Indolizines. Part VI.[1] Ring-opening Reactions of 3-Amino- and 3-Nitroso-indolizines

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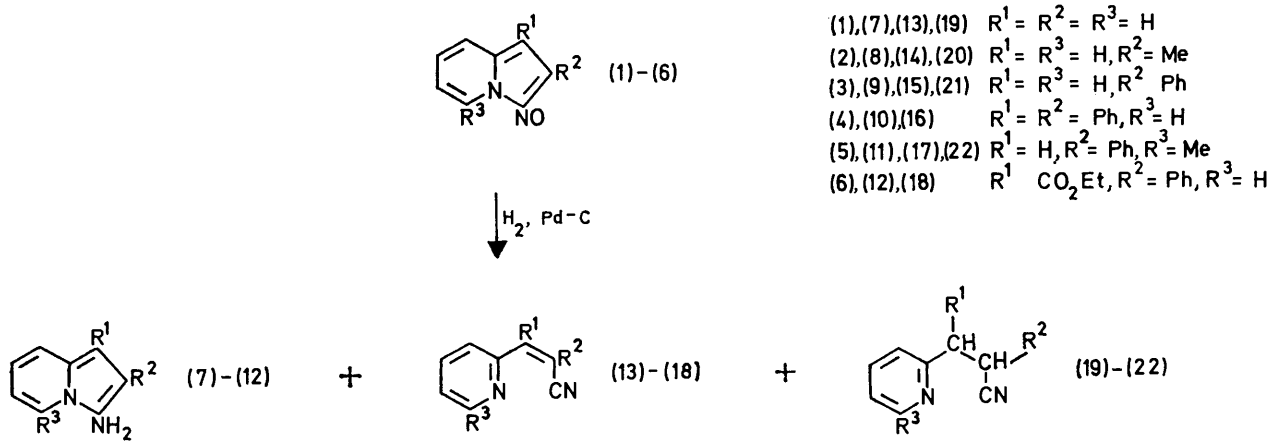
Catalytic hydrogenation of 3-nitrosoindolizines has been shown to yield *cis*-3-(2-pyridyl)-acrylonitriles and -propionitriles in addition to 3-aminoindolizines. A number of syntheses of the acrylonitriles both from 3-nitroso-indolizines under reductive conditions, and from 3-aminoindolizines under oxidative conditions, have been accomplished and the nature of the intermediates in these reactions is discussed. Hydrolysis of 3-aminoindolizines with hydrochloric acid is shown to yield 3-(2-pyridyl)propionic acids.

WE have previously reported the cleavage of the pyrrole ring of 3-nitrosoindolizines [2] and 7-nitrosopyrrolo[1,2-*c*]-pyrimidines [3] to yield 3-(2-pyridyl)- and 3-(pyrimidin-4-yl)-acrylonitriles and -propionitriles in the attempted reduction of nitroso-compounds to the corresponding amines. It has additionally been shown that the amines of amine, acrylonitrile, and propionitrile are shown in Table 1. Hydrogenation of 2-methyl-3-nitroindolizine under similar conditions gave the amine (7) (42%), the acrylonitrile (13) (34%) and the propionitrile (19) (24%) but hydrogenation of 3-(4-carboxyphenylazo)-2-phenyl-indolizine in dimethylformamide yielded 3-amino-2-



may be converted into the acrylonitriles by treatment with lead tetra-acetate or palladium–charcoal. We have now investigated these reactions in the indolizine series with a view to determining the scope and mechanisms of the reactions, and the optimum conditions for ring opening.

A series of 3-nitrosoindolizines were hydrogenated under identical conditions (3 atm) in ethanol over palladium–charcoal. After 1 h the reactions were stopped, catalyst and solvent rapidly removed, and the proportions of the various products and unchanged starting materials estimated by t.l.c., i.r., and n.m.r. measurements. The approximate proportional yields

[1] Part V, J. A. Hickman and D. G. Wibberley, preceding paper.

phenylindolizine and *p*-aminobenzoic acid with no ring-opened nitrile.

TABLE 1

3-Nitroso-indolizine	Amine	%	Acrylonitrile	%	Propionitrile	%
(1)	(7)	29	(13)	12	(19)	59
(2)	(8)	39	(14)	37	(20)	24
(3)	(9)	27	(15)	52	(21)	21
(4)	(10)	85	(16)	15		
(5)	(11)	38	(17)	17	(22)	45
(6)	(12)	93	(18)	7		

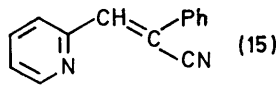
The preparation of 2-phenyl-3-(2-pyridyl)acrylonitrile (15) was then investigated under a variety of reaction

[2] W. J. Irwin and D. G. Wibberley, *Chem. Comm.*, 1968, 878.
[3] W. J. Irwin and D. G. Wibberley, *J. Chem. Soc.* (*C*), 1971, 3237.

conditions (Table 2). It is apparent from these experiments that it is not only, as implied in our earlier papers,[2,3] the palladium–charcoal which is effecting the oxidative ring cleavage of the 3-amino-compounds to the acrylonitriles. In those ring-opening reactions effected by treatment of the amine with palladium–charcoal the additional presence of either oxygen or a dehydrogenating agent was shown to be necessary. The last two reactions in Table 2 are evidence that nitrosoindolizines can behave as oxidising agents and therefore presumably also perform such a function in the preparation of acrylonitriles by catalytic hydrogenation of the 3-nitroso-compounds.

TABLE 2

Routes used for the synthesis of the acrylonitrile (15)



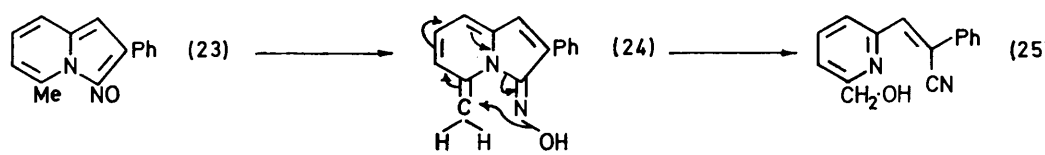
Reagents	Reaction Conditions	Time (h)	Yield (%)
3-Nitroso-2-phenylindolizine (3) (1·0 g) + Pd–C (0·2 g) + cyclohexene (3 cm³) + EtOH (20 cm³)	Reflux	48	68
3-Nitroso-2-phenylindolizine (3) (1·0 g) + $P(OEt)_3$ (2·0 g)	100°	6	80
3-Amino-2-phenylindolizine (9) (1·0 g) + $Pb(OAc)_4$ (2·0 g) + C_6H_6 (50 cm³)	Reflux	1	77
3-Amino-2-phenylindolizine (9) (1·0 g) + Pd–C (0·2 g) + EtOH (25 cm³) + air	Reflux	18	89
3-Amino-2-phenylindolizine (9) (1·0 g) + Pd–C (0·2 g) + EtOH (25 cm³) + O_2	Room temp.	1	94
3-Amino-2-phenylindolizine (9) (1·0 g) + Pd–C (0·2 g) + EtOH (25 cm³) + N_2		1	0
3-Amino-2-phenylindolizine (9) (1·0 g) + Pd–C (0·2 g) + EtOH (25 cm³) + cyclohexene (3·0 cm³) + N_2	Reflux	4	80
3-Amino-2-phenylindolizine (9) (1·0 g) + 3-nitroso-2-phenylindolizine (3) (1·1 g) + EtOH (50 cm³) + Pd–C (0·2 g) + N_2	Room temp.	1	71 *
3-Amino-2-phenylindolizine (9) (1·0 g) + 3-nitroso-2-phenylindolizine (3) (1·1 g) + EtOH (50 cm³)	Reflux	4	73

* Together with 19% unchanged starting material.

A ring-opening reaction in which no external reagent was necessary was the previously reported [1] conversion of 5-methyl-3-nitrosoindolizine (23) into 3-(6-hydroxymethyl-2-pyridyl)acrylonitrile (25) on heating under reflux in ethanol. Alkylindolizines are known to be easily oxidised [4] and an intermolecular reduction of a 3-nitroso-group was presumably responsible for the formation of the acrylonitrile (14) from a preparation of 2-methyl-3-nitrosoindolizine; this possibly explains our failure to nitrosate 1,2-dimethylindolizine.

In view of the formation of the same acrylonitrile by such a variety of reactions, the formation of a common intermediate, such as the isomeric 3-nitrene (28) is attractive. Both the deoxygenation of other *C*-nitroso-compounds [5] and the oxidation of other *C*-amines [6,7] with lead tetra-acetate are reactions which have previously been suggested by some workers to proceed *via* nitrenes. We were unable, however, to demonstrate the presence of indolizin-3-ylnitrenes (28) by intermolecular trapping reactions with cyclohexene or to prepare 3-azidoindolizines, which could conceivably decompose *via* nitrenes. The preparation of 3-nitroso- or 3-amino-2-phenyl-5-styrylindolizine was attempted for an investigation of possible alternative intramolecular nitrene insertion reactions into the styryl double bond, but failed at the starting material stage. It therefore appears equally probable at this stage that nitrenes are not formed in these reactions and that, as in related examples,[8] more complex adducts such as (26) or (27) are the immediate precursors of the acrylonitriles (29).

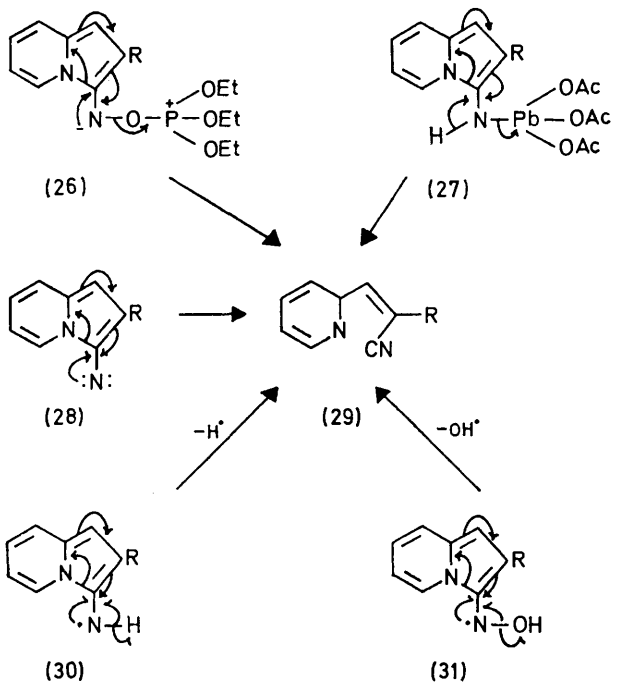
Other intermediates must be formed in those reactions not involving triethyl phosphite or lead tetra-acetate, and the suggestion [9] that amino-radicals (33a) are possible intermediates in the formation of β-azoacrylonitriles (35) and bis-azo-compounds (34) by the oxidation of 5-aminopyrazoles (32) appears relevant. Similar amino-radical intermediates (30) can be postulated for those preparations of the 2-pyridylacrylonitriles which are accomplished by oxidation of the 3-aminoindolizines by an oxidising agent such as oxygen, lead tetra-acetate, or a 3-nitrosoindolizine. In the last case there is evidence [10] that nitroso-compounds can abstract hydrogen atoms, and the concurrent reduction of the nitrosoindolizine could yield a hydroxylamino-radical species



[4] W. L. Mosby, 'Heterocyclic Systems with Bridgehead Nitrogen Atoms,' Interscience, London, 1961, Part I.
[5] J. I. G. Cadogan, *Quart. Rev.*, 1968, **22**, 222.
[6] C. D. Campbell and C. W. Rees, *Chem. Comm.*, 1965, 192.
[7] J. B. Aylward, *Quart. Rev.*, 1971, **25**, 407.
[8] T. L. Gilchrist and C. W. Rees, 'Carbenes, Nitrenes, and Aryres,' Nelson, London, 1969.
[9] P. A. S. Smith, G. J. W. Breen, and M. Hajek, American Chemical Society 155th National Meeting, San Francisco, California, 1968, Abstracts p55-*O*.
[10] G. A. Russell, E. G. Geels, F. J. Smentowski, K. Y. Chang, J. Reynolds, and G. Kaup, *J. Amer. Chem. Soc.*, 1967, **89**, 3821; G. T. Knight and M. J. R. Loadman, *J. Chem. Soc.* (*B*), 1971, 2107.

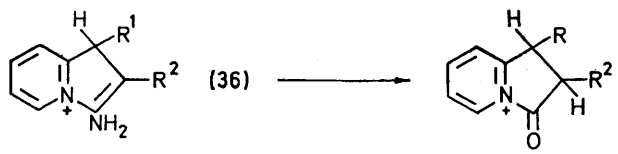
(31) capable of fragmentation to the nitrile (29). Also an intramolecular redox reaction of the 5-methyl-3-nitrosoindolizine (23) could yield radical or ionic intermediates [*e.g.* (24)] capable of bond isomerisation to the hydroxymethyl-2-pyridylacrylonitrile (25).

In contrast to work with other aromatic and heterocyclic systems, azo-compounds were not obtained in the



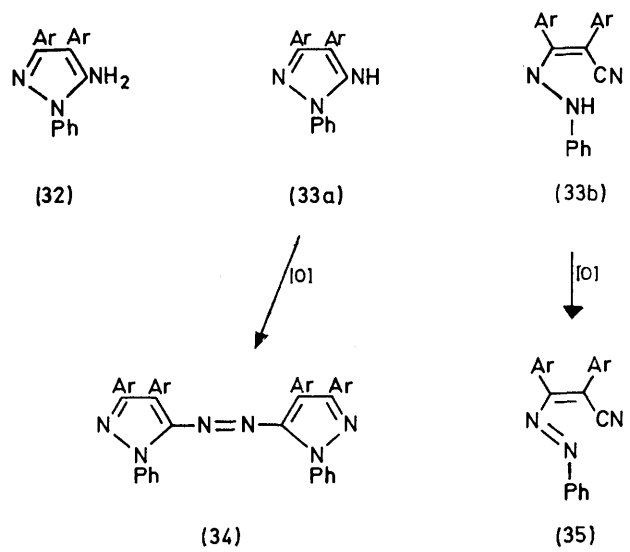
reaction of the 3-aminoindolizine (9) with the 3-nitrosoindolizine.

In view, additionally, of the high stability of the 3-phenylazoindolizines [1] we consider it unlikely that any N–N bonded azo-, azoxy-, or hydrazo-compounds are intermediates in the formation of the acrylonitriles. 3-Hydroxylaminoindolizines remained as possible precursors but attempts to prepare 3-hydroxylamino-2-phenylindolizine by treatment of the 3-nitroso-compound

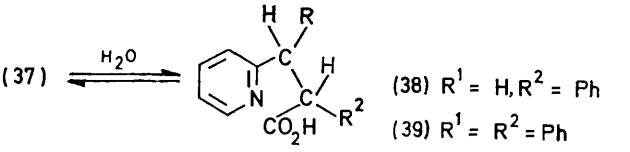


(3) with sodium borohydride in propan-2-ol in the presence of palladium–charcoal yielded the 3-(2-pyridyl)-propionitrile (21) in 87% yield.

Treatment of the amines (9) and (10) with dilute or concentrated hydrochloric acid caused hydrolysis and ring cleavage to yield the propionic acids (38) and (39) and ammonium chloride. Similar hydrolysis appeared to be taking place with 3-acetamido-2-methyl- and 3-acetamido-1,2-dimethyl-indolizine, and ammonium chloride was again formed, but the products decomposed during work-up. Hydrolysis of the nitrile (21) also yielded the acid (38), identical with the product of hydrolysis of 3-diacetylamino-2-phenylindolizine. This



acid has previously been suggested to be the corresponding 3-hydroxyindolizine. Presumably the 3-oxo-tautomers (37) of the protonated 3-hydroxyindolizines are intermediates in this hydrolysis of the protonated 3-aminoindolizines (36), and such compounds will be as susceptible to cleavage of the N–CO bond as any *N*-acylpyridinium sa



EXPERIMENTAL

Spectra were determined as described in the preceding paper.

Catalytic Hydrogenation of 3-Nitrosoindolizines.—A solution of the 3-nitrosoindolizine (1·0 g) in sufficient ethanol to effect dissolution (*ca.* 30 cm³) containing 10% palladium–charcoal (0·2 g) was shaken with hydrogen at 3 atm for 1 h. The mixture was filtered through Celite and the solvent removed. The approximate estimation of the proportions of products and unchanged starting material (Table 1) was made at this stage by i.r. and n.m.r. spectroscopy. The mixtures were separated by column chromatography on alumina with benzene as eluant. 3-Nitrosoindolizine (1) yielded 3-aminoindolizine (7),[1] 3-(2-*pyridyl*)*acrylonitrile* (13) as an oil (Found: M^+, 130·05310. $C_8H_6N_2$ requires M, 130·05316), $\nu_{max.}$ (film) 2250 (C≡N) cm^{-1}, τ ($CDCl_3$) 1·35 (1H, d, J 5 Hz, pyridyl 6-H), 2·1—2·9 (3H, m, pyridyl 3-, 4-, and 5-H), 2·81 (1H, d, J 12 Hz, *cis*-CH=C*H*–CN), and 4·43 (1H, d, J 12 Hz, *cis*-C*H*=CH·CN) [a small quantity of the *trans*-isomer was slowly formed at room temperature: τ ($CDCl_3$) 3·45 (1H, d, J 16 Hz *trans*-C*H*=CH–CN)], and 3-(2-pyridyl) propionitrile (19) as an oil which formed a picrate, m.p.

140—141° (decomp.) [lit.,[11] 140—142° (decomp.)], $\nu_{max.}$ (film) 2240 (C≡N) cm^{-1}, τ ($CDCl_3$) 1·53 (1H, d, *J* 5 Hz, pyridyl 6-H), 2·3—2·9 (3H, m, pyridyl 3-, 4-, and 5-H), 7·15 (4H, m, $-CH_2-CH_2-CN$). 2-Methyl-3-nitrosoindolizine (2) gave 3-amino-2-methylindolizine (8),[1] *2-methyl-3-(2-pyridyl)acrylonitrile* (14) as an oil [*picrate*, m.p. 128—129° (decomp.) (Found: C, 48·0; H, 3·0; N, 18·6. $C_{15}H_{11}N_5O_7$ requires C, 48·3; H, 2·9; N, 18·6%)] (Found for the oil: M^+, 144·06917. $C_9H_8N_2$ requires *M*, 144·06875), $\nu_{max.}$ (film) 2250 (C≡N) and 1640 (C=O) cm^{-1}, τ 1·31 (1H, d, *J* 5 Hz pyridyl 6-H), 2·3—3·0 (3H, m, pyridyl 3-, 4-, and 5-H), 2·87 (1H, q, *J* 2 Hz C*H*=CMe·CN), 7·84 (3H, d, *J* 2 Hz, CH=C*Me*·CN), and *2-methyl-3-(2-pyridyl)propionitrile* (20) as an oil (Found: M^+, 146·08531. $C_9H_{10}N_2$ requires *M*, 146·08441), $\nu_{max.}$ (film) 2250 (C≡N) cm^{-1}, τ ($CDCl_3$) 1·40 (1H, d, *J* 5 Hz, pyridyl 6-H), 2·3—3·0 (3H, m, pyridyl 3-, 4-, and 5-H), 6·9 (3H, m, CH_2·C*H*Me·CN), and 8·65 (3H, d, *J* 6 Hz, CH_2·CH*Me*·CN). 3-Nitroso-2-phenylindolizine (3) gave 3-amino-2-phenylindolizine (9),[1] *2-phenyl-3-(2-pyridyl)-acrylonitrile* (15), needles, m.p. 61—68° [from light petroleum (b.p. 60—80°)] (Found: C, 81·5; H, 5·0; N, 13·4%; M^+, 206. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%; *M*, 206), $\nu_{max.}$ ($CHCl_3$) 2250 (C≡N) and 1630 (C=C) cm^{-1}, τ ($CDCl_3$) 1·40 (1H, d, *J* 5 Hz, pyridyl 6-H), 2·0—2·8 (9H, m, 2-Ph, pyridyl 3-, 4-, and 5-H and C*H*=CPh·CN), and 2-phenyl-3-(2-pyridyl)propionitrile (21), m.p. 53—54°, identical with an authentic sample,[12] $\nu_{max.}$ 2250 (C≡N) cm^{-1}, τ ($CDCl_3$) 1·4 (1H, d, *J* 5 Hz, pyridyl 6-H), 2·6 (8H, m, Ph, pyridyl 3-, 4-, and 5-H), 5·5 (1H, t, *J* 8 Hz, CH_2·C*H*·CN), and 6·8 (2H, d, *J* 8 Hz, CH_2·CH·CN). 3-Nitroso-1,2-diphenylindolizine (4) gave 3-amino-1,2-diphenylindolizine (10) [1] and *2,3-diphenyl-3-(2-pyridyl)acrylonitrile* (16), needles, m.p. 145—146° [from light petroleum (b.p. 60—80°)] (Found: C, 85·3; H, 5·0; N, 9·8%; M^+, 282. $C_{20}H_{14}N_2$ requires C, 85·1; H, 5·0; N, 9·8%; *M*, 282), $\nu_{max.}$ ($CHCl_3$) 2220 (C≡N) cm^{-1}, τ ($CDCl_3$) 1·35 (1H, d, *J* 5 Hz, pyridyl 6-H), and 2·3—3·0 (13H, 2- and 3-Ph, pyridyl 3-, 4-, and 5-H). 5-Methyl-3-nitroso-2-phenylindolizine (5) gave 3-amino-5-methyl-2-phenylindolizine (11),[1] *3-(6-methyl-2-pyridyl)-2-phenylacrylonitrile* (17), prisms, m.p. 69—70° [from light petroleum (b.p. 60—80°)] (Found: C, 81·9; H, 5·5; N, 12·7%; M^+, 220. $C_{15}H_{12}N_2$ requires C, 81·7; H, 5·5; N, 12·5%; *M*, 220), $\nu_{max.}$ ($CHCl_3$) 2250 (C≡N) and 1640 (C=C) cm^{-1}, τ ($CDCl_3$) 2·1—2·9 (9H, m, 2-Ph, pyridyl 3-, 4-, and 5-H and C*H*=CPh·CN), 7·45 (3H, s, pyridyl 6-Me), and *3-(6-methyl-2-pyridyl)-2-phenylpropionitrile* (22), as an oil [*picrate*, m.p. 166—167° (Found: C, 55·7; H, 3·9; N, 15·4%; M^+, 222. $C_{21}H_{17}N_5O_7$ requires C, 55·6; H, 3·8; N, 15·5%; *M*, 222)], $\nu_{max.}$ ($CHCl_3$) 2250 (C≡N) cm^{-1}, τ ($CDCl_3$) 2·4—3·1 (8H, m, 2-Ph, pyridyl 3-, 4-, and 5-H), 5·57 (1H, t, *J* 8 Hz, CH_2·C*H*Ph·CN), 6·83 (2H, d, *J* 8 Hz, CH_2·CHPh·CN), and 7·50 (3H, s, pyridyl 6-Me). Ethyl 3-nitroso-2-phenylindolizine-1-carboxylate (6) gave ethyl 3-amino-2-phenylindolizine-1-carboxylate (12)[1] and the acrylonitrile (18) in too small a yield to be isolated.

2-Phenyl-3-(2-pyridyl)acrylonitrile was prepared by the reactions recorded in Table 2.

2-Methyl-3-(2-pyridyl)acrylonitrile was similarly prepared in 55% yield by transfer hydrogenation of the nitroso-compound (2) with cyclohexene.

3-(6-Hydroxymethyl-2-pyridyl)-2-phenylacrylonitrile (25). —A solution of 5-methyl-3-nitroso-2-phenylindolizine (23) (1·18 g) in absolute ethanol (50 cm^3) was refluxed for 17 h. The solvent was removed and the black solid extracted with light petroleum (b.p. 60—80°). Concentration of the extract gave the *acrylonitrile* (25), needles (0·48 g, 41%), m.p. 103—104° [from light petroleum (b.p. 60—80°)] (Found: C, 76·0; H, 5·2; N, 11·7%; M^+, 236. $C_{15}H_{12}N_2O$ requires C, 76·3; H, 5·1; N, 11·9%; *M*, 236), $\nu_{max.}$ ($CHCl_3$) 3450 (OH) and 2225 (C≡N) cm^{-1}, τ ($CDCl_3$) 2·05—2·80 (9H, m, pyridyl 3-, 4-, and 5-H, C*H*=CPh·CN), 5·12 (2H, s, pyridyl 6-CH_2·OH), and 5·82 (1H, s, pyridyl 6-CH_2·O*H*, exchangeable).

2-Phenyl-3-(2-pyridyl)propionitrile (21) (0·45 g, 87%) was additionally prepared by treatment of the nitroso-compound (3) (0·55 g) in propan-2-ol (25 cm^3) with palladium–carbon (0·1 g), sodium borohydride (0·1 g), and propan-2-ol (30 cm^3) in the presence of nitrogen.

2,3-Diphenyl-3-(2-pyridyl)acrylonitrile (16) was obtained in 82% yield by treatment of the 3-aminoindolizine (10) with lead tetra-acetate.

Attempted Preparations of 2-Phenyl-5-styrylindolizine.—(a) *From 5-methyl-2-phenylindolizine.* Benzaldehyde (0·58 g) 5-methyl-2-phenylindolizine (1·04 g), acetic anhydride (0·55 g), and dioxan were heated together under reflux for 17 h. The solvents and excess of reagents were distilled off and the dark tarry residue was chromatographed on a column of neutral alumina (elution with benzene). Material from a cream band was collected to give *αα-bis-(5-methyl-2-phenylindolizin-3-yl)toluene* (1·05 g, 42%), pale cream needles, m.p. 213° (decomp.) (from ethanol) (Found: M^+, 502·24089. $C_{37}H_{30}N_2$ requires *M*, 502·23967), $\nu_{max.}$ 1610, 1540 (aryl), and 1430 (alkyl) cm^{-1}, τ ($CDCl_3$) 2·70—2·90 (11H, m, 2- and 2′-Ph 8- and 8′-H, 3·50—3·75 (7H, m, 1-, 6-, and 7-H, 1′-, 6′-, 7′-H, and C*H*Ph), and 7·67 (6H, s, 5- and 5′-Me).

(b) *From 2-methyl-6-styrylpyridine.* All attempts to form a quaternary salt from 2-methyl-6-styrylpyridine and phenacyl bromide were unsuccessful.

Reaction of 3-Aminoindolizines with Hydrochloric Acid.—*2-Phenyl-3-(2-pyridyl)propionic acid* (38).—(*a*) 3-Amino-2-phenylindolizine (0·5 g) and concentrated hydrochloric acid (5 cm^3) were heated under reflux for 0·5 h. The mixture was cooled to yield the *propionic acid* (38) *hydrochloride* (0·53 g, 90%), needles, m.p. 200—202° (from ethanol–ether) (Found: C, 63·4; H, 5·4; N, 5·4%; M^+, 227. $C_{14}H_{14}NO_2$ requires C, 63·8; H, 5·5; N, 5·3%; *M*, 227), $\nu_{max.}$ (Nujol) 2600 (OH) and 1700 (C=O) cm^{-1}. Treatment of the hydrochloride with aqueous sodium hydrogen carbonate solution yielded the free *acid* (40), needles, m.p. 150—151° (from ethanol) (Found: C, 74·2; H, 5·8; N, 6·0. $C_{14}H_{13}NO_2$ requires C, 74·0; H, 5·8; N, 6·2%), $\nu_{max.}$ (Nujol, Me_2SO, or pyridine) 2400 (OH) and 1700 (C=O) cm^{-1}, τ ($CDCl_3$) −0·75 (1H, s, CO_2H, exchangeable), 1·32 (1H, d, *J* 6 Hz, pyridyl 6-H), 2·25—2·84 (8H, m, 2-Ph, pyridyl 3-, 4-, and 5-H), 5·73 (1H, t, *J* 7·5 Hz, CH_2·C*H*Ph), 6·32 (1H, q, *J* 14·5 and 7·5 Hz, CH*H*·CHPh), and 6·73 (1H, q, *J* 14·5 and 7·5 Hz, C*H*H·CHPh), τ (pyridine) −0·73 (1H, s, CO_2H, exchangeable).

(*b*) Similar hydrolysis of 3-acetamido-2-phenylindolizine gave the same acid (76%); (*c*) hydrolysis of the amine with 2N-hydrochloric acid also gave the acid (38) (73%).

(*d*) A solution of 2-phenyl-3-(2-pyridyl)propionitrile (3·0 g) in concentrated hydrochloric acid (5 cm^3) was heated under reflux for 3 h. The solid was collected after cooling and neutralised with sodium hydrogen carbonate to yield

[11] V. Bockelkeide, W. J. Linn, P. O'Grady, and M. Lamburg, *J. Amer. Chem. Soc.*, 1953, **75**, 3243.

[12] J. Hurst, T. Melton, and D. G. Wibberley, *J. Chem. Soc.*, 1965, 2948.

the acid (3·4 g, 96%), identical with a sample prepared by method (*a*).

2,3-*Diphenyl*-3-(2-*pyridyl*)*propionic Acid* (39).—Treatment of 3-amino-1,2-diphenylindolizine by the preceding method (*a*) yielded the *acid* (39) *hydrochloride* (87%), pale cream prisms, m.p. 214° (decomp.) (from ethanol) (Found: C, 70·4; H, 5·4; N, 4·3%; M^+, 303. $C_{20}H_{18}ClNO_2$ requires C, 70·7; H, 5·3; N, 4·1%; *M*, 303), $\nu_{max.}$ (Nujol) 2300 (OH) and 1700 cm^{-1}. The acid (39) was obtained by treatment of the hydrochloride with sodium hydrogen carbonate and separated as pale cream prisms, m.p. 181° (decomp.) (from ethanol), $\nu_{max.}$ (Nujol) 2300 (OH) and 1700 (C=O) cm^{-1}, τ ($CDCl_3$) −1·5br (1H, s, CO_2H, exchangeable, 1·4 (1H, d, *J* 5 Hz, pyridyl 6-H), 2·5—2·9 (13H, m, 2- and 3-Ph, pyridyl 3-, 4-, and 5-H), and 5·32 (2H, d, *J* 10 Hz, C*H*Ph·C*H*Ph). The same acid (39) was obtained from 3-acetamido-1,2-diphenylindolizine with conc. hydrochloric acid (72%) and from the amine with dilute hydrochloric acid. Attempted hydrolysis of 3-acetamido-1,2-dimethylindolizine with conc. hydrochloric acid yielded ammonium chloride (78%) and an unstable green oil, the n.m.r. spectrum of which, although poorly resolved, suggested the presence of 2,3-methyl-3-(2-pyridyl)propionic acid.

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