Reaction between 3*H*-Pyrrolizines and Acetylenedicarboxylic Esters. Part I. Preparation of 3-(Alkoxycarbonylmethylene)-3*H*-pyrrolizines

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3*H*-Pyrrolizine reacts with dimethyl or diethyl acetylenedicarboxylate to give the 3-[alkoxycarbonyl(alkoxycarbonylmethyl)methylene]-3*H*-pyrrolizines (5) and (8). 1-Methyl-3*H*-pyrrolizine and 6,7-dimethylpyrrolizine give the similar compounds (6) and (7) with the dimethyl ester: with the diethyl ester 1-methyl-3*H*-pyrrolizine gives a 3*H*-pyrrolizin-5-ylmaleate (13) shown to be an intermediate in the production of the expected compound (10). A mechanism for the reaction has been proposed, and tested by deuterium-labelling experiments. 3-Diphenylmethylene-3*H*-pyrrolizine undergoes cycloaddition with dimethyl acetylenedicarboxylate to give a dihydrocyclo[3.2.2]azine (dimethyl 5,6-dihydro-5,5-diphenylpyrrolo[2.1.5-*cd*']indolizine-6,7-dicarboxylate) (14).

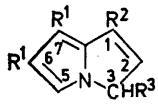
We have been investigating routes to pyrroloazepines;[1-3] some of the routes involve valence isomerisation reactions, and attempts have been made to bring about a photochemical addition of acetylenes to 3*H*-pyrrolizine (1). During these experiments we discovered that 3*H*-pyrrolizine and acetylenedicarboxylic esters undergo a dark reaction giving two major classes of product. When equimolar proportions of a 3*H*-pyrrolizine and an ester were used the principal products were 1 : 1 adducts; with an excess of ester the principal products were adducts containing two ester molecules and one of the 3*H*-pyrrolizine. The evidence for the structure of the 1 : 1 adducts is given here; that for the structure of the 1 : 2 adducts is in Part II.

When a toluene solution of 3*H*-pyrrolizine (1) and dimethyl acetylenedicarboxylate in equimolar proportions was left in the dark for 200 h or was boiled (5 h) the major product, isolated in up to 71% yield, was an orange compound. The mass spectrum (Table 1) and analysis showed this to be an adduct of one molecule of 3*H*-pyrrolizine (1) with one molecule of acetylenedicarboxylate. The u.v. and visible absorption of the compound (Table 1) was similar to that reported[4,5] for compound (11), obtained by the reaction of the 4-azapentalenyl anion with benzophenone. The n.m.r. spectrum (Table 2) of the adduct showed three pyrrole proton absorptions, two deshielded alkene signals (J 6 Hz), and a methylene singlet, normally obscured by the ester methyl singlets but clearly visible when benzene was added to the solution. These spectral data were in accord with structure (5); subsequent comparison with the n.m.r. spectrum of compound (12)[6] (Table 2), which has been prepared from pyrrolizin-3-one and methoxycarbonylmethylenetriphenylphosphorane, confirmed the proposed structure.

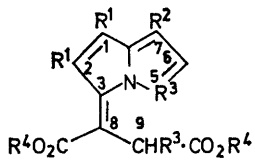
Since 3*H*-pyrrolizine has a very low acidity at position 3,[4,5] an anionic intermediate seems unlikely, although the addition of potassium t-butoxide to the original mixture does accelerate the production of compound (5). A number of substituted 3*H*-pyrrolizines were

[1] E. W. Collington and G. Jones, *J. Chem. Soc.* (*C*), 1969, 1028.
[2] E. W. Collington, G. R. Cliff, and G. Jones, *J. Chem. Soc.* (*C*), 1970, 1490.
[3] G. R. Cliff and G. Jones, *J. Chem. Soc.* (*C*), 1971, 3418.
[4] W. H. Okamura and T. J. Katz, *Tetrahedron*, 1967, **23**, 2941.
[5] W. Flitsch and R. Heidhues, *Chem. Ber.*, 1968, **101**, 3843.
[6] Prof. W. Flitsch, personal communication.

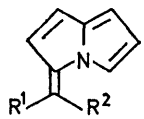
used to discover the position of substitution by the acetylenedicarboxylate. From 1-methyl-3*H*-pyrrolizine (2) and dimethyl acetylenedicarboxylate a compound



(1) $R^1 = R^2 = R^3 = H$
(2) $R^1 = R^3 = H$, $R^2 = Me$
(3) $R^1 = Me$, $R^2 = R^3 = H$
(4) $R^1 = R^2 = H$, $R^3 = D$

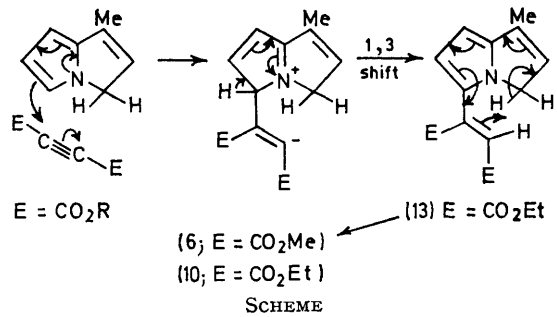


(5) $R^1 = R^2 = R^3 = H$, $R^4 = Me$
(6) $R^1 = R^3 = H$, $R^2 = R^4 = Me$
(7) $R^1 = R^4 = Me$, $R^2 = R^3 = H$
(8) $R^1 = R^2 = R^3 = H$, $R^4 = Et$
(9) $R^1 = R^2 = H$, $R^3 = H$ or D (1 : 1), $R^4 = Et$
(10) $R^1 = R^3 = H$, $R^2 = Me$, $R^4 = Et$



(11) $R^1 = R^2 = Ph$
(12) $R^1 = CO_2Et$, $R^2 = H$

(6) was obtained, having a similar chromophore to that of the parent compound (5) (Table 1). The n.m.r. spectrum showed two major changes from that of compound (5) (Table 2); in the pyrrole proton region one signal (a β-proton absorption) was absent, and a singlet (3H) near δ 2·0 p.p.m. was present. This leaves little doubt that initial substitution was at position 5 in the 3*H*-pyrrolizine; the position of substitution was firmly established by the use of 6,7-dimethyl-3*H*-pyrrolizine (3), prepared by Schweizer's method [7] from 3,4-dimethylpyrrole-2-carbaldehyde. The product (7) from the dimethylpyrrolizine again showed the characteristic chromophore (Table 1); the n.m.r. spectrum showed three pyrrole proton absorptions but no deshielded alkene protons were present. Hence the methyl groups were in the ring bearing the exocyclic double bond and the point of substitution by the acetylenedicarboxylate was position 5. A mechanism for this reaction is shown in the Scheme and has been tested by deuteriation experiments.



SCHEME

In the first attempt to obtain a suitably deuteriated 3*H*-pyrrolizine, pyrrole was subjected to acid-catalysed exchange with deuterium oxide, giving [$^2H_5$]pyrrole (estimated incorporation 94%).[8] Formylation gave [3,4,5-$^2H_3$]pyrrole-2-carbaldehyde; treatment of the deuteriated pyrrolecarbaldehyde with vinyltriphenylphosphonium bromide and sodium hydride gave a 3*H*-pyrrolizine randomly deuteriated; randomisation has been reported in Wittig reactions with deuteriated ketones when sodium hydride was used as the base.[9] By treating 3*H*-pyrrolizine (1) with n-butyl-lithium and subsequently with deuterium oxide, [3-^{2}H]pyrrolizine (4) was obtained;[4] further anion formation and treatment with deuterium oxide gave incorporation also into the other ring positions. The monodeuteriated pyrrolizine (4) reacted with dimethyl acetylenedicarboxylate to give a 1 : 1 adduct which was purified by preliminary column chromatography on Woelm alumina (necessary to remove the 1 : 2 adduct which was also formed). Such purified specimens were shown

TABLE 1

U.v.–visible and mass spectra

Compound	$\lambda_{max.}$/nm (log ε) (in 95% EtOH)	*m/e* (%)
(11)	209 (4·34), 242 (4·11), 342 (4·19), 405sh	
(5)	209·5 (4·14), 230sh, 322·5 (4·30), 420 (3·29)	247 (*M*+, 72), 215 (11), 188 (100), 160 (33), 128 (33)
(6)	211·5 (4·18), 235sh, 346 (4·31), 423 (3·44)	261 (*M*+, 43) 229 (5), 202 (100), 174 (25), 142 (41)
(3)	210 (3·77), 285·5 (3·88)	133 (*M*+, 80), 132 (46), 118 (100)
(7)	210 (4·10), 320 (4·09), 400sh	
(8)	209·5 (4·15), 230sh, 333 (4·30), 419 (3·29)	275 (*M*+, 68), 229 (14), 202 (100), 174 (41), 129 (73)
(9)	209·5 (4·15), 230sh, 333 (4·30), 419 (3·29)	276 (*M*+, 81), 203 (100), 176 (31), 130 (46)
(10)	210·5 (4·22), 235sh, 346 (4·32), 432 (3·46)	289 (*M*+, 67), 244 (9), 216 (100), 142 (25)
(13)	215sh, 240 (4·19), 247sh, 377 (4·32)	289 (*M*+, 95), 244 (50), 243 (100), 216 (55), 215 (96), 187 (46), 171 (26), 142 (72)
(14)	212 (4·36), 240sh, 370 (4·04), 480 (3·22)	411 (*M*+, 100), 396 (10), 352 (50), 334 (10), 320 (52)
(15)	211 (4·31), 301·5 (4·19)	413 (*M*+, 100), 398 (38), 354 (76), 336 (69), 322 (26)

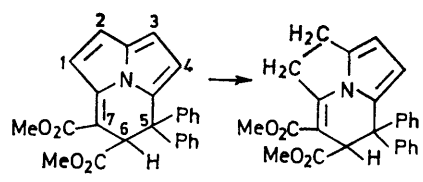
[7] E. E. Schweizer and K. K. Light, *J. Org. Chem.*, 1966, **31**, 870.

[8] F. A. Miller, *J. Amer. Chem. Soc.*, 1942, **62**, 1543.

[9] T. B. Malloy, R. M. Hedges, and F. Fisher, *J. Org. Chem.*, 1970, **35**, 4256.

by ^{1}H n.m.r. to have 40% deuterium content at position 5 but none elsewhere. When 3*H*-pyrrolizine (1) reacted with diethyl acetylenedicarboxylate no 1 : 2 adduct was formed; consequently the adduct (8) could be purified without alumina chromatography. A specimen (9) prepared from the deuteriated pyrrolizine (4) showed 50% deuterium content at position 5 and 25% deuterium content in the methylene group (position 9). All the original deuterium from compound (4) was still present in the adduct, and the transfer from position 3 of the pyrrolizine to the methylene group must be intramolecular. A sample of the deuteriated compound (9) passed through an alumina column lost all deuterium from position 9.

The reaction between pyrrolizines and diethyl acetylenedicarboxylate was slow, and very small amounts of 1 : 2 adducts were formed, even when a large excess of ester was used. From 1-methyl-3*H*-pyrrolizine (2) the major product was a yellow isomer of the expected compound (10) (which was present in small amounts) (Table 1). The n.m.r. spectrum of this product was similar to that of the pyrrolizine (2) except for two methyl singlets and one sharp singlet (1H) at δ 5·72 p.p.m. (a maleate hydrogen atom); the α-pyrrole absorption was absent. The yellow material was thus a pyrrolizin-5-ylmaleate (13). Prolonged boiling of a toluene solution of compound (13) gave the adduct (10), proving that the compound (13) was an intermediate, as shown in the Scheme.



(14) (15)

Pyrrolizines with exocyclic double bonds offer attractive intermediates for cyclazine synthesis; Farquhar and Leaver have used such an approach to cycl[3,3,3]azines.[10] The diphenyl derivative (11) reacted rapidly with dimethyl acetylenedicarboxylate to give cycl[3,2,2]azine (pyrrolo[2,1,5-*cd*]indolizine) derivative (14). The u.v. absorption was similar to that of compound (5) (Table 1); the n.m.r. spectrum also resembled closely those of the 1 : 1 adducts, with additional signals at δ 4·6 (1H) and 7·27 p.p.m. (10H). The cyclazine (14) was readily reduced to a colourless dihydro-derivative; the n.m.r. spectrum showed the absence of the double bond protons (1 and 2) and the appearance of signals (4H) in the δ 3—4 p.p.m. region. The dihydro-derivative has therefore formula (15). In contrast compound (5) proved inert to dienophiles; prolonged treatment with acetylenedicarboxylate, either thermal or in a photochemical reactor, gave no adducts. The compound (5) also failed to react with styrene, which has been successfully used for dienes having 'inverse electron demand.'[11]

TABLE 2

N.m.r. data for 1 : 1 adducts and 6,7-dimethyl-3*H*-pyrrolizine (3)

Compound	δ (p.p.m.) H-1	H-2	H-3	H-5	H-6	H-7	Ester CH_2	Ester CH_3	Others	*J*/Hz
(5) [a]	7·17(d)	6·59(d)		6·93(d)	6·10(t)	5·95(d)			CH_2, 3·5—3·8(m)	$J_{1,2}$ 6, $J_{5,6}$ 3, $J_{6,7}$ 3
(12) [b]	7·03	6·57		6·95	5·95	5·80	4·17	1·28	H, 5·76	
(6) [a]	7·13(d)	6·61(d)		6·82(d)	5·90(d)	Me, 2·06(s)		3·77, 3·65 (s)	CH_2, 3·60(s)	$J_{1,2}$ 6, $J_{5,6}$ 3,
(3) [a]	5·59(d)	5·99(t)	CH_2, 4·0(m)	6·61(s) †	Me, 1·82(s)	Me, 1·82(s)				$J_{1,2}$ 4
(7) [a]	Me, 1·95(s)	Me, 1·82(s)		6·92(d)	6·02(t)	5·76(d)		3·75, 3·65 (s)	CH_2, 3·59(s)	$J_{5,6}$ 3, $J_{6,7}$ 3
(8) [a]	7·19(d)	6·59(d)		6·95(d)	6·08(t)	5·93(d)	4·19 (qui) §	1·25(q)	CH_2, 3·62(s)	$J_{1,2}$ 6, $J_{5,6}$ 3, $J_{6,7}$ 3
(9) [a]	7·19(d)	6·59(d)		6·95 (0·5H,d)	6·08(t) ‡	5·93(d)	4·19 (qui)	1·25(q)	CH_2 (1·5H), 3·62(s)	$J_{1,2}$ 6, $J_{5,6}$ 3, $J_{6,7}$ 3
(10) [a]	7·14(d)	6·59(d)		6·86(d)	5·90(d)	Me, 2·10(s)	4·18 (qui)	1·25(q)	CH_2, 3·58(s)	$J_{1,2}$ 6, $J_{5,6}$ 3

[a] In CCl_4. [b] In CS_2. † Broad. ‡ Collapsing triplet. § qui = quintet.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. Column chromatography was performed on Woelm alumina (activity III) and preparative layer chromatography (p.l.c.) on 40 cm plates with Merck silica gel PF_{254}. N.m.r. shifts (δ) are given in p.p.m. from tetramethylsilane.

3*H*-Pyrrolizine and 1-methyl-3*H*-pyrrolizine were prepared as described by Schweizer and Light.[7]

3-[*Methoxycarbonyl*(*methoxycarbonylmethyl*)*methylene*]-3H-*pyrrolizine* (5).—A solution of 3*H*-pyrrolizine (525 mg, 5 mmol) and dimethyl acetylenedicarboxylate (710 mg, 5 mmol) in dry toluene (100 ml) was kept in the dark under nitrogen, at room temperature (9 days). Alternatively, the solution was boiled (5 h), then left overnight. The toluene was evaporated off under reduced pressure, and the residual red oil chromatographed on alumina (75 g). The column was made up in petroleum (b.p. 60—80°); the oil was applied in toluene and eluted with petroleum–toluene (1 : 1). An orange band was eluted; evaporation left a red oil which slowly solidified and was crystallised from petroleum (b.p. 60—80°) to give the *diester* (5), m.p. 76° (880 mg, 71%) (Found: C, 63·2; H, 5·4; N, 5·6.

[10] D. Farquhar and D. Leaver, *Chem. Comm.*, 1969, 24.

[11] See D. L. Fields, T. H. Regan, and J. C. Dignan, *J. Org. Chem.*, 1968, **33**, 390; C. K. Bradsher and J. A. Stone, *ibid.*, p. 519.

$C_{13}H_{13}NO_4$ requires C, 63·15; H, 5·3; N, 5·65%), $\nu_{max.}$ 1735 and 1700 cm^{-1}.

A second band eluted from the alumina column (toluene) gave the diadduct (200 mg); see Part II.

3-[*Methoxycarbonyl*(*methoxycarbonylmethyl*)*methylene*]-1-*methyl*-3H *pyrrolizine* (6).—Prepared similarly the *diester* (6) (35%) had m.p. 105—108° (Found: C, 64·7; H, 5·65; N, 5·3. $C_{14}H_{15}NO_4$ requires C, 64·7; H, 5·8; N, 5·35%), $\nu_{max.}$ 1730 and 1690 cm^{-1}.

3,4-*Dimethylpyrrole*-2-*carbaldehyde*.—Formylation of 3,4-dimethylpyrrole [12] was performed as described for pyrrole; [13] the product crystallised from benzene–petroleum (b.p. 40—60°) as needles (50%), m.p. 133° (lit.,[14] 133°), $\nu_{max.}$ ($CHCl_3$) 3450, 3260, and 1630 cm^{-1}; δ ($CDCl_3$) 2·0 (3H, s, Me), 2·25 (3H, s, Me), 6·9 (1H, d, *J* 3 Hz), 9·6 (1H, s, CHO), and 9·9—10·7 (1H, m, N–H).

6,7-*Dimethyl*-3H-*pyrrolizine* (3).—From 3,4-dimethylpyrrole-2-carbaldehyde (1·6 g) and vinyltriphenylphosphonium bromide (5·0 g) by the method used for 3*H*-pyrrolizine,[7] 6,7-*dimethyl* 3H-*pyrrolizine* (3) was obtained as a pale yellow, unstable oil, b.p. 87—90° at 16 mmHg (1·15 g, 67%), *m/e* 133 (M^+) and 118 (100%).

3-[*Methoxycarbonyl*(*methoxycarbonylmethyl*)*methylene*]-6,7-*dimethyl*-3H-*pyrrolizine* (7).—Prepared like compound (5) in boiling toluene (5 h) the *diester* (7) was an orange liquid (34%) (Found: C, 65·6; H, 6·25; N, 5·1. $C_{15}H_{17}NO_4$ requires C, 65·4; H, 6·25; N, 5·1%), $\nu_{max.}$ 1725 and 1690 cm^{-1}.

[3,4,5-$^2H_3$]*Pyrrole*-2-*carbaldehyde*.—The method [13] used to formylate pyrrole was used on [$^2H_5$]pyrrole [8] (11·7 g; 94% ^2H content). The crude aldehyde, after distillation, was dissolved in benzene, and partitioned three times with water. The dried (Na_2SO_4) benzene solution was evaporated and the solid residue recrystallised from petroleum (b.p. 40—60°) to give [3,4,5-$^2H_3$]*pyrrole*-2-*carbaldehyde* as needles, m.p. 44·5° (lit.,[13] 44—45° for pyrrole-2-carbaldehyde). Deuterium content at positions 3, 4, and 5 was estimated as 90% by n.m.r. measurement.

3H-*Pyrrolizine from* [3,4,5-$^2H_3$]*Pyrrole*-2-*carbaldehyde*.—From the labelled aldehyde (9·5 g) and vinyltriphenylphosphonium bromide (38 g) by the usual method [7] a deuteriopyrrolizine (5·68 g, 54%), b.p. 67—69° at 16 mmHg, was obtained. The n.m.r. spectrum showed less intense signals throughout, and the mass spectrum showed molecular ions at *m/e* 105 (51%), 106 (77%), 107 (53%), and 108 (23%).

Reaction between [3-^2H]*Pyrrolizine* (4) *and Dimethyl Acetylenedicarboxylate*.—A solution of the deuteriated pyrrolizine (4) and dimethyl acetylenedicarboxylate in toluene was boiled (5 h), and worked up as usual; the recrystallised adduct was identical with compound (5) in m.p. but showed a signal for H-5 in the n.m.r. spectrum only 60% as intense as that expected. The CH_2 signal at 3·60 p.p.m. showed no reduction in intensity.

Reaction between Diethyl Acetylenedicarboxylate and 3H-*Pyrrolizine or* [3-^2H]*Pyrrolizine*.—(*a*) From 3*H*-pyrrolizine (1) and diethyl acetylenedicarboxylate in boiling toluene (5 h) a crude product was obtained containing no detectable diadduct. Recrystallisation from petroleum (b.p. 60—80°) gave the *diester* (8), m.p. 84—85° (86%) (Found: C, 65·5; H, 6·35; N, 5·0. $C_{15}H_{17}NO_4$ requires C, 65·4; H, 6·25; N, 5·1%), $\nu_{max.}$ 1730 and 1693 cm^{-1}.

(*b*) A similar reaction with [3-^2H]pyrrolizine (4) gave the deuteriated adduct (9); the n.m.r. signal for H-5 was 50% as intense as that of the adduct (8); the CH_2 signal was 75% as intense as that of the adduct (8). The deuteriated adduct showed *m/e* 276 (80%) and 203 (100%); *cf.* 275 (68%) and 202 (100%) for adduct (8).

Reaction between 1-*Methyl*-3H-*pyrrolizine* (2) *and Diethyl Acetylenedicarboxylate*.—(*a*) A solution of the pyrrolizine (2) (595 mg) and diethyl acetylenedicarboxylate (850 mg) in toluene (100 ml) was boiled for 5 h and then left overnight.

(*b*) Similar treatment of a solution containing the pyrrolizine (357 mg) and the acetylenedicarboxylate (2·5 g) gave an increased proportion of di-adduct.

The combined solutions were evaporated and the residue was chromatographed on alumina (250 g). Elution of an orange band (fraction 1) with petroleum (b.p. 60—80°)–toluene (1 : 1) was followed by elution of a deep red band (fraction 2) with toluene.

Fraction 1 was treated with petroleum (b.p. 60—80°) to give a yellow solid. P.l.c. of the red gum obtained from the mother liquors (chloroform) gave more yellow solid, and a mixture which could not be separated. The yellow solid, after recrystallisation, gave *diethyl* 1-*methyl*-3H-*pyrrolizin*-5-*ylmaleate* (13); m.p. 110°, as yellow plates (from petroleum) (500 mg, 19%) (Found: C, 66·5; H, 6·7; N, 4·8. $C_{16}H_{19}NO_4$ requires C, 66·4; H, 6·65; N, 4·85%), $\nu_{max.}$ 1700 cm^{-1}; δ (CCl_4) 1·29 (6H, 2 × CH_2·CH_3), 2·05 (3H, m, Me), 3·9—4·6 (6H, m, 2 × O·CH_2·CH_3 and pyrrolizine CH_2), 5·72 (1H, s), 6·07 (1H, s), 6·07 (1H, d, *J* 2 Hz), and 6·54 (1H, d, *J* 3 Hz). P.l.c. of fraction 2 [chloroform–benzene (4 : 1)] gave a little of compound (13) and a di-adduct (102 mg).

Isomerisation of Compound (13).—A solution of the pyrrolizinylmaleate (13) (100 mg) in dry toluene (30 ml) was boiled (32 h) and evaporated. P.l.c. of the residual red oil [chloroform–benzene (4 : 1)] gave starting material (51 mg) and the *diester* (10) as orange needles, m.p. 57—59° [from petroleum (b.p. 40—60°)] (21 mg, 21%) (Found: C, 66·5; H, 6·45; N, 4·9. $C_{16}H_{19}NO_4$ requires C, 66·4; H, 6·65; N, 4·85%), $\nu_{max.}$ ($CHCl_3$) 1727 and 1692 cm^{-1}. By boiling a solution of the compound (13) in ethanol (18 h) the yield of compound (10) was improved to 62%.

Dimethyl 5,6-*Dihydro*-5,5-*diphenylpyrrolo*[2,1,5-cd]*indolizine*-6,7-*dicarboxylate* (14).—A solution of compound (11) (240 mg) and dimethyl acetylenedicarboxylate (400 mg) in dry toluene (400 ml) was boiled (8 h) then left overnight. After evaporation of the solvent, the residual red oil was chromatographed on alumina (75 g); elution with petroleum (b.p. 60—80°) removed a yellow band (starting material). Elution with toluene removed a maroon band, giving a maroon solid. Recrystallisation from aqueous ethanol gave the *dihydrocyclazine* (14), m.p. 158° (254 mg, 69%) (Found: C, 75·55; H, 5·4; N, 3·35. $C_{36}H_{21}NO_4$ requires C, 75·85; H, 5·15; N, 3·4%), $\nu_{max.}$ 1725 and 1685 cm^{-1}; δ ($CDCl_3$) 3·11 (3H, s, O·CH_3), 3·80 (3H, s, O·CH_3), 4·60 (1H, s, H-6), 5·93 (1H, d, *J* 3 Hz) and 6·03 (1H, d, *J* 3 Hz) (H-3 and H-4), 6·47 (1H, d, *J* 6 Hz, H-1), 6·59 (1H, d, *J* 6 Hz, H-2), and 7·27br (10H, s).

Dimethyl 1,2,5,6-*Tetrahydro*-5,5-*diphenylpyrrolo*[2,1,5-cd]*indolizine*-6,7-*dicarboxylate* (15).—A solution of the cyclazine (14) (80 mg) in methanol (80 ml) with palladium–carbon

[12] R. L. Hinman and S. Theodoropulous, *J. Org. Chem.*, 1963, **28**, 3052.

[13] R. M. Silverstein, E. E. Ryskiewicz, and C. Willard, *Org. Synth.*, 1963, Coll. Vol. IV, p. 831.

[14] H. Fischer and H. Hofelmann, *Annalen*, 1938, **533**, 216.

(10%; 30 mg) was hydrogenated at atmospheric temperature and pressure until uptake ceased. The catalyst was filtered off and the solvent removed to give virtually pure *tetrahydrocyclazine* (15), recrystallised from aqueous ethanol as cream needles, m.p. 189—190° (80 mg, 97%) (Found: C, 75·4; H, 5·65; N, 3·2. $C_{26}H_{23}NO_4$ requires C, 75·5; H, 5·6; N, 3·4%), $\nu_{max.}$ ($CHCl_3$) 1725 and 1690 cm^{-1}; δ ($CDCl_3$) 3·08 (5H, m, O·CH_3 and CH_2), 3·45 (2H, m), 3·79 (3H, s, O·CH_3), 4·66 (1H, s, H-6), 5·91 (1H, d, *J* 3 Hz) and 6·42 (1H, d, *J* 3 Hz) (H-3 and H-4), and 7·25 (10H, m).

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