Addition Reactions of Heterocyclic Compounds. Part LXV.[1] Synthesis, Tautomerism, and Rearrangement of Some 2*H*- and 4*H*-Quinolizine Esters

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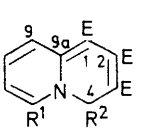
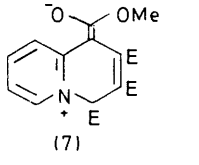
Tetramethyl 4*H*-quinolizine-1.2.3.4-tetracarboxylates on selective alkaline hydrolysis and decarboxylation give trimethyl 2*H*- and 4*H*-quinolizine-1.2.3-tricarboxlyates, which can be interconverted and which were identified from their u.v. and n.m.r. spectra. The non-equivalence of the 4-protons in the 4*H*-isomers at low temperatures is associated with an sp^2-hybridised nitrogen atom and restricted rotation of the ester groups. The formation of indolizines from all these quinolizines with nitric acid or with phenol has been investigated. and mechanistic schemes are proposed. Some 2*H*-quinolizines have been synthesised from ethyl 2-(2-pyridyl)cinnamate and acetylenecarboxylates.

SIMPLE theoretical calculations [2] have suggested that 4*H*-quinolizines will be more stable than their 2*H*- and 9a*H*-isomers and that nucleophilic attack on the unsubstituted aromatic quinolizinylium cation will take place preferentially at position 4. The initial products, trapped by hydrogenation, from reactions of quinolizinylium salts with Grignard reagents [3] or lithium aluminium hydride [4] are very unstable 4*H*-quinolizines, and earlier syntheses designed to yield 4*H*-quinolizine itself gave only the valence tautomer 2-(buta-1,3-dienyl)-pyridine.[5] In contrast, tetramethyl 9a*H*- and 4*H*-quinolizine-1,2,3,4-tetracarboxylates [*e.g.* (1)] are well known [6] and their stability is associated with resonance involving the 1- and 3-ester groups [*e.g.* (7)]. The molecular parameters, deduced from an *X*-ray examination,[7] of tetramethyl 9*H*-pyrido[2,1-*b*]benzothiazole-6,7,8,9-tetracarboxylate (8), which is structurally similar to our 4*H*-quinolizines, support this concept. The bonds joining the 6- and 8-ester groups to the ring are shorter than those for the other ester groups, and distances between other atoms show corresponding variations. From the atomic co-ordinates published [7] we have now calculated that the nitrogen atom is placed only 0.058 Å from the mean plane of its attached carbon



	R^1	R^2
(1)	H	E
(2)	H	CO_2Na
(3)	H	H
(4)	Me	E
(5)	Me	CO_2Na
(6)	Me	H

E = CO_2Me (throughout)



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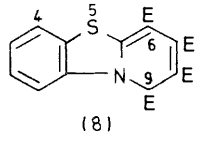

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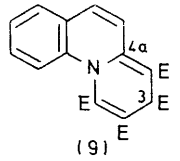


(9)

atoms, that the nitrogen atom and C-5a, -6, -7, and -8 are essentially coplanar (max. deviation 0.075 Å), and

[1] Part LXIV, R. M. Acheson, M. G. Bite, and M. W. Cooper, *J.C.S. Perkin I*, preceding paper.
[2] R. M. Acheson and D. M. Goodall, *J. Chem. Soc.*, 1964, 3225.
[3] T. Miyadera, E. Ohki, and I. Iwai, *Chem. and Pharm. Bull. (Japan)*, 1964, **12**, 1344.
[4] T. Miyadera and Y. Kishida, *Tetrahedron*, 1969, 397.
[5] V. Boekelheide and W. G. Gall, *J. Amer. Chem. Soc.*, 1954, **76**, 1832.
[6] R. M. Acheson, *Adv. Heterocyclic Chem.*, 1963, **1**, 125.
[7] H. Ogura, K. Kikuchi, H. Takayanagi, K. Furuhata, Y. Iitaka, and R. M. Acheson, *J.C.S. Perkin I*, 1975, 2316.

that the 6-, 7-, and 8-ester groups (mean C–CO_2 planes) subtend angles of 8.3, 74.4, and 26.0°, respectively, to this plane.

It is therefore of interest to ascertain the minimum number of ester groups necessary to stabilise the bicyclic 4*H*-quinolizine system, and the possibility of selective removal of ester groups from quinolizine tetraesters has been investigated. Heating the tetraester (1) with phenol, formic acid, dilute nitric acid, or potassium hydroxide causes ring contraction to indolizines,[8] whereas hydrolysis with aqueous hydrochloric acid gives 2-carboxy-1,4-dihydroquinolizinylium chloride.[9] We have now found that 1 mol. equiv. of sodium hydroxide in homogeneous solution selectively hydrolyses the 4-ester groups of the tetraesters (1) and (4) yielding the yellow salts (2) and (5). Their u.v. spectra indicate the presence of the 4*H*-quinolizine chromophore and their n.m.r. spectra indicate that the 1-ester group, which deshields the 9-proton, is intact and show that the highest field ester groups have been hydrolysed. These groups must have been present at position 4 to fit in with the data now considered.

Acidification of these salts caused immediate decarboxylation and gave mixtures of the corresponding red 2*H*- [(11) and (12)] and yellow 4*H*-quinolizines [(3) and (6)]. The 4*H*-compounds closely resembled the parent tetraesters in the u.v., and showed the expected similarities in their n.m.r. spectra to the tetraesters. The only 2*H*-quinolizine of this type described previously is the unstable tetramethyl 3*H*-benzo[*c*]quinolizine-1,2,3,4-tetracarboxylate (9), obtained by irradiation of the 4a*H*-isomer.[10]

The n.m.r. spectra of the 4*H*-triesters (3) and (6) show the signals for the two protons at position 4 as singlets at room temperature, but, surprisingly, as a pair of doublets (τ 5.00 and 5.76; J *ca.* 13 Hz) at −60 °C, coalescence being observed at −27 ± 1 °C. In contrast the 4*H*-quinolizine-1,3-dicarboxylate[11] (15) showed equivalence of the 4-protons at −60 °C. Assuming that the nitrogen atom is sp^2-hybridised in these compounds, as is very probable from the *X*-ray data discussed earlier, the non-equivalence of the 4-protons of the triesters at low temperatures can be associated with a restriction of rotation of the 3-ester group enhanced by

TABLE 1

N.m.r. spectra (solvent deuteriochloroform; 60 MHz; tetramethylsilane as internal standard; τ values; J in Hz)

Compound	Protons	OMe
(2) [a]	4-H, 4.23s; 6-H, 2.11d; 7-H, 3.04m; 8-H, 2.35app. t; 9-H, 1.81d; $J_{6,7}$ 7, $J_{7,8}$ 7, $J_{8,9}$ 9	6.08, 6.22, 6.32
(3)	4-H_2, 5.38s; 6-H, 2.56d; 7-H, 3.30m; 8-H, 2.60app. t; 9-H, 1.56d; $J_{6,7}$ 7, $J_{7,8}$ 7, $J_{8,9}$ 10	6.16, 6.32, 6.32
(6)	4-H_2, 5.42s; 6-Me, 7.46; 7-H, 3.34d; 8-H, 2.70q; 9-H, 1.62d; $J_{7,8}$ 7, $J_{8,9}$ 9	6.18, 6.33, 6.33
(11)	2-H, 5.04s; 4-H, 2.58s; 6-H, 3.11d; 7-H, 4.11app. t; 8-H, 3.35m; 9-H, 1.73d; $J_{6,7}$ 7, $J_{7,8}$ 7, $J_{8,9}$ 10	6.25, 6.31, 6.41
(12)	2-H, 4.99s; 4-H, 2.31s; 6-Me, 7.72; 7-H, 4.18d; 8-H, 3.40q; 9-H, 1.74d; $J_{7,8}$ 7, $J_{8,9}$ 10	6.21, 6.29, 6.41
(13) [b]	1-H, 4.78app. d; 2-H, 5.09app. d;[c] 4-H, 1.60s; 6-H, 1.04d; 7-H, 9-H, 1.6—1.95m; 8-H. 1.20app. t; $J_{6,7}$ 6, $J_{7,8}$ + $J_{8,9}$ 17, $J_{1,2}$ 1	5.98, 6.20, 6.25
(14) [b]	1-H, 4.85app. d; 2-H, 5.09app. d;[c] 4-H, 1.55s; 6-Me, 6.96; 7-, 8-, 9-H, 1.4—2.1m; $J_{1,2}$ 1	5.95, 6.20, 6.24
(16)	4-H, 3.92s; ArH(5), 6-H, 8-H, 2.1—2.4m; 7-H, 3.34t; 9-H, 1.34d; $J_{6,7}$ 8, $J_{7,8}$ 8, $J_{8,9}$ 10	6.41,[d] 9.41,[e] 6.64, 6.35
(18)	4-H, 4.04s; 6-H, 2.51d; 7-H, 3.34m; 8-H, 2.70app. t; 9-H, 1.26d; $J_{6,7}$ 7, $J_{7,8}$ 7, $J_{8,9}$ 9	5.91,[d] 8.85,[e] 6.16, 6.28, 6.34
(22)	ArH(5), 2.80s; 2-H, 4.74s; 6-H, 3.13d; 7-H, 4.11app. t; 8-H, 3.34m; 9-H, 1.77d; $J_{6,7}$ 7, $J_{7,8}$ 7, $J_{8,9}$ 10	5.87,[d] 8.74,[e] 6.10, 6.30
(23) [f]	ArH(5) 2.6—2.7m; 2-H, 4.83s; 4-H, 2.66s; 6-H, 3.13d; 7-H, 4.11app. t; 8-H, 3.35m; 9-H, 1.73d; $J_{6,7}$ 7, $J_{7,8}$ 7, $J_{8,9}$ 10	5.96,[d] 8.70,[e] 6.30
(24)	ArH(5), 2.68s; 3-CH_2, 6.30s; 5-H, 2.10d; 6-H, 3.28app. t; 7-H, 2.90app. t; 8-H, 1.71d; $J_{5,6}$ 8, $J_{7,8}$ 9	5.89,[d] 8.94,[e] 6.37, 6.40
(A)	4-H, 4.29s; 6-H, 2.25d; 7-H, 3.21m; 8-H, 2.50app. t; 9-H, 1.85d; $J_{6,7}$ 7, $J_{7,8}$ 7, $J_{8,9}$ 9	6.13, 6.32

(A) Disodium 1,2-dimethyl 4*H*-quinolizine-1,2,3,4-tetracarboxylate dihydrate.

[a] In D_2O. [b] In CF_3CO_2H. [c] Assigned by comparison with spectrum run in $CF_3{\cdot}CO_2D$. [d] $CH_2{\cdot}CH_3$, q, J 7. [e] $CH_2{\cdot}CH_3$, t, J 7. [f] At 270 MHz.

TABLE 2

U.v. spectra

Compd.	Solvent [a]	$\lambda_{max.}$/nm ($10^{-4}\varepsilon$)
(2)	M	258 (0.25), 314 (0.33), 348 (0.40), 435 (0.30)
(3)	M	211 (1.41), 260 (0.80), 312 (1.60), 346 (1.09), 444 (1.00)
	A	214 (1.22), 252infl, 313 (1.32), 340infl, 442 (0.38)
(6)	M	212 (1.10), 264 (0.80), 314 (1.05), 344 (1.32), 461 (0.93)
	A	217 (1.35), 317 (1.15), 450 (0.43)
(11)	M	208 (1.5), 264 (2.40), 296infl (0.60), 465 (0.59)
	A	208 (1.40), 283 (1.28)
(12)	M	213 (1.00), 263 (1.17), 305 (0.70), 265 (0.57)
	A	208 (1.40), 287 (0.90)
(16)	M, A	214 (1.30), 280 (1.12), 335 (0.46), 348infl (0.34), 410 (0.61)
	P	224 (2.43), 262infl (0.85), 290 (1.15)
(22)	M	208 (2.04), 271 (2.01), 312infl (0.68), 465 (0.41)
	A	208 (2.24), 278 (0.98)
(23)	M	208 (2.31). 268 (3.08), 310infl (0.63), 470 (0.60)
	A	208 (0.73), 280 (0.70)
(A)	M	208 (1.32), 245 (0.78), 313 (0.96), 328infl (0.70), 440 (0.63)
	A	208 (1.30), 270 (0.46), 314infl (0.11)

(A) Disodium 1,2-dimethyl 4*H*-quinolizine-1,2,3,4-tetracarboxylate dihydrate.

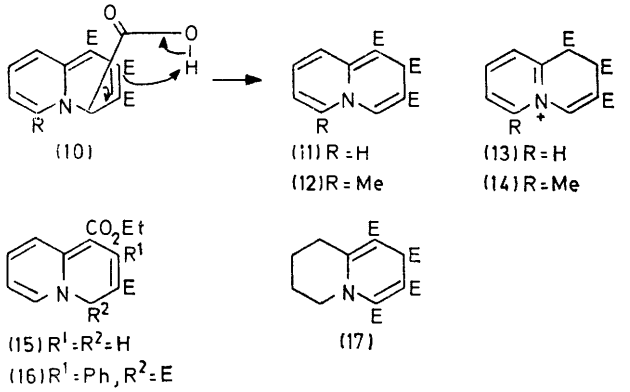
[a] M, methanol; A, methanol acidified with one drop of 72% perchloric acid. P, 1 : 1 (v/v) methanol–72% perchloric acid.

[8] R. M. Acheson and G. A. Taylor, *J. Chem. Soc.*, 1960, 4600.
[9] R. M. Acheson and J. M. F. Gagan, *J. Chem. Soc.*, 1963, 1903.
[10] A. O. Plunkett, *Tetrahedron Letters*, 1974, 4181.
[11] R. M. Acheson and J. McK. Woollard, *J. Chem. Soc.* (*C*), 1971, 3296.

the buttressed 2-ester group. The steric effect of the 2-ester group is shown up in the u.v. spectra of the compounds, for the long-wavelength band of the diester (15), where there is effectively no steric inhibition of resonance of the type shown in structure (7), is considerably more towards the visible than the long-wavelength bands of the triesters (3) and (6), where coplanarity of the 1- and 3-ester groups with the rest of the conjugated system is markedly reduced.

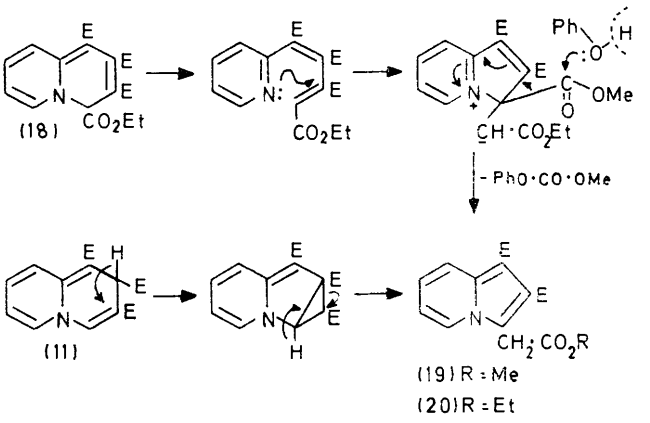
The n.m.r. spectra of our 2*H*-quinolizines, which could be formed by a concerted decarboxylation as indicated (10), showed one-proton singlets at τ 2.58 and 5.04, and (11) has the characteristic four-proton system of a quinolizine. The u.v. spectra showed an absorption at 465 nm, indicative of a highly conjugated chromophore. N.m.r. spectra of the 2*H*-quinolizines in trifluoroacetic acid solution showed that protonation takes place at the 1-position to give the cations (13) and (14). The 1- and 2-protons are apparently coupled, and the 2-proton did not exchange in deuteriated trifluoroacetic acid.

At room temperature trimethyl 2*H*-quinolizine-1,2,3-tricarboxylate, treated with acid or passed through a

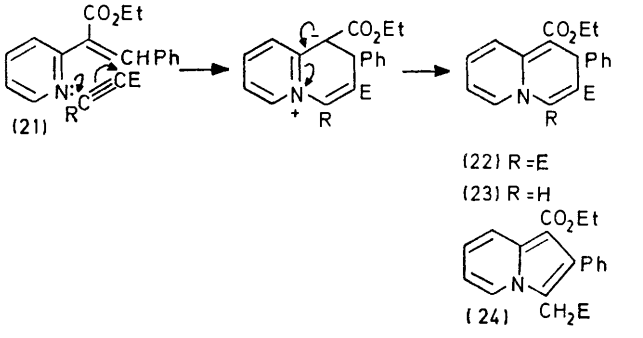


silica column, is converted almost entirely into the 4*H*-isomer, in accord with the calculations [2] concerning the stabilities of quinolizines. However in refluxing toluene these 2*H*- and 4*H*-quinolizines yield a 2 : 1 mixture of the 2*H*- and 4*H*-isomers after 45 h. The position of equilibrium could not be established because of the decomposition of the 4*H*-isomer, and the mechanism of the equilibration is not clear. These quinolizines may be considered as 1,4- and 1,2-dihydropyridines, respectively; compounds of these types have been directly interconverted only in the presence of hydrogenation catalysts.[12] Partial reduction of the 4*H*-quinolizine tetraester (1) gives a 2*H*-quinolizine derivative (17).[13] The chemical shift of the 2-proton in this compound (in $CDCl_3$) is τ 4.93, between the values observed for the complex 2*H*-quinolizine (9) and our examples.

On refluxing in phenol for 10 min the 2*H*- (11) and 4*H*-triesters (3), and the 4*H*-tetraester (1) gave the indolizine-3-acetate (19). It was of interest to determine which ester group of the tetraester was eliminated. The sodium salt (2) with ethyl bromide gave a mixture of 4*H*-quinolizine tetraester (18) and its decarboxylation products (3) and (11). Warm dilute nitric acid converted the tetraester in this mixture into trimethyl indolizine-1,2,3-tricarboxylate, proving that the ester group originally at position 4 of the tetraester was lost. In similar experiments the stability of the triesters (3) and (4) to dilute nitric acid was demonstrated. However refluxing the mixture of the ethyl ester (18), (3), and (11) in phenol gave a mixture of the ethyl dimethyl (20) and the trimethyl indolizinetricarboxylate (19), the proportion of (20) corresponding to that of the original ethyl ester (18) present. A mechanism consistent with the retention of the 4-ester group is shown in Scheme 1. The quinolizine triesters must rearrange by a different pathway, which was shown to be acid-catalysed and may proceed *via* (11) as outlined. The n.m.r. spectra of the 4*H*-quinolizine triester (3) and the tetraester [14] (1) in trifluoroacetic acid solution show that protonation occurs at position 3. The 4-proton exchanges rapidly only in the case of the tetraester.[14]



SCHEME 1



SCHEME 2

Ethyl 2-(2-pyridyl)cinnamate (21) with dimethyl acetylenedicarboxylate gave the 2*H*-quinolizine (22), presumably *via* nucleophilic attack from the nitrogen atom followed by a Michael-type cyclisation. Methyl propiolate gave a very low yield of the quinolizine (23),

[12] R. M. Acheson and G. Paglietti, *J.C.S. Perkin I*, 1976, 45; R. E. Lyle and S. E. Mallett, *Ann. New York Acad. Sci.*, 1967, **145**, 83.

[13] R. M. Acheson and G. A. Taylor, *J. Chem. Soc.*, 1960, 1691.

[14] R. M. Acheson, R. S. Feinberg, and J. M. F. Gagan, *J. Chem. Soc.*, 1965, 948.

and but-3-yn-2-one gave no identifiable products. The u.v. and n.m.r. spectra of these 2*H*-quinolizines were closely similar to those of the 2*H*-quinolizines obtained by the decarboxylation route. The 2*H*-quinolizine (22) was isomerised on a silica column to a mixture of the 4*H*-quinolizine (16) and the indolizine-3-acetate (24). The n.m.r. signals of the 1- and 3-ester groups of the 4*H*-quinolizine were at markedly higher field than those of the 2*H*-isomer, indicating that the 2-phenyl group of the 4*H*-quinolizine is forced into a position perpendicular to the heterocyclic ring plane.

EXPERIMENTAL

The instruments used have been described previously.[15] I.r. spectra and analytical data for the new compounds are available as Supplementary Publication No. SUP 21820 (3 pp.).†

Alkaline Hydrolysis of Tetramethyl 4H-*Quinolizine*-1,2,3,4-*tetracarboxylate* (1).—(i) The tetraester [13] (1) (3.63 g) was dissolved in acetonitrile (70 ml) and heated to 50 °C. Aqueous M-sodium hydroxide (10.0 ml) was added dropwise with stirring, the temperature being maintained, and after 1 h more at 50 °C cooling precipitated *sodium* 1,2,3-*trimethyl* 4H-*quinolizine*-1,2,3,4-*tetracarboxylate dihydrate* (2), yellow prisms (3.58 g) [from acetonitrile–water (3 : 1 v/v)], m.p. 195—196° (decomp.). The compound turned red on drying at 60 °C *in vacuo*, remained red on cooling, but turned yellow rapidly in air (hydrate formation?).

This salt (8.12 g) in water (100 ml) was acidified by dropwise addition of aqueous M-hydrochloric acid with stirring, at 50 °C. After neutralization and cooling, the precipitate of *trimethyl* 4H- and 2H-*quinolizine*-1,2,3-*tricarboxylates* (2 : 3 ratio by n.m.r.) (4.5 g) was collected and chromatographed over alumina. Elution with toluene gave the 2*H*-quinolizine (11) (1.40 g), red needles from aqueous methanol, m.p. 172—173°; further elution with toluene–chloroform yielded the 4*H*-isomer (3) (1.36 g), yellow needles from aqueous methanol, m.p. 165° (decomp.).

(ii) The tetraester (3.63 g) dissolved in warm acetonitrile was treated with aqueous M-sodium hydroxide (20 ml) and methanol (70 ml) and stirred for 4 h at 50 °C. The precipitate obtained on cooling gave *disodium* 1,2-*dimethyl* 4H-*quinolizine*-1,2,3,4-*tetracarboxylate dihydrate* (A) yellow prisms (3.3 g) (from aq. EtOH), decomp. *ca.* 180°. Acidification under a variety of conditions gave tars.

Interconversion of Trimethyl 2H- *and* 4H-*Quinolizine*-1,2,3-*tricarboxylates*.—(i) The 2*H*-isomer (11) (0.5 g) was refluxed in toluene for 17 h, and the product chromatographed on alumina. Benzene eluted the 2*H*-isomer (0.43 g) and benzene containing 5% (v/v) of chloroform the 4*H*-compound (0.06 g) (3).

(ii) The 4*H*-isomer (0.5 g) similarly, but under reflux for 21 h, gave a mixture of the 2*H*- (0.21 g) and 4*H*-quinolizines (0.28 g). Both quinolizines, as reactants or products, were shown to be pure by t.l.c., m.p., and u.v. spectroscopy.

(iii) N.m.r. observations on the isomers (3) and (11) in pyridine at 95—100 °C showed that the 2*H*-isomer (11) was unchanged after 1 day while the 4*H*-isomer (3) both isomerised and decomposed; after 3 days both samples had given several products. In nitrobenzene after 9 h at 60 °C no changes had occurred; after 12 h at 110 °C the 2*H*-isomer had given 50% of the 4*H*-isomer while the 4*H*-compound had given 5% of the 2*H*-compound; neither starting material was detectable after 12 h at 150 °C.

(iv) The 2*H*-quinolizine (0.2 g) was stable in refluxing methanol (25 ml) for 20 h, but after addition of 5 drops of 10M-HCl refluxing for 3 h gave a 3 : 2 mixture of the 2*H*- and 4*H*-isomers.

(v) The 2*H*-quinolizine (200 mg) after being applied to a silica t.l.c. plate, or a silica column, in chloroform and left overnight yielded the 4*H*-isomer (160 mg) in >95% purity (n.m.r.).

Alkaline Hydrolysis of Tetramethyl 6-*Methyl*-4H-*quinolizine*-1,2,3,4-*tetracarboxylate* (4).—The quinolizine (1.9 g) in acetonitrile (90 ml) was stirred rapidly and aqueous M-sodium hydroxide (5.3 ml) was added dropwise. After refluxing for 40 min, water (20 ml) was added and the acetonitrile removed *in vacuo*. The aqueous residue was extracted with chloroform, the extract yielding unchanged quinolizine (0.72 g), and acidified (2M-HCl). After neutralisation (solid $NaHCO_3$), extraction with chloroform yielded a red oil which was chromatographed on alumina. Elution with benzene–ether (20 : 1 v/v) gave *trimethyl* 6-*methyl*-2H-*quinolizine*-1,2,3-*tricarboxylate* (12), red crystals (0.34 g) (from MeOH), m.p. 147°, and, in the ratio 1 : 1, the 4H-*isomer* (6), yellow needles (0.34 g) (from MeOH), m.p. 170° (decomp.).

Hydrolysis of the Trimethyl 2H- *and* 4H-*Quinolizine*-1,2,3-*tricarboxylates*.—(i) The 4*H*-ester (3) (820 mg) in aqueous 5M-hydrochloric acid (40 ml) was refluxed for 3 h. Only traces of fluorescent material (indolizines?) were extracted by chloroform. The aqueous phase was evaporated to dryness and the residue recrystallised from methanol to give 2-carboxy-1,4-dihydroquinolizinylium chloride (420 mg), identical with an authentic sample.[9]

(ii) The 4*H*-ester (1 mg) was unchanged in hexamethylphosphoramide (1 ml) after 20 min at 180 °C, but similar treatment in the presence of 1 drop of acetic acid caused complete conversion into the indolizine (19), shown by t.l.c. comparisons.

(iii) The 2*H*-ester, treated as in (i) gave a 1 : 4 mixture (from n.m.r.) (710 mg) of 2-carboxy-1,4-dihydroquinolizinylium chloride and a dicarboxy-1,2-dihydroquinolizinylium chloride. Attempts to separate these salts by ion-exchange chromatography, or conversion into their methyl esters and crystallisation, failed.

4-*Ethyl* 1,2,3-*Trimethyl* 4H-*quinolizine*-1,2,3,4-*tetracarboxylate* (18).—Sodium 1,2,3-trimethyl 4*H*-quinolizine-1,2,3,4-tetracarboxylate hydrate (4 g) in water (10 ml) was refluxed with ethyl bromide (25 ml) in ethanol (25 ml) for 2 days, and the mixture evaporated. The chloroform-soluble part of the residue gave a solid (1.5 g) (B) identified from its n.m.r. spectrum as a mixture containing 30—70% of the trimethyl ethyl ester with trimethyl 2*H*- and 4*H*-quinolizine-1,2,3-tricarboxylates which could not be resolved by fractional crystallisation or chromatography. The proportion of the ethyl ester was variable. The mixture (900 mg) was added to aqueous 2M-nitric acid and heated on a steam-bath until dissolved. After dilution with water (85 ml), extraction with chloroform yielded trimethyl indolizine-1,2,3-tricarboxylate,[16] yellow needles (from aq. MeOH) (80 mg, 40% based on the initial ethyl ester), m.p. and mixed m.p. 143°. Trimethyl 2*H*- and

† See Notice to Authors No. 7, *J.C.S. Perkin I*, 1975, Index issue.

[15] R. M. Acheson and D. F. Nisbet, *J. Chem. Soc.* (*C*), 1971, 3291.

[16] O. Diels and R. Meyer, *Annalen*, 1934, **513**, 129.

4*H*-quinolizine-1,2,3-tricarboxylates were recovered from similar treatment.

Methyl 1,2-*Bismethoxycarbonylindolizine*-3-*acetate* (19).—(i) Tetramethyl 4*H*-quinolizine-1,2,3,4-tetracarboxylate (1.0 g) well mixed with phenol (5 g) was refluxed for 10 min, cooled, and diluted with chloroform (50 ml). The solution was extracted with aqueous 2M-sodium hydroxide (50 ml), combined with chloroform washings of the aqueous layers, dried, and evaporated. Recrystallisation of the residue (from aq. MeOH) gave methyl 1,2-dimethoxycarbonylindolizine-3-acetate (650 mg, 77%), m.p. 65—66° (lit.,[17] 68°).

(ii) Trimethyl 2*H*- and 4*H*-quinolizine-1,2,3-tricarboxylates gave the same product (64 and 71%, respectively) by the same procedure.

(iii) 4-Ethyl 1,2,3-trimethyl-4*H*-quinolizine-1,2,3,4-tetracarboxylate containing the triesters [mixture (B)] as above gave a mixture of ethyl and methyl 1,2-bismethoxycarbonylindolizine-3-acetates (62%), in the same ratio as the initial constituents (n.m.r.), which could not be separated.

Ethyl 2-(2-*Pyridyl*)*cinnamate*.—This was obtained as a liquid by the procedure described,[18] but in much higher yield (88%) and as a *cis–trans* mixture (from n.m.r.) (*trans* only reported).

2-*Phenyl*-2H-*quinolizines*.—(i) The above ethyl cinnamate (2.53 g) in toluene was treated slowly with dimethyl acetylenedicarboxylate (1.42 g), and after 12 h at room temperature the mixture was refluxed for 1 h. Chromatography on alumina and elution with toluene gave 1-*ethyl* 3,4-*dimethyl* 2-*phenyl*-2H-*quinolizine*-1,3,4-*tricarboxylate* (22), red rhombs (450 mg) (from methanol), m.p. 119—120°. This compound (200 mg) in toluene (10 ml) was placed on a silica column (*ca.* 60 ml) and left overnight; the column was then eluted with toluene followed by chloroform. The first (blue-fluorescing) band yielded methyl 1-ethoxycarbonyl-2-phenylindolizine-3-acetate (24) (*ca.* 30 mg), identified from its u.v. and n.m.r. spectra, and 1-*ethyl* 3,4-*dimethyl* 2-*phenyl*-4H-*quinolizine*-1,3,4-*tricarboxylate* (16), yellow rhombs (110 mg) (from MeOH), m.p. 206—207°.

(ii) The ethyl cinnamate (2.53 g) and methyl propiolate (0.84 g), as above but refluxed for 4 h, gave 1-ethyl 3-methyl 2-phenyl-2*H*-quinolizine-1,3-dicarboxylate (23), red rhombs (from MeOH) (30 mg), m.p. 173—174.5°. No identified product was obtained in a similar reaction with but-3-yn-2-one.

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[17] O. Diels and K. Alder, *Annalen*, 1933, **505**, 103.
[18] G. Van Zyl, D. I. DeVries, R. H. Decker, and E. T. Niles, *J. Org. Chem.*, 1961, **26**, 3373.