Synthesis of Pyrrolidine-2,4-diones (Tetramic acids) and Some Derivatives

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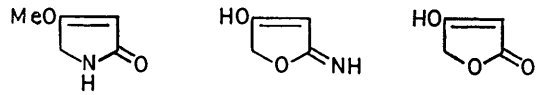
Pyrrolidine-2,4-dione (tetramic acid) has been obtained by heating its 3-ethoxycarbonyl derivative with water or nitromethane. Prolonged heating with water yields 4-hydroxy-3,4'-bi-Δ^3-pyrrolinyl-2,2'-dione, the anhydro-derivative of the dione. 1- and 5-Methylpyrrolidine-2,4-diones and their anhydro-derivatives have been obtained similarly. Previously reported syntheses of these pyrrolidine-2,4-diones are shown to be in error; the products obtained appear to have been the corresponding anhydro-derivatives, or their hydrates. Other derivatives of the diones are described. Condensation of ethyl-4-hydroxy-2-oxo-Δ^3-pyrroline-3-carboxylate with aromatic aldehydes yields mainly the (*E*)-5-arylmethylene derivatives.

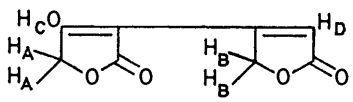
PYRROLIDINE-2,4-DIONE (tetramic acid) (XVII) and its 1- and 5-methyl derivatives [(XVIII) and (XIX)] have been synthesised (Scheme 1), apparently for the first time, although their synthesis has been claimed previously. Pyrrolidine-2,4-dione has hitherto been obtained [1] only as its enol methyl ether, 4-methoxy-Δ^3-pyrrolin-2-one (I) The first reported synthesis [2,3] of the corresponding dione (XVII) was shown [4,5] later to give the isomeric compound (II) ('iminotetronic acid'); the correction has not always been noted.[6,7] More recently Isowa and Ohta [8] have reported that hydrolysis of methyl 4-hydroxy-2-oxo-Δ^3-pyrroline-3-carboxylate (XVI) with boiling aqueous barium hydroxide gives the dione (XVII) ($C_4H_5NO_2$), but the u.v. absorption quoted by these authors is not consistent with this structure. The strong maxima (log $\varepsilon > 3$) at 239 and 320 nm in water, and similar absorption in aqueous sodium hydroxide show that their product contained a more highly conjugated chromophore than could be present in a tautomer of pyrrolidine-2,4-dione. Their material was probably mainly the monohydrate of the anhydrodimer (XX) (see later), derived from the initially formed dione in the same way as anhydrotetronic acid (IV) is formed from tetronic acid (III).[9]

[1] D. J. Cram, O. Theander, H. Jager, and M. K. Stanfield, *J. Amer. Chem. Soc.*, 1963, **85**, 1430.
[2] E. Benary, *Ber.*, 1907, **40**, 1079.
[3] E. Benary, *Ber.*, 1911, **44**, 1759.
[4] R. Anschütz, *Ber.*, 1912, **45**, 2374.
[5] E. Benary, *Ber.*, 1912, **45**, 3682.
[6] R. N. Lacey, *J. Chem. Soc.*, 1954, 850.
[7] C. E. Stickings, *Biochem. J.*, 1959, **72**, 332.
[8] Y. Isowa and M. Ohta, *Bull. Chem. Soc. (Japan)*, 1962, **35**, 1941.
[9] D. H. Marrian, P. B. Russell, A. R. Todd, and W. S. Waring, *J. Chem. Soc.*, 1947, 1365.

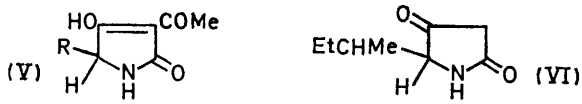
Isowa and Ohta [8] reported a similar synthesis of 5-methylpyrrolidine-2,4-dione (5-methyltetramic acid) (XIX). The published data are scanty, but the apparent insolubility of their product in water shows



(I) (II) (III)



(IV)



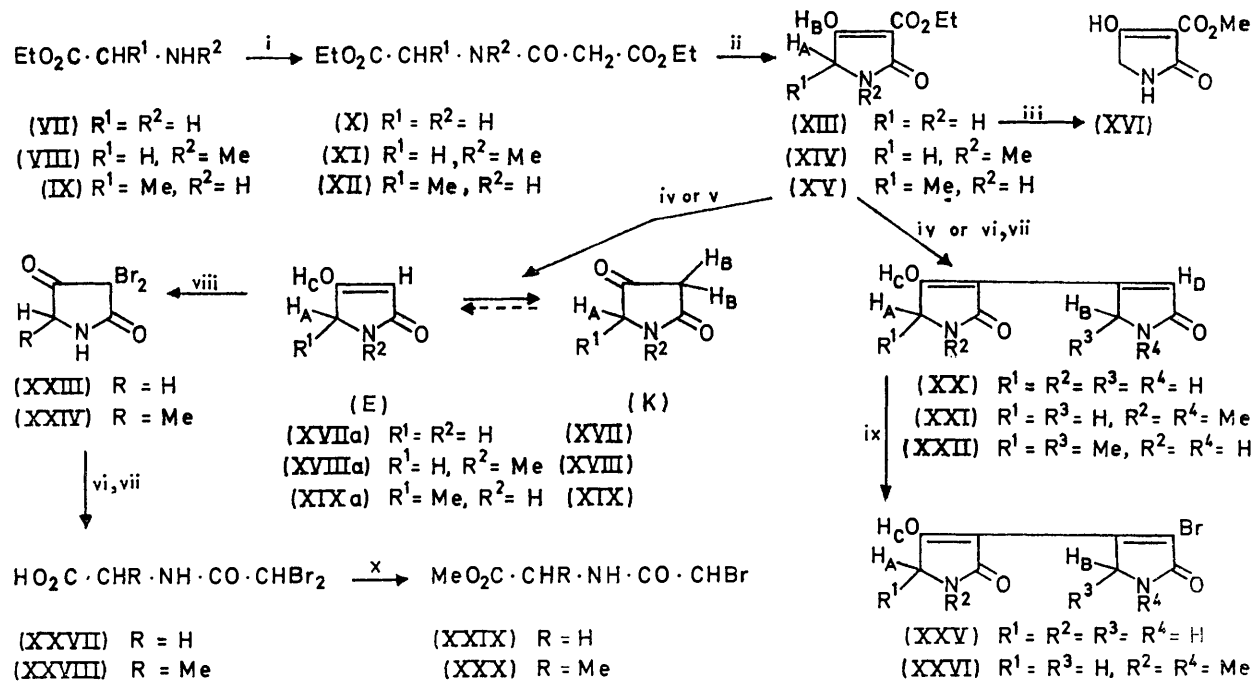
(V) (VI)

(see later) that it was unlikely to have been the dione, which is soluble in water.

Schmidt and Geiger [10] obtained a compound which they considered to be 1-methylpyrrolidine-2,4-dione (XXII) were obtained from the ethyl 4-hydroxy-2-oxo-Δ^3-pyrroline-3-carboxylates (XIII)—(XV). The esters (XIII)—(XV) were prepared from the corresponding amino-acid ethyl esters (VII)—(IX) by conversion into their *N*-ethoxycarbonylacetyl derivatives (X)—(XII), which were cyclised with sodium ethoxide in benzene.

The cyclic esters gave intense red colours with ferric ions. They were less acidic (Table 1) than 3-ethoxycarbonyltetronic acid (p*K* 1·8).[11] The n.m.r. signal (Table 2) at τ 6·1 for the ring methylene group of the ester (XIII) diminished on deuteriation, suggesting the involvement of a tautomeric form other than (XIII) [in the 5-methyl analogue (XV) the C-5 proton did not appear to exchange and in the *N*-methyl analogue (XIV) the relevant part of the spectrum was obscured by the HOD signal]. Crystallisation of the ethyl ester (XIII) from boiling methanol resulted in rapid conversion into the sparingly soluble methyl ester (XVI), which has been obtained [8] by cyclising the intermediate (X) with sodium methoxide.

When the cyclic esters (XIII), (XIV), and (XV) were heated in boiling water, with aqueous ferric chloride as external indicator to monitor the reaction,



SCHEME 1 Reagents: i, $ClCO{\cdot}CH_2{\cdot}CO_2Et$–$K_2CO_3$; ii, NaOEt–$C_6H_6$; iii, MeOH; iv, H_2O; v, $MeNO_2$; vi, OH^-; vii, H^+; viii, Br_2–H_2O; ix, Br_2–NaOAc; x, CH_2N_2

(XVIII) by heating the corresponding 3-methoxycarbonyl derivative with water. The elemental analytical figures, m.p., and blue colour with ferric ions reported for this product are consistent with its formulation as the anhydro-monohydrate (XXI), which we have also prepared.

In the present work the pyrrolidine-2,4-diones (XVII)—(XIX) and their anhydro-dimers (XX)—the indicator colours changed progressively from the red of starting material to brown, and finally to blue. Recovery of the products at the intermediate stage (about 6 min) yielded the water-soluble pyrrolidine-2,4-diones (XVII)—(XIX), which were usually ac-

[10] U. Schmidt and F. Geiger, *Annalen*, 1963, **664**, 168.
[11] W. Baker, K. D. Grice, and A. B. Jansen, *J. Chem. Soc.*, 1943, 241.

companied by small proportions of the corresponding anhydro-derivatives of the diones; isolation at the terminal stage gave only the latter [(XX)—(XXII); see later]. Refluxing the ester (XIII) in nitromethane also gave pyrrolidine-2,4-dione (XVII); this method was more convenient than the first, but gave lower yields.

Pyrrolidine-2,4-dione could not be obtained from the ester (XIII) by pyrolysis, and when the three esters were hydrolysed with cold alkali, the only products isolated were the anhydro-derivatives of the diones. The related dione, deacetyltenuazonic acid (VI), has been prepared [7] from its 3-acetyl derivative [tenuazonic acid (V; R = CHMeEt)] by hot acidic hydrolysis, but similar treatment of the readily available [6] 3-acetyl-4-hydroxy-Δ^3-pyrrolin-2-one (V; R = H) did not give the dione (XVII); this result is to be expected because of the instability of this dione in aqueous media. Attemps to cyclise diethyl chloroacetylmalonate [12] to the dione (XVII) with aqueous ammonia resulted in fission to give chloroacetamide.

TABLE 1

Compound	pK in H_2O	$\lambda_{max.}$/nm (ε) H_2O	0·1N-NaOH	0·1N-HCl
(XIII)	2·34	227 (13,700) 261 (11,700)	228 (14,000) 261 (12,700)	
(XIV)	2·55	229 (15,900) 269 (9470)	230 (15,900) 269 (9690)	
(XV)			229 (14,600) 262 (12,100)	
(XVII), (XVIIa)	6·4	258 (1240)	260 (12,900)	Nil
(XVIII), (XVIIIa)	7·05		267 (9500)	Nil
(XIX), (XIXa)	6·42	260 (890)	261 (12,100)	Nil
(XX)	3·19		*ca.* 223 (7860) 267 (10,700) 317 (18,000)	236 (11,400) 285 (13,000)
(XXI)	3·46	*ca.* 233 (9560) 274 (10,600) 327 (16,300)	*ca.* 230 (9380) 273 (11,700) 328 (17,900)	243 (14,800) 295 (11,000)
(XXII)	3·09		*ca.* 233 (8630) 268 (10,400) 322 (16,600)	236 (12,700) 286 (11,700)
(XXV)			*ca.* 225 (7070) 266 (9430) 329 (14,800)	227 (12,400) 284 (7950)
(XXVI)		*ca.* 228 (8670) 278 (7980) 328 (9220)		236 (12,800) 289 (6350)
(IV)		253 (15,100) 308 (24,900)	254 (17,100) 309 (24,500)	218 (6810) 253 (11,000) 312 (13,700)

The new pyrrolidine-2,4-diones exist in the keto-form (K) ($\nu_{max.}$ *ca.* 1780 cm^{-1}) as solids, in deuteriochloroform (n.m.r.), and in dilute hydrochloric acid (no u.v. max.), but are enolised to a minor extent (E) in [$^2H_6$]dimethyl sulphoxide and in water (Table 1). The enolate ions absorb between 260 and 267 nm (*cf.* tetronic acid,[13] 248 nm) and there are no maxima in the region 300—330 nm (u.v. spectra were determined immediately after dissolution of the sample). The *N*-methyl analogue (XVIII) was hygroscopic and in undried air soon (1—2 h) became partly converted (i.r. and u.v. absorption) into its anhydro-derivative (XXI). The diones were only weakly acidic (pK > 6), and when freshly prepared gave slight or negligible brown colours with aqueous ferric chloride. The n.m.r. spectra showed resemblances to those of analogous tetronic acids which also are less highly enolised in deuteriochloroform than in [$^2H_6$]dimethyl sulphoxide. As in the spectra of many tetronic acids [14] there was weak (*J ca.* 1 Hz) long-range coupling between the C-5 and C-3 protons in the keto and enol forms of the pyrrolidine-2,4-diones. Additionally, in the keto-form (XVIII) of the *N*-methyl analogue there was coupling between the *N*-methyl and C-3 protons; the *N*-methyl signal reverted to a singlet when the latter were removed by deuteriation. No evidence was obtained that any of the pyrrolidinediones underwent deuteriation at positions 5 [*cf.* (XIII)].

The pyrrolidinediones gave 2,4-dinitrophenylhydrazones, and a thiosemicarbazone was obtained from the 5-methyl analogue (XIX). Bromination of the diones in aqueous sodium acetate gave products which decomposed during attempted recovery. Bromination with bromine water failed with the *N*-methyl analogue (XVIII), but the diones (XVII) and (XIX) yielded the corresponding 3,3-dibromo-derivatives (XXIII) and (XXIV). These dibromides were immediately cleaved by cold aqueous sodium hydroxide, giving the acyclic acids (XXVII) and (XXVIII), respectively, from which the methyl esters (XXIX) and (XXX) were obtained by treatment with diazomethane.

The position of the bromine substituents in the dibromopyrrolidine-2,4-diones was established by i.r. (NH), n.m.r. (see Experimental section), and mass spectroscopy. The last showed *inter alia*, fragments of *m/e* (^{79}Br) 213 [$(\overline{CBr_2 \cdot CO \cdot NH^+}$], 198 [$(Br_2C{=}C{=}\overset{+}{O})$], and 170 [$(CBr_2^+)$].

The dibromopyrrolidinedione (XXIII), m.p. 135—136° (decomp.), may be identical with the dibromopyrrolidine-2,4-dione, m.p. 143—144°, obtained by Cram *et al.*[1] from the bromination of 4-methoxy-Δ^3-pyrrolin-2-one (I). Although these authors assigned the alternative 1,3-dibromo-substitution pattern to their product, the quoted i.r. absorption includes bands [$\nu_{max.}$ ($CHCl_3$) 3180 and 3380 cm^{-1}] assignable to an NH group; the other strong maxima are similar to those shown by our product (XXIII), except that the latter gives rise to a very strong band at 1210 cm^{-1} in chloroform instead of at 1255 cm^{-1}. Structures analogous to (XXIII) and (XXVII) may probably be assigned respectively to the dibromo-derivative $C_8H_{11}Br_2NO_2$ and its alkali-fission product $C_8H_{13}Br_2N_2O_3$, obtained [7] from deacetyltenuazonic acid (VI) by Stickings.

[12] L. J. Haynes, J. R. Plimmer, and A. J. Stanners, *J. Chem. Soc.*, 1956, 4661.

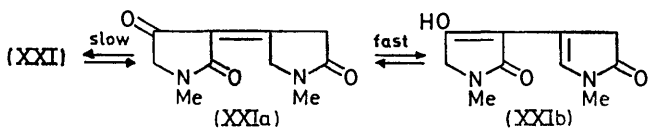
[13] L. J. Haynes and J. R. Plimmer, *Quart. Rev.*, 1960, **14**, 292.

[14] T. P. C. Mulholland, unpublished results.

The high-melting anhydro-derivatives of the pyrrolidine-2,4-diones (XVII)—(XIX) were assigned the bipyrrolinyl structures (XX)—(XXII), respectively, by analogy with anhydrotetronic acid (IV),[9] which can be obtained similarly, but less readily, from tetronic acid by treatment with hot water. 4-Hydroxythiophen-2(5*H*)-one (thiotetronic acid)[15] also yields[16] an anhydro-derivative, but 5-methyltetronic acid does not.[9]

The *NN'*-dimethylbipyrrolinyl (XXI), only obtained as its monohydrate, is undoubtedly the product isolated by Schmidt and Geiger.[10] The analogues (XX) and (XXII) were isolated in anhydrous form, and the former also as a hemihydrate which was difficult to dehydrate further. As with anhydrotetronic acid, bromination of the bipyrrolinyls (XX) and (XXI) gave monobromo-derivatives. These [(XXV) and (XXVI)] were unstable in solution and could not be advantageously recrystallised. The u.v. spectra were almost identical with those of the unbrominated precursors; in alkali all showed maxima near 225, 270, and 325 nm (Table 1) and in acid near 240 and 290 nm. The unbrominated bipyrrolinyls were markedly acidic, though less so than anhydrotetronic avid (IV) (pK 1·99).[9] The n.m.r. spectra also showed similarities with that of the last compound (we thank Dr. B. Hesp for a sample). The spectra of anhydrotetronic acid and the bipyrrolinyls (XX) and (XXI) showed resolved signals due to both ring-methylene groups; the higher-field signals were not coupled, but the lower-field signals showed the usual long-range coupling to the vinyl protons. In the bipyrrolinyls (XX) and (XXI) the methylene signals appeared at about τ 6·1 (hydroxylated ring) and at τ 5·7; the latter signals reverted to singlets when the vinyl protons (τ 3·7) were replaced by bromine in the corresponding monobromo-derivatives (XXV) and (XXVI). The doubling of signals in the spectrum of the 5,5'-dimethyl analogue (XXII) is ascribed to the presence of two diastereoisomeric racemates.

Deuteriation of the *NN'*-dimethylbipyrrolinyl (XXI) resulted both in replacement of the vinyl proton and a diminution (*ca.* 50% in 2 days) of the methylene signal at τ 5·73, while the methylene group (τ 6·03) of the hydroxylated ring was unaffected. It seems likely that, as with the cyclic ester (XIII), more than one isomer or tautomer of this bipyrrolinyl may exist, probably as a result of an equilibrium between the structures (XXI), (XXIa), and (XXIb).



The i.r. spectra of the bipyrrolinyls are difficult to interpret, but may indicate that as solids, the tautomeric states differ. No evidence was obtained that deuteriation of the 5'-position occurred in the bipyrrolinyls (XXII) and (XX) or the bromobipyrrolinyl (XXVI). Neither methylene group present in anhydrotetronic

TABLE 2

^{1}H N.m.r. data (τ values)

Compound [a]	Solvent [b]	R^1	R^3	H_A	H_B	CO_2Et					
(XIII)	A	$=H_A$	*c*	6·10(s) [d]	*c*	5·75(q), 8·75(t)					
(XIV)	A	$=H_A$	7·20(s)	6·06(s)	*c*	5·85(q), 8·80(t)					
(XV)	A	8·58(d)	2·9(d)	5·80(q)	−0·2 [e]	5·60(q), 8·63(t)					
		$K(H_A)$	$K(H_B)$	$E(H_A)$	$E(H_B)$	$K(R^1)$	$E(R^1)$	$K(R^2)$	$E(R^2)$	$E(H_A)$	%E
(XVII) and (XVIIa) [e]	A	6·2(m)	7·08 [d] (J_{AB} 1 Hz)	6·2(m)	5·25(t) [d] (J_{AB} 1 Hz)	$=H_A(K)$	$=H_A(E)$	1·8br [d]	2·9br	−1·2br [d]	19
(XVIII)	B	6·13(t) (J_{AB} 1 Hz)	7·0br(m) [d]			$=H_A(K)$		7·00br			0
(XVIII) and (XVIIIa)	A	6·1br(m)	7·0br(m) [d]	6·1br(m)	5·21 [d]	$=H_A(K)$	$=H_A(E)$	7·16(t) (J_{B_2B} 1 Hz)	7·23	−1·2br [d]	13
(XIX)	B	5·92br(q)	7·00(d) [d] (J_{AB} 1 Hz)			8·64(d) (J_{R^1A} 7 Hz)		2·4 [d]			0
(XIX) and (XIXa)	A + B	6·0(q)	7·0(d) [d] (J_{AB} 1 Hz)	6·0(q)	5·25br [d]	8·76(d) (J_{R^1A} 7 Hz)	8·76(d) (J_{R^1A} 7 Hz)	1·6br [d]	2·9br [d]	−1·2br [d]	20
		H_A	H_B	R^1	R^3	R^2,R^4	H_C	H_D			
(XX)	A	6·14(s)	5·80br	$=H_A$	$=H_B$	2·5, 2·5	2·1 [d]	3·75br [d]			
(XXI)	A	6·03(s)	5·73br [d]	$=H_A$	$=H_B$	7·10, 7·16	*c*	3·73br [d]			
(XXII) [f]	A	5·92 (2 × q)	5·42 (2 × q)	8·75 (2 × d)	8·85 (2 × d)	2·4, 2·4	2·1 [d]	3·79 [d]			
(XXV)	A	6·10(s)	5·85(s)	$=H_A$	$=H_B$	2·4, 1·5	−0·5				
(XXVI)	A	6·05(s)	5·76(s)	$=H_A$	$=H_B$	7·04(s), 7·18(s)	−1·3 [d]				
(IV)	A	5·28(s)	4·90 (J_{BD} 1·5 Hz)				*c*	3·92(t) (J_{BD} 1·5 Hz)			

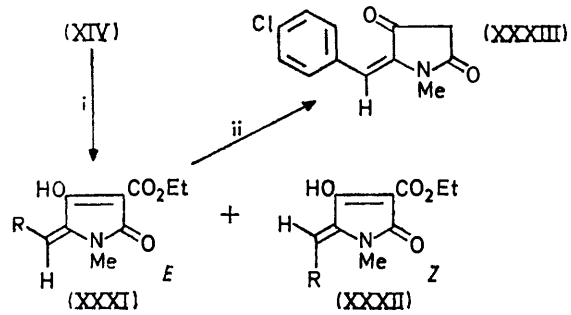
[a] See Scheme 1. [b] A, $(CD_3)_2SO$; B, $CDCl_3$. [c] Exchanges with water in the solvent. [d] Can be deuteriated. [e] Insoluble in $CDCl_3$. [f] Mixture of diastereoisomeric racemates.

[15] E. Benary, *Ber.*, 1913, **46**, 2103.
[16] G. J. Stacey, unpublished results.

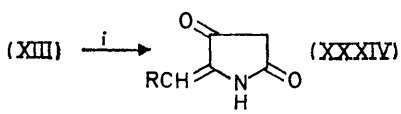
acid (IV) was affected by subjection to deuteriation conditions for 2 days.

Ethyl 4-hydroxy-1-methyl-2-oxo-Δ^3-pyrroline-3-carboxylate (XIV) condensed with several aromatic aldehydes (Scheme 2) in acidic media. Depending on the aldehyde, the product was either a single, *E*-isomer,[17] or a mixture of the *E*- and a smaller amount of the *Z*-isomer. One mixed product was resolved by crystallisation giving both the major (*E*) (XXXIa) and minor (*Z*) (XXXIIa) isomers. Neither product melted sharply, but progress in the resolution could be followed by n.m.r. spectroscopy.

The n.m.r. spectra of the predominant isomers (XXXI) showed singlets at about τ 3·6 and 6·9 for the vinyl and *N*-methyl protons, respectively; the minor isomers, when formed, gave rise to a corresponding pair of signals at about τ 3·3 and 7·2. Configurational assignments, predicted on steric grounds, were established by n.m.r. spectroscopy. Double resonance experiments with the mixture of the isomers (XXXIa)



	% *Z*-Isomer in crude product
a; R = *p*-ClC_6H_4	20 — 25
b; R = *p*-FC_6H_4	25 — 30
c; R = *p*-BrC_6H_4	Trace
d; R = *m*-ClC_6H_4	Trace
e; R = *p*-$ClC_6H_4 \cdot C_6H_4$-*p*	0



SCHEME 2 Reagents: i, RCHO–H^+; ii, EtOAc, heat

and (XXXIIa) showed that a significant nuclear Overhauser effect[18] was demonstrable for the major product. Irradiation (degassed deuteriochloroform solution) at the frequency of the *N*-methyl protons in the major product (τ 6·88) resulted in an enhancement (9·2, 11·2%) of the absorption intensity of the corresponding vinyl proton signal at τ 3·63, whereas similar irradiation at the frequency of the *N*-methyl protons of the minor isomer (τ 7·15) had no effect on the vinyl signal at τ 3·28. Thus the major product contains the vinyl hydrogen atom and *N*-methyl group in spatial proximity and is the *E*-isomer (XXXIa).

Heating the latter isomer with ethyl acetate removed the ester group, yielding the dione (XXXIII), which is assumed to retain the original *E*-configuration, and, like the 3,5-unsubstituted pyrrolidinediones, exists in the keto-form in the solid state. Esters analogous to (XXXI) were not obtained from the reaction of ethyl 4-hydroxy-2-oxo-Δ^3-pyrroline-3-carboxylate (XIII) with *p*-chloro- and *p*-fluoro-benzaldehyde because the ester group was more labile and was largely lost during the condensations; only the 3-unsubstituted 5-arylmethylene derivatives (XXXIVa and b) were isolated.

EXPERIMENTAL

M.p.s are corrected, and unless stated otherwise were determined with Kofler hot-stage apparatus; some decomposition points were determined for samples in unsealed capillaries [denoted (cap.)]. Light petroleum had b.p. 60—80° and organic solutions were dried with sodium sulphate. Molecular weights were obtained by low resolution mass spectroscopy (Hitachi RMU-6E instrument), n.m.r. spectra with Perkin-Elmer R12 60 MHz or Varian HA-100 spectrometers, and i.r. spectra with a Perkin-Elmer model 457 spectrometer.

Ethyl 2-Oxo-Δ^3-pyrroline-3-carboxylates.—(i) *Ethyl 4-hydroxy-2-oxo-Δ^3-pyrroline-3-carboxylate* (XIII). A mixture of ethyl *N*-(ethoxycarbonylacetyl)glycinate (X) (36·2 g, 0·17 mol) [m.p. 71—72° (lit.,[8] 64—65°)], benzene (250 ml), and a solution of sodium (3·83 g, 0·17 g atom) in ethanol (77 ml) was stirred and boiled for 3 h, cooled, and mixed with water (160 ml). The aqueous layer, combined with water-washings of the organic layer, was washed with ether, then acidified at 0° with dilute (1 : 1) sulphuric acid. The *product* separated as cream-coloured needles (12·3 g, 41%) which were used without further purification. A sample crystallised quickly from water formed needles of the hemihydrate. When the compound was heated rapidly (cap.) there was transient melting at *ca.* 140°, followed by resolidification and no further melting to 300°; when it was heated slowly it blackened, but did not melt [Found (dried at 100°): C, 47·2; H, 5·1; N, 7·7. $C_7H_9NO_4$,0·5H_2O requires C, 46·7; H, 5·6; N, 7·8%] [Found: M^+, 171 ($C_7H_9NO_4$)], $\nu_{max.}$ (Nujol) 3210br,m (NH), *ca.* 3100br (OH), 1716vs and 1665s (CO), and 1632 cm^{-1} (C=C). This ester and the analogues (XIV)—(XVI) gave intense red colours with aqueous ferric chloride.

Heating the ester (XIII) with methanol resulted in rapid separation of the sparingly soluble methyl 4-hydroxy-2-oxo-Δ^3-pyrroline-3-carboxylate (XVI) as needles, m.p. >300° (lit.,[8] >360°) (Found: C, 46·0; H, 4·7; N, 8·7%; equiv., 156. Calc. for $C_6H_7NO_4$: C, 45·9; H, 4·5; N, 8·9%; equiv., 157), $\lambda_{max.}$ (0·1N-NaOH) 229 and 262 nm (ε 12,700 and 12,000).

(ii) *Ethyl 4-hydroxy-1-methyl-2-oxo-Δ^3-pyrroline-3-carboxylate* (XIV). Ethoxycarbonylacetyl chloride (29·4 g, 0·2 mol) was added dropwise to a vigorously stirred solution of sarcosine ethyl ester hydrochloride (30·3 g, 0·2 mol) in aqueous 50% potassium carbonate (130 ml) below 0°. The mixture was stirred at room temperature for 18 h,

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[18] F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 1965, **87**, 5250.

then extracted with chloroform. The extract was washed with water, dried, and evaporated, giving the *N*-ethoxycarbonylacetyl derivative (XI) as an oil (33·9 g). This oil (27·7 g) was cyclised by the method described in (i) yielding the *product* (16·0 g), m.p. 190—192° (decomp.; cap.) (Found: C, 52·0; H, 5·8; N, 7·5%; *M*, 185. $C_8H_{11}NO_4$ requires C, 51·9; H, 6·0; N, 7·6%; *M*, 185), $\nu_{max.}$ (Nujol) 2450vbr, 1840br, 1709s, 1644ms, 1612vs, and 1540vw cm^{-1}. The ester could be recrystallised from ethanol, though with slight decomposition.

(iii) (±)-*Ethyl 4-hydroxy-5-methyl-2-oxo-*Δ^3*-pyrroline-3-carboxylate* (XV). The crude oily *N*-ethoxycarbonylacetyl derivative (XII) [8] of (±)-alanine ethyl ester hydrochloride, was cyclised with sodium ethoxide as described in (i). After the acidification step the liberated *product* (73%) was recovered in chloroform, and crystallised from ethyl acetate in prisms, m.p. 134—136° (Found: C, 52·3; H, 6·1; N, 7·7%; *M*, 185. $C_8H_{11}NO_4$ requires C, 51·9; H, 6·0; N, 7·6%; *M*, 185), $\nu_{max.}$ (Nujol) 3190ms, *ca.* 3000br, 1728vs, 1666s, and 1639ms cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 3460mw, *ca.* 3230br, 1704vs, 1662s, and 1628ms cm^{-1}.

Pyrrolidine-2,4-diones and their Bipyrrolinyl Derivatives.—(i) *Pyrrolidine-2,4-dione* (XVII). (*a*) The ester (XIII) (5·0 g) was added to deaerated water (160 ml) preheated to 98°. The mixture was refluxed under nitrogen until (6 min) samples gave only a weak brown colour with aqueous ferric chloride, and was then cooled rapidly to 0°. Initially the mixture gave a red colour with ferric ions (starting material) which was succeeded by brown; if heating was continued until the colour began to acquire a purple tinge, yields of product were reduced. The solution was evaporated at room temperature at *ca.* 10^{-2} mmHg (rotatory evaporator) and the residual dried (P_2O_5) solid was digested with cold acetonitrile. Evaporation of the extract gave the *dione* (1·3 g, 47%) which showed no max. at 320 nm. Material for analysis was obtained as a colourless crystalline solid by sublimation *in vacuo*, or, less efficiently, by crystallisation from acetonitrile. When the dione was heated slowly it blackened, but did not melt at 300°; when heated rapidly from 110° (cap.) there was a transient m.p. at *ca.* 140—150° (decomp.) followed by resolidification and no further melting to 300° (Found: C, 48·7; H, 5·1; N, 14·0%; *M*, 99. $C_4H_5NO_2$ requires C, 48·5; H, 5·1; N, 14·1%; *M*, 99), $\nu_{max.}$ (Nujol) 3230ms, *ca.* 3120w, 1782s, 1696vs, and 1670vs cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 3440mw (NH), 1782mw, 1755w, 1712vs, 1615m, and 1264m cm^{-1}. This dione and the following analogues gave detectable, but very weak brown colours with aqueous ferric chloride.

(*b*) The ester (XIII) (1·00 g) was boiled with nitromethane (25 ml) for 25 min under nitrogen. The solution was evaporated *in vacuo*, and the residue was worked up as described in (*a*) giving (after sublimation) the dione (XVII) (0·20 g, 36%).

The 4-(2,4-*dinitrophenylhydrazone*), obtained by storage of the dione with Brady's reagent at room temperature overnight, crystallised from methanol as yellow prisms, m.p. 212—214° (decomp.) [Found (dried at 100°): C, 43·3; H, 3·2; N, 24·6%; *M*, 279. $C_{10}H_9N_5O_5$ requires C, 43·0; H, 3·2; N, 25·1%; *M*, 279].

(ii) 1-*Methylpyrrolidine-2,4-dione* (XVIII). The ester (XIV) (1·50 g.) was heated with water as described in (i) for 6 min (weak brown colour with ferric ions). The acetonitrile-soluble portion of the product was extracted with ether, and the solid recovered from the extract was sublimed *in vacuo* at 40°, yielding the *dione* (0·39 g) as a hygroscopic crystalline solid, m.p. 48—51° (Found: C, 53·3; H, 6·6; N, 12·4%; *M*, 113. $C_5H_7NO_2$ requires C, 53·1; H, 6·2; N, 12·4%; *M*, 113), $\nu_{max.}$ ($CHCl_3$) 3020m, 1782ms, 1696vs, and 1264ms cm^{-1}.

The 4-(2,4-*dinitrophenylhydrazone*) formed red prisms, m.p. 173—175° (decomp.) (from methanol) [Found (dried at 85°): C, 45·0; H, 3·9; N, 23·1. $C_{11}H_{11}N_5O_5$ requires C, 45·0; H, 3·8; N, 23·9%. Found (dried at 50°): C, 44·1; H, 4·1; N, 21·5. $C_{11}H_{11}N_5O_5$,CH_3OH requires C, 44·3; H, 4·6; N, 21·6%].

(iii) (±)-5-*Methylpyrrolidine-2,4-dione* (XIX) *and* (±)-4-*hydroxy-5,5′-dimethyl-3,4′-bi-*Δ^3*-pyrrolinyl-2,2′-dione* (XXII). The ester (XV) (6·5 g) was heated with water until the solution gave a brown colour with ferric ions (7 min) and the crude dry product was digested with cold acetonitrile as described in (i), giving a solution and an undissolved residue (A).

Evaporation of the solution gave the *dione* (XIX) (3·73 g, 85%), m.p. 110—116°, raised to 115—117° by crystallisation (prisms) from acetonitrile or sublimation *in vacuo* (Found: C, 53·1; H, 6·1; N, 12·7%; *M*, 113. $C_5H_7NO_2$ requires C, 53·1; H, 6·2; N, 12·4%; *M*, 113), $\nu_{max.}$ (Nujol) 3200ms, 3100w, 1772ms, 1746w, 1696vs, and 1272ms cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 3435m, 3025m, 1770ms, 1733vs, and 1264ms cm^{-1}.

The 4-(2,4-*dinitrophenylhydrazone*) crystallised from methanol in yellow needles, m.p. 222—225° (decomp.) (Found: C, 44·8; H, 4·1; N, 23·9%; *M*, 293. $C_{11}H_{11}N_5O_5$ requires C, 45·0; N, 3·8; N, 23·9%; *M*, 293).

The 4-*thiosemicarbazone*, obtained by heating an aqueous solution of the dione and thiosemicarbazide at 50° for 15 min, crystallised from ethanol in needles, m.p. 223° (decomp.) (Found: C, 39·0; H, 5·2; N, 29·7. $C_6H_{10}N_4OS$ requires C, 38·7; H, 5·4; N, 30·1%).

The acetonitrile-insoluble residue (A) (0·43 g, 12%) consisted of the (±)-*bipyrrolinyl derivative* (XXII) of the dione (XIX), and crystallised from water in prisms, m.p. *ca.* 260° (decomp.) (Found: C, 57·9; H, 5·9; N, 13·4%; *M*, 208. $C_{10}H_{12}N_2O_3$ requires C, 57·7; H, 5·8; N, 13·5%; *M*, 208), $\nu_{max.}$ (Nujol) 3230br,m, 2640br,m, 1697vs, 1674ms, 1652s, and 1578 cm^{-1}. This compound and the analogues (XX) and (XXI) gave blue colours with aqueous ferric chloride.

(iv) 4-*Hydroxy-3,4′-bi-*Δ^3*-pyrrolinyl-2,2′-dione* (XX). The ester (XIII) (1·0 g) was boiled with water (35 ml) under nitrogen until (16 min) a sample of the solution gave a blue colour with aqueous ferric chloride. Concentration of the solution yielded the *product* (0·33 g) which crystallised from water as microcrystals which blackened on heating, but did not melt at 300° (Found: C, 53·7; H, 4·1; N, 15·3%; *M*, 180. $C_8H_8N_2O_3$ requires C, 53·3; H, 4·5; N, 15·55%; *M*, 180), $\nu_{max.}$ (Nujol) 3200br,m, 2550br, 1870br, 1718m, 1672s, 1618ms, and 1582m cm^{-1}.

(v) 4-*Hydroxy-1,1′-dimethyl-3,4′-bi-*Δ^3*-pyrrolinyl-2,2′-dione* (XXI). The ester (XIV) (8·0 g) was boiled with water for 20 min (blue colour with ferric ions) as in (iv). Recovery gave the monohydrated *product* (2·6 g), which crystallised from water in prisms, m.p. 254—256° (decomp., cap.) [Found (dried at 100°): C, 53·3; H, 5·8; N, 12·4%; equiv., 225. $C_{10}H_{12}N_2O_3$,H_2O requires C, 53·1; H, 6·2; N, 12·4%, equiv., 226] [Found: M^+, 208 ($C_{10}H_{12}N_2O_3$)], $\nu_{max.}$ (Nujol) 3530, 3390 (H_2O), 2500br, 1850br, 1690s,sh, 1672s, 1658sh, 1600sh, and 1583ms cm^{-1}.

Bromo-derivatives of the Pyrrolidine-2,4-diones and Bipyrrolinyl Derivatives.—(i) 3,3-*Dibromopyrrolidine-2,4-dione*

(XXIII). Bromine water was added dropwise to a solution of pyrrolidine-2,4-dione (XVII) (89 mg) in water (5 ml) at room temperature until the bromine colour was no longer discharged. After the removal of a small excess of bromine *in vacuo* the product was recovered in ethyl acetate, giving the *dibromo-dione* (220 mg) which crystallised from benzene in needles, m.p. 136—138° (decomp.) [Found: C, 19·0; H, 1·5; N, 5·3%; M(^{79}Br), 255. $C_4H_3Br_2NO_2$ requires C, 18·7; H, 1·2; N, 5·45%; M(^{79}Br), 255], $\nu_{max.}$ (Nujol) 3250br,ms, 1812vw, 1778ms, 1726vs, and 1698vs cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 3420w, 1806vw, 1782w, 1731vs, and 1210vs cm^{-1}, τ[$(CD_3)_2SO$] 0·9br (NH) and 5·76 (2H, s, CH_2).

(ii) (±)-*3,3-Dibromo-5-methylpyrrolidine-2,4-dione* (XXIV). Bromination of (±)-5-methylpyrrolidine-2,4-dione (XIX) (0·5 g) as described in (i) gave the *dibromo-derivative* (1·0 g) as prisms, m.p. 110—111° (from benzene) [Found: C, 22·2; H, 2·1; N, 5·3%; M (^{79}Br), 269. $C_5H_5Br_2NO_2$ requires C, 22·15; H, 1·8; N, 5·1%; M (^{79}Br), 269], $\nu_{max.}$ (Nujol) 3210br,ms, 1792ms, 1731vs, and 1695vs cm^{-1}, $\nu_{max.}$ ($CDCl_3$) 3410w, 1792m, and 1730vs cm^{-1}, τ[$(CD_3)_2SO$] 0·8br (NH), 5·44 (q, J 7Hz, C*H*·CH_3), and 8·65 (3H, d J 7 Hz, CH·C*H*$_3$).

(iii) *3-Bromo-4′-hydroxy-1,1′-dimethyl-3,4′-bi-Δ³-pyrrolinyl-2,2′-dione* (XXVI). A stirred suspension of 4-hydroxy-1,1′-dimethyl-3,4′-bi-Δ³-pyrrolinyl-2,2′-dione monohydrate (XXI) (1·04 g, 4·8 mmol) in a solution of sodium acetate trihydrate (1·86 g, 11·9 mmol) in water (40 ml) was treated dropwise at 0° with bromine (0·78 g, 4·8 mmol). The microcrystalline *bromo-derivative* (0·54 g) was filtered off and a second crop (0·72 g) was obtained by acidifying with hydrochloric acid. The derivative blackened when heated (cap.) but did not melt at 300°, and could not be recrystallised without substantial decomposition (Found: C, 42·3; H, 3·9; N, 9·75%; equiv., 280. $C_{10}H_{11}BrN_2O_3$ requires C, 41·8; H, 3·9; N, 9·8%; equiv. 287), $\nu_{max.}$ (Nujol) *ca.* 3220br,m, 2610br,mw, 1686s, 1649ms, and 1582m cm^{-1}. This derivative and that following gave slate-blue colours with ferric ions.

(iv) *3-Bromo-4′-hydroxy-3,4′-bi-Δ³-pyrrolinyl-2,2′-dione* (XXV). 4-Hydroxy-3,4-bi-Δ³-pyrrolinyl-2,2′-dione (XX) (0·90 g) was brominated by the method described in (iii) and the resulting solution, on acidification, deposited a microcrystalline solid consisting essentially of the bromo-derivative. This did not melt at 300° (cap.), but blackened on heating, and could not be recrystallised (Found: C, 38·1; H, 3·1; N, 10·9. $C_8H_7BrN_2O_3$ requires C, 37·1; H, 2·7; N, 10·8%). The n.m.r. spectrum revealed the presence of a small amount of starting material.

Action of Sodium Hydroxide on the Dibromopyrrolidine-2,4-diones.—(i) *3,3-Dibromopyrrolidine-2,4-dione* (XXIII). The dibromo-dione (205 mg) was added to N-sodium hydroxide (1·8 ml) below 5°. After *ca.* 2 min the resulting yellow solution was acidified with hydrochloric acid. Recovery of the product in ethyl acetate gave *N-dibromoacetylglycine* (XXVII) (170 mg) as needles, m.p. 154—156° (decomp.) (from ethyl acetate–light petroleum) (Found: C, 17·7; H, 1·7; N, 5·4. $C_4H_5Br_2NO_3$ requires C, 17·5; H, 1·8; 5·1%), $\nu_{max.}$ (Nujol) 3290s, 3075mw, 3015mw, 3200—2600br, 1730s, 1668vs, and 1554ms cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 1739s, 1692vs, and 1502m cm^{-1}, τ[$(CD_3)SO$)] 1·3 (t, NH), 3·64 (s, $CHBr_2$), and 6·20 (2H, d, J 5 Hz, CH_2·N).

The *methyl ester* (XXIX), obtained with diazomethane, formed needles, m.p. 107° (from light petroleum) (Found: C, 21·2; H, 2·6; N, 4·9. $C_5H_7Br_2NO_3$ requires C, 20·8; H, 2·4; N, 4·8%), $\nu_{max.}$ ($CHCl_3$) 3410m, 1749s, 1690vs, and 1510m cm^{-1}, τ($CDCl_3$) 3·0br (NH), 4·13 (s, $CHBr_2$), 5·90 (2H, d, J 5 Hz, CH_2·N), and 6·20 (3H, s, OMe).

(ii) (±)-*3,3-Dibromo-5-methylpyrrolidine-2,4-dione* (XXIV). The dibromo-dione (266 mg) was treated with N-sodium hydroxide as in (i). Acidification of the solution caused separation of (±)-*N-dibromoacetylalanine* (XXVIII) (164 mg) which formed prisms, m.p. 190° (decomp.) (from aqueous ethanol) (Found: C, 21·0; H, 2·7; N, 4·8. $C_5H_7Br_2NO_3$ requires C, 20·8; H, 2·4; N, 4·8%), $\nu_{max.}$ (Nujol) 3290s, 3070w, 3035w, 3200—2600br, 1728s, 1660vs, and 1550ms cm^{-1}, τ[$(CD_3)_2SO$] 1·2 (d, J 7 Hz, NH), 3·65 (s, $CHBr_2$), 5·8 (quint, J 7 Hz, C*H*·CH_3), and 8·70 (3H, d, J 7 Hz, CH·C*H*$_3$).

The *methyl ester* (XXX) crystallised from light petroleum in needles, m.p. 100—101° (Found: C, 24·2; H, 3·1; N, 4·6. $C_6H_9Br_2NO_3$ requires C, 23·8; H, 3·0; N, 4·6%), $\nu_{max.}$ (Nujol) 3300s, 3070w, 3015mw, 1747s, 1666vs, and 1553ms cm^{-1}, τ($CDCl_3$) 3·0br (NH), 4·16 (s, $CHBr_2$), 5·4 (q, J 7 Hz, C*H*·CH_3), 6·23 (3H, s, OMe), and 8·52 (3H, d, J 7 Hz, CH·C*H*$_3$).

Condensation of Ethyl 4-Hydroxy-1-methyl-2-oxo-Δ³-pyrroline-3-carboxylate (XIV) *with Aldehydes.*—(i) *p-Chlorobenzaldehyde.* Hydrogen chloride was passed into a mixture of the ester (XIV) (5·9 g, 32 mmol) and *p*-chlorobenzaldehyde (5·0 g, 36 mmol) in ethanol (80 ml) for 2·5 h at 0°, then for 2·5 h at 60° (bath). The ester gradually dissolved and later a yellow solid separated. The mixture was cooled, resaturated with hydrogen chloride, stored for 18 h at room temperature, then evaporated *in vacuo* below 40°. The solid (7·4 g) obtained by trituration of the residue with ether was a mixture (3 : 1) of *E*- and *Z*-isomers with about 5% of starting material (n.m.r. spectrum).

The crude product (21 g) was crystallised twice from ethyl acetate below 70° giving mother-liquors (A) and the major product, *ethyl* (E)-*5-p-chlorobenzylidene-4-hydroxy-1-methyl-2-oxo-Δ³-pyrroline-3-carboxylate* (XXXIa) (4·8 g) as yellow prisms, m.p. *ca.* 120—130° (decomp.) (Found: C, 58·6; H, 4·6; N, 4·5. $C_{15}H_{14}ClNO_4$ requires C, 58·6; H, 4·6; N, 4·55%), $\nu_{max.}$ (Nujol) 3300—2500 (OH), 1703s (amide CO), 1666ms, and 1655sh (ester CO) cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 1700vs, 1652m, 1640sh, and 1592s cm^{-1}, $\lambda_{max.}$ (MeOH) 238 and 312 nm (ε 19,700 and 22,200), τ($CDCl_3$) 2·52 and 2·9 (4H, AA′BB′, aromatic), 3·63 (s, CH), 6·88 (3H, s, NMe), and 5·64 and 8·65 (5H, q and t, CO_2Et).

Heating the product (XXXIa) with ethyl acetate under reflux for 30 min gave (*E*)-*5-p-chlorobenzylidene-1-methylpyrrolidine-2,4-dione* (XXXIII), which formed yellow prisms, m.p. 104—105° (from benzene–light petroleum) (Found: C, 61·7; H, 4·5; N, 5·6. $C_{12}H_{10}ClNO_2$ requires C, 61·2; H, 4·3; N, 5·9%), $\nu_{max.}$ (Nujol) 1740ms (conj. CO), 1715s (amide CO), and 1603ms cm^{-1} (*exo*-C=C), $\lambda_{max.}$ (0·1N-NaOH) 233 and 312 nm (ε 8400 and 21,800), τ($CDCl_3$) 2·4 and 2·71 (4H, AA′BB′, aromatic), 4·07 (s, CH), 6·83 (3H, s, NMe), and 6·89 (2H, s, CO·CH_2·CO).

The material recovered from the mother-liquors (A) was fractionally recrystallised from the same solvent and from benzene–light petroleum; the resolution was followed by n.m.r. spectroscopy. Ultimately the minor product, *ethyl* (Z)-*5-p-chlorobenzylidene-4-hydroxy-1-methyl-2-oxo-Δ³-pyrroline-3-carboxylate* (XXXIIa) (1·0 g) was isolated as yellow prisms, m.p. *ca.* 120—130° (decomp.) (Found: C, 58·4; H, 4·8; N, 4·3%), $\nu_{max.}$ (Nujol) 3200br, 1714s, 1663ms, 1655sh, 1648sh, 1602ms, and 1586ms cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 3000br, 1750w, 1708vs, 1658ms, 1640sh, and 1610s cm^{-1}, $\lambda_{max.}$ (MeOH) 237 and 304 nm (ε 15,600 and 20,800),

$\tau(CHCl_3)$ 2·62 and 2·72 (4H, AA'BB', aromatic), 3·28 (s, CH), 7·15 (3H, s, NMe), and 5·58 and 8·62 (5H, q and t, CO_2Et).

Condensation of the ester (XIV) with other aldehydes under conditions similar to those described in (i) gave the following products. The ratios of the *E*- and *Z*-isomers in the crude products, determined by n.m.r. spectra, are listed in Scheme 2.

(ii) *p*-Fluorobenzaldehyde gave a mixture of *ethyl* (*E*)- and (*Z*)-5-p-*fluorobenzylidene*-4-*hydroxy*-1-*methyl*-2-*oxo*-Δ^3-*pyrroline*-3-*carboxylates* (XXXIb) and (XXXIIb), yellow prisms, m.p. *ca.* 90—100° (decomp.) (from ethyl acetate) (Found: C, 62·4; H, 4·9; N, 4·8. $C_{15}H_{14}FNO_4$ requires C, 61·9; H, 4·8; N, 4·8%), $\tau(CDCl_3)$ 2·2—3·1 (4H, m, aromatic), 3·6 (s) and 6·88 (s) [CH and NMe of major *E*-isomer], 3·3 (s) and 7·16 (s) [CH and NMe of minor *Z*-isomer], and 5·64 and 8·63 (5H, q and t, CO_2Et).

(iii) *p*-Bromobenzaldehyde gave *ethyl* (E)-5-p-*bromobenzylidene*-4-*hydroxy*-1-*methyl*-2-*oxo*-Δ^3-*pyrroline*-3-*carboxylate* (XXXIc), obtained in lower yield than the analogous derivatives described, crystallised from chloroform–light petroleum in yellow prisms, m.p. *ca.* 130—140° (decomp.) (Found: C, 51·1; H, 4·0; N, 3·7. $C_{15}H_{14}BrNO_4$ requires C, 51·1; H, 4·0; N, 4·0%), $\nu_{max.}$ (Nujol) 3300—2500br, 1706s, 1660ms, 1646sh, 1638sh, and 1593ms cm^{-1}, $\tau(CHCl_3)$ 2·5 (4H, s, aromatic), 3·58 (s, CH), 6·83 (3H, s, NMe), and 5·58 and 8·58 (5H, q and t, CO_2Et).

(iv) *m*-Chlorobenzaldehyde gave *ethyl* (E)-5-m-*chlorobenzylidene*-4-*hydroxy*-1-*methyl*-2-*oxo*-Δ^3-*pyrroline*-3-*carboxylate* (XXXId), yellow prisms, m.p. *ca.* 112—125° (decomp.) (from benzene) (Found: C, 58·4; H, 4·5; N, 4·55. $C_{15}H_{14}ClNO_4$ requires C, 58·6; H, 4·6; N, 4·55%), $\nu_{max.}$ (Nujol) 3200, 1727s, 1664ms, 1650sh, 1640sh, and 1604ms cm^{-1}, $\tau(CHCl_3)$ 2·1—2·8 (4H, m, aromatic), 3·58 (s, CH) 6·80 (3H, s, NMe), and 5·58 and 8·58 (5H, q and t, CO_2Et).

(v) *p*-Chlorophenylbenzaldehyde gave *ethyl* (E)-5-[p-(p-*chlorophenyl*)*benzylidene*]-4-*hydroxy*-1-*methyl*-2-*oxo*-Δ^3-*pyrroline*-3-*carboxylate* (XXXIe), yellow prisms, m.p. (rapid heating) *ca.* 150° (decomp.), resolidifying and remelting 180° (decomp.) (from ethyl acetate) (Found: C, 65·4; H, 4·8; N, 3·2. $C_{21}H_{18}ClNO_4$ requires C, 65·7; H, 4·7; N, 3·6%), $\nu_{max.}$ (Nujol) 3300—2500br, 1703vs, 1662ms, 1655sh, 1637m, and 1594s cm^{-1}, $\tau(CDCl_3)$ 2·2—2·8 (8H, m, aromatic), 3·51 (s, CH), 6·84 (3H, s, NMe), and 5·60 and 8·63 (5H, q and t, CO_2Et).

Condensation of Ethyl 4-*Hydroxy*-2-*oxo*-Δ^3-*pyrroline*-3-*carboxylate* (XIII) *Hemihydrate with Aldehydes.*—The condensations and isolation of crude products were carried out as described for the analogue (XIV).

(i) p-*Chlorobenzaldehyde.* The crude product contained only a small amount of ester-bearing material (n.m.r.); recrystallisation from nitromethane gave 5-p-*chlorobenzylidenepyrrolidine*-2,4-*dione* (XXXIVa) as yellow needles, m.p. 210—213° (decomp.) (Found: C, 59·8; H, 3·9; N, 6·0. $C_{11}H_8ClNO_2$ requires C, 59·6; H, 3·6; N, 6·3%), $\nu_{max.}$ (Nujol) 3200mw (NH), 1754ms (conj. CO), 1719vs (amide CO), and 1639s cm^{-1} (*exo*-C=C), $\tau[(CD_3)_2SO]$ −1·7, −0·9, and 0·57 [all br,s, NH (keto), NH (enol), and OH (enol)], 2·3—2·8 (4H, m, aromatic), 3·79 (s) and 3·88 (s) (=CHAr, keto and enol), 5·03 [s, CH·CO, enol (*ca.* 60%)], and 6·81 [s, $CO{\cdot}CH_2{\cdot}CO$, keto (*ca.* 40%)].

(ii) p-*Fluorobenzaldehyde.* The largely de-esterified product crystallised from nitromethane giving 5-p-*fluorobenzylidenepyrrolidine*-2,4-*dione* (XXXIVb) as yellow prisms, m.p. 202—206° (decomp.) (Found: C, 64·5; H, 4·1; N, 6·6. $C_{11}H_8FNO_2$ requires C, 64·4; H, 3·9; N, 6·8%), $\nu_{max.}$ (Nujol) 3220mw, 1758ms, 1719s, and 1649s cm^{-1}, $\tau[(CD_3)_2SO]$ −1·7, −0·9, and 1·6 [all br,s, NH (keto), NH (enol), OH (enol)], 2·2—3·0 (4H, m, aromatic), 3·74 (s) and 3·82 (s) (=CHAr, keto and enol), 5·02 [s, =CH·CO, enol (*ca.* 60%)], and 6·80 [s, $CO{\cdot}CH_2{\cdot}CO$, keto (*ca.* 40%)].

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