The Synthesis and Chemistry of Azolenines.† Part 2.[1] A General Synthesis of Pyrrole-2-carboxylic Acid Derivatives by the Reaction of 2H-Azirines with Enamines, and the Crystal and Molecular Structure of Ethyl 3-Phenyl-4,5,6,7-tetrahydroindole-2-carboxylate

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A new general synthesis of 1H-pyrrole-2-carboxylic acid derivatives is described. Reaction between appropriately substituted 2H-azirines and enamines gives a mixture of 2,3- and 3,4-dihydropyrroles, which on acid treatment yields the title compounds in moderate to high yields. Attempts to extend the reaction to the preparation of 2H- and 3H-pyrroles were unsuccessful; reasons are discussed. The crystal and molecular structure of ethyl 3-phenyl-4,5,6,7-tetrahydroindole-2-carboxylate has been determined. The molecules pack in highly coplanar, centrosymmetric, hydrogen-bonded pairs.

As part of a search for new synthetic approaches to 2H- and 3H-pyrroles,[2] we were interested in a potential reaction between 2H-azirines and enamines. 2H-Pyrroles have been prepared from 2H-azirines by photochemical cleavage of the C—C bond,[3-5] thermal cleavage of the C—N bond,[6-9] or Mo(CO)6-catalysed cleavage of the C=N bond,[10] each in the presence of alkynes, or of substituted alkenes serving as masked alkynes. Recently, attack by enolate anions at the 2H-azirine C=N bond has led to 2H-pyrroles [11,12] by what is claimed to be the most convenient general route to these compounds.[11c] It seemed that both 2H- and the little-known 3H-pyrroles might be prepared by reaction between 2H-azirines and suitably substituted enamines, the latter being structural analogues of enolate anions. Two alternative pathways were envisaged (Scheme 1), each involving loss of pyrrolidine from a 1 : 1 adduct.

Results and Discussion

In preliminary exploratory reactions we selected substrates having R^3 and R^6 = H, the anticipated products being 1H-pyrroles (7) or (8) (Scheme 2). This was to establish both the appropriate conditions and the orientation of any addition, prior to extension of the reaction to 2H- and 3H-pyrroles.

Reactions in which R^3 and R^6 = H.—Pyrrolidin-1-ylcyclohexene (1b) reacted exothermally with the azirine ester (2n) at room temperature and the mixture after being heated at 100 °C for 15 min yielded a 1H-pyrrole (21%; m.p. 200.5 °C) whose i.r. and [1]H n.m.r. spectra were consistent with structures (7bn) or (8bn).‡ Attempts to distinguish these by [13]C n.m.r. spectroscopy were inconclusive; the structure was established as (8bn) by X-ray crystallography (see below), thus demonstrating that reaction between substrates (1b) and (2n) was via path B and not path A.

This being a new synthetic route to 1H-pyrroles (8), efforts were turned to establishing the scope and mechanism of the reaction, and to optimising yields.§ Equimolar amounts of reactants (1b) and (2n) when stirred at room temperature until

the azirine i.r. band near 1 770 cm⁻¹ had disappeared gave a 1 : 1 adduct ($M^{+ \cdot}$ 340); neutralisation of a dry methanolic solution with hydrogen chloride gas at 0 °C led to the pyrrole (8bn) in 84% yield.

Extension to a wide range of enamines (1a—h) and azirine esters (2n—q), using a 2—4 h reaction time prior to HCl treatment (Method A), gave additional 1H-pyrroles (8) most of which are novel (Table 1). In some cases carbon tetrachloride gave better results than methanol (Method B); yields were good to excellent. For the less reactive enamines (1i) and (1j) yields were lower even after prolonged (72 h) reaction times before HCl treatment; no 1H-pyrroles could be isolated from (1k), which gave instead a small amount (7.5%) of the pyrazine (10). ¶

In view of the known sensitivity of 1H-pyrroles to strong acids, decomposition of the enamine–azirine (1 : 1) adduct was attempted with acetic acid in methanol, and with ammonium chloride or ammonium acetate in liquid ammonia. Of these modifications, the first (Method C), and the last (Method D) gave improved yields in certain cases when R^4 = Me, but not when R^4 = Ph. Reactions using the highly reactive diester (2r) were carried out in a solvent (chloroform) at 0 °C (Method E). Although L'abbé and co-workers isolated 1H-pyrroles from this azirine and enamines without acid treatment,[13] we found that the yield of (8fr) was increased from 8 to 25% if the reaction mixture was treated in methanol with HCl.
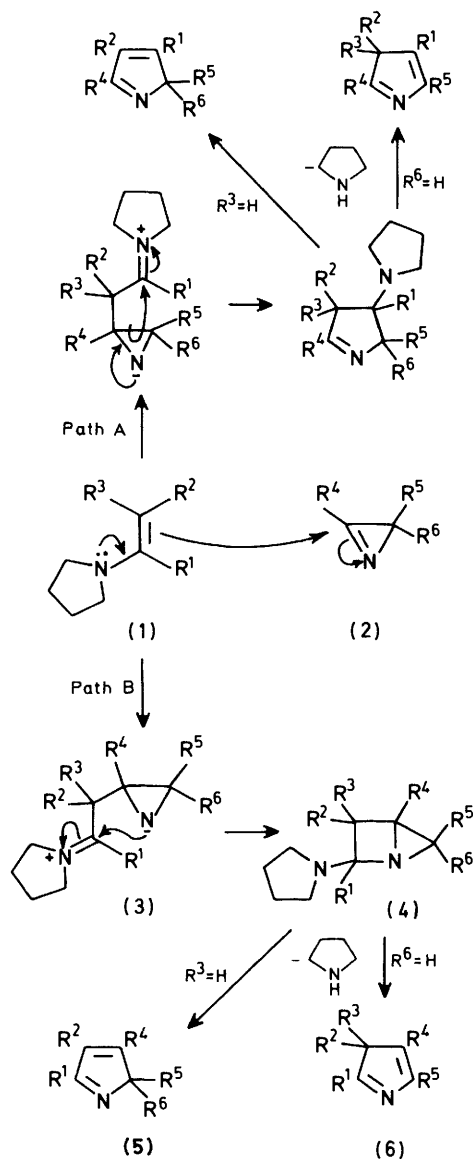
The Nature of the Intermediate 1 : 1 Adduct.—L'abbé and co-workers proposed that the initial adduct of type (4) ring-opened to a 2,5-dihydropyrrole of type (11) (Scheme 3) prior to loss of the secondary amine.[13] We believe that the bicycles (4) are instead converted into a mixture of a 2,3-dihydropyrrole (12) and a 3,4-dihydropyrrole (13), possibly in equilibrium, and with the former being the major (>75%) component. Liquid film i.r. spectra for a series of intermediates having R^4 = Ph and R^5 = CO₂Me show common peaks at 1 746w [$v_{C=O}$ of (13)], 1 685vs [$v_{C=O}$ of (12) but not (11)], 1 545s (somewhat broad), 1 385s, 1 270s, and 1 120s cm⁻¹. There is only weak absorption in the NH region. Likewise, [1]H n.m.r. spectra show typical pyrrolidine multiplets

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† The term azolenines refers to non-aromatic isomers of azoles.
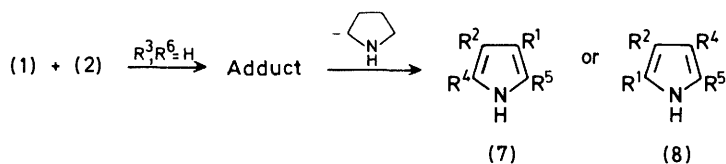‡ The known isomer (9) melts at 107 °C [L. Bernadi, P. Masi, and G. Rosini, *Ann. Chim. (Rome)*, 1973, **63**, 601].
§ During the course of this work, two examples were reported of 1H-pyrroles prepared by this method.[13]

¶ Pyrazines, derived apparently from dimerisation and oxidation of azirines, were isolated as by-products in a number of these reactions, and especially those involving the azirine (2w).
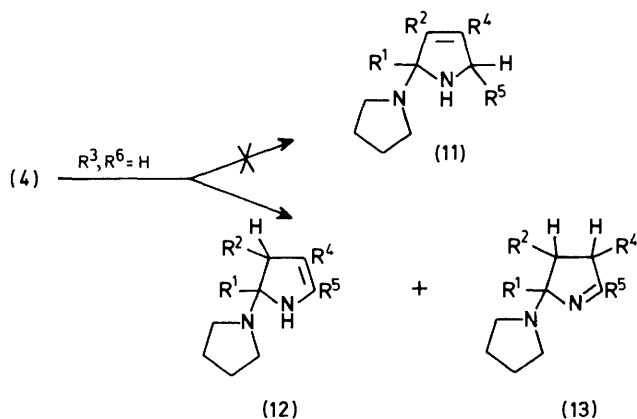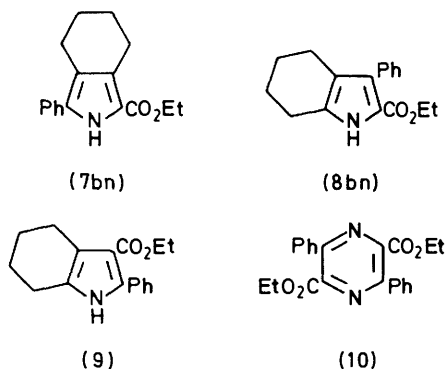
Scheme 1.

near δ 1.7 and 3.1 [assigned to structure (12)], with a weak multiplet near δ 3.6 [assigned to structure (13)]; also δ 3.25 (CO_2CH_3) and 7.2 (Ph; essentially a singlet). A doublet (J 7 Hz) is observed for $R^2 = CH_3$, inconsistent with structure (11).

Other substituents R^5. The tertiary amide (2s) also gave 1*H*-pyrroles with enamines, although elimination of pyrrolidine was much slower. Optimum yields were obtained by leaving the methanolic HCl solution of the 1 : 1 adduct overnight before isolation of the product (Method F). In contrast the primary amide (2t) gave only tars. The aldehyde (2u) was highly reactive, giving only tarry products; in contrast its diethyl acetal (2v), and the azirines (2w) and (2x), while reacting cleanly with enamines, failed to yield 1*H*-pyrroles under a variety of work-up procedures. It seems that for successful formation of 1*H*-pyrroles, R^5 should be an ester or tertiary amide function; we thus report an important new general method for preparing 1*H*-pyrrole-2-carboxylic acid derivatives.

I.r. and ^{1}H n.m.r. spectra for 1*H*-pyrroles prepared are given in Table 2.

Azirines (2) *having* R^5 *and* $R^6 \neq$ H.—By analogy, reactions of 2,2-disubstituted 2*H*-azirines with enamines (1a—h) were expected to lead to 2*H*-pyrroles (5). In practice, neither of the azirines (2y) or (2z) reacted with enamines at room temperature or on gentle warming, as shown by monitoring the i.r. 1 770 cm^{-1} band. At 100 °C tars were formed, but 2*H*-pyrroles could not be isolated. The low reactivity probably results from steric effects involving R^6.

Enamines (1) *having* R^2 *and* $R^3 \neq$ H.—3*H*-Pyrroles (6) were the expected products from the enamines (1l) and (1m) on reaction with azirines having $R^6 =$ H. While reaction occurred cleanly [*e.g.* with azirines (2o) and (2w)] to give 1 : 1 adducts, these were clearly different from structures (11)—(13). N.m.r. spectra (^{1}H and ^{13}C) showed the presence of a Me_2CH group, and while off-resonance spectra of adducts from (1l) had a doublet near δ 160, those from (1m) showed a singlet. Spectra of the adduct from (1l) and (2o) were fully consistent with the open-chain structure (14), formed apparently as shown in Scheme 4. An analogous sequence, without the final prototropic shift, has been observed with azirines and the enolate anions from $\alpha\alpha$-disubstituted ketones.[14] While the latter authors propose a two-stage ring

(7)   (8)

	R^1	R^2	R^3		R^4	R^5	R^6
(1a)		[CH$_2$]$_3$	H	(2n)	Ph	CO$_2$Et	H
(1b)		[CH$_2$]$_4$	H	(2o)	Ph	CO$_2$Me	H
(1c)		[CH$_2$]$_5$	H	(2p)	Me	CO$_2$Et	H
(1d)		[CH$_2$]$_6$	H	(2q)	Me	CO$_2$Me	H
(1e)	Et	Me	H	(2r)	CO$_2$Me	CO$_2$Me	H
(1f)	Et	Ph	H	(2s)	Ph	CONMe$_2$	H
(1g)	Ph	H	H	(2t)	Ph	CONH$_2$	H
(1h)	Ph	Me	H	(2u)	Ph	CHO	H
(1i)	Me	Ac	H	(2v)	Ph	CH(OEt)$_2$	H
(1j)	Me	CO$_2$Et	H	(2w)	Ph	H	H
(1k)	Ph	CO$_2$Et	H	(2x)	Ph	Me	H
(1l)	H	Me	Me	(2y)	Ph	CO$_2$Me	Me
(1m)	Ph	Me	Me	(2z)	Ph	Me	Me

Scheme 2.

(7bn)

(8bn)

(9)

(10)

(11)

(4)   R³,R⁶= H

(12)   (13)

Scheme 3.

(1l)   (2o)

(14)

Scheme 4.

(15)   (2n),(2o)

(16) R = Et
(17) R = Me

Scheme 5.

opening sequence, we believe it to be concerted as shown; the isopropyl carbon atom is an unfavourable site for a carbanion. Adducts from the azirine (2w) appear to be mixtures of isomeric compounds.

Reaction between 2H-*Azirines and Ynamines.*—Such reactions should give 1H-pyrroles directly, as was found to be the case. The ynamine (15) (Scheme 5) reacted with azirines (2n) and (2o) (Method G) to give low yields of the aminopyrroles (16) and (17) (Table 1).

Crystal Structure of the Tetrahydroindole (8bn).—The crystal structure of this compound is of interest from a number of points of view. Besides establishing the orientation of addition between azirines and enamines, it is the first reported structure of a tetrahydroindole. Further, few crystal structures of pyrrole-2-carboxylic esters have been determined,[15] and this one is found to contain centrosymmetrically-related hydrogen-bonded pairs of molecules (Figure).

Bond lengths and angles (Table 3) compare well with the corresponding values for related ethyl pyrrole-2-carboxylates;[15b] they also agree very closely with those for a series of 2-benzoylpyrroles.[16] The carbonyl group, which is essentially coplanar with the pyrrole ring [Table 4; the relevant torsion angle is 170(8)°], is *syn* relative to the C(2)⁻ N bond; examples are known where it is both *anti*[15] and *syn*.[15b] The phenyl-group, which is rotated out of the plane of the pyrrole ring by 51(4)°, has normal bond lengths and angles. Puckering of the cyclohexene moiety to relieve strain results in C(6) and C(7) lying respectively below and above a plane defined by the pyrrole ring atoms (Table 4). The unusually short (1.464 Å) C(6)⁻C(7) bond, and enlarged (115—116°) C(5)⁻C(6)⁻C(7) and C(6)⁻C(7)⁻C(8) angles, possibly arise
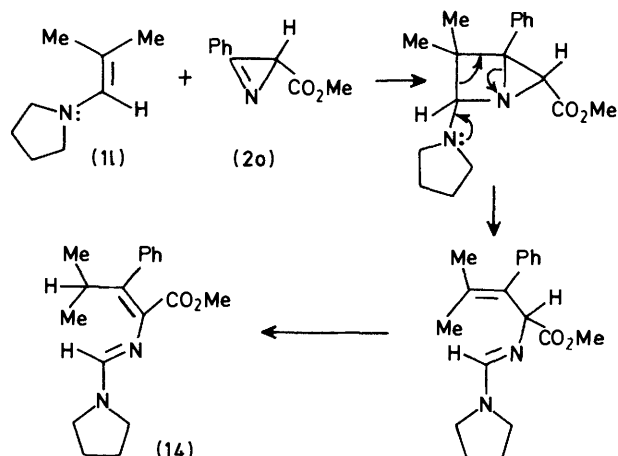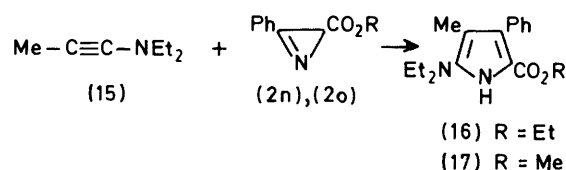
from large thermal motions for C(6) and C(7) ($U_{22} = 0.122$ and 0.132 respectively; Table 8). The most closely related structure we have been able to find (3,4,5,6-tetrahydrophthalimide[17]) does not show this effect.

All the atoms making up the ten-membered ring hydrogen-bonding site are remarkably coplanar (Table 4), deviations from the plane defined by O(1), O(1)′, N, and N′ all being less than 0.1 Å. Relevant N⁻H · · · O=C bond lengths and angles are given in Table 5. There has been only one other report of simple dimeric H-bonded structures in the pyrrole series,[16] although a bifurcated system is known.[15b]

Experimental

I.r. spectra were recorded on a Perkin-Elmer 577 spectrophotometer and calibrated with polystyrene; n.m.r. spectra were recorded on Perkin-Elmer R-20 (¹H) and JEOL FX-90Q (¹H and ¹³C) instruments with internal SiMe₄ being used in calibration; and mass spectra on a Hitachi RMS-4 spectrometer. Enamines were prepared by well-known methods; the ynamine (15) as reported by Hubert and Viehe.[18] Known azirines were prepared by published procedures: (2n),[19] (2o),[19] (2p),[20] (2r),[21] (2t),[22] (2u),[23] (2v),[23] (2w),[24] (2x),[11b] and (2z);[11b] they were characterised by i.r. and ¹H n.m.r. spectroscopy. Established methods were used for new azirines: (2q),[20] 34% (from methyl crotonate), $v_{max.}$ (film) 1 798 and 1 729 cm⁻¹; δ (CDCl₃) 3.72 (3 H, s), 2.52 (3 H, s), and 2.43 (1 H, s); (2s),[22] 92%, $v_{max.}$ (film) 1 760 and 1 643 cm⁻¹; δ (CDCl₃) 7.75 (2 H, m), 7.45 (3 H, m), 3.29 (3 H, s), and 2.96 (3 H, + 1 H); and (2y),[19] 81%, $v_{max.}$ (film) 1 758 and 1 726 cm⁻¹; δ (CDCl₃) 7.75 (2 H, m), 7.51 (3 H, m), 3.62 (3 H, s), and 1.60 (3 H, s).

Preparation of 1H-*Pyrroles* (8).—*Method A.* To the azirine (2) (0.01 mol) was added dropwise, with stirring and cooling, the enamine (1) (0.01 mol). The mixture was stirred at 25 °C until i.r. absorption at 1 770 cm⁻¹ had disappeared (2—72 h);

Table 1. Preparative, physical, and analytical data for pyrrole-2-carboxylic acid derivatives (8), (16), and (17)

Compd.	R¹	R²	R⁴	R⁵	Yield (%)	Method [a]/ solvent [b]	M.p. (°C)	Found (%) (Requires) C	H	N	Molecular formula
(8an)		[CH₂]₃	Ph	CO₂Et	65	A/I	162	75.0 (75.25)	6.8 6.7	5.4 5.5)	$C_{16}H_{17}NO_2$
(8bn)		[CH₂]₄	Ph	CO₂Et	84	A/I	200.5	75.5 (75.8)	6.8 7.1	5.2 5.2)	$C_{17}H_{19}NO_2$
(8cn)		[CH₂]₅	Ph	CO₂Et	80	A/I	190	76.3 (76.3)	7.3 7.5	5.0 4.95)	$C_{18}H_{21}NO_2$
(8dn)		[CH₂]₆	Ph	CO₂Et	64	A/II	147.5	76.8 (76.75)	8.0 7.8	4.8 4.7)	$C_{19}H_{23}NO_2$
(8en)	Et	Me	Ph	CO₂Et	66	A/I	103	74.7 (74.7)	7.4 7.45	5.3 5.45)	$C_{16}H_{19}NO_2$
(8ao)		[CH₂]₃	Ph	CO₂Me	73	A/I	184	74.6 (74.65)	6.2 6.25	5.6 5.8)	$C_{15}H_{15}NO_2$
(8bo)		[CH₂]₄	Ph	CO₂Me	62	B/III	190	75.4 (75.25)	6.9 6.7	5.6 5.5)	$C_{16}H_{17}NO_2$
(8co)		[CH₂]₅	Ph	CO₂Me	58	A/I	185	75.5 (75.8)	7.1 7.1	5.4 5.2)	$C_{17}H_{19}NO_2$
(8do)		[CH₂]₆	Ph	CO₂Me	72	A/III	157	76.2 (76.3)	7.7 7.5	4.95 4.95)	$C_{18}H_{21}NO_2$
(8eo)	Et	Me	Ph	CO₂Me	81	B/II	125	74.2 (74.05)	7.1 7.05	5.7 5.75)	$C_{15}H_{17}NO_2$
(8fo)	Et	Ph	Ph	CO₂Me	63	A/I	198.5	78.4 (78.65)	6.2 6.3	4.4 4.6)	$C_{20}H_{19}NO_2$
(8go)	Ph	H	Ph	CO₂Me	38	A/IV	182	78.3 (78.0)	5.55 5.45	4.05 5.05)	$C_{18}H_{15}NO_2$
(8ho)	Ph	Me	Ph	CO₂Me	48	A/I	138	78.3 (78.3)	6.0 5.9	4.5 4.8)	$C_{19}H_{17}NO_2$
(8io)	Me	COMe	Ph	CO₂Me	31	A/I	150.5	69.85 (70.0)	5.8 5.9	5.6 5.45)	$C_{18}H_{15}NO_3$
(8jo)	Me	CO₂Et	Ph	CO₂Me	24	A/I	140	67.1 (66.9)	6.1 5.95	4.9 4.9)	$C_{16}H_{17}NO_4$
(8bp)		[CH₂]₄	Me	CO₂Et	44	D/II	110 [c]				
(8cp)		[CH₂]₅	Me	CO₂Et	51	A/II	106	70.7 (70.55)	8.7 8.65	6.6 6.3)	$C_{13}H_{19}NO_2$
(8ep)	Et	Me	Me	CO₂Et	65	C/II	72	68.0 (67.7)	9.1 8.8	7.2 7.2)	$C_{11}H_{17}NO_2$
(8fp)	Et	Ph	Me	CO₂Et	27	C/I	147	74.7 (74.7)	7.8 7.45	5.7 5.45)	$C_{16}H_{19}NO_2$
(8bq)		[CH₂]₄	Me	CO₂Me	45	D/I	156	68.5 (68.35)	7.8 7.8	7.3 7.25)	$C_{11}H_{15}NO_2$
(8gq)	Ph	H	Me	CO₂Me	25	C/I	127	72.4 (72.5)	6.3 6.1	6.6 6.5)	$C_{13}H_{13}NO_2$
(8ar)		[CH₂]₃	CO₂Me	CO₂Me	15	E/V	127 [d]				
(8br)		[CH₂]₄	CO₂Me	CO₂Me	21	E/I	137.5 [d,e]				
(8cr)		[CH₂]₅	CO₂Me	CO₂Me	19	E/I	116	61.8 (62.1)	6.5 6.8	5.4 5.6)	$C_{13}H_{17}NO_4$
(8fr)	Et	Ph	CO₂Me	CO₂Me	25	E/V	177.5 [d]				
(8gr)	Ph	H	CO₂Me	CO₂Me	7	D/II	132 [f]				
(8bs)		[CH₂]₄	Ph	CONMe₂	27	F/VI	252	76.2 (76.1)	7.55 7.5	10.45 10.4)	$C_{17}H_{20}N_2O$
(8cs)		[CH₂]₅	Ph	CONMe₂	40	F/I	265	76.45 (76.55)	8.15 7.85	10.0 9.9)	$C_{18}H_{22}N_2O$
(8fs)	Et	Ph	Ph	CONMe₂	47	F/V	197	79.0 (79.2)	6.9 6.95	8.7 8.8)	$C_{21}H_{22}N_2O$
(16)	NEt₂	Me	Ph	CO₂Et	15	G/V	117	72.3 (72.0)	8.1 8.05	9.3 9.3)	$C_{18}H_{24}N_2O_2$
(17)	NEt₂	Me	Ph	CO₂Me	18	G/V	112.5	71.5 (71.3)	7.8 7.75	9.3 9.8)	$C_{17}H_{22}N_2O_2$

[a] See Experimental section. [b] Solvents for recrystallisation: I, CCl₄; II, light petroleum (b.p. 60—80 °C); III, MeOH; IV, CHCl₃; V, CCl₄–light petroleum; VI, EtOAc. [c] Lit. m.p. 110—111 °C (V. I. Shvedov, L. B. Altukhova, and A. N. Grinev, *Khim. Geterotsikl. Soedin.*, 1972, 342). [d] Lit. m.p.s (8ar) 114—116 °C; (8br) 133—135 °C; (8fr) 170—172 °C (R. Baumes, R. Jacquier, and G. Tarrago, *Bull. Soc. Chim. Fr.*, 1974, 1147). [e] Lit. m.p. 139 °C (V. Bardakos, W. Sucrow, and A. Fehlauer, *Chem. Ber.*, 1975, **108**, 2161). [f] Lit. m.p. 134—135 °C (J. Barluenga, F. Palacios, and V. Gotor, *Synthesis*, 1975, 642); 140 °C (T. Sheradsky, *Tetrahedron Lett.*, 1970, 25); 149 °C (ref. 13).

Table 2. I.r. (Nujol), and ^{1}H n.m.r. (CDCl$_3$) spectroscopic data for 1H-pyrroles (8), (16), and (17)

Compd.	R^1	R^2	R^4	R^5	$\nu_{max.}$/cm^{-1} NH	C=O	^{1}H N.m.r./δ R^1	R^2	R^4	R^5	NH
(8an)	[CH$_2$]$_3$		Ph	CO$_2$Et	3 295	1 648	1.70 (m) 2.63 (m)		7.30 (m)	1.20 (t) 4.13 (q)	8.80 (br)
(8bn)	[CH$_2$]$_4$		Ph	CO$_2$Et	3 290	1 655	1.75 (m) 2.56 (m)		7.34 (m)	1.15 (t) 4.16 (q)	8.90 (br)
(8cn)	[CH$_2$]$_5$		Ph	CO$_2$Et	3 293	1 652	1.72 (m) 2.41 and 2.72 (m)		7.31 (m)	1.08 (t) 4.10 (q)	9.05 (br)
(8dn)	[CH$_2$]$_6$		Ph	CO$_2$Et	3 305	1 652	1.60 (m) 2.49 and 2.80 (m)		7.31 (m)	1.08 (t) 4.12 (q)	9.30 (br)
(8en)	Et	Me	Ph	CO$_2$Et	3 320	1 658	1.22 (t) 2.60 (q)	1.86 (s)	7.20 (m)	1.07 (t) 4.05 (q)	8.75 (br)
(8ao)	[CH$_2$]$_3$		Ph	CO$_2$Me	3 294	1 650	2.60 (m)		7.25 (m)	3.67 (s)	8.80 (br)
(8bo)	[CH$_2$]$_4$		Ph	CO$_2$Me	3 292	1 662	1.75 (m) 2.40 (m)		7.23 (m)	3.63 (s)	8.75 (br)
(8co)	[CH$_2$]$_5$		Ph	CO$_2$Me	3 302	1 657	1.70 (m) 2.42 and 2.73 (m)		7.18 (m)	3.57 (s)	8.95 (br)
(8do)	[CH$_2$]$_6$		Ph	CO$_2$Me	3 325	1 660	1.43 (m) 2.35 and 2.72 (m)		7.18 (m)	3.57 (s)	8.75 (br)
(8eo)	Et	Me	Ph	CO$_2$Me	3 312	1 668	1.22 (t) 2.65 (q)	1.86 (s)		3.59 (s)	8.90 (br)
(8fo)	Et	Ph	Ph	CO$_2$Me	3 310	1 667	1.20 (t) 2.62 (q)	7.02 (s)	7.02 (s)	3.63 (s)	9.05 (br)
(8go)	Ph	H	Ph	CO$_2$Me	3 310	1 669	7.41 (m)	6.53 (d)	7.30 (m)	3.75 (s)	9.30 (br)
(8ho)	Ph	Me	Ph	CO$_2$Me	3 292	1 680	7.34 (s)	2.06 (s)	7.25 (s)	3.62 (s)	8.95 (br)
(8io)	Me	COMe	Ph	CO$_2$Me	3 330	1 654 1 671	2.52 (s)	1.77 (s)	7.21 (m)	3.57 (s)	9.75 (br)
(8jo)	Me	CO$_2$Et	Ph	CO$_2$Me	3 295	1 672 1 697	2.52 (s)	0.94 (t) 3.94 (q)	7.16 (m)	3.56 (s)	9.45 (br)
(8bp)	[CH$_2$]$_4$		Me	CO$_2$Et	3 287	1 655	1.73 (m) 2.43 (m)		2.18 (s)	1.30 (t) 4.19 (q)	8.65 (br)
(8cp)	[CH$_2$]$_5$		Me	CO$_2$Et	3 312	1 659	1.73 (m) 2.55 (m)		2.23 (s)	1.32 (t) 4.26 (q)	8.85 (br)
(8ep)	Et	Me	Me	CO$_2$Et	3 331	1 661	1.18 (t) 2.56 (q)	1.90 (s)	2.24 (s)	1.32 (t) 4.28 (q)	8.80 (br)
(8fp)	Et	Ph	Me	CO$_2$Et	3 300	1 656	1.16 (t) 2.61 (q)	7.27 (m)	2.26 (s)	1.45 (t) 4.33 (q)	8.95 (br)
(8bq)	[CH$_2$]$_4$		Me	CO$_2$Me	3 295	1 660	1.75 (m) 2.45 (m)		2.22 (s)	3.83 (s)	8.85 (br)
(8gq)	Ph	H	Me	CO$_2$Me	3 322	1 681	7.45 (m)	6.36 (d)	2.48 (s)	3.88 (s)	9.15 (br)
(8ar)	[CH$_2$]$_3$		CO$_2$Me	CO$_2$Me	3 273	1 668 1 722	2.48 (m) 2.70 (m)		3.86 (s)^a	3.84 (s)^a	9.55 (br)
(8br)	[CH$_2$]$_4$		CO$_2$Me	CO$_2$Me	3 300 3 275	1 664 1 707 1 719	1.77 (m) 2.60 (m)		3.85 (s)^b	3.85 (s)^b	9.40 (br)
(8cr)	[CH$_2$]$_5$		CO$_2$Me	CO$_2$Me	3 288	1 670 1 725	1.70 (m) 2.58 (m)		3.72 (s)^a	3.78 (s)^a	9.05 (br)
(8fr)	Et	Ph	CO$_2$Me	CO$_2$Me	3 275	1 681 1 738	1.17 (t) 2.61 (q)	7.20 (m)	3.65 (s)^a	3.79 (s)^a	9.55 (br)
(8gr)	Ph	H	CO$_2$Me	CO$_2$Me	3 273	1 678 1 725	7.33 (m) 7.54 (m)	6.91 (d)	3.85 (s)^a	3.87 (s)^a	10.02 (br)
(8bs)	[CH$_2$]$_4$		Ph	CONMe$_2$	3 225	1 591	1.76 (m) 2.57 (m)		7.29 (m)	2.67 (s)	9.50 (br)
(8cs)	[CH$_2$]$_5$		Ph	CONMe$_2$	3 250	1 590	1.72 (m) 2.62 (m)		7.27 (m)	2.60 (s)	9.60 (br)
(8fs)	Et	Ph	Ph	CONMe$_2$	3 270	1 592	1.05 (t) 2.63 (q)	7.06 (m)	7.14 (m)	2.65 (s)	c
(16)	NEt$_2$	Me	Ph	CO$_2$Et	3 330	1 660	1.06 (t)^b 3.04 (q)	1.82 (s)	7.19 (m)	1.06 (t)^b 4.03 (q)	8.45 (br)
(17)	NEt$_2$	Me	Ph	CO$_2$Me	3 335	1 668	1.05 (t) 3.05 (q)	1.81 (s)	7.18 (m)	3.56 (s)	8.45 (br)

^{a} Assignments may be interchanged. ^{b} Signals superimposed. ^{c} Signal not observed.

the 1 : 1 adduct was then dissolved in dry MeOH (15 ml) and dry HCl was passed into the solution at 0 °C until it was neutral. The solvent was removed under reduced pressure and the pyrrole was isolated by column chromatography (SiO$_2$; CHCl$_3$) and finally recrystallised.

Method B. As for Method A, only CCl$_4$ was used in place of MeOH.

Method C. The 1 : 1 adduct (0.01 mol) was dissolved in MeOH (15 ml) as in Method A, and the solution neutralised with AcOH at 0 °C. The mixture was allowed to stand over-
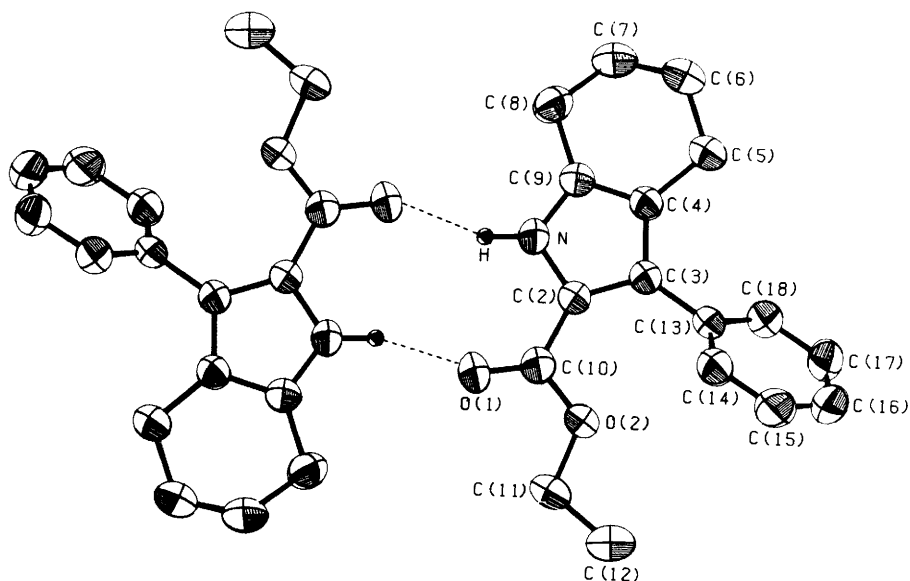
Figure. ORTEP Drawing of the tetrahydroindole (8bn) showing the atom numbering scheme used, and the centrosymmetric arrangement of a hydrogen-bonded pair of molecules

Table 3. Bond lengths and angles for the tetrahydroindole (8bn), with e.s.d.s in parentheses

Bond lengths (Å)

N–C(2)	1.385(3)	C(10)–O(1)	1.215(3)
C(2)–C(3)	1.394(3)	C(10)–O(2)	1.336(3)
C(3)–C(4)	1.414(3)	O(2)–C(11)	1.458(3)
C(4)–C(5)	1.503(3)	C(11)–C(12)	1.493(3)
C(5)–C(6)	1.508(3)	C(3)–C(13)	1.478(3)
C(6)–C(7)	1.464(4)	C(13)–C(14)	1.387(3)
C(7)–C(8)	1.520(3)	C(14)–C(15)	1.387(3)
C(8)–C(9)	1.492(3)	C(15)–C(16)	1.373(4)
C(9)–C(4)	1.377(3)	C(16)–C(17)	1.370(4)
C(9)–N	1.355(3)	C(17)–C(18)	1.393(3)
C(2)–C(10)	1.447(3)	C(18)–C(13)	1.383(3)

Angles (°)

C(9)–N–C(2)	109.4(2)	C(8)–C(9)–N	125.3(2)
N–C(2)–C(3)	107.5(2)	C(4)–C(9)–N	108.7(2)
N–C(2)–C(10)	117.9(2)	C(2)–C(10)–O(1)	125.0(2)
C(10)–C(2)–C(3)	134.4(2)	C(2)–C(10)–O(2)	112.9(2)
C(2)–C(3)–C(4)	106.8(2)	O(1)–C(10)–O(2)	122.1(2)
C(2)–C(3)–C(13)	127.9(2)	C(10)–O(2)–C(11)	117.5(2)
C(13)–C(3)–C(4)	125.2(2)	O(2)–C(11)–C(12)	106.6(2)
C(3)–C(4)–C(9)	107.6(2)	C(3)–C(13)–C(14)	121.1(2)
C(3)–C(4)–C(5)	130.4(2)	C(3)–C(13)–C(18)	120.7(2)
C(9)–C(4)–C(5)	122.0(2)	C(18)–C(13)–C(14)	118.2(2)
C(4)–C(5)–C(6)	111.4(2)	C(13)–C(14)–C(15)	121.0(2)
C(5)–C(6)–C(7)	115.7(2)	C(14)–C(15)–C(16)	119.9(2)
C(6)–C(7)–C(8)	115.6(2)	C(15)–C(16)–C(17)	120.2(3)
C(7)–C(8)–C(9)	108.7(2)	C(16)–C(17)–C(18)	119.9(2)
C(8)–C(9)–C(4)	126.0(2)	C(17)–C(18)–C(13)	120.9(2)

Table 4. Least-squares mean planes, and displacements (Å) of atoms from those planes. Equations are in the form $pax + qby + rcz = s$; atoms used in the calculation are marked with an asterisk

Plane (1)—Pyrrole ring

p	0.4693	C(2)*	0.01	C(6)	−0.23
q	−0.8737	C(3)*	−0.01	C(7)	0.37
r	−0.2631	C(4)*	0.01	C(8)	−0.01
s	6.870	C(9)*	0.00	C(10)	0.12
		N*	0.00	C(13)	−0.13
		C(5)	0.03	O(1)	0.04
				O(2)	0.35

Plane (2)—H-Bonding site

p	0.4587	N*	0.00	C(2)′	0.00
q	−0.8710	N′*	0.00	C(10)	0.09
r	−0.2704	O(1)*	0.00	C(10)′	−0.09
s	6.962	O(1)′*	0.00	H(N)	0.05
		C(2)	−0.00	H(N)′	−0.05

Table 5. Bond lengths (Å) and angles (°) at the hydrogen-bonding site, with e.s.d.s in parentheses

N–H	0.92(2)	N–H · · · O(1)′	160(2)
H · · · O(1)′	1.96(2)	H · · · O(1)′–C(10)′	154(1)
N · · · O(1)′	2.847(2)		

night at 25 °C, after which water (50 ml) was added and the product extracted with Et_2O (3 × 50 ml). The ether extract was washed with water (50 ml), dried ($MgSO_4$), and evaporated, and the residue purified as for Method A.

Method D. The 1 : 1 adduct (0.01 mol), prepared as in Method A, was dissolved in liquid NH_3 (50 ml) in a thermally insulated flask, dry NH_4OAc (0.5 g, 0.03 mol) was added, and the mixture was stirred until the NH_3 had evaporated. The

residue was purified by column chromatography, and the product recrystallised.

Method E. As for Method A only the azirine and enamine were separately dissolved in $CHCl_3$ (25 ml) before mixing at 0 °C; the $CHCl_3$ was removed prior to MeOH/HCl treatment.

Method F. As for Method A, only the MeOH solution was allowed to stand overnight after HCl treatment and before isolation of the product.

Attempts to Prepare 2H-*Pyrroles from Azirines* (2y) *and* (2z).—The azirines were unchanged when stirred with the enamines (1a—c), and (1e) both at room temperature and on gentle warming. At 100 °C tars were formed.

Table 6. Fractional atomic co-ordinates ($\times 10^4$) for non-hydrogen atoms with e.s.d.s in parentheses

Atom	x	y	z
N	2 875(2)	6 330(2)	10 061(1)
C(2)	2 764(3)	6 708(2)	8 945(2)
C(3)	4 516(2)	7 594(2)	8 780(2)
C(4)	5 678(2)	7 772(2)	9 839(2)
C(5)	7 696(3)	8 635(3)	10 177(2)
C(6)	8 386(3)	8 226(3)	11 282(2)
C(7)	7 226(3)	8 063(3)	12 236(2)
C(8)	5 294(3)	6 816(3)	11 807(2)
C(9)	4 628(3)	6 965(2)	10 595(2)
C(10)	985(3)	6 251(3)	8 271(2)
C(11)	−703(3)	6 564(3)	6 598(2)
C(12)	−273(3)	7 263(3)	5 523(2)
C(13)	5 112(2)	8 146(3)	7 686(2)
C(14)	4 563(3)	7 054(3)	6 517(2)
C(15)	5 162(3)	7 564(3)	5 496(2)
C(16)	6 331(3)	9 166(4)	5 635(2)
C(17)	6 913(3)	10 260(3)	6 782(2)
C(18)	6 306(3)	9 750(3)	7 808(2)
O(1)	−420(2)	5 378(2)	8 526(1)
O(2)	1 021(2)	6 919(2)	7 327(1)

Attempts to Prepare 3H-*Pyrroles from Enamines* (11) *and* (1m).—Reactions were carried out as for Method A. Spectroscopic data for adduct (14) were; $v_{max.}$ (film) 1 685(s), 1 620(m), 1 530 (s), 1 395 (s), 1 265 (s), and 1 105 (s) cm⁻¹; δ (¹H) (CDCl₃) 1.10 (6 H, d, J 6.5 Hz), 1.75 (4 H, m), 2.5 (1 H, m), 3.10 (3 H, s), 3.40 (4 H, m), 7.2 (5 H, s), and 7.56 (1 H, d, J 4.5 Hz); δ (¹³C) (CDCl₃) 19.5 (q), 25.5 (t), 34.8 (d), 50.0 (q), 52.3 (t), 115.0 (s), 127.9 (d), 128.1 (d), 128.8 (d), 138.7 (s), 151.1 (s), 161.7 (d), and 167.1 (s).

Preparation of the Amino-pyrroles (16) *and* (17).—*Method G.* The propynamine (15) and the appropriate azirine were combined as in Method A. After 72 h at 25 °C, the mixture was chromatographed (SiO₂/CHCl₃), and the isolated product was recrystallised.

Crystal Structure Determination for the Tetrahydroindole (8bn).—C₁₇H₁₉NO₂, $M = 269.34$. Triclinic, space group $P\bar{1}$, $a = 8.024(1)$, $b = 8.973(1)$, $c = 11.293(2)$ Å, $\alpha = 103.32(1)$, $\beta = 93.34(1)$, $\gamma = 110.98(1)°$, $U = 729.8$ Å³, $Z = 2$, $D_c = 1.226$ g cm⁻³, $F(000) = 288$, $\mu(Mo$-$K_\alpha) = 0.86$ cm⁻¹. Intensity data were collected on a Nicolet R3m automated diffractometer using the θ—2θ scanning technique, with variable scan speeds from 2.02 to 8.37° min⁻¹ and a scan range from 1° below the K_{α_1} peak to 1° above the K_{α_2} peak. Background counts were taken for half the scan time at each end of the scan range. All reflections within the (h, $\pm k$, $\pm l$) quadrants extending to $2\theta = 55°$ were measured. A total of 2 578 independent reflections were obtained of which 1 969 with $|F_o| > 3\sigma(|F_o|)$ were considered to be observed and used in subsequent calculations.

The structure was solved by direct methods with MULTAN 78.[25] Refinement was carried out by full-matrix least-squares methods. The quantity minimized was $\Sigma w(F_o^2 - F_c^2)^2$, with weight $w = 1/\sigma^2(F_o^2)$. Atomic scattering factors were obtained from International Tables.[26] Calculations were carried out on an IBM 3031 computer using the CRYM system.[27]

After several cycles of least-squares adjustment of the co-

ordinates and anisotropic thermal parameters of the non-hydrogen atoms the R-index was reduced to 0.10. At this stage positions of all the hydrogen atoms were recovered from a difference Fourier map.

In the last least-squares cycle a list of 258 parameters were adjusted: atomic co-ordinates, anisotropic thermal parameters of the non-hydrogen atoms, isotropic thermal parameters of the hydrogen atoms, a scale factor, and a secondary extinction factor. The parameters of the hydrogen atoms were kept in one matrix and the rest of the parameters in another.

The final R-index for 1 969 reflections was 0.049, the 'goodness of fit', $[\Sigma w(F_o^2 - F_c^2)^2/(m - s)]^{\frac{1}{2}} = 2.49$, where m is the number of reflections and s is the number of parameters. The final value of the secondary extinction parameter was $(3.77 \pm 0.08) \times 10^{-7}$. Atomic parameters for non-hydrogen atoms are listed in Table 6. Those for hydrogen atoms (Table 7), observed and calculated structure factors and thermal parameters (Table 8) are in a Supplementary Publication (SUP No. 23723, 9 pages).*

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