_3$, unless otherwise stated.

(E)-1,3-*Diphenylpropene* (5b).—Prepared by the procedure of Dieckmann and Kämmerer,[15] the alkene (5b) had the same i.r. and u.v. absorption as reported,[16] but differed in ^{1}H n.m.r. from the reported figures; we were unable to resolve the vinyl signal at δ 6.4 into two signals, at 60 or at 100 MHz. A sample of our alkene gave, with bromine, the dibromide, m.p. 109 °C (lit.,[15] 110 °C).

(Z)-1,3-*Diphenylpropene* (5a).—(*a*) A solution of phenethyl bromide (3 g) and triphenylphosphine (4.2 g) in anhydrous dimethylformamide (30 ml) was boiled under reflux (20 h). Removal of the solvent under reduced pressure gave a viscous oil (7.2 g). Trituration with anhydrous tetrahydrofuran gave a solid *phosphonium salt*, m.p. 89—90 °C

(Found: C, 69.8; H, 5.35. $C_{26}H_{24}BrP$ requires C, 69.65; H, 5.55%).

(*b*) A suspension of sodium amide (from 1.8 g of sodium) in anhydrous ether (100 ml) was treated with the phosphonium salt (33 g) and the mixture was boiled (30 h). The ether was replaced by anhydrous benzene (100 ml), benzaldehyde (7.8 g) was added, and the mixture was boiled (3 h). Removal of the solvent and distillation of the residue gave a mixture (4.6 g, 32%) of *Z*- and *E*-alkenes (5a) and (5b) (78 : 22 by n.m.r.). P.l.c. (multiple elution with petroleum) gave the pure *Z*-propene (5a) (Found: C, 93.0; H, 7.0. Calc. for $C_{15}H_{14}$: C, 92.8; H, 7.2%); δ 3.6 (2 H, d, *J* 7 Hz, CH_2CH=CH), 5.7 (1 H, d t), 6.5 (1 H, d, *J* 12 Hz), and 7.1 (10 H, m); $\lambda_{max.}$ 242 nm (lit.,[16] 242 nm).

erythro-1-*Azido*-2-*iodo*-1,3-*diphenylpropane*.—Iodine monochloride (3.66 g) was added slowly (10 min) to a stirred, cooled slurry of sodium azide (3 g) in freshly distilled acetonitrile (20 ml). After a further 10 min, (*E*)-1,3-diphenylpropene (5b) (3.88 g) was added. The mixture was allowed to warm to room temperature, and was stirred (20 h). The mixture was poured into water (50 ml) and extracted (ether; 3 × 50 ml), the organic extracts were washed [sodium thiosulphate (5%; 120 ml); water (18 ml)] and dried. Removal of the solvent under reduced pressure left a brown oil (5.1 g), purified by chromatography on alumina (150 g; III). Elution with petroleum (b.p. 40—60 °C) gave substantially pure *iodo-azide*, further purified by p.l.c. (Found: C, 49.7; H, 4.0; N, 11.1. $C_{15}H_{14}N_3I$ requires C, 49.6; H, 3.85; N, 11.55%); δ 2.1 (2 H, m, CH_2CHI), 4.3 (1 H, m, CHI), 4.8 (1 H, d, *J* 4 Hz, CHN_3), and 7.1 (10 H, m).

(E)-1-*Azido*-1,3-*diphenylpropene* (6b).—The foregoing iodoazide (0.7 g) in anhydrous ether (10 ml) was added to a cooled, stirred suspension of potassium t-butoxide (from 0.1 g of potassium), also in ether. The mixture was stirred (ice bath; 48 h). Water (50 ml) was added and the organic layer was separated and dried, then evaporated to give a yellow oil (0.5 g). P.l.c. (elution with petroleum, b.p. 40—60 °C) gave the *vinyl azide* (6b) (Found: C, 76.4; H, 6.0; N, 17.25. $C_{15}H_{13}N_3$ requires C, 76.6; H, 5.55; N, 17.85%); $\nu_{max.}$ 2 120 cm^{-1}; δ 2.9 (2 H, d, *J* 8 Hz), 5.5 (1 H, t, *J* 8 Hz), and 6.8 (10 H, m).

threo-1-*Azido*-2-*iodo*-1,3-*diphenylpropane and* (Z)-1-*Azido*-1,3-*diphenylpropene* (6a).—(*a*) The addition of iodine azide was performed with the *Z*-propene (5b) as described for the *E*-propene (5a), giving the *threo*-iodo-azide in 40% yield. Analyses were inconsistent, and the compound was unstable even at 0 °C; δ 2.7 (2 H, m), 3.6 (1 H, m), 4.8 (1 H, d, *J* 5 Hz), and 7.1 (10 H, m).

(*b*) Elimination of hydrogen iodide as described above gave, in 33% yield, (Z)-1-*azido*-1,3-*diphenylpropene* (6a) (Found: C, 77.05; H, 5.75; N, 17.2%); $\nu_{max.}$ 2 120 cm^{-1}; *m/z* 235 (34%, M^+), 207 (53%, *M* − 28), and 91 (100%, C_7H_7).

2-*Benzyl*-1,3-*diphenylpropene*.—Triphenyl(phenethyl)-phosphonium bromide (43.2 g) was added to a stirred suspension of sodium hydride (4.8 g; 50% suspension in paraffin) in anhydrous benzene (1 l); the mixture was boiled under reflux (2 h). A solution of 1.3-diphenylpropan-2-one (21 g) in benzene (100 ml) was added and boiling continued (120 h). The mixture was filtered, the solvent removed from the filtrate under reduced pressure, and the residue extracted with petroleum. Evaporation left an oil, which was purified by chromatography on alumina (100 g; IV), eluting with petroleum (b.p. 40—60 °C). The pure *alkene* was obtained in 96% yield (Found: C, 92.55; H, 7.3. $C_{22}H_{20}$ requires C, 92.9; H, 7.1%); δ 3.3 (2 H, s), 3.5 (2 H, s), 6.5 (1 H, s), and 7.2 (10 H, m).

1-*Azido*-2-*benzyl*-1,3-*diphenylpropene* (7).—The iodo-azide was prepared as described above, using 2-benzyl-1,3-diphenylpropene (5.6 g). The product (2.9 g, 37%) was, from its ^1H n.m.r. spectrum, a mixture of the two regioisomeric iodo-azides. The mixture was treated with potassium t-butoxide; only one isomer can eliminate hydrogen iodide. The *propene* (7) was obtained after p.l.c. in 19% yield (Found: C, 81.05; H, 6.3; N, 12.7. $C_{22}H_{19}N_3$ requires C, 81.25; H, 5.85; N, 12.9%); $\nu_{max.}$ 2 120 cm^{-1}; δ 3.5 (4 H, br, s) and 7.2 (15 H, m).

Decomposition of the Vinyl Azides (6a), (6b), *and* (7).—The azide (6b) was decomposed in boiling [$^2H_6$]benzene (9 h); the azide (6a) in trichlorobenzene at 180 °C; the azide (7) in trichlorobenzene at 100 °C. All, after removal of solvent, gave oils, containing at least six products. The n.m.r. spectra of the crude materials showed no signals characteristic of pyrroloazepines, and p.l.c. produced many bands from which no characterized materials were obtained.

N-(3-*Oxobutyl*)*pyrrole*-2-*carbaldehyde* (10).—A solution of benzyltrimethylammonium hydroxide (3 ml; 40% in methanol) was added to a cooled (ice-bath), stirred solution of pyrrole-2-carbaldehyde (17 g, 0.18 mol) and but-3-en-2-one (20.4 g, 0.28 mol) over 10 min, and the mixture was stirred for 45 min. The solution was poured into water (1.5 l), and neutralized with dilute hydrochloric acid. The solution was extracted (dichloromethane; 3 × 500 ml), the combined extracts were dried, and the solvent was removed under reduced pressure. The *oxo-aldehyde* (10) had b.p. 81 °C at 0.5 mmHg (yield 20.2 g, 68%) (Found: C, 65.25; H, 6.25; N, 9.0. $C_9H_{11}NO_2$ requires C, 65.45; H, 6.65; N, 8.5%); $\nu_{max.}$ ($CHCl_3$) 1 720 and 1 660 cm^{-1}; $\lambda_{max.}$ 221, 280sh, and 300 nm ($\log_{10}$ ε 3.41, —, and 3.54); δ 2.05 (3 H, s, CH_3CO), 2.9 (2 H, t, *J* 7 Hz, CH_2CO), 4.4 (2 H, t, *J* 7 Hz, CH_2N), 6.15 (1 H, m), 6.9 (2 H, m), and 9.35 (1 H, s, CHO); *m/z* 165 (41%, M^+) 122 (50%, *M* − 43), 94 (68%), 66 (32%), 44 (27%), 43 (100%, CH_3CO), and 39 (45%).

Cyclisation of the Oxo-aldehyde (10).—(*a*) A solution of the oxo-aldehyde (10) (10 g, 0.06 mol) in absolute ethanol (10 ml) was added over 5 min to a boiling, stirred solution of sodium ethoxide [from sodium (1.4 g)] in absolute ethanol (500 ml). The mixture was boiled under reflux (40 min), then most of the solvent was removed under reduced pressure. The brown residue was partitioned between water (300 ml) and dichloromethane (500 ml). The aqueous phase was exhaustively extracted with dichloromethane (5 × 500 ml); the combined organic extracts were dried and evaporated under reduced pressure. The residual brown gum was purified on an alumina column (120 g; IV). Elution with benzene–light petroleum (30 : 70) gave 5,6-*dihydropyrrolo*-[1,2-a]*azepin*-7-*one*, (11) (3.5 g, 40%), which crystallized from hexane as yellow crystals, m.p. 55—56 °C (Found: C, 73.35; H, 6.4; N, 9.7. C_9H_9NO requires C, 73.45; H, 6.1; N, 9.5%); $\nu_{max.}$ ($CHCl_3$) 1 610 and 1 665 cm^{-1}; δ 2.85 (2 H, m, CH_2CO), 4.05 (2 H, m, CH_2N), 5.9 (1 H, d, *J* 11 Hz, H-8), 6.15 (1 H, m, H-1), 6.4 (1 H, m, H-2), 6.8 (1 H, m, H-3), and 7.05 (1 H, d, *J* 11 Hz, H-9); *m/z* 147 (13%, M^+), 146 (100%), 118 (57%), 117 (73%), 90 (40%), 64 (19%), and 39 (16%). Further elution with the same solvents (40 : 60) gave 6-*acetyl*-3H-*pyrrolizine* (13), yellow needles (from hexane), m.p. 60—61 °C (2.7 g, 31%) (Found: C, 73.1; H, 5.85; N, 9.6. C_9H_9NO requires C, 73.45; H, 6.1; N, 9.5%); $\nu_{max.}$ (Nujol) 1 710 and 1 650 cm^{-1}; $\lambda_{max.}$ 250 and 292 nm ($\log_{10}$

ε 3.31 and 2.95); δ 2.35 (3 H, s, CH_3CO), 4.45 (2 H, br, s, H-3), 6.2 (1 H, m, H-1, $J_{1,2}$ 5 Hz), 6.28 (1 H, br, s, H-7), 6.5 (1 H, m, H-2, $J_{1,2}$ 5 Hz), and 7.5 (1 H, br, s, H-5); *m/z* 147 (48%, M^+), 146 (100%), 132 (37%, $M - CH_3$), 131 (92%), 118 (48%), 104 (47%, $M - CH_3CO$), 103 (100%, $M - 1 - CH_3CO$), and 39 (26%).

(*b*) A solution of n-butyl-lithium (4.2 ml; 1.6M in hexane) was added to a stirred, cooled solution of di-isopropylamine (0.6 ml; freshly distilled) in anhydrous tetrahydrofuran (THF) (50 ml), followed by the oxo-aldehyde (10) (1 g) in THF (10 ml). The mixture was stirred (4 h) at −78 °C then allowed to warm to room temperature, and a saturated solution of ammonium chloride in ammonia (s.g. 0.880) (50 ml) was added. The organic material was extracted with ether, and the extract dried and evaporated, to give a yellow oil. Chromatography as before gave first *2-acetyl-3H-pyrrolizine* (12), purified by p.l.c. (0.24 g, 27%) (Found: C, 73.25; H, 6.2; N, 9.65. C_9H_9NO requires C, 73.45; H, 6.15; N, 9.5%); $\nu_{max.}$ ($CHCl_3$) 1 650 and 1 565 cm^{-1}; $\lambda_{max.}$ 242 and 373 nm ($\log_{10}$ ε 3.31 and 4.07); δ 2.35 (3 H, s, $COCH_3$), 4.6 (2 H, br, s, H-3), 6.2 (2 H, m, H-1 and H-7), 6.9 (1H, m, H-6), and 7.2 (1H, m, H-5); *m/z* 147 (90%, M^+), 146 (98%), 131 (91%), 117 (28%), 105 (21%), 104 (100%, $M - CH_3CO$), 103 (100%, $M - 1 - CH_3CO$), 102 (44%), 76 (94%), 75 (97%), and 39 (51%). Later fractions from the column yielded the ketone (11) (0.14 g, 16%) and starting material (0.31 g, 31%).

2-Acetyl-1-(3-oxobutyl)pyrrole (15) *and its Cyclization.*—From 2-acetylpyrrole and but-3-en-2-one as described for compound (10), the diketone (15) was prepared in crude yield of 97%; δ 2.0 (3 H, s), 2.3 (3 H, s), 2.8 (2 H, t, *J* 6 Hz, H-6), 4.35 (2 H, t, *J* 6 Hz, H-5), 5.9 (1 H, m), and 6.8 (2 H, m). Cyclization, as described for compound (10), using sodium ethoxide in ethanol, gave an oil, purified by p.l.c. (ethyl acetate–toluene, 1 : 3). From the band at R_F 0.71 was obtained *6-acetyl-7-methyl-3H-pyrrolizine* (17) (Found: C, 74.2; H, 6.6; N, 8.8. $C_{10}H_{11}NO$ requires C, 74.5; H, 6.9; N, 8.7%); $\nu_{max.}$ 1 665 and 1 640 cm^{-1}; δ 2.3 (3 H, s), 2.4 (3 H, s), 4.5 (2 H, br, s, H-3), 6.1 (1 H, m), 6.7 (1 H, m), and 6.9 (1 H, m); *m/z* 161 (40%, M^+), 160 (29%), 146 (16%, $M - CH_3$), 145 (29%), 144 (19%), 135 (11%), 130 (18%), 120 (16%), 118 (84%, $M - CH_3CO$), 117 (22%), 109 (100%), 94 (97%), 44 (93%), and 39 (36%). From the band of R_F 0.49 was obtained *5,6-dihydro-7-methylpyrrolo[1,2-a]azepin-9-one* (16) (Found: C, 73.85; H, 6.3; N, 8.85. $C_{10}H_{11}NO$ requires C, 74.5; H, 6.9; N, 8.7%); $\nu_{max.}$ ($CHCl_3$) 1 670 and 1 590 cm^{-1}; δ 2.0 (3 H, br, s, coupled to signal at δ 5.95), 2.6 (2 H, m, H-6), 4.1 (2 H, m, H-5), 5.95 (2 H, m), 6.5 (1 H, m), and 6.85 (1 H, m); *m/z* 161 (28%, M^+), 160 (89%), 148 (11%), 146 (4%), 145 (21%), 132 (56%), 131 (95%), 130 (17%), 118 (22%), 117 (100%), 116 (56%), 108 (35%), 93 (44%), 78 (28%), 69 (46%), and 39 (35%).

8-Bromo-5,6-dihydropyrrolo[1,2-a]azepin-7-one (18) and *3,8-Dibromo-5,6-dihydropyrrolo[1,2-a]azepin-7-one* (19).—(*a*) A solution of bromine in carbon tetrachloride (2 ml; 5% solution) was added dropwise to a stirred mixture of the ketone (11) (0.1 g), calcium carbonate (0.5 g), and carbon tetrachloride (30 ml) at room temperature. The mixture was stirred (4 h) and filtered, and the filtrate evaporated at room temperature, giving a brown oil (0.13 g). P.l.c. gave two bands (ethyl acetate–toluene, 35 : 65). The band of R_F 0.83, after extraction, gave the *dibromo-ketone* (19), m.p. 125 °C (yellow crystals from ether) (65 mg, 31%) (Found: C, 35.3; H, 2.8; N, 4.45. $C_9H_7Br_2NO$ requires C, 35.4; H, 2.6; N, 4.6%); $\nu_{max.}$ (CCl_4) 1 660 and 1 585 cm^{-1}; δ 3.0 (2 H, m, H-6), 4.2 (2 H, m, H-5), 6.1 (1 H, d, *J* 4 Hz, H-2), 6.4 (1 H, d, *J* 4 Hz, H-1), and 7.5 (1 H, s, H-9); *m/z* 307 (19%), 305 (37%), 303 (20%, M^+), 227 (13%), 226 (40%), 224 (42%, M − Br), 150 (100%), 118 (20%), 117 (38%), 93 (40%), 91 (43%), and 39 (19%). The second band, R_F 0.66, gave, as a yellow oil, the *bromo-ketone* (18) (42 mg, 27%) (Found: C, 47.2; H, 3.5; N, 6.3. C_9H_8BrNO requires C, 47.8; H, 3.5; N, 6.2%); $\nu_{max.}$ (CCl_4) 1 660 and 1 585 cm^{-1}; δ 3.0 (2 H, m, H-6), 4.15 (2 H, m, H-5), 6.05 (1 H, m), 6.4 (1 H, m), 6.7 (1 H, m), and 7.6 (1 H, s, H-9); *m/z* 227 (34%), 225 (34%, M^+), 147 (36%), 145 (50%), 118 (69%), 117 (34%), 109 (21%), 93 (100%), 91 (94%), and 81 (53%).

(*b*) Phenyltrimethylammonium tribromide (0.25 g) was added to a stirred solution of the ketone (11) (0.1 g) in anhydrous THF (30 ml) with calcium carbonate (0.5 g), under nitrogen, and stirring was continued, at room temperature, for 4.5 h. The filtered solution was shaken with aqueous sodium hydrogencarbonate (50 ml; 5%) and dichloromethane; the separated organic layer was dried and evaporated. The residual oil was purified by p.l.c. (ethyl acetate–toluene, 36 : 65) to give starting material and the monobromo-ketone (18) (5%).

7H-Pyrrolo[1,2-a]azepin-7-one (3).—(*a*) A solution of the ketone (11) (1 g) and DDQ (3.1 g) in anhydrous benzene (100 ml) was boiled under reflux (7 h), under nitrogen. The filtered mixture was evaporated under reduced pressure, and the residue chromatographed on alumina (30 g; IV). Elution with chloroform–benzene (1 : 4) gave the *azepinone* (3), yellow needles (from hexane), m.p. 119—120 °C (10 mg, 1%) (Found: C, 74.7; H, 4.6; N, 9.45. C_9H_7NO requires C, 74.45; H, 4.85; N, 9.65%); $\nu_{max.}$ ($CDCl_3$) 1 650 and 1 620 cm^{-1}; $\lambda_{max.}$ 260, 290, 307, and 360 nm ($\log_{10}$ ε 4.66, 3.77, 3.67, and 3.47); $\lambda_{max.}$ (96%, H_2SO_4) 297, 356, and 455 nm ($\log_{10}$ ε 4.04, 3.86, and 2.87); ^1H n.m.r. given in main text (Table); *m/z* 145 (91%, M^+), 144 (38%), 142 (43%), 117 (100%), 90 (49%), 89 (28%), and 39 (26%).

(*b*) A mixture of the ketone (11) (0.5 g) and palladium–charcoal (10%; 0.5 g) was heated under nitrogen at atmospheric pressure (20 h). The mixture was extracted with dichloromethane (150 ml), the extract evaporated, and the residual oil purified as already described, or by p.l.c. (ethyl acetate–toluene, 1 : 3) to give the ketone (3) in variable yield (up to 40%), some dihydro-ketone (11) being recovered.

5,6,8,9-Tetrahydropyrrolo[1,2-a]azepin-7-one (21).—A mixture of the dihydroazepinone (11) (0.2 g), and palladium–charcoal (10%; 0.2 g) in decalin (30 ml) was boiled under reflux, under nitrogen (1.5 h). The mixture was cooled and filtered, and the filtrate partitioned with methanol (4 × 10 ml). The combined methanolic extracts were evaporated, and the residue was purified by p.l.c. (ethyl acetate–toluene, 1 : 4). The faster running fraction was naphthalene; the slower gave the *tetrahydroazepinone* (21) as cream-coloured needles (from hexane), m.p. 93—94 °C (18 mg, 9%) (Found: C, 72.05; H, 7.4; N, 9.2. $C_9H_{11}NO$ requires C, 72.45; H, 7.45; N, 9.4%); $\nu_{max.}$ 1 700 cm^{-1}; δ 2.8 (6 H, m), 4.1 (2 H, m, H-5), 6.05 (2 H, m), and 6.6 (1 H, d d, *J* 2 Hz); *m/z* 149 (15%, M^+), 148 (100%), 147 (89%), 105 (92%), and 78 (29%).

Deuteriation of the Dihydropyrroloazepinone (11).—The ketone (11) (0.15 g) was stirred with lithium deuteroxide in 1,2-dimethoxyethane–D_2O (20 : 5) for 1 h. Dilution and extraction with dichloromethane gave, after removal of the solvent, a sample of the ketone (24) differing from the ketone (11) in the absence of the n.m.r. multiplet at δ 2.85 due to H-6; *m/z* 149 (46%) and 148 (12%).

Enolate of Compound (11).—This was prepared from the ketone (11) and a slight excess of lithium di-isopropylamide in 1,2-dimethoxyethane; treatment with D_2O gave a mixture of ketones (11) and (24). If, instead of D_2O, a trapping agent was added (methyl iodide or chlorotrimethylsilane) no product was isolated; starting ketone (11) was recovered.

6,7-*Dihydro*-7-*methylene*-5H-*pyrrolo*[1,2-a]*azepine* (25).—A solution of n-butyl-lithium (4 ml; 1.6M in hexane) was added to a stirred suspension of triphenylmethylphosphonium bromide (2 g) in anhydrous THF (100 ml), under nitrogen. After 30 min, a red solution was obtained, then a solution of the ketone (11) (0.8 g) in THF (10 ml) was added, and the mixture stirred (3 h). The filtered solution was evaporated to give a yellow oil, purified by chromatography on alumina (25 g; IV). Elution with petroleum (b.p. 40—60 °C) gave the *methylene compound* (25), b.p. 155 °C at 0.05 mmHg (bulb tube) (0.37 g, 47%) (Found: C, 82.3; H, 7.4; N, 9.3. $C_{10}H_{11}N$ requires C, 82.7; H, 7.65; N, 9.65%); δ 2.5 (2 H, m, H-6), 3.8 (2 H, m, H-5), 4.7 (2 H, m, CH_2=C), 5.8 (3 H, m, H-8, H-9, H-1), 6.3 (1 H, m, H-2), and 6.9 (1 H, m, H-3); *m/z* 145 (52%, M^+), 144 (100%), 143 (75%), 142 (67%), 141 (36%), 129 (53%), 117 (53%), 116 (82%), 114 (76%), 104 (58%), 103 (67%), 90 (79%), 77 (36%), 65 (52%), and 39 (67%).

6,7-*Dihydro*-7-*hydroxy*-7-*methyl*-5H-*pyrrolo*[1,2-a]*azepine* (27).—A solution of methyl-lithium–lithium bromide (0.7 ml of a 1.4M-solution in ether), was added to a stirred, cooled (−78 °C) solution of the dihydroazepinone (11) (0.15 g) in anhydrous THF (40 ml). The mixture was stirred at −78 °C (4 h) then at room temperature (2 h). Water (20 ml) was added, and the mixture extracted with ether (2 × 50 ml). The dried extracts were evaporated to give an oil (0.15 g). P.l.c. (ethyl acetate–toluene, 1 : 3) gave two products, 2-formylpyrrole (20%), and the *alcohol* (27) (0.8 g, 56%) (Found: C, 74.4; H, 6.4; N, 9.1. $C_{10}H_{13}NO$ requires C, 74.5; H, 6.9; N, 8.7%); $\nu_{max.}$ (film) 3 410 cm^{-1}; δ 1.3 (3 H, s), 2.05 (2 H, m, H-6), 3.9 (1 H, br, s, exch. D_2O), 4.1 (2 H, m, H-5), 5.32 (1 H, d, *J* 12.4 Hz, H-8), 5.93 (1 H, dd, *J* 3.1 and 2.6 Hz, H-1), 6.05 (1 H, m, H-2), 6.15 (1 H, d, *J* 12.4 Hz, H-9), and 6.69 (1 H, m, H-3); *m/z* 163 (14%, M^+), 148 (20%, $M - CH_3$), 147 (20%), 146 (21%), 145 (100%, $M - H_2O$), 144 (70%), 130 (58%), 119 (23%), 118 (18%), 104 (12%), 103 (10%), 91 (14%), 77 (14%), 65 (12%), 63 (8%), 51 (13%), and 39 (16%).

7-*Methyl*-5H-*pyrrolo*[1,2-a]*azepine* (26) *and* 6,7-*Dihydro*-7-*methylene*-5H-*pyrrolo*[1,2-a]*azepine* (25).—(*a*) Compound (25) (0.15 g) in anhydrous dimethyl sulphoxide (30 ml) was heated at 50 °C with potassium t-butoxide [from potassium (0.05 g)] for 19 h. Work-up by dilution and extraction gave a mixture of compound (25) and the azepine (26) in the ratio 6 : 4. ^1H N.m.r. signals due to the 7-methyl group at δ 2.1 and to the 5 H methylene group at δ 4.3 (*J* 5 Hz) were observed.

(*b*) Boiling a solution of the alcohol (27) in benzene with a few crystals of toluene-*p*-sulphonic acid gave compounds (25) and (26) in the ratio 1 : 1.

6,7-*Dihydro*-7-*hydroxy*-5H-*pyrrolo*[1,2-a]*azepine* (28).—(*a*) A solution of the dihydroazepinone (11) (0.15 g, 1 mmol) in ethanol (10 ml) was added, under nitrogen, dropwise, to a stirred, cooled (ice-bath) mixture of sodium borohydride (0.02 g, 0.5 mmol) in ethanol (15 ml). The mixture was stirred at 0 °C (2 h), then at room temperature overnight. The mixture was concentrated to 5 ml under reduced pressure, and partitioned between water (50 ml) and dichloromethane (50 ml). The organic layer was separated, washed [saturated aqueous sodium chloride (30 ml); water (30 ml)], dried, and evaporated to give a yellow oil (0.1 g). The oil was purified by p.l.c. (ethyl acetate–toluene, 1 : 3) to give the *alcohol* (28) (50 mg, 31%) (Found: C, 72.2; H, 7.35; H, 9.6. $C_9H_{11}NO$ requires C, 72.45; H, 7.45; N, 9.4%); $\nu_{max.}$ (film) 3 380 cm^{-1}; $\lambda_{max.}$ 278 nm ($\log_{10}$ ε 3.02); δ 2.1 (2 H, m, H-6), 3.1 (1 H, br, s, OH), 4.0 (2 H, m, H-5), 4.5 (1 H, m, H-7), 5.4 (1 H, dd, *J* 11 and 4 Hz, H-8), 5.9 (2 H, m), 6.2 (1 H, d, *J* 11 Hz, H-9), and 6.6 (1 H, m); *m/z* 149 (2%, M^+), 132 (100%, M — OH), 118 (36%), 104 (15%), 51 (13%), and 39 (47%).

(*b*) Reduction of the azepinone (3) under the same conditions gave the alcohol (28) in 14% yield.

5H-*Pyrrolo*[1,2-a]*azepine* (2).—A solution of the alcohol (28) (60 mg) in anhydrous benzene (30 ml) with toluene-*p*-sulphonic acid (3 crystals) was stirred at room temperature (24 h) then boiled under reflux (2 h). The mixture was washed [saturated aqueous sodium hydrogencarbonate (50 ml); water (50 ml)], dried, and evaporated to give a brown oil. The oil was percolated through alumina to give the *pyrroloazepine* (2) (15 mg, 31%) (Found: C, 81.65; H, 6.5; N, 11.25. C_9H_9N requires C, 82.4; H, 6.9; N, 10.7%); $\lambda_{max.}$ 272 nm ($\log_{10}$ ε 2.74); δ 4.5 (2 H, d, *J* 5 Hz, H-5), 6.0 (5 H, m), 6.6 (1 H, m), and 6.7 (1 H, d, *J* 7 Hz); *m/z* 147 (16%, M^+), 130 (3%), 111 (42%), 97 (67%), 95 (74%), 69 (100%), and 39 (16%).

7-*Methylene*-7H-*pyrrolo*[1,2-a]*azepine* (30).—A solution of n-butyl-lithium (0.9 ml; 0.7M in hexane) was added to a stirred mixture of triphenylmethylphosphonium bromide (0.25 g) in anhydrous THF (50 ml), under nitrogen. The mixture was stirred (20 min) then a solution of the pyrroloazepinone (3) (0.1 g) in THF (10 ml) was added. The mixture was stirred (3 h) and the solvent was then removed under reduced pressure; ether (150 ml) was added, precipitating a solid. The filtrate was evaporated to give an oil (0.1 g), purified by p.l.c. (ethyl acetate–toluene, 1 : 9). The major product was the *methylene compound* (30) (20 mg, 20%) (Found: C, 83.2; H, 6.6; N, 9.4. $C_{10}H_9N$ requires C, 83.85; H, 6.35; N, 9.8%); $\lambda_{max.}$ 258 and 319 nm ($\log_{10}$ ε 3.02 and 2.08); $\lambda_{max.}$ (CF_3CO_2H) 475 nm; δ 5.8 (2 H, br, s, CH_2=C) and 7.1—7.5 (7 H, m); *m/z* 143 (42%, M^+), 129 (92%, $M - CH_2$), 117 (43%), and 39 (100%).

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REFERENCES

[1] Part 4, G. R. Cliff, G. Jones, and J. Stanyer, *J. Chem. Soc. C*, 1971, 3426.
[2] E. W. Collington and G. Jones, *J. Chem. Soc. C*, 1969, 1028.
[3] G. R. Cliff, E. W. Collington, and G. Jones, *J. Chem. Soc. C*, 1970, 1490.
[4] G. R. Cliff and G. Jones, *J. Chem. Soc. C*, 1971, 3418.
[5] W. Flitsch, B. Müter, and W. Wolf, *Chem. Ber.*, 1973, **106**, 1993.
[6] W. Flitsch, F. Kappenberg, and H. Schmidt, *Chem. Ber.*, 1978, **111**, 2407.
[7] R. N. Carde and G. Jones, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2066.
[8] R. N. Carde, G. Jones, W. H. McKinley, and C. Price, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1211.

[9] T. Gilchrist, C. W. Rees, and J. A. R. Rodrigues, *J. Chem. Soc., Chem. Commun.*, 1979, 627; C. W. Rees, personal communication.
[10] H. Hemetsberger and D. Knittel, *Monatsh.*, 1972, **103**, 194, and references therein.
[11] F. W. Fowler, A. Hassner, and D. Levy, *J. Am. Chem. Soc.*, 1967, **89**, 2077.
[12] A. Hassner and F. W. Fowler, *J. Org. Chem.*, 1968, **33**, 2686.
[13] G. Jones and P. M. Radley, submitted to *J. Chem. Research*, 1982, (*S*), **54**; (*M*), 0385.
[14] H. Guenther, H. Schmickler, E. M. Guenther, and D. Cramer, *Org. Magn. Reson.*, 1977, **9**, 420.
[15] W. Dieckmann and M. Kämmerer, *Ber.*, 1906, **39**, 3046.
[16] E. K. Raunio and W. A. Bonner, *J. Org. Chem.*, 1966, **31**, 396.