Enamine Chemistry. Part XXI.[1] Condensation of L-Sodium or L-Ethyl Prolinate with Ketones to give Substituted Polyhydropyrrolo[1,2*a*]-indoles and -pyrrolizines

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The effect of substituents and ring size on the cyclization of enamines derives from L-ethyl pyrrolidine-2-carboxylate and cyclic ketones, to give 1,2,3,5,6,7,8,9a-octahydropyrrolo[1,2-*a*]indol-9-ones, has been investigated and the conversion of the parent system into the perhydropyrrolo[1,2-*a*]indol-9-one is reported. Application of the reaction to simple acyclic ketones, β-diketones, and β-oxo-esters gives the corresponding substituted pyrrolizines.

PREVIOUS work has shown that when diethyl 4-oxocyclohexane-1,1-dicarboxylate (I; $R^1 = R^2 = H$, $R^3 = R^4 = CO_2Et$) was heated with L-ethyl prolinate (II), the pyrrolo[1,2-*a*]indole (IV; $R^1 = R^2 = H$, $R^3 = R^4 = CO_2Et$) was obtained.[1,2] The reaction proceeds *via* an intramolecular cyclization [3] involving an enamine intermediate (III). Similarly cyclohexanone gives the pyrrolo[1,2-*a*]indole (IV; $R^1 = R^2 = R^3 = R^4 = H$).[4] We have now studied the effects of substituents and ring size on this reaction, and its application to acyclic ketones, diketones, and oxo-esters.

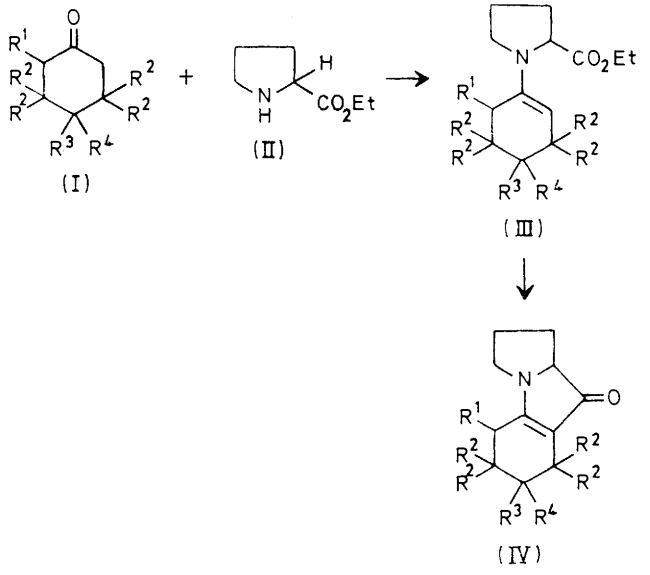
As might be expected from stereochemical considerations, when the cyclohexanone ring is substituted in the 2-position the reaction is critically dependent upon the size of the substituent. Thus the 5-methylpyrrolo-[1,2-*a*]indole (IV; $R^1 = Me$, $R^2 = R^3 = R^4 = H$) was obtained from L-ethyl prolinate and 2-methylcyclohexanone merely by heating the reagents in benzene for 28 h, under reflux in the presence of toluene-*p*-sulphonic acid. However, in the case of 2-phenyl- and 2-benzylcyclohexanones, no reaction occurred under these conditions. The former required boiling toluene (for 3 days) and the latter boiling xylene (for 2 days) to yield the corresponding 5-phenyl and 5-benzyl analogues, respectively. Similarly, treatment of 2-isopropylcyclohexanone in *p*-xylene at reflux temperatures gave the 5-isopropylpyrrolo[1,2-*a*]indole (IV; $R^1 = Pr^i$, $R^2 = R^3 = R^4 = H$) after 8 days. When the size of the 2-substituent was still greater, as in 2-t-butylcyclohexanone, spiro[5.5]-undecan-1-one, and camphor, no reaction occurred in boiling xylene, and the method of White and Weingarten,[5] with titanium tetrachloride, gave an intractable tar. When these hindered ketones were heated with a

[1] Part XX, P. W. Hickmott, K. N. Woodward, and R. Urbani, *J.C.S. Perkin I*, 1975, 1885.
[2] R. Urbani, Ph.D. Thesis, Salford, 1975.
[3] N. A. Nelson, J. E. Ladbury, and R. Hsi, *J. Amer. Chem. Soc.*, 1958, **80**, 6633; U. K. Pandit, K. de Jonge, and G. T. Koomen, *Tetrahedron Letters*, 1967, 3529; Z. Horii, K. Morikawa, C. Iwata, and I. Ninomiya, *Chem. and Pharm. Bull.* (*Japan*), 1968, **16**, 1686; A. I. Meyers, A. H. Reine, J. C. Sircar, K. B. Roo, S. Singh, H. Weidmann, and M. Fitzpatrick, *J. Heterocyclic Chem.*, 1968, **5**, 151; J. M. Bobbitt and C. P. Dutta, *Chem. Comm.*, 1968, 1429.
[4] K. Hiroi, K. Achiwa, and S. Yamada, *Chem. and Pharm. Bull.* (*Japan*), 1972, **20**, 246.
[5] W. A. White, and H. Weingarten, *J. Org. Chem.*, 1967 **32**, 213.

Ketone	Method	Solvent	Temp. (°C)	Reaction time	Cyclization yield (%)	Product B.p. (m.p.)	Product Structure
Cyclohexanone	A′	Benzene	80	20 h	[a]		
	D		150	24 h	90	124° at 0.05 mmHg	(IV; $R^1 = R^2 = R^3 = R^4 = H$)
	E	Dimethylformamide	100	2 h	0		
2-Methylcyclohexanone	A	Benzene	80	24 h	60	143° at 0.2 mmHg	(IV; $R^1 = Me$, $R^2 = R^3 = R^4 = H$)
2-Isopropylcyclohexanone	A	*p*-Xylene	138	8 days	27	146° at 0.1 mmHg	(IV; $R^1 = Pr^i$, $R^2 = R^3 = R^4 = H$)
2-Phenylcyclohexanone	A	Toluene	110	3 days	48	174° at 0.05 mmHg	(IV; $R^1 = Ph$, $R^2 = R^3 = R^4 = H$)
2-Benzylcyclohexanone	A	*p*-Xylene	138	2 days	59	198° at 0.05 mmHg	(IV; $R^1 = PhCH_2$, $R^2 = R^3 = R^4 = H$)
2-t-Butylcyclohexanone	A	*p*-Xylene	138	3 days	0		
	B	Benzene	20	8 days	0		
	C		150	36 h	0 [b]		
Spiro[5.5]undecan-1-one	A	*p*-Xylene	138	4 days	0		
	B	Benzene	20	8 days	0		
	C		150	36 h	0 [b]		
Camphor	A	*p*-Xylene	138	8 days	0		
	B	Benzene	20	8 days	0		
	C		150	36 h	0 [b]		
3,3,5,5-Tetramethylcyclohexanone	A	Benzene	80	4 days	0 [c]		
	D		150	36 h	41	147° at 0.05 mmHg	(IV; $R^2 = Me$, $R^1 = R^3 = R^4 = H$)
4-t-Butylcyclohexanone	A	Benzene	80	72 h	62	155° at 0.15 mmHg	(IV; $R^4 = Pr^i$, $R^1 = R^2 = R^3 = H$)
Diethyl 4-oxocyclohexane-1,1-dicarboxylate	A	Benzene	80	20 h	68	164° at 0.05 mmHg	(IV; $R^3 = R^4 = CO_2Et$, $R^1 = R^2 = H$)
N-Methylpiperidin-4-one	A	Benzene	80	0.5 h	44	144° at 0.1 mmHg	(VII)
Cyclohexane-1,4-dione	A′	Benzene	80	22 h	0 [d]		
	D		170	36 h	0 [e]		
Cyclohex-2-enone	E	Dimethylformamide	100	2 h	0		
	F	Benzene	80	72 h	0		
Isophorone	A	Benzene	80	48 h	0 [g]		
	D		150	36 h	0		
Cyclopentanone	A	Benzene	80	48 h	0 [f]		
	A	Toluene	110	48 h	0		
	A	*p*-Xylene	138	48 h	0		
Cyclopentenone	E	Dimethylformamide	100	3 h	0		
	F	Benzene	80	72 h	0		
Cycloheptanone	A	Benzene	80	72 h	82	134° at 0.03 mmHg	(VIII; $n = 2$)
Cyclo-octanone	A	Benzene	80	96 h	61	151° at 0.04 mmHg	(VIII; $n = 3$)
Acetone	A	Benzene	80	24 h	0		
Ethyl methyl ketone	A	Benzene	80	3 days	45	141° at 0.7 mmHg	(XII; $R^1 = Et$, $R^2 = H$) and (XII; $R^1 = R^2 = Me$)
Diethyl ketone	A	Benzene	80	4 days	22	144° at 0.5 mmHg	(XII; $R^1 = Et$, $R^2 = Me$)
	E	Dimethylformamide	100	2 h	0		
Ethyl isopropyl ketone	A	*p*-Xylene	138	24 h	39	172° at 0.2 mmHg	(XII; $R^1 = Pr^i$, $R^2 = Me$)
Dibenzyl ketone	A	*p*-Xylene	138	72 h	0		
Pentatriacontan-18-one	A	*p*-Xylene	138	6 days	0		
Acetophenone	A	*p*-Xylene	138	48 h	0		
Acetylacetone	E	Dimethylformamide	100	2 h	32	(93°)	(XVI; $R^1 = Me$, $R^2 = Ac$)
	F	Benzene	80	24 h	11		
Benzoylacetone	E	Dimethylformamide	100	2 h	0		
	F	Benzene	80	72 h	0		
2,2,6,6-Tetramethylheptane-3,5-dione	E	Dimethylformamide	145	18 h	0		
Methyl acetoacetate	E	Dimethylformamide	100	2 h	62	(67.5°)	(XVI; $R^1 = Me$, $R^2 = CO_2Me$)
	F	Benzene	80	24 h	21		
Ethyl acetoacetate	E	Dimethylformamide	100	2 h	57	(107°)	(XVI; $R^1 = Me$, $R^2 = CO_2Et$)
	F	Benzene	80	2 h	15		
Ethyl benzoylacetate	E	Dimethylformamide	100	2 h	0		
	F	Benzene	80	72 h	0		

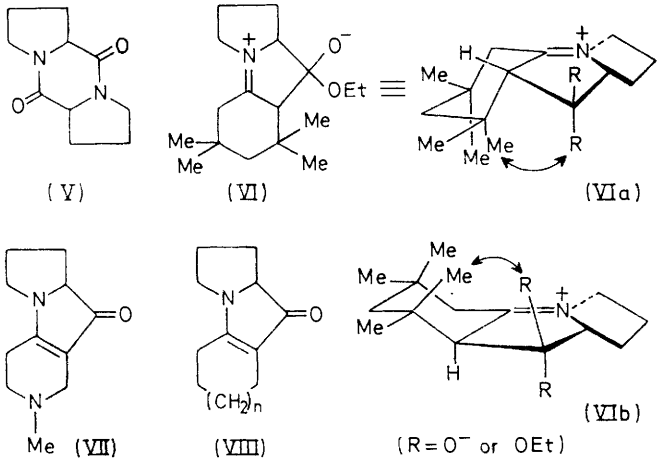
[a] Product was a mixture of mainly 1-(2-ethoxycarbonylpyrrolidin-1-yl)cyclohexene, together with the cyclization product (IV; $R^1 = R^2 = R^3 = R^4 = H$). [b] 60—70% yield of L-proline anhydride (V) obtained, m.p. 148—149° [lit., 149° (Heilbron's 'Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965, vol. 5)]. [c] Product was 3,3,5,5-tetramethyl-1-(2-ethoxycarbonylpyrrolidin-1-yl)cyclohexene (III; $R^1 = R^3 = R^4 = H$, $R^2 = Me$), b.p. 107° at 0.2 mmHg (81%). [d] Product was 1,4-bis-(2-ethoxycarbonylpyrrolidin-1-yl)cyclohexa-1,3-diene (XVII), M^+ 362; $\nu_{max.}$ (film) 1 740 (CO) and 1 620 cm^{-1} (C:C); τ($CDCl_3$) 5.08 (2 H, =CH), 6.15 (4 H, q, $CH_2{\cdot}CH_3$), 6.71 (2 H, m, $N{\cdot}CH{\cdot}CO_2Et$), 7.75 (4 H, $N{\cdot}CH_2$), 7.78 (4 H, s, $CH_2{\cdot}CH_2$), 8.31 (8 H, m, $CH_2{\cdot}CH_2$), and 8.83 (6 H, t, $CH_2{\cdot}CH_3$). [e] Complex mixture of approximately eight components. [f] Product was 1-(2-ethoxycarbonylpyrrolidin-1-yl)cyclopentene (IX), b.p. 82° at 0.02 mmHg (61%), M^+ 209; $\nu_{max.}$ (film) 1 730 (CO) and 1 633 cm^{-1} (C:C); τ($CDCl_3$) 5.8 (2 H, q, $CH_2{\cdot}CH_3$) 6.0 (2 H, m, =CH and $N{\cdot}CH{\cdot}CO_2Et$), 6.50—7.15 (2 H, $N{\cdot}CH_2$), 7.2—8.50 (10 H, CH_2 envelope), and 8.75 (3 H, t, $CH_2{\cdot}CH_3$). [g] Product was a mixture of dienamines (XI), b.p. 123° at 0.4 mmHg; M^+ 263; $\nu_{max.}$ (film) 1 730 (CO) and 1 610 and 1 580 cm^{-1} (C:C); τ($CDCl_3$) 4.95(s), 5.3(m), 5.8(m), 6.65(m), 8.2(m), 8.75(t), and 9.05(s).

slight excess of L-ethyl prolinate at 150 °C in a sealed tube for 36 h, the main product (*ca.* 70%) was the proline



anhydride (V), there being no evidence for formation of the intermediate enamine or the cyclization product.

Since in no case where the reaction failed was any of the corresponding enamine isolated, the effect of 2-substituents can be simply rationalized in terms of the ease of enamine formation. The larger the substituent the greater are the steric interactions (1,3-diaxial or *A*-strain [6]) in the resulting enamine. When the conditions



were sufficiently vigorous to ensure enamine formation, then cyclization to the pyrrolo[1,2-*a*]indole followed.

When the substituents are further removed from the carbonyl group, as at the 3-position, there is no impediment to enamine formation. The reaction of 3,3,5,5-tetramethylcyclohexanone, however, stopped at this intermediate stage, yielding the enamine (III; R^2 = Me, $R^1 = R^3 = R^4$ = H). Attempted cyclization of this enamine failed in boiling *p*-xylene, in the presence of toluene-*p*-sulphonic acid, but was achieved by the action of heat in a sealed tube at 150 °C for 24 h, to give the 6,6,8,8-tetramethylpyrrolo[1,2-*a*]indole (IV; R^2 = Me, $R^1 = R^3 = R^4$ = H). Models show that there are severe steric interactions between the geminal methyl groups at C-8 and the R groups at C-9 in the intermediate (VI). These interactions presumably prevent cyclization of the intermediate enamine under mild conditions, but under more forceful conditions cyclization occurs and the steric interactions are subsequently alleviated by expulsion of ethoxide anion in the re-formation of the carbonyl group at C-9.

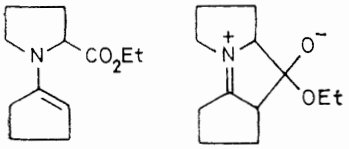
The question of whether the cyclization occurs by way of axial attack by the ester carbonyl group on the enamine double bond, or by attack from the equatorial side of the cyclohexene system, cannot be resolved at present. In passing it may be said that although the developing orbital bias,[7] in a reaction which might be expected to proceed *via* a product-like transition state, would favour axial attack, equatorial attack would be favoured by the constraint imposed by the coplanarity of positions 8a and 9a in the intermediate zwitterion (VI). This means that, from which ever side cyclization occurs, the resulting bond must be equatorially oriented to the cyclohexane ring to give (VIa) (by equatorial attack) or (VIb) (by axial attack and ring inversion).

When the substituents are more remote there is no steric impediment to formation of the enamine or to subsequent cyclization. Thus the 7-t-butylpyrrolo-[1,2-*a*]indole (IV; $R^1 = R^2 = R^3$ = H, $R^4 = Bu^t$) and the diester (IV; $R^1 = R^2$ = H, $R^3 = R^4 = CO_2Et$) were both readily formed by heating the corresponding ketone with L-ethyl prolinate in benzene for 72 h under reflux in the presence of toluene-*p*-sulphonic acid. Similarly *N*-methylpiperidin-4-one gave the pyridopyrrolizine (VII).

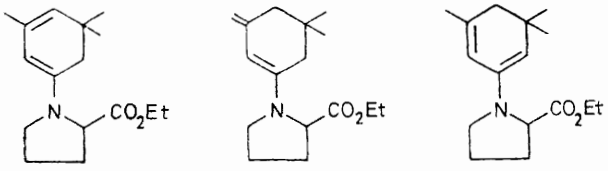
Application of the reaction to larger cyclic ketones presented no difficulty. Thus cycloheptanone and cyclo-octanone gave the cycloalkenopyrrolizines (VIII; n = 2 or 3) after 96 h in benzene under reflux. The reaction failed, however, when the ring size of the ketone was decreased. Thus cyclopentanone gave the enamine (IX), but all attempts to cyclize this were unsuccessful, presumably owing to the increased angle strain which would arise in formation of the zwitterionic intermediate (X). The reaction also failed with αβ-unsaturated cyclic ketones. Thus cyclopent-2-enone and cyclohex-2-enone gave only polymeric products, from which no pure compound could be isolated, and isophorone gave a mixture of the two linear dienamines (XIa and b) in the ratios indicated. There was no evidence for the formation of the cross-conjugated isomer (XIc), in agreement with previous results,[8] and attempts to cyclize these dienamines were unsuccessful. Treatment of cyclohexane-1,4-dione

[6] F. Johnson, *Chem. Rev.*, 1968, **68**, 375.
[7] P. W. Hickmott and K. N. Woodward, *J.C.S. Chem. Comm.*, 1974, 275.
[8] N. F. Firrel and P. W. Hickmott, *J. Chem. Soc.* (*B*), 1969, 293.

with L-ethyl prolinate in benzene gave the crude dienediamine (XVII), but attempts to cyclize this to (XVIII) were also unsuccessful.

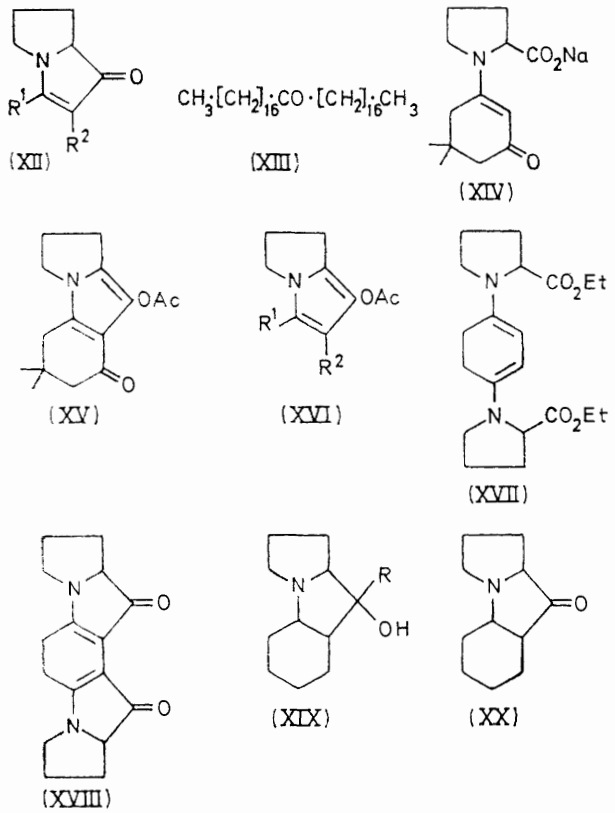


(IX) (X)



(XIa) (43%) (XIb) (57%) (XIc) (0%)

Application of the reaction to acyclic ketones (diethyl, ethyl isopropyl, and ethyl methyl ketone) gave the corresponding pyrrolizines (XII) (in the last case a 3 : 2 mixture of two isomers). The reaction failed, however,



(XII) (XIII) (XIV) (XV) (XVI) (XVII) (XVIII) (XIX) (XX)

with acetone, which gave polymeric products, and with dibenzyl ketone, acetophenone, and pentatriacontan-18-one.

[9] R. J. Friary, R. W. Frank, and J. F. Tobin, *Chem. Comm.*, 1970, 283.

Friary *et al.* have reported [9] that treatment of dimedone with L-sodium prolinate in dimethylformamide gives the enamino-ketone (XIV), which cyclizes to the pyrrolo-[1,2-*a*]indole (XV) on treatment with acetic anhydride. In a similar way we have shown that a number of acyclic 1,3-dicarbonyl compounds may be converted into the corresponding dihydropyrrolizines. Thus ethyl acetoacetate, methyl acetoacetate, and acetylacetone gave the corresponding cyclic products (XVI). The same products may be obtained by initial condensation of L-ethyl prolinate with the appropriate 1,3-dicarbonyl compound in benzene, followed by cyclization with acetic anhydride, but in lower purity and yield. However attempted application of the reaction to ethyl benzoylacetate, benzoylacetone, and 2,2,6,6-tetramethylheptane-3,5-dione, by either method, failed completely. Surprisingly, when the L-sodium prolinate–dimethylformamide method was applied to cyclohexanone or diethyl ketone, only unchanged ketone was isolated, in almost quantitative recovery.

Reduction of 1,2,3,5,6,7,8,9a-octahydropyrrolo[1,2-*a*]-indol-9-one (IV; $R^1 = R^2 = R^3 = R^4 = H$) has been studied with a view to obtaining the ketone (XX) and hence the phenethanolamines (XIX; R = aryl) required for pharmacological evaluation. Attempted selective reduction of the C:C bond has proved unsuccessful. Thus use of lithium hydride (at 0 or 20 °C) or sodium borohydride in pyridine, or catalytic methods (rhodium–alumina) gave only unchanged enamino-ketone (IV). Use of diborane gave an organoborane derivative (ν_{BH}2 400 cm^{-1}) which was not solvolysed in methanol, and iron pentacarbonyl [10] gave complex mixtures. More vigorous reduction, with lithium aluminium hydride in boiling ether–tetrahydrofuran, gave a mixture of the saturated alcohol (XIX; R = H) and the ketone (XX). Treatment of a solution of this mixture in acetone with aqueous sulphuric acid followed by Jones reagent gave the required ketone (XX). The yields of this ketone were much lower if the initial treatment with acid was omitted. Milder methods (use of silver oxide or manganese dioxide, Oppenauer oxidation, and the modified procedure [11] developed by Woodward for compounds containing basic nitrogen) were ineffective or gave considerably lower yields.

EXPERIMENTAL

I.r. spectra were determined with a Perkin-Elmer 257 spectrometer, n.m.r. spectra with a Varian A60 spectrometer, and mass spectra with A.E.I. MS9 and MS12 instruments.

General Methods.—(*A*) The ketone (0.0156 mol), L-ethyl prolinate (0.0175 mol), and a catalytic amount of toluene-*p*-sulphonic acid were heated in a hydrocarbon solvent (70 ml) under reflux until the theoretical amount of water had been eliminated and collected in a Dean–Stark trap. The solvent was removed *in vacuo* and the residual oil distilled to give the pure product.

[10] R. Noyori, I. Umeda, and T. Ishigami, *J. Org. Chem.*, 1972, **37**, 1542.

[11] R. B. Woodward, N. L. Wendler, and F. J. Brutsech, *J. Amer. Chem. Soc.*, 1945, **67**, 1425.

(*A'*) As method (*A*) except that no toluene-*p*-sulphonic acid was used and the crude product obtained after removal of the solvent was not distilled.

(*B*) The ketone (0.03 mol) and L-ethyl prolinate (0.049 mol) were stirred in dry benzene (70 ml) at 5 °C under nitrogen. Titanium tetrachloride in dry benzene was added dropwise over 30 min and the mixture was stirred at ambient temperature for several days. Samples were removed at intervals to determine whether any reaction had taken place.

(*C*) The ketone (0.03 mol) and L-ethyl prolinate (0.049 mol) were heated in a sealed tube in an electric furnace at 150 °C for 36 h. The tube was allowed to cool and the contents lixiviated with light petroleum (b.p. 60—80°) and the solid product was recrystallized from benzene–light petroleum.

(*D*) The intermediate enamine obtained by method (*A*) or (*A'*) was heated in a sealed tube in an electric furnace at 150—170 °C and the product was purified by distillation.

(*E*) The β-diketone or β-oxo-ester (0.0157 mol) and L-sodium prolinate were stirred in dry dimethylformamide (25 ml) at 100—145 °C for 2—18 h. The mixture was cooled and diluted with dry ether (50 ml) and the solid collected, washed with dry ether, and dissolved in acetic anhydride (25 ml). The solution was heated under reflux for 2 h, cooled, and filtered, and the filtrate was stirred with water (50 ml) for 0.5 h. The aqueous phase was extracted several times with ether, and the combined extracts were washed with water (2 × 20 ml), dried ($MgSO_4$), and concentrated to give the product, which was recrystallized from light petroleum (b.p. 60—80°) or cyclohexane.

(*F*) The β-diketone or β-oxo-ester (0.0157 mol) and L-ethyl prolinate (0.0164 mol) were dissolved in benzene (70 ml) and heated under reflux in the presence of a catalytic amount of toluene-*p*-sulphonic acid until the theoretical amount of water had been collected in a Dean–Stark trap. The solvent was removed *in vacuo* and the residue dissolved in acetic anhydride (25 ml). The solution was heated under reflux for 2 h, cooled, and stirred with water (50 ml). The solution was then extracted with ether and the extracts were washed, dried, and concentrated to give the crude product, which was purified by column chromatography [silica; benzene–acetone (95 : 5)].

The experimental details for the reactions are given in the Table and the analytical and spectral data for the cyclization products are summarized below. All liquids were further purified by fractionation in a Kugerlröhr apparatus at 0.001—0.005 mmHg, and the purity of the fraction which was subjected to accurate mass measurement was established by t.l.c. on silica [benzene–acetone (90 : 10) or benzene–acetone–ethyl acetate (85 : 5 : 10)].

1,2,3,5,6,7,8,9a-*Octahydropyrrolo*[1,2-a]*indol*-9-*one* (IV; $R^1 = R^2 = R^3 = R^4 = H$) (Found: C, 74.1; H, 8.0; N, 8.2%; M^+, 177.1154. $C_{11}H_{15}NO$ requires C, 74.6; H, 8.5; N, 7.9%; *M*, 177.1157) showed $\nu_{max.}$ (film) 1 665 (CO) and 1 585 cm^{-1} (C:C); $\tau(CDCl_3)$ 6.2 (1 H, m, N·CH·CO), 6.7—7.2 (2 H, m, N·CH_2), and 7.5—8.8 (CH_2 envelope).

For *Diethyl* 2,3,5,6,7,8,9,9a-*Octahydro*-9-*oxo*-1H-*pyrrolo*-[1,2-a]*indole*-7,7-*dicarboxylate* (IV; $R^1 = R^2 = H$, $R^3 = R^4 = CO_2Et$) see Part XX.[1]

1,2,3,5,6,7,8,9a-*Octahydro*-5-*methylpyrrolo*[1,2-a]*indol*-9-*one* (IV; R^1 = Me, $R^2 = R^3 = R^4 = H$) (Found: M^+, 191.1300. $C_{12}H_{17}NO$ requires *M*, 191.1310) showed $\nu_{max.}$ (film) 1 670 (CO) and 1 580 cm^{-1} (C:C); $\tau(CDCl_3)$ 5.70—8.7 (14 H, CH_2 envelope) and 8.80 (3 H, d, CH_3).

1,2,3,5,6,7,8,9a-*Octahydro*-5-*isopropylpyrrolo*[1,2-a]*indol*-9-*one* (IV; $R^1 = Pr^i$, $R^2 = R^3 = R^4 = H$) (Found: M^+, 231.1627. $C_{14}H_{21}NO$ requires *M*, 231.1623) showed $\nu_{max.}$ (film) 1 670 (CO) and 1 585 cm^{-1} (C:C); $\tau(CDCl_3)$ 5.79 (1 H, m, N·CH), 6.45 (2 H, t, N·CH_2), and 7.39—8.55 (18 H, m, CH_2 envelope and Pr^i).

1,2,3,5,6,7,8,9a-*Octahydro*-5-*phenylpyrrolo*[1,2-a]*indol*-9-*one* (IV; R^1 = Ph, $R^2 = R^3 = R^4 = H$) (Found: M^+, 253.1477. $C_{17}H_{19}NO$ requires *M*, 253.1467) showed $\nu_{max.}$ (film) 1 665 (CO) and 1 580 cm^{-1} (C:C); $\tau(CDCl_3)$ 2.80 (5 H, s, Ph) and 5.8—9.1 (14 H, m, CH_2 envelope).

5-*Benzyl*-1,2,3,5,6,7,8,9a-*octahydropyrrolo*[1,2-a]*indol*-9-*one* (IV; $R^1 = PhCH_2$, $R^2 = R^3 = R^4 = H$) (Found: M^+, 267.1626. $C_{18}H_{21}NO$ requires *M*, 267.1623) showed $\nu_{max.}$ (film) 1 680 (CO) and 1 580 cm^{-1} (C:C) $\tau(CDCl_3)$ 2.83 (5 H, s, Ph) and 5.22—9.05 (16 H, m, CH_2 envelope and $PhCH_2$).

1,2,3,5,6,7,8,9a-*Octahydro*-6,6,8,8-*tetramethylpyrrolo*-[1,2-a]*indol*-9-*one* (IV; $R^1 = R^3 = R^4 = H$, R^2 = Me) (Found: M^+, 233.1765. $C_{15}H_{23}NO$ requires *M*, 233.1780) showed $\nu_{max.}$ (film) 1 675 (CO) and 1 580 cm^{-1} (C:C); $\tau(CDCl_3)$ 6.3 (1 H, N·CH), 6.98 (2 H, N·CH_2), 7.65—8.50 (6 H, CH_2 envelope), 8.66 (2 H, 7-H_2), 8.82 (6 H, s, CH_3), and 9.00s (6 H, CH_3).

1,2,3,5,6,7,8,9a-*Octahydro*-7-*t*-*butylpyrrolo*[1,2-a]*indol*-9-*one* (IV; $R^1 = R^2 = R^3 = H$, $R^4 = Bu^t$) (Found: M^+, 233.1786. $C_{15}H_{23}NO$ requires *M*, 233.1780) showed $\nu_{max.}$ (film) 1 670 (CO) and 1 600 cm^{-1} (C:C); $\tau(CDCl_3)$ 6.05 (1 H, m, N·CH), 6.85 (2 H, m, N·CH_2), 7.32—8.90 (11 H, m), and 9.19 (9 H, s, CH_3).

1,2,3,4,6,7,8,8a-*Octahydro*-2-*methylpyrido*[3,4-b]*pyrrolizin*-9-*one* (VII) (Found: M^+, 192.1247. $C_{11}H_{16}N_2O$ requires *M*, 192.1263) showed $\nu_{max.}$ (film) 1 665 (CO) and 1 595 cm^{-1} (C:C); $\tau(CDCl_3)$ 6.18—6.93 (3 H, m, CH·N·CH_2) and 7.10—8.34 [13 H, m, CH_2 envelope and N·CH_3 (s, at 7.60)].

1,2,3,6,7,8,9,10a-*Octahydrocyclohepta*[b]*pyrrolizin*-10-(5H)-*one* (VIII; *n* = 2) (Found: M^+, 191.1303. $C_{12}H_{17}NO$ requires *M*, 191.1310) showed $\nu_{max.}$ (film) 1 655 (CO) and 1 580 cm^{-1} (C:C); $\tau(CDCl_3)$ 6.17 (1 H, m, N·CH), 6.79 (2 H, m, N·CH_2), and 7.16 (14 H, m).

1,2,3,5,6,7,8,9,10,11a-*Decahydrocyclo-octa*[b]*pyrrolizin*-11-*one* (VIII; *n* = 3) (Found: M^+, 205.1468. $C_{13}H_{19}NO$ requires *M*, 205.1467) showed $\nu_{max.}$ (film) 1 665 (CO) and 1 580 cm^{-1} (C:C); $\tau(CDCl_3)$ 6.11 (1 H, m, N·CH), 6.71 (2 H, N·CH_2), and 7.14—8.80 (16 H, m).

3-*Ethyl*-5,6,7,7a-*tetrahydro*-2-*methylpyrrolizin*-1-*one* (XII; R^1 = Et, R^2 = Me) [Found: M^+, 165; $(M-1)^+$, 164.1069.* $C_{10}H_{15}NO$ requires *M*, 165; (*M* − 1), 164.1075]; $\nu_{max.}$ (film) 1 665 (CO) and 1 585 cm^{-1} (C:C); $\tau(CDCl_3)$ 5.9—6.46 (1 H, m, N·CH), 6.85 (2 H, m, N·CH_2), 7.22—8.25 (6 H, m, CH_2 envelope), 8.38 (3 H, s, CH_3), and 8.84 (3 H, t, CH_2·CH_3).

3-*Ethyl*-5,6,7,7a-*tetrahydropyrrolizin*-1-*one* (XII; R^1 = Et, R^2 = H) and 5,6,7,7a-*tetrahydro*-2,3-*dimethylpyrrolizin*-1-*one* (XII; $R^1 = R^2$ = Me) (Found: M^+, 151.0994. $C_9H_{13}NO$ requires *M*, 151.0997) showed $\nu_{max.}$ (film) 1 675 (CO) and 1 590 cm^{-1} (C:C); $\tau(CDCl_3)$ 5.75 (s, =CH), 6.20—7.16 (3 H, CH_2·N and N·CH), and 7.30—9.2 (CH_2 envelope and CH_3).

3-*Isopropyl*-5,6,7,7a-*tetrahydro*-2-*methylpyrrolizin*-1-*one* (XII; $R^1 = Pr^i$, R^2 = Me)(Found: M^+, 179.1314. $C_{11}H_{17}NO$ requires *M*, 179.1309) showed $\nu_{max.}$ (film) 1 670 (CO) and 1 590 cm^{-1} (C:C); $\tau(CDCl_3)$ 6.2 (1 H, m, N·CH), 6.9 (2 H, t, N·CH_2), and 7.5—9.15 (14 H, m, CH_2 envelope and CH_3).

7-*Acetoxy*-6-*acetyl*-2,3-*dihydro*-5-*methyl*-1H-*pyrrolizine*

* Molecular ion too weak to be measured accurately.

(XVI; R^1 = Me, R^2 = Ac) (Found: C, 65.6; H, 7.0; N, 6.7%; M^+, 221. $C_{12}H_{15}NO_3$ requires C, 65.1; H, 6.8; N, 6.3%; M, 221) showed $\nu_{max.}$ (Nujol) 1 755 and 1 645 (CO), and 1 605 cm^{-1} (C:C); τ($CDCl_3$) 6.15 (2 H, t, N·CH_2), 6.68 (3 H, s, CH_3), 6.71 (3 H, s, CH_3), 6.99 (4 H, CH_2·CH_2), and 7.55 (3 H, s, CH_3).

Methyl 7-acetoxy-2,3-dihydro-5-methyl-1H-pyrrolizine-6-carboxylate (XVI; R^1 = Me, R^2 = CO_2Me) (Found: C, 60.35; H, 6.5; N, 6.0%; M^+, 237. $C_{12}H_{15}NO_4$ requires C, 60.7; H, 6.4; N, 5.9%; M, 237) showed $\nu_{max.}$ (Nujol) 1 760 and 1 695 (C:O) and 1 617 cm^{-1} (C:C); τ($CDCl_3$) 6.16 (2 H, m, N·CH_2), 6.25 (3 H, s, CH_3), 7.01—7.52 (4 H, m, CH_2·CH_2), 7.60 (3 H, s, CH_3), and 7.64 (3 H, s, CH_3).

Ethyl 7-acetoxy-2,3-dihydro-5-methyl-1H-pyrrolizine-6-carboxylate (XVI; R^1 = Me, R^2 = CO_2Et) (Found: C, 61.9; H, 7.0; N, 5.5%; M^+, 251. $C_{13}H_{17}NO_4$ requires C, 62.1; H, 6.8; N, 5.6%; M, 251) showed $\nu_{max.}$ (Nujol) 1 760 and 1 685 (CO) and 1 605 cm^{-1} (C:C); τ($CDCl_3$) 5.88 (2 H, q, CH_2·CH_3), 6.20 (2 H, t, N·CH_2), 7.14—7.60 (4 H, m, CH_2·CH_2), 7.63 (3 H, s, CH_3), 7.79 (3 H, s, CH_3), and 8.72 (3 H, t, CH_2·CH_3).

Perhydropyrrolo[1,2-a]*indol-9-one* (XX).—A solution of the octahydropyrroloindolone (IV; R^1 = R^2 = R^3 = R^4 = H) (13 g) in dry tetrahydrofuran (250 ml) was added dropwise to lithium aluminium hydride (25 g) in dry ether (300 ml) at ambient temperature, and the mixture was heated under reflux for 48 h. The cooled solution was poured into ice–water and filtered through Celite. The aqueous and solid phases were extracted with ether and the extracts combined, dried (Na_2SO_4), and evaporated to give the crude alcohol (XIX; R = H) (12.7 g) [m.p. 111—112.5° (from chloroform)] contaminated with the ketone (XX) [$\nu_{max.}$ (film) 3 400 (OH) and 1 750 cm^{-1} (CO)]. The crude product was dissolved in acetone (300 ml) and concentrated sulphuric acid (8 g) in water (25 ml) was added. The solution was vigorously stirred and Jones reagent (116 ml) in acetone (200 ml) was added over 10 min. The solution was stirred overnight, and basified with 20% sodium hydroxide, and the resulting suspension was filtered through Celite. The aqueous and solid phases were extracted with ether and the extracts combined, dried (Na_2SO_4), and evaporated to give a red-brown oil (8.01 g). Distillation gave the ketone (XX) (1.91 g, 15%), b.p. 133° at 0.7 mmHg, M^+ 179; $\nu_{max.}$ (film) 1 750 cm^{-1} (CO); τ($CDCl_3$) 6.14—9.16 (CH_2 envelope); *dinitrophenylhydrazone*, m.p. 157° (from ethanol) (Found: C, 57.4; H, 5.6; N, 19.3. $C_{17}H_{21}N_5O_4$ requires: C, 57.1; H, 5.9; N, 19.45%).

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