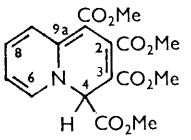
## 173. *Addition Reactions of Heterocyclic Compounds. Part XXI.* The Nuclear Magnetic Resonance Spectra of Some Quinolizines and their Salts, and New Adducts from Alkylpyridines.*

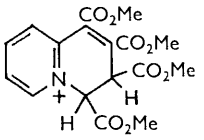
By R. M. Acheson, R. S. Feinberg, and J. M. F. Gagan.

The nuclear magnetic resonance spectra of some tetramethyl 4*H*-quinolizine-1,2,3,4-tetracarboxylates have been measured in deuterochloroform and trifluoroacetic acid and the positions of protonation ascertained. New adducts have been obtained from 2-methyl-, 2-ethyl-, 2-ethyl-6-methyl-, and 2,6-dimethyl-pyridine with dimethyl acetylenedicarboxylate.

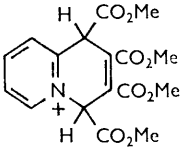
The nuclear magnetic resonance (n.m.r.) spectra of some of the quinolizines in the Tables have been reported [1-3] in sufficient detail to establish that the lone proton is at position 4 or 9a only. In the case of the 4*H*-quinolizines (I) and (IV)—(VII) in deuterochloroform the aliphatic proton appears as a sharp singlet at about 3·95 τ whereas in the 6-methyl and 6-ethyl derivatives (II) and (III) it is at lower field, possibly because the alkyl group alters the stereochemistry of the 4*H*-atom. The assignments for the aromatic protons in the 8-methyl derivative (V) are unambiguous without reference to the other 4*H*-quinolizines, for which allocations have been made after considering the effect of the methyl groups at the various positions. The only possible ambiguity is with the 9-methyl derivative (VI). The triplet must be due to the hydrogen atom at position 7, and the 6- and 8-hydrogen atoms have been assigned by analogy with the positions of those of the 7-methyl derivative (IV), where there is no uncertainty.



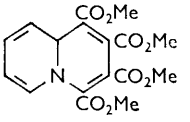
(I)
(II) 6-Me
(III) 6-Et
(IV) 7-Me
(V) 8-Me
(VI) 9-Me
(VII) 7,9-diMe



(VIII)
(IX) 6-Me
(X) 7-Me
(XI) 8-Me



(XII) 9-Me
(XIII) 7,9-diMe



(XIV) 6-Me
(XV) 6-Et
(XVI) 9-Me
(XVII) 7,9-diMe
(XVIII) 9a-Me
(XIX) 9a-Et
(XX) 6,9a-diMe
(XXI) 9a-Et-6-Me

The 4*H*-quinolizines (I)—(VII) are vinylogous pyridones [4] and a comparison of the resonance positions of the aromatic hydrogen atoms with those of 1-methylpyridone where the 3-, 4-, 5-, and 6-protons appear at 3·43, 2·74, 3·85, and 2·69 τ, respectively [5] shows slightly greater deshielding in the quinolizines at positions 6 and 8, more at position 7, and very much more at position 9. This suggests that the quinolizines possess a greater ring current than the pyridone and the appearance of the 9-proton at such a low field position must be due to the effect of the 1-ester group.[6]

It was concluded [1] from ultraviolet spectrum studies that tetramethyl 4*H*-quinolizine-1,2,3,4-tetracarboxylates [*e.g.*, (I)] protonate at position 3 yielding cations such as (VIII),

* Part XX, *J.*, 1964, 3229.

[1] Acheson, Taylor, Richards, and Higham, *J.*, 1960, 1691.
[2] Jackman, Johnson, and Tebby, *J.*, 1960, 1579.
[3] Acheson, Hands, and Woolven, *J.*, 1963, 2082.
[4] Acheson, *Adv. Heterocyclic Chem.*, 1963, **1**, 149.
[5] Elvidge and Jackman, *J.*, 1961, 859.
[6] Cf. Jackman, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," Pergamon, London, 1959, pp. 123—124.

TABLE 1.

Proton resonances ($\tau$ values) and coupling constants of quinolizines (in deuterochloroform).

| Compound | 4-H | 6-H | 7-H | 8-H | 9-H | 9a-H | *ester*-Me |
|---|---|---|---|---|---|---|---|
| | | | Assignments | | | | |
| (I) [a] | 3·94 | 2·3—2·6(m) | 3·15(t) [b]<br>$J_{6,7} + J_{7,8} = 14$ | 2·3—2·6(m) | 1·32q<br>$J_{8,9} + J_{7,9} = 11$ | | 6·07, 6·20, 6·24, 6·28 |
| (II) | 3·44 | 7·42(Me) | 3·22(d) [b] | 2·56(q)<br>$J_{7,8} + J_{8,9} = 16$ | 1·42(d) [b]<br>$J_{8,9} = 9$ | | 6·08, 6·20, 6·27, 6·31 |
| (III) | 3·46 | 7·12(q)($CH_2$)<br>8·69(t)(Me), $J = 8$ | 3·20(q)<br>$J_{7,8} + J_{7,9} = 9$ | 2·54(q)<br>$J_{7,8} + J_{8,9} = 17$ | 1·45(q)<br>$J_{8,9} + J_{7,9} = 10$ | | 6·08, 6·21, 6·27, 6·33 |
| (IV) [a] | 3·98 | 2·62(d)<br>$J_{6,8} = 1$ | 7·71(Me) | 2·52(q)<br>$J_{8,9} + J_{6,8} = 10$ | 1·38(d)<br>$J_{8,9} = 9$ | | 6·05, 6·18, 6·23, 6·26 |
| (V) [c] | 3·99 | 2·53(d)<br>$J_{6,7} = 7$ | 3·28(d) [b]<br>$J_{6,7} = 7$ | 7·61(Me) | 1·47 [b] | | 6·10, 6·23, 6·28, 6·31 |
| (VI) [a] | 3·89 | 2·48(q)<br>$J_{6,7} + J_{6,8} = 8$ | 3·07(t)<br>$J_{6,7} + J_{7,8} = 14$ | 2·33(q)<br>$J_{7,8} + J_{6,8} = 8$ | 7·72(Me) | | 6·06, 6·24, 6·27, 6·31 |
| (VII) [a] | 3·92 | 2·60 [b] | 7·73(Me) | 2·47 [b] | 7·73(Me) | | 6·06, 6·26, 6·30, 6·30 |
| (XIV) | | 8·04(Me) | 3·9—4·2(m) | (2 protons) | 4·35(d) [b]<br>$J_{8,9} = 9$ | 5·03(t)<br>$J + J = 4$ | 6·12, 6·16, 6·24, 6·33 |
| (XV) | | 7·76(q)($CH_2$)<br>8·86(t)(Me), $J = 8$ | 3·85—4·1(m) | (2 protons) | 4·38(d) [b]<br>$J_{8,9} = 9$ | 5·05(t)<br>$J + J = 4$ | 6·13, 6·18, 6·24, 6·34 |
| (XVI) [a] | | 3·78(d) [b]<br>$J_{6,7} \sim 7$ | 4·05—4·22(m) | (2 protons) | 8·19(Me) | 5·01(d)<br>$J = 1$ | 6·09, 6·09, 6·24, 6·29 |
| (XVII) [a] | | 3·93 | 8·17(Me) or<br>8·19(Me) | 4·22(d)<br>$J_{8,9a} \sim 2$ | 8·17(Me) or<br>8·19(Me) | 4·92(d)<br>$J_{8,9a} \sim 2$ | 6·11, 6·11, 6·25, 6·31 |
| (XVIII) | | 3·63(d) [b] | 4·43(t) [b]<br>$J_{6,7} + J_{7,8} = 14$ | 3·80(q) [d]<br>$J_{7,8} + J_{8,9} = 16$ | 4·14(d) [b]<br>$J_{8,9} = 9$ | 8·78(Me) | 6·02, 6·19, 6·19, 6·28 |
| (XIX) | | 3·62(d) [b]<br>$J_{6,7} = 7$ | 4·60(t) [b]<br>$J_{6,7} + J_{7,8} = 13$ | 3·81(q) [d]<br>$J_{7,8} + J_{8,9} = 16$ | 4·25(d)<br>$J_{8,9} = 10$ | 7·9—8·9(m)($CH_2$)<br>9·13(Me)(t), $J_{Me_2CH,} = 8$ | 6·03, 6·22, 6·24, 6·28 |
| (XX) | | 8·10(Me) | 4·92(d) [b]<br>$J_{7,8} = 7·5$ | 3·98(q)<br>$J_{7,8} + J_{8,9} \sim 16$ | 4·22(d) [b]<br>$J_{8,9} = 9$ | 8·69(Me) | 6·12, 6·18, 6·21, 6·28 |
| (XXI) | | 8·08(Me) | 4·98(d)<br>$J_{7,8} = 6$ | 3·88(q)<br>$J_{7,8} + J_{8,9} = 16$ | 4·38(d)<br>$J_{8,9} = 10$ | 7·9—8·9(m)($CH_2$)<br>9·07(t)Me<br>$J_{Me,CH,} = 7$ | 6·13, 6·16, 6·22, 6·24 |
| (XXII) | | 3·89 | 8·27(Me) | 7·5—8·4(m) | (3 protons)<br>8·86(d)(Me)<br>$J_{9H,9Me} = 7$ | 5·18 | 6·06, 6·12, 6·26, 6·33 |
| (XXIII) [e] | 3·99 | 2·25(d) [b]<br>$J_{6,7} = 7$ | 37·4(t) [b]<br>$J_{6,7} + J_{7,8} = 14$ | 3·12(t) [b]<br>$J_{7,8} + J_{8,9} = 16$ | 2·78(d) [b]<br>$J_{8,9} = 9$ | | 6·01, 6·20, 6·32 |

d, doublet; t, triplet; q, quartet; m, multiplet.

[a] For preparation see ref. 1. [b] With some further splitting. [c] For preparation see ref. 2. [d] Only part of multiplet clearly observable.
[e] Me at position 1 appears at $\tau$ 7·81.

except when a 9-methyl group is present, *e.g.*, (VI) and (VII), when the cations (XII) and (XIII) are formed. The n.m.r. spectra of the 4*H*-quinolizines in trifluoroacetic acid (Table 2) are consistent with a similar protonation occurring under these conditions. The aromatic-hydrogen atom assignments have been made as before and it is clear that the proton must have added to the ester-containing ring. The resonance positions of the aromatic 7- and 9-hydrogen atoms in appropriate cations are now very similar so that the effect of the 1-ester group on the 9-hydrogen atom must have vanished. This could be due either to protonation giving cations of type (XII) or to the alteration of the stereochemistry associated with the formation of the isomeric cations (VIII)—(XI).

TABLE 2.

Proton resonances ($\tau$ values) and coupling constants of quinolizines (in trifluoroacetic acid).

| | Assignments | | | | | | |
|---|---|---|---|---|---|---|---|
| Compound | H-3 | H-4 | H-6 | H-7 | H-8 | H-9 | *ester*-Me |
| (VIII) | 4·72 | 3·54 | 0·89(d) [a] | 1·68(t) [a,b] | 1·14(t) [a] | 1·62(d) [a] | 5·80, 5·86, |
| | | | $J_{6,7} = 6$ | | $J_{7,8} + J_{8,9} = 16$ | $J_{8,9} = 8$ | 6·01, 6·12 |
| (IX) | 4·67 | 3·31 | 6·86(Me) | 1·86(d) [c] | 1·35(t) | 1·86(d) [c] | 5·82, 5·86, |
| | | | | $J_{6,7} = 8$ | $J_{6,7} + J_{7,8} = 16$ | $J_{7,8} = 8$ | 6·01, 6·13 |
| (X) | 4·80 | 3·67 | 1·13 [a] | 7·29(Me) | 1·40(d) [a] | 1·87(d) | 5·85, 5·91, |
| | | | | | $J_{8,9} = 8$ | $J_{8,9} = 8$ | 6·05, 6·16 |
| (XI) | 4·79 | 3·66 | 1·14(d) | 1·93(d) [b] | 7·17(Me) | 1·87 | 5·85, 5·90, |
| | | | $J_{6,7} = 7$ | | | | 6·05, 6·15 |
| (XII) | 4·28 [d] | 3·11 | 1·09(d) [a] | 1·85(t) [a] | 1·34(d) [a] | 7·16(Me) | 5·88, 5·88, |
| | | | $J_{6,7} = 7$ | $J + J = 15$ | $J_{7,8} = 8$ | | 6·02, 6·08 |
| (XIII) | 4·34 [d] | 3·22 | 1·32 [a] | 7·22(Me) or | 1·55 [a] | 7·22(Me) or | 5·89, 5·89, |
| | | | | 7·33(Me) | | 7·33(Me) | 6·02, 6·09 |

d, doublet; t, triplet; q, quartet.

[a] With some further splitting. [b] Only part of multiplet clearly observable. [c] Two superimposed doublets. [d] These protons are at position 1.

Excluding the 9-methyl compounds (VI) and (VII), the downfield shifts of the 4-, 6-, 7-, and 8-hydrogen atoms caused by protonation are about 0·3, 1·4, 1·44, and 1·1 p.p.m., respectively, and it is notable that the 9-hydrogen atom shifts upfield by about 0·4 p.p.m. With the 9-methyl compounds the situation is similar except that the 4-hydrogen atom shows a bigger downfield shift, about 0·75 p.p.m., when protonation takes place. This, considered with the other n.m.r. data, can only be accounted for on the assumption that the 9-methyl compounds (VI) and (VII) give the cations (XII) and (XIII) and that the others give the more conjugated type (VIII)—(XI) where the added proton is more shielded.

The added proton, which must exchange rapidly since it does not couple, must be responsible for the 4·80 $\tau$ peak in the spectrum of the cation from the 7-methyl compound (IV), as in deuterotrifluoroacetic acid this peak was absent; that at 3·67 $\tau$ had diminished somewhat, presumably due to some exchange, but otherwise the spectrum was identical to that in trifluoroacetic acid. In the case of the 9-methyl derivative, exchange in the cation (XII) was more rapid, as the two one-proton singlets present in trifluoroacetic acid were absent in the deuterated acid. The resonance positions of the aromatic hydrogen atoms of the cations of both types, *i.e.*, (VIII) and (XII), generally resemble those of comparable pyridinium salts.[5]

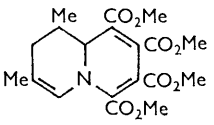
The n.m.r. spectra of the 9a*H*-quinolizines (XIV)—(XXI) (Table 1) show that the unsubstituted ring is aliphatic in character and that the bridgehead proton couples about equally with the 8 and 9 ring-hydrogen atoms.

The assignment of the 6- and 8-protons in the 7,9-dimethyl derivative (XVII) has been made on the assumption that the one nearest to the 9a-hydrogen atom is that which couples, and the lower-field proton is then the one nearer to the nitrogen atom. In the 9a-methyl (XVIII) and -ethyl (XIX) compounds the lower-field doublet has been assigned

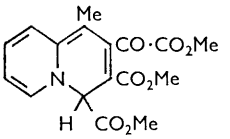
to the proton nearest the nitrogen atom and then the spectra of these compounds and their derivatives form a regular pattern. The n.m.r. spectrum of the dihydro-derivative [1] of the 7,9-dimethyl-9a*H*-quinolizine (XVII) shows that it must have structure (XXII).

We have now obtained tetramethyl 6-methyl-9a*H*-quinolizine-1,2,3,4-tetracarboxylate (XIV) as well as the 9a-methyl isomer [3] (XVIII) from 2-methylpyridine and dimethyl acetylenedicarboxylate. The structure of the first adduct was deduced from its n.m.r. spectrum, from the similarity of its ultraviolet and infrared spectra to those of analogous 9a*H*-quinolizines,[1,7] and from the fact that it isomerises even on standing for some days in chloroform solution to the 4*H*-quinolizine (II), which was the only product isolated by Jackman, Johnson, and Tebby [2] from the ester and 2-methylpyridine. Diels and Pistor,[8] who first examined this reaction, isolated the 9a-methyl-9a*H*-quinolizine (XVIII) and a red isomer which, although having the same melting point as that of our 6-methyl-9a*H*-quinolizine, had different chemical properties and may be analogous in structure to the product from quinaldine and the acetylenic ester, which possesses no *C*-methyl group [9] and which we are investigating.

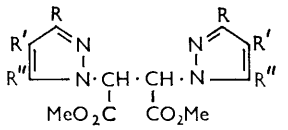
2-Ethylpyridine and the ester similarly gave a mixture of the 6- and 9a-ethyl-9a*H*-




(XXII)




(XXIII)




(XXIV) R = R′ = R″ = H
(XXV) R = R″ = Me
(XXVI) R = R′ = R″ = Me

quinolizines (XV) and (XIX), but a third product, tentatively formulated as compound (XXIII), was also isolated. Its ultraviolet spectrum was similar to that of Kashimoto's compound,[1] but after acidification resembled those [1] of the cations (VIII)—(XI).

2-Ethyl-6-methyl- and 2,6-dimethyl-pyridine and the ester gave the corresponding 6-methyl-9a-alkyl-9a*H*-quinolizines (XXI) and (XX). The ethyl derivative (XXI), and

TABLE 3.

Proton resonances ($\tau$ values) and coupling constants of pyrazoles (in deuterochloroform).

| Compound | Side-chain | H-3 | H-4 | H-5 | *ester*-Me |
|---|---|---|---|---|---|
| (XXIV) | 4·01 | 2·38(d) or 2·58(d) | 3·68(t) | 2·58(d) or 2·38(d) | 6·27 |
| | | $J_{3,4} = 2$ | $J_{3,4} + J_{4,5} = 4$ | $J_{4,5} = 2$ | |
| (XXV) | 4·08 | 7·56(Me) or 7·81(Me) | 4·17 | 7·81(Me) or 7·56(Me) | 6·24 |
| (XXVI) | 4·05 | 7·67(Me) or 7·81(Me) | 8·11(Me) | 7·81(Me) or 7·67(Me) | 6·44 |

d, doublet; t, triplet.

the 9a-ethyl-9a*H*-quinolizine (XIX), with hot dimethyl acetylenedicarboxylate gave tetramethyl 2-ethylpyridine-3,4,5,6-tetracarboxylate by an addition-elimination sequence described previously,[3] which confirms the structures proposed.

The n.m.r. spectra (Table 3) of the pyrazoles (XXIV)—(XXVI) confirm the structures proposed,[10] as the aliphatic protons appear at far too low a field for the isomeric dimethyl αα-di-1-pyrazolylsuccinate structures to pertain.

## EXPERIMENTAL

The n.m.r. spectra were measured at 34° and 60 Mc./sec. using a Perkin-Elmer spectrometer. The trifluoroacetic acid solutions were examined as soon as possible after preparation. The

[7] Acheson and Hole, *J.*, 1962, 748.
[8] Diels and Pistor, *Annalen*, 1937, **530**, 87.
[9] Crabtree, Jackman, and Johnson, *J.*, 1962, 4417.
[10] Acheson and Poulter, *J.*, 1960, 2138.

deuterotrifluoroacetic acid was obtained from deuterium oxide and trifluoroacetic anhydride. The ultraviolet spectra are for methanol solutions and are given in mμ, $10^{-4}\varepsilon$ being in parenthesis, and the infrared spectra are for Nujol mulls. Inflections are marked with an asterisk. Solvent (A) was methanol–72% perchloric acid (2 : 1, v/v).

*2-Methylpyridine and Dimethyl Acetylenedicarboxylate.*—2-Methylpyridine (10 g.), previously refluxed over calcium hydride for 2 hr. and redistilled, was added in small portions during 30 min. to the ester (28 g.) in sodium-dried ether (200 ml.) at 0° and the mixture left at 0° for 3 days. The ether was decanted from the viscous tar, which was washed with ether (30 ml.). As the combined ether solutions on standing in an open container slowly evaporated to *ca.* 50 ml. a crystalline precipitate (5·5 g.) formed and was combined with that (8·5 g.) obtained by triturating the tar with methanol (30 ml.). The solid was dissolved in the minimum amount of chloroform. The solution, diluted with an equal volume of benzene, was chromatographed on a deactivated alumina [10] (600 ml.) column (3·5 cm. diam.) prepared in benzene. Elution with benzene gave first some dimethyl fumarate, m. p. 104—105°, and then a yellow fraction which, after removal of solvent and trituration with methanol, gave tetramethyl 9a-methyl-9a*H*-quinolizine-1,2,3,4-tetracarboxylate (XVIII) (4·5 g.), m. p. 140° (from methanol) (lit.,[3] 139°). Further elution gave a mixture followed by a red band which on elution and treatment as before yielded *tetramethyl 6-methyl-*9aH-*quinolizine-1,2,3,4-tetracarboxylate* (XIV) (6 g.) which separated from methanol as orange needles, m. p. 126° (Found: C, 57·5; H, 5·1; N, 3·8; OMe, 32·7. $C_{17}H_{19}NO_8$ requires C, 57·3; H, 5·1; N, 3·8; 4 OMe, 32·9%), $\lambda_{max.}$ 236 (1·61), 294 (1·2), and 433 (0·52), $\nu_{max.}$ 5·75, 5·84, 5·86, 6·09, 6·19, 6·67, 6·88, and 6·98 μ.

Refluxing in benzene for 28 hr., shaking in acetic acid with Adams catalyst for 4 hr., or standing in chloroform for a few days gave the 4*H*-isomer (II), orange needles, m. p. 239° (from methanol) (lit.,[2] 238—239°), $\lambda_{max.}$ 266 (0·92), 307 (1·08), 349 (1·14), and 443 (1·05), and after acidification, 321 (1·12), showing that the cation (IX) was formed.[1]

*Hydrogenation of Tetramethyl 6-Methyl-*9aH-*quinolizine-1,2,3,4-tetracarboxylate* (XIV).—The quinolizine (0·5 g.) in methanol (100 ml.) was shaken overnight with 10% palladised charcoal (0·1 g.), the solution was filtered and evaporated, and recrystallisation of the residue from methanol gave a *dihydro-derivative* as ochre prisms, m. p. 127—128° (Found: C, 57·1; H, 5·6; OMe, 32·6. $C_{18}H_{21}NO_8$ requires C, 57·0; H, 5·6; OMe, 32·7%). $\lambda_{max.}$ (unchanged by acid) 236 (0·95), 278 (1·48), and 417 (0·69), $\nu_{max.}$ 5·73, 5·84, 5·91, 6·21, 6·65, 6·87, 6·96, and 7·01 μ.

*2-Ethylpyridine and Dimethyl Acetylenedicarboxylate.*—Freshly distilled 2-ethylpyridine (3·6 ml.) in methyl cyanide (10 ml.) was added slowly to the ester (9·5 ml.) in methyl cyanide (20 ml.) at 0° and the mixture kept at this temperature for 4 days. The solvent was removed *in vacuo* and the residue, in the minimum of chloroform, was diluted with an equal volume of benzene and chromatographed on alumina (500 ml.; 3·5 cm. diam. column) made up in benzene. Elution with benzene (500 ml.) gave the 4H-*quinolizine* (XXIII) (0·18 g.), lemon needles, m. p. 146° (from methanol) (Found: C, 59·1; H, 4·8; N, 4·1; OMe, 25·9. $C_{17}H_{17}NO_7$ requires C, 58·9; H, 4·9; N, 4·0; 3OMe, 25·6%), $\lambda_{max.}$ 266 (1·10), 278* (0·76), 339 (0·59), 440 (2·40), and (in solvent A) 267 (1·96), 306 (0·68), and 490 (0·29), $\nu_{max.}$ 5·71, 5·82, 5·94, 6·08,* 6·15, 6·39, 6·70,* 6·80, 6·90, and 7·00 μ.

Elution with benzene–chloroform (3 : 1) gave, in the first 300 ml., *tetramethyl* 9a-*ethyl*-9aH-*quinolizine-1,2,3,4-tetracarboxylate* (XIX) (0·44 g.), orange prisms, m. p. 116° (from methanol) (Found: C, 58·4; H, 5·5; N, 3·7; OMe, 31·5. $C_{19}H_{21}NO_8$ requires C, 58·3; H, 5·4; N, 3·6; 4OMe, 31·7%), $\lambda_{max.}$ 281 (1·16), 334 (0·45), and 418 (0·64), unchanged in solvent (A), $\nu_{max.}$ 5·76, 5·84, 6·02, 6·23, 6·53, 6·88,* and 6·97 μ.

Further elution (1·2 l.) gave *tetramethyl 6-ethyl-*9aH-*quinolizine-1,2,3,4-tetracarboxylate* (XV) (1·5 g.), deep yellow prisms, m. p. 125° (from methanol) (Found: C, 58·2; H, 5·6; N, 3·7; OMe, 31·5. $C_{19}H_{21}NO_8$ requires C, 58·3; H, 5·4; N, 3·6; 4OMe, 31·7%), $\lambda_{max.}$ 236 (1·56), 294 (0·91), and 430 (0·55), $\nu_{max.}$ 5·68,* 5·71, 5·80, 5·89, 6·11, 6·31w, 6·60, 6·96, and 7·04 μ.

*Tetramethyl 6-Ethyl-*4H-*quinolizine-1,2,3,4-tetracarboxylate* (III).—The 9a*H*-isomer (1·0 g.) was refluxed in methanol (50 ml.) and acetic acid (25 ml.) for 48 hr., the solvents were removed *in vacuo*, and the residue, on trituration with methanol, gave the 4H-*quinolizine*, square yellow plates (0·8 g.), m. p. 188° (from methanol) (Found: C, 58·1; H, 5·2; N, 3·6; OMe, 31·4. $C_{19}H_{21}NO_8$ requires C, 58·3; H, 5·4; N, 3·6; 4OMe, 31·7%), $\lambda_{max.}$ 266 (0·90), 307 (1·04), 350 (1·15), and 445 (1·15), and (in solvent A) 322 (1·23) and 329 * (1·11), $\nu_{max.}$ 5·74, 6·02, 6·16, 6·36, 6·50, 6·81, and 6·97 μ.

Isomerisation was not effected by refluxing for 11 hr. in benzene containing a trace of acetic

acid, but took place slowly in chloroform at room temperature, possibly because of hydrogen chloride impurity.

*Tetramethyl* 6,9a-*dimethyl*-9aH-*quinolizine*-1,2,3,4-*tetracarboxylate* (XX).—(*a*) Freshly distilled 2,6-dimethylpyridine (3·6 ml.; b. p. 142—143°) was refluxed with dimethyl acetylenedicarboxylate (9·5 ml.) in dry benzene (150 ml.) for 12 hr., and the solution was concentrated and chromatographed on alumina (500 ml.). Elution with benzene gave the 9aH-*quinolizine* (0·9 g.), red-orange prisms, m. p. 103° (from methanol) Found: C, 58·4; H, 5·4; N, 3·8; OMe, 31·4. $C_{19}H_{21}NO_8$ requires C, 58·3; H, 5·4; N, 3·6; 4OMe, 31·7%), $\lambda_{max.}$ 294 (1·20), 330 (0·29), and 445 (0·44), $\nu_{max.}$ 5·77, 5·83, 5·88,* 5·99, 6·16, 6·25, 6·57, 6·87, and 6·97 μ.

(*b*) The pyridine (3·6 ml.) in methyl cyanide (10 ml.) was added slowly to the ester (9·5 ml.) in methyl cyanide (20 ml.) at 0° and set aside at room temperature for 20 days. The solvent was removed *in vacuo* and the residual tar gave the 9a*H*-quinolizine (0·3 g.) on trituration with methanol. The soluble material, on chromatography in benzene as in (*a*), gave a further 2·2 g. of the quinolizine.

*Tetramethyl* 9a-*Ethyl*-6-*methyl*-9aH-*quinolizine*-1,2,3,4-*tetracarboxylate* (XXI).—(*a*) This quinolizine (0·4 g.) was obtained using 2-ethyl-6-methylpyridine (4 ml.) instead of the dimethylpyridine in (*a*) above, and separated from methanol as orange leaflets, m. p. 132° (Found: C, 59·1; H, 5·7; N, 3·6; OMe, 30·1. $C_{20}H_{23}NO_8$ requires C, 59·2; H, 5·7; N, 3·5; 4OMe, 30·6%), $\lambda_{max.}$ 294 (0·93), 335 * (0·25), and 450 (0·40), $\nu_{max.}$ 5·78, 5·89, 5·98w, 6·18, 6·56, 6·84,* 6·93, and 6·97 μ.

(*b*) The reaction, carried out in methyl cyanide as in (*b*) above, gave the quinolizine (1·95 g.).

*Tetramethyl* 9a-*Ethyl*-9aH-*quinolizine*-1,2,3,4-*tetracarboxylate* (XIX) *and Dimethyl Acetylenedicarboxylate*.—The quinolizine (1·5 g.) and the ester (2 ml.) were heated at 100° for 48 hr. and the product, in benzene–light petroleum (b. p. 40—60°) (4 ml.; 1 : 1), was chromatographed on alumina (70 ml.) made up in light petroleum. Elution with the last solvent gave the unchanged acetylene, and subsequently benzene eluted *tetramethyl* 2-*ethylpyridine*-3,4,5,6-*tetracarboxylate* (0·9 g.) which crystallised on trituration with ether and separated from ether–light petroleum (5 : 1) as needles, m. p. 51° (Found: C, 53·6; H, 5·2; N, 3·8. $C_{15}H_{17}NO_8$ requires C, 53·1; H, 5·1; N, 4·1%), $\lambda_{max.}$ 284 (0·36). The corresponding 2-methyl derivative [3] had $\lambda_{max.}$ 283 (0·33).

*Tetramethyl* 9a-*Ethyl*-6-*methyl*-9aH-*quinolizine*-1,2,3,4-*tetracarboxylate* (XXI) *and Dimethyl Acetylenedicarboxylate*.—The quinolizine (0·36 g.) and the ester (0·5 ml.) were heated at 100° for 72 hr., and the product was chromatographed on a thin layer of silica gel. After development with benzene the band corresponding to the position of that of a test portion of tetramethyl 2-ethylpyridine-3,4,5,6-tetracarboxylate was eluted with methanol and the product, after crystallisation from ether–light petroleum, gave material (0·14 g.) identical (m. p. and infrared spectrum) to this pyridine.

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