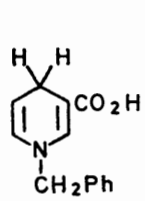
Addition Reactions of Heterocyclic Compounds. Part LI.[1] Cyclobuta-[*b*]pyridines from Reactions of Dimethyl Acetylenedicarboxylate with 1-Alkyl-1,4-dihydropyridines and the Cycloelimination of Amide and Carboxy-groups

By R. M. Acheson,* N. D. Wright, and (in part) P. A. Tasker, Department of Biochemistry, South Parks Road, Oxford OX1 3QU

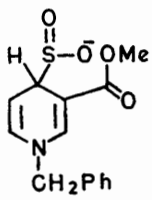
Several 1,3-disubstituted 1,4-dihydropyridines with dimethyl acetylenedicarboxylate in acetonitrile at room temperature gave 1,4.4a,6a-tetrahydrocyclobuta[*b*]pyridines and where a 3-carboxy- or a 3-carbamoyl group was present, a novel cycloelimination of this group occurred to give the corresponding 3-(*cis*-1,2-dimethoxycarbonylvinyl) derivative. 1-Benzyl-1,4-dihydroquinoline-4-carbonitrile gave the 3-(*cis*-1,2-dimethoxycarbonylvinyl) derivative quantitatively, and 2-benzyl-1,2-dihydroisoquinoline-1-carbonitrile formed a phenanthridine.

THE zwitterions formed by nucleophilic attack of nitrogen-containing heterocycles upon acetylenic esters [2] generally react further by proton abstraction, nucleophilic attack upon another molecule of the acetylene (usually followed by cyclisation) or, if initial attack was effected by the carbon atom α or β to the heteroatom, by cyclisation.[3,4]

The reactions of *N*-substituted dihydropyridines and some similar compounds with dimethyl acetylenedicarboxylate in calcium hydride-dried acetonitrile at room temperature have now been investigated, and the formation of products by each of the above routes has been observed.[5] The dihydropyridines were obtained by reactions of the corresponding pyridinium salts with sodium dithionite,[6] a noteworthy feature being that 1-benzyl-3-methoxycarbonylpyridinium chloride gave the reduced acid (1) as the sole product, rapid hydrolysis perhaps having taken place *via* anchimeric assistance from the SO_2^- group of the anticipated intermediate (2).



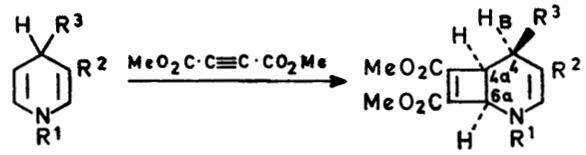
(1)



(2)

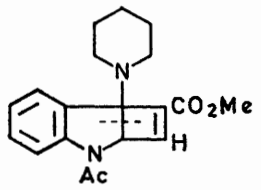
By analogy with alicyclic enamines,[7] the expected attack by the carbon atom β to the nitrogen atom of the dihydropyridines (3)—(5) on the ester, followed by a presumably non-concerted cyclisation, was observed to give the cyclobutene derivatives (6)—(8), respectively, but in contrast to the observed benzazepine formation from 1-methylindole with dimethyl acetylenedicarboxylate,[8] no ring-expanded products were obtained even after refluxing the cyclobutenes (6) and (7) for 2 days in dioxan. No adducts were isolated from the dihydropyridines (10)—(12).

Compounds (6) and (7) thus appear to be the first known crystalline, thermally stable cyclobutenes formed from dimethyl acetylenedicarboxylate and enamine



(3) $R^1 = CH_2Ph$, $R^2 = CO{\cdot}NPhEt$, $R^3 = H_A$ (6)
(4) $R^1 = CH_2Ph$, $R^2 = CN$, $R^3 = H_A$ (7)
(5) $R^1 = Me$, $R^2 = CN$, $R^3 = H_A$ (8)
(10) $R^1 = CH_2Ph$, $R^2 = CO{\cdot}NH_2$, $R^3 = CN$
(11) $R^1 = CH_2Ph$, $R^2 = CN$, $R^3 = CN$
(12) $R^1 = CH_2Ph$, $R^2 = Ac$, $R^3 = CN$

systems [7,9] although Snieckus [4] has isolated the stable, crystalline compound (9) formed from 1-acetyl-3-piperidinoindole with methyl propiolate. On refluxing



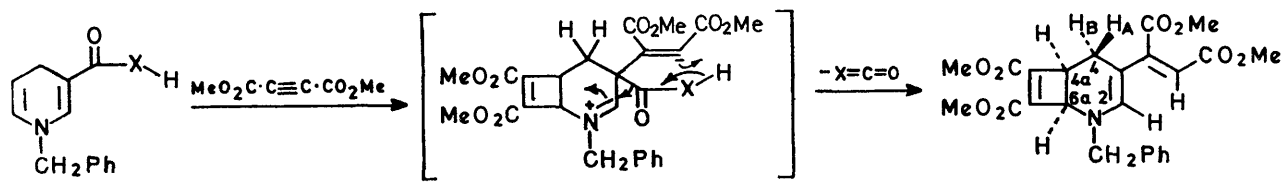
(9)

for 44 h in dioxan the corresponding benzazepine was formed.

In contrast, when the dihydropyridines (1), (13), and (14), each containing a 3-substituent with a suitably placed removable hydrogen atom, were treated with the ester, displacement of these groups occurred together with cyclobutene formation to give the 1 : 2 adduct (16) in yields of 0·5, 14, and 4%, respectively. It is thought that intramolecular *proton abstraction* by the postulated zwitterionic intermediate (15) occurs by way of a six-membered cyclic transition state involving cycloelimination of an isocyanate, or of carbon dioxide in the case of (1),

[1] Part L, R. M. Acheson, P. J. Abbott, M. W. Foxton, N. R. Raulins, and G. E. Robinson, *J.C.S. Perkin I*, 1972, 2182.
[2] R. M. Acheson, *Adv. Heterocyclic Chem.*, 1963, **1**, 125.
[3] A. Galbraith, T. Small, R. A. Barnes, and V. Boekelheide, *J. Amer. Chem. Soc.*, 1961, **83**, 453.
[4] V. Snieckus and M.-S. Lin, *J. Org. Chem.*, 1971, **36**, 645.
[5] Preliminary report, R. M. Acheson and N. D. Wright, *Chem. Comm.*, 1971, 1421.
[6] D. Mauzerall and J. H. Westheimer, *J. Amer. Chem. Soc.*, 1955, **77**, 2261.
[7] C. F. Hueber, L. Dorfman, M. M. Robison, E. Donoghue, W. G. Pierson, and P. Strachan, *J. Org. Chem.*, 1963, **28**, 3134.
[8] R. M. Acheson, J. M. Bridson, and T. S. Cameron, *J.C.S. Perkin I*, 1972, 968.
[9] G. A. Berchtold and G. F. Uhlig, *J. Org. Chem.*, 1963, **28**, 1459.

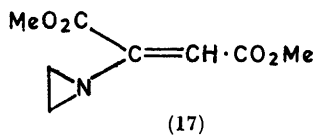
Owing to the high τ value (4·70) of the vinyl proton signal, the ester groups are assumed to be *cis*, for the corresponding signals for protons of the maleate and fumarate isomers of (17) appear at τ 4·69 and 3·85, respectively.[10]



(1) X = O
(13) X = NH
(14) X = N·CH$_2$·CH$_2$Ph

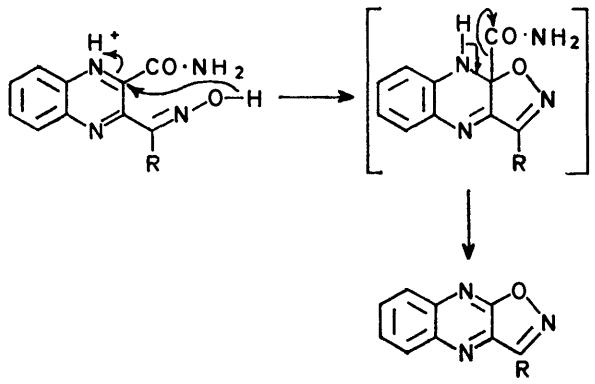
(15) (16)

The only other examples of the remarkable displacement of an unsubstituted carbamoyl group have been described by Dahn and his associates. They showed [11]



(17)

that the oximes and phenylhydrazones of 3-aroylquinoxaline-2-carboxamides cyclised readily to isoxazolo-[4,5-*b*]quinoxalines (18) and pyrazolo[3,4-*b*]quinoxalines, respectively, nucleophilic attack by the appropriate oxygen or nitrogen atom being followed by elimination of the carbamoyl group as indicated.



(18)

The cyclobutapyridines (6)—(8) and (16) have similar n.m.r. spectra (Table 1), and the 60 MHz spectra of compounds (6) and (7) have been accurately computer-simulated. Spin-tickling and -decoupling experiments carried out at 100 MHz for compound (16) confirmed the nature of the five-proton system 2-H, 4-H$_A$, 4-H$_B$, 4a-H, and 6a-H. Irradiation at τ 6·35 (4a-H) collapsed the multiplets due to 4-H$_A$ and 4-H$_B$ to doublets, of which that due to 4-H$_A$ is slightly broadened because of additional coupling with the 2-proton. This 2-H signal appeared as a clear doublet when the 6a-proton was irradiated, and as an apparent singlet when 4-H$_A$ was decoupled. Although the doublet assigned to 6a-H is partially obscured in the 60 and 100 MHz spectra by one peak of the quartet caused by the two non-equivalent benzylic protons, good separation was obtained at 220 MHz (Table 1). The different magnitudes of the coupling constants of 4a-H with 4-H$_A$ and with 4-H$_B$ (8·0 and 1·9 Hz, respectively) can be attributed to the quasi-diaxial relationship of 4-H$_A$ and 4a-H in contrast to the quasi-equatorial–axial orientation of 4-H$_B$ and 4a-H, and these can be predicted from the Karplus equation.

The vicinal coupling constants between 4a-H and 6a-H in the four cyclobutene adducts range between 4·4 and 5·0 Hz, in agreement with the values (1·6—4·9 Hz) quoted by Jackman,[12] and our high values confirm the *cis*-orientation of the two protons. The shifts to higher field of signals for the four protons 4-H$_A$, 4-H$_B$, 4a-H, and 6a-H, compared with their resonance positions in the original dihydropyridines, indicate the presence of an additional ring and the available data exclude alternative structures.

The n.m.r. spectra of the cyclobutenes (6), (7), and (16) in trifluoroacetic acid showed similar downfield shifts of the signals due to the 2- (Δτ 1·7—2·8) and 6a- and benzylic protons (Δτ *ca.* 1·0), consistent with protonation at position 3. In the case of compound (6), the presence of twice the number of peaks for the multiplets assigned to 4-H$_A$ and 4-H$_B$, as compared with compounds (7) and (16), seemed to indicate that the proton has added to give the two possible geometric isomers in similar proportions. Also, for compound (16), acidification of a methanolic solution gave a decreased $\lambda_{max.}$ in the u.v. spectrum (Table 2), but in contrast, this procedure does not appear to protonate the nitrile (7) as its u.v. spectrum is unchanged. Conjugation in the amide (6) seems to increase on acidification, and the proton under these conditions could add at the carbonyl oxygen atom to give a resonance-stabilised cation.

The cyclobutenes (6) and (7) readily added 1 mol of hydrogen, over palladised charcoal, to give the crystalline cyclobutanes (19) and (20), the u.v. spectra of which were virtually identical, except in extinction coefficients, with those of the original cyclobutenes (Table 2).

[10] J. E. Dolfini, *J. Org. Chem.*, 1965, **30**, 1298.
[11] H. Dahn and J. P. Fumeau, *Bull. Soc. vaudoise Sci. Nat.*, 1970, **70**, 313; H. Dahn and J. Nussbaum, *Helv. Chim. Acta*, 1969, **52**, 1661; H. Dahn and H. Moll, *ibid.*, 1966, **49**, 2426.
[12] L. M. Jackman and S. Sternhell, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 1969, p. 287.

TABLE 1

60 MHz N.m.r. spectra (τ values; J in Hz) for solutions in deuteriochloroform, with internal tetramethylsilane as reference

Compound	Proton assignments	Ester methyls
(1) [a]	2·6—3·0 (m, Ar-H_5, 2-H), 6·92 (m,[b] 4-H_2), 5·22 (dt, $J_{4,5}$ 3·3, $J_{5,6}$ 8·0, 5-H), 4·33 (m,[c,d] 6-H), 5·75 (s, 1-PhCH_2).	
(3) [e]	2·6—2·9 (m, Ar-H_{10}), 3·58 (d, J 1·6, 2-H), 7·28 (q, $J_{4,5}$ 3·4, J 1·3, 4-H_2), 5·53 (dt, $J_{5,6}$ 7·9, 5-H), 4·45 (m,[c,d] 6-H), 6·22 (q, J 7·0, CH_3·CH_2), 8·89 (t, CH_3·CH_2), 5·97 (s, 1-PhCH_2).	
(4)	2·6—2·8 (m, Ar-H_5), 3·55 (d, J 1·4, 2-H), 6·95 (m,[f] 4-H_2), 5·43 (dt, $J_{4,5}$ 3·3, $J_{5,6}$ 8·0, 5-H), 4·38 (m,[d,g] 6-H), 5·84 (s, 1-PhCH_2).	
(5)	3·65 (d, J 1·3, 2-H), 6·98 (m,[h] 4-H_2), 5·45 (dt, $J_{4,5}$ 3·3, $J_{5,6}$ 8·0, 5-H), 4·45 (m,[d,g] 6-H), 7·14 (s, 1-Me).	
(6)	2·6—3·1 (m, Ar-H_{10}), 3·52 (q, $J_{2,4_A}$ 2·0, $J_{2,6a}$ 1·0, 2-H), 8·05 (m,[j] $J_{4_A,4_B}$ 16·0, $J_{4_A,4a}$ 6·6, 4-H_A), 7·58 (q, $J_{4_B,4a}$ 2·0, 4-H_B), 6·58 (m,[j] $J_{4a,6a}$ 4·8, 4a-H), 6·06 (q, 6a-H), CH_3·CH_2,[k] 8·91 (t, J 6·9, CH_3·CH_2—), 5·59 (d) and 6·08 (d) (J 15·3, 1-PhCH_2).	6·26 (3H), 6·31 (3H)
(6)	2·4—2·9 (m, Ar-H_{10}), 1·07 (s, 2-H), 7·78—8·31 (m,[m] 4-H_A), 7·31 (m,[n] $J_{4_A,4_B}$ 14·8, 4-H_B), 4a-H,[k] 4·86 (d, $J_{4a,6a}$ 4·0, 6a-H), CH_3·CH_2,[k] 8·83 (t, J 7·0, CH_3·CH_2), 4·35 (d) and 4·70 (d) (J 14·7, 1-PhCH_2).	6·08 (3H), 6·12 (3H)
(7) [i,o]	2·72 (s, Ar-H_5), 3·21br (s, 2-H), 7·60 (m, $J_{4_A,4_B}$ 16·0, $J_{4_A,4a}$ 8·0, 4-H_A), 7·50 (m, $J_{4_B,4a}$ 1·9, 4-H_B), 6·46 (m, 4a-H), 5·86 (q, $J_{4a,6a}$ 4·4, $J_{2,6a}$ 0·9, 6a-H), 5·37 (d) and 5·78 (d) (J 14·9, 1-PhCH_2).	6·23 (6H)
(7)	2·4—2·7 (m, Ar-H_5), 1·51br (s, 2-H), 7·63 (q, $J_{4_A,4_B}$ 14·5, $J_{4_A,4a}$ 6·0, 4-H_A), 7·02 (d, 4-H_B), 4a-H,[k] 4·84 (d, $J_{4a,6a}$ 4·4, 6a-H), 4·48 (d) and 4·97 (d) (J 16·0, 1-PhCH_2).	6·02 (6H)
(8)	3·33br (s, 2-H), 7·50—7·72 (m, 4-H_2), 4a-H,[k] 5·88 (d, $J_{4a,6a}$ 4·8, 6a-H), 7·02 (s, 1-Me).	6·23 (6H)
(10) [p]	2·72 (s, Ar-H_5), 2·66 (d, J 1·3, 2-H), 5·51 (d, $J_{4,5}$ 4·7, 4-H), 5·28 (q, $J_{5,6}$ 7·3, 5-H), 3·71 (d, 6-H), 3·12br (s, NH_2), 5·59 (s, 1-PhCH_2).	
(11)	2·5—3·0 (m, Ar-H_5), 3·29 (d, J 1·2, 2-H), 5·62 (d,[q] 4-H), 5·27 (q, $J_{4,5}$ 4·1, $J_{5,6}$ 7·8, 5-H), 4·02 (d,[d] 6-H), 5·68 (s, 1-PhCH_2).	
(12) [e]	2·6—3·0 (m, Ar-H_5, 2-H), 4-H,[q] 5·08 (q, $J_{4,5}$ 4·7, $J_{5,6}$ 7·8, 5-H), 3·96 (d,[d] 6-H), 5·51 (s, 1-PhCH_2) 7·85 (s, Ac).	
(13)	2·6—2·8 (m, Ar-H_5), 2·93 (d, J 1·3, 2-H), 6·91 (m,[f] 4-H_2), 5·33 (dt, $J_{4,5}$ 3·3, $J_{5,6}$ 8·0, 5-H), 4·34 (m,[r] 6-H), 4·08br (s, NH_2), 5·78 (s, 1-PhCH_2).	
(14) [e]	2·4—2·8 (m, Ar-H_{10}), 2·87 (s, 2-H), 6·8—7·3 (m, 4-H_2, 2 × CH_2), 5·27 (dt, $J_{4,5}$ 3·2, $J_{5,6}$ 8·0, 5-H), 4·31 (m, 6-H), 5·67 (s, 1-PhCH_2).	
(16)	2·72 (s, Ar-H_5), 3·58br (s, 2-H), 7·82 (m, $J_{2,4_A}$ 1·9, $J_{4_A,4_B}$ 16·0, $J_{4_A,4a}$ 8·0, 4-H_A), 7·37 (q, $J_{4_B,4a}$ 1·9, 4-H_B), 6·35[t] (m, 4a-H), 5·84 (d, $J_{4a,6a}$ 5·0, 6a-H), 4·70 (s, vinyl H), 5·31 (d) and 5·75 (d) (J 15·0, 1-PhCH_2).	6·24 (9H), 6·43 (3H)

TABLE 1 (*Continued*)

Compound	Proton assignments	Ester methyls
(16) [i]	2·50 (s, Ar-H_5), 0·81 (s, 2-H), 7·37 (q, $J_{4_A,4_B}$ 16·0, $J_{4_A,4a}$ 6·5, 4-H_A), 6·46 (d, 4-H_B), 4a-H [k], 4·76 (d, $J_{4a,6a}$ 4·7, 6a-H), 4·41 (s, vinyl H), 4·28 (d) and 4·65 (d) (J 15·0, 1-PhCH_2).	6·01 (3H), 6·08 (3H), 6·20 (6H)
(19)	2·7—3·0 (m, Ar-H_{10}), 3·02 (d, J 2·4, 2-H), 6·1—8·0, (m, 4-H_A, 4-H_B, 4a-H, 5-H, 6-H, 6a-H, CH_3·CH_2). 5·96 (s, 1-PhCH_2), 8·90 (t, J 7, CH_3·CH_2).	6·49 (3H), 6·53 (3H)
(20)	2·6—3·0 (m, Ar-H_5), 3·14 (d, J 1·7, 2-H), 6·0—8·0 (m, 4-H_A, 4-H_B, 4a-H, 5-H, 6-H, 6a-H), 5·79 (s, 1-PhCH_2).	6·38 (6H)
(21)	2·6—3·6 (m, Ar-H_9), 3·80 (q, $J_{2,3}$ 7·7, $J_{2,4}$ 0·9, 2-H), 5·47 (q,[q] $J_{3,4}$ 4·0, 3-H), 5·12 (d, 4-H), 5·39 (s, 1-PhCH_2).	
(22)	2·5—3·3 (m, Ar-H_9), 3·37 (s, 2-H), 5·02 (s, 4-H), 4·32 (s, vinyl H), 5·19 (s, 1-PhCH_2).	6·20 (3H), 6·32 (3H)
(23)	2·6—3·2 (m, Ar-H_9), 4·92br (s, 1-H), 3·84 (q, $J_{1,3}$ 0·9, $J_{3,4}$ 7·6, 3-H), 4·39 (d, 4-H), 5·72 (s, 2-PhCH_2).	
(24)	2·3—2·8 (m, Ar-H_8), 6-H,[k] 2·17 (d, $J_{10,11}$ 6·0, 10-H), 5·35 (s, PhCH_2).	6·2—6·5 (12H)

[a] Measured down to τ 2. [b] Apparent quartet, ΣJ 5·1 Hz. [c] Apparent pair of doublets, J 1·6 Hz. [d] Further splitting. [e] At 100 MHz. [f] Apparent quartet, ΣJ 4·7 Hz. [g] Apparent pair of doublets, J 1·4 Hz. [h] ΣJ 4·7 Hz. [i] Resonance line positions for the five interacting protons of the four- and six-membered rings were accurately computer-simulated from the parameters given. [j] Four pairs of doublets. [k] Obscured by ester absorption. [l] In trifluoroacetic acid. [m] Apparent quartet. [n] Six lines observed. [o] The small couplings of 2-H were neglected in the computer simulation. [p] In Me_2SO. [q] Partially obscured by benzylic CH_2 absorption. [r] Partially obscured by amide NH_2 absorption. [s] Also at 100 and 220 MHz. [t] Predicted from decoupling experiments at 100 MHz.

TABLE 2

U.v. absorption spectra (methanol)

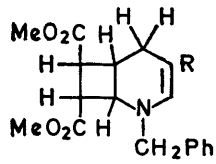
Compound	$\lambda_{max.}$/nm (10^{-4} ε)
(1)	352
(3)	360 (6·49)
(4)	338 (6·86)
(5)	340 (5·60)
(6)	311 (14·1)
(6) [a]	336 (18·9)
(7)	278 (17·9)
(7) [a]	278 (17·9)
(8)	277
(10)	336 (4·36)
(11)	329 (4·36)
(12)	349 (7·65)
(13)	356 (11·4)
(14)	349
(16)	231 (11·0), 360 (29·0)
(16) [a]	263 (17·3)
(19)	238 (15·2), 312 (23·4)
(19) [a]	338 (25·0)
(20)	276 (22·5)
(21)	300 (8·60)
(22)	255 (27·6), 377 (52·4)
(23)	337 (4·02)
(24)	353 (13·3)

[a] Solution acidified with 70% perchloric acid.

Dimethyl fumarate was readily split off in the mass spectrometer. The aliphatic regions of the n.m.r. spectra were very complex and consistent with the structures proposed.

1-Benzyl-1,4-dihydroquinoline-4-carbonitrile (21) did

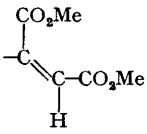
not react with the acetylenic ester to form a cyclobutene, but instead gave a quantitative yield of the 3-maleate



(19) R = CO·NPhEt
(20) R = CN

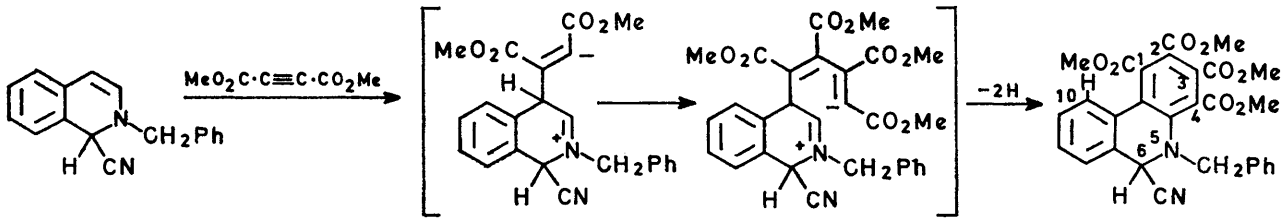
(22), formed by *proton abstraction* by the postulated zwitterionic intermediate. Comparison of the n.m.r. spectra of compounds (21) and (22) suggested that the

(21) R = H

(22) R = 

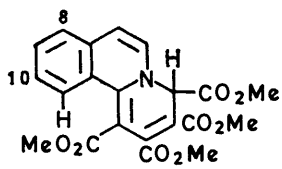
resonance at τ 4·32 was due to the vinyl proton, further comparisons with compounds (16) and (17) indicating that the ester groups are *cis*.

2-Benzyl-1,2-dihydroisoquinoline-1-carbonitrile (23) gave, in contrast, the phenanthridine (24) in 4% yield, formed presumably by *cyclisation* with 2 mol of the ester



(23) (24)

followed by oxidation as shown. It showed a low-field aromatic doublet similar to that (τ 1·94) due to the 11-H of the quinolizine (25),[13] and the downfield shift of the benzylic proton signal, compared with the starting material, can be attributed to the influence of the ester groups together with the additional aromatic ring formed. The relatively high frequency (2238 cm^{-1}) of



(25)

the cyanide stretching vibration indicates that this group remains attached to a saturated carbon atom; the frequency is higher than the usual value of *ca.* 2220 cm^{-1} observed for other compounds in this study bearing a nitrile group in a similar position.

EXPERIMENTAL

The instruments and general procedures have been described previously.[1] Petroleum had b.p. 40—60°, and acetonitrile was dried by refluxing over calcium hydride followed by distillation. I.r. spectra were obtained for Nujol mulls or liquid films. N.m.r. spectra at 60 MHz were measured with a Perkin-Elmer R12 instrument; the 100 MHz decoupled spectrum and also the 220 MHz spectrum were measured with Varian HA-100 and HA-220 spectrometers operating at 33°. Computer-simulated spectra were obtained with the seven-spin program prepared by Wilkins and Klopfenstein.[14] Columns were in all cases made up in ether; silica used was Kieselguhr PF_{254}. All analyses for new compounds were within accepted limits for C, H, and N.* Molecular ion and base peaks are quoted for the mass spectra, details of which can be obtained from the Mass Spectral Data Centre A.W.R.E., Aldermaston.

The Dihydropyridines (3)—(5) *and* (13).—Sodium dithionite (15·0 g, 0·085 mol) and anhydrous sodium carbonate (9·0 g, 0·085 mol) in water (150 ml) were added dropwise to stirred aqueous (75 ml) 1-benzyl-3-cyanopyridinium bromide [15] (13·3 g, 0·05 mol). After 2 h at room temperature, when the yellow mixture had become dark red and returned to yellow, the solid precipitate was collected, washed with water, and thoroughly dried *in vacuo*; further solid separated after 2 days at 0°. The solid was dissolved in the minimum of dry ether at room temperature; addition of petroleum and cooling to 0° precipitated 1-*benzyl*-1,4-*dihydropyridine*-3-*carbonitrile* (4) (4·0 g, 44%), pale yellow needles, m.p. 53—54°, unstable in air, $\nu_{max.}$ 2186, 1679, 1640, and 1600 cm^{-1}.

3-Cyano-1-methylpyridinium iodide similarly gave the dihydropyridine (5) (44%), m.p. 31° (lit.,[16] 29—30°). The dihydropyridine (13) was obtained in 58% yield (also obtained as reported [6,17]), and compound (3) in 32% yield, m.p. 80—83° (lit.,[18] 82—85·5°).

1-*Benzyl*-3-(N-*phenethylcarbamoyl*)*pyridinium Salts*.—*N*-Phenethylnicotinamide [19] (4·6 g) and benzyl chloride (2·6 g) in ethyl acetate (20 ml) were refluxed for 10 h. The

* Details are given in Supplementary Publication No. SUP 20545 (7 pp., 1 microfiche) [see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20].

[13] R. M. Acheson, J. M. F. Gagan, and D. R. Harrison, *J. Chem. Soc.*, 1968, 362.
[14] C. L. Wilkins and C. E. Klopfenstein, *J. Chem. Educ.*, 1966, **43**, 10.
[15] G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonner, and F. E. Ziegler, *J. Amer. Chem. Soc.*, 1966, **88**, 3099.
[16] K. Schenker and J. Druey, *Helv. Chim. Acta*, 1959, **42**, 1960.
[17] D. Mauzerall and F. H. Westheimer, *J. Amer. Chem. Soc.*, 1957, **79**, 712.
[18] A. G. Anderson, jun., and G. Berkelhammer, *J. Amer. Chem. Soc.*, 1958, **80**, 992.
[19] W. D. Crow and J. H. Hodgkin, *Austral. J. Chem.*, 1964, **17**(1), 119.

pyridinium chloride separated out as a pale brown oil (6·1 g, 85%); the *picrate* crystallised as golden yellow plates (from 1 : 1 water–ethanol), m.p. 123—125°.

1-*Benzyl*-1,4-*dihydro*-N-*phenethylpyridine*-3-*carboxamide* (14).—The foregoing pyridinium chloride in water (100 ml) was treated with a 0·03M solution of sodium dithionite and sodium carbonate as in the preparation of compound (4). The red oil (14) (3·0 g) obtained after extraction with chloroform (3 × 30 ml), removal of solvent, and drying *in vacuo* could not be crystallised; $\nu_{max.}$ 3400—3240, 1640, 1589, and 1540 cm^{-1}.

1-*Benzyl*-1,4-*dihydronicotinic Acid* (1).—Solid sodium dithionite (17·4 g, 0·1 mol) was slowly added to a stirred solution of 1-benzyl-3-methoxycarbonylpyridinium bromide [15] (9·2 g, 0·03 mol) and anhydrous sodium carbonate (10·6 g, 0·1 mol) in water (200 ml), and the mixture was left at room temperature for 1 h. The solution went directly from brown-yellow to cloudy yellow, and a precipitate started to form. The solid was filtered off, washed with water, dried *in vacuo* for 5 h, and recrystallised from acetonitrile to give 1-*benzyl*-1,4-*dihydronicotinic acid* (1) (2·3 g, 34%), as pale yellow needles, m.p. 95—97° (decomp.), $\nu_{max.}$ 3460—3400, 1678, 1650, 1598, and 1572 cm^{-1}.

The Cyclobuta[b]*pyridines* (6)—(8).—*General method.* The dihydropyridine (0·05 mol) in acetonitrile (50 ml) was treated with dimethyl acetylenedicarboxylate (0·07 mol) and the mixture was left for 1 week at room temperature. The solvent was removed *in vacuo* and the residual oil dissolved in benzene was chromatographed on an alumina column (*ca.* 100 ml). Elution of orange bands with ether yielded the products.

The dihydropyridine (3) gave *dimethyl* 1-*benzyl*-3-(N-*ethyl*-N-*phenylcarbamoyl*)-1,4,4a,6a-*tetrahydrocyclobuta*[b]-*pyridine*-5,6-*dicarboxylate* (6) (32%), orange prisms (from methanol), m.p. 120—122°, $\nu_{max.}$ 1740, 1720, 1650, 1629, 1593, 1582, and 1556 cm^{-1}, *m/e* 460 (M^+, 10%) and 340 (100).

1-Benzyl-1,4-dihydropyridine-3-carbonitrile (4) gave *dimethyl* 1-*benzyl*-3-*cyano*-1,4,4a,6a-*tetrahydrocyclobuta*[b]-*pyridine*-5,6-*dicarboxylate* (7) (52%), golden-yellow plates (from methanol), m.p. 140—141°, $\nu_{max.}$ 2180, 1731, 1718, 1655, and 1623 cm^{-1}, *m/e* 338 (M^+, 100%).

1,4-Dihydro-1-methylpyridine-3-carbonitrile (5) gave dimethyl 3-cyano-1,4,4a,6a-tetrahydro-1-methylcyclobuta-[*b*]pyridine-5,6-dicarboxylate (8) as a red oil which could not be induced to crystallise, $\nu_{max.}$ (film) 2186, 1720, and 1620 cm^{-1}.

1-Benzyl-1,4-dihydronicotinamide (13) after 2 weeks and with 300 ml of alumina, gave *dimethyl* 1-*benzyl*-3-(cis-1,2-*dimethoxycarbonylvinyl*)-1,4,4a,6a-*tetrahydrocyclobuta*[b]-*pyridine*-5,6-*dicarboxylate* (16) (14%), yellow needles (from methanol), m.p. 175—178°, $\nu_{max.}$ 1725, 1693, 1658, 1613, and 1545 cm^{-1}, *m/e* 455 (M^+, 100%).

1-Benzyl-1,4-dihydro-*N*-phenethylpyridine-3-carboxamide (14), treated like compound (13), gave compound (16) (4%).

1-Benzyl-1,4-dihydronicotinic acid (1), treated similarly but chromatographed on silica, gave compound (16) (0·5%).

The only crystalline products isolable when compounds (10), (11), and (12) were each treated like compound (3) were traces of (11) and (12).

[20] F. Kröhnke, H. Dickhäuser, and I. Vogt, *Annalen*, 1961, **644**, 93.

Hydrogenation of the Cyclobuta[b]*pyridines* (6) *and* (7).—Compound (6) (0·46 g) in methanol (100 ml) was shaken with 5% palladium–charcoal (0·25 g) under hydrogen (5 atm) for 1 h. After filtration, evaporation of the solvent gave a yellow oil, which after trituration with ether gave *dimethyl* 1-*benzyl*-3-(N-*ethyl*-N-*phenylcarbamoyl*)-1,4,4a,5,6,6a-*hexahydrocyclobuta*[b]*pyridine*-5,6-*dicarboxylate* (19) (0·27 g), white microcrystals [from methanol–ether (1 : 2)], m.p. 137—139°, $\nu_{max.}$ 1732, 1711, 1630, 1595, 1582, and 1555 cm^{-1}, *m/e* 462 (M^+, 10%) and 342 (100).

Compound (7) (0·34 g) similarly gave *dimethyl* 1-*benzyl*-3-*cyano*-1,4,4a,5,6,6a-*hexahydrocyclobuta*[b]*pyridine*-5, 6-*dicarboxylate* (20) (0·24 g), prisms (from acetone), m.p. 129—131°, $\nu_{max.}$ 2185, 1742, 1721, and 1630 cm^{-1}, *m/e* 340 (M^+, 13%) and 196 (100).

The 4-*Cyano*-1,4-*dihydro-pyridines and -quinolines, and the Isoquinoline* (23).—Potassium cyanide (1·5 g, 0·02 mol) in water (20 ml) was added dropwise to a stirred solution of 1-benzylquinolinium bromide [20] (5·0 g, 0·02 mol) in water (100 ml); after 20 min, the oil obtained was collected with methylene chloride (2 × 30 ml) and dried. It crystallised from ether to give 1-*benzyl*-1,4-*dihydroquinoline*-4-*carbonitrile* (21) (3·0 g, 73%), pale green prisms, m.p. 89—91°, $\nu_{max.}$ 2221, 1668, 1600, and 1571 cm^{-1}.

2-*Benzyl*-1,2-*dihydroisoquinoline*-1-*carbonitrile* (23) (82%) was similarly obtained from 2-benzylisoquinolinium bromide [21] as pale yellow needles [from ether–petroleum (1 : 1)], m.p. 83—84°, $\nu_{max.}$ 2220, 1620, 1600, and 1569 cm^{-1}.

1-*Benzyl*-1,4-*dihydropyridine*-3,4-*dicarbo-nitrile* (11) was obtained from 1-benzyl-3-cyanopyridinium bromide [15] as pale yellow prisms (83%) (from sodium-dried ether), m.p. 70—72°, $\nu_{max.}$ 2192, 1681, and 1590 cm^{-1}.

1-*Benzyl*-4-*cyano*-1,4-*dihydronicotinamide* (10), prepared similarly, was filtered from the reaction mixture as white prisms (96%), m.p. 128—130°, $\nu_{max.}$ 3445, 3170, 2220, 1679, 1640, and 1599 cm^{-1}.

3-*Acetyl*-1-*benzyl*-1,4-*dihydropyridine*-4-*carbonitrile* (12), from 3-acetyl-1-benzylpyridinium chloride,[18] precipitated from the reaction mixture and crystallised as pale yellow prisms (92%) from sodium-dried ether, m.p. 108—111° (decomp.), $\nu_{max.}$ 2220, 1680, 1626, and 1570 cm^{-1}.

1-*Benzyl*-3-(cis-1,2-*dimethoxycarbonylvinyl*)-1,4-*dihydroquinoline*-4-*carbonitrile* (22).—The dihydroquinoline (21) (1·5 g) in acetonitrile (30 ml) and dimethyl acetylenedicarboxylate (1·15 g) were left at room temperature for 12 h. Evaporation of the solvent gave the *adduct* (22) (1·4 g, 90%), powdery yellow microcrystals (from methanol), m.p. 173—175°, $\nu_{max.}$ 2222, 1736, 1700, 1630, and 1560 cm^{-1}, *m/e* 388 (M^+, 33%) and 329 (100).

Tetramethyl 5-*Benzyl*-6-*cyano*-5,6-*dihydrophenanthridine*-1,2,3,4-*tetracarboxylate* (24).—The isoquinoline (23) (3·0 g) and dimethyl acetylenedicarboxylate (3·0 g) were left at room temperature for 4 days; the solvent was removed and the residue was chromatographed with chloroform–petroleum (5 : 3) as eluant. The *adduct* (24) (0·2 g, 4%), yellow prisms (from methanol), had m.p. 189—192°, $\nu_{max.}$ 2238, 1750, 1715infl, 1695, 1685infl, 1620, 1600, and 1568 cm^{-1}, *m/e* 528 (M^+, 90%) and 431 (100).

[2/1191 *Received*, 25*th May*, 1972]

[21] J. E. Baldwin and J. A. Duncan, *J. Org. Chem.*, 1971, **26**, 627.