Synthesis of Peri-fused Indolizines and Azaindolizines by Intramolecular 1,3-Dipolar Cycloaddition of 3-(Phenylpropynoyloxyalkyl)pyridine *N*-Ylides

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Treatment of 3-(phenylpropynoyloxymethyl)-*N*-aminopyridinium salt with potassium carbonate in methanol gave unexpectedly 4-methyl-2-phenylpyrazolo[1,5-*a*]pyridine and methyl 6- and 4-hydroxymethyl-2-phenylpyrazolo[1,5-*a*]pyridine-3-carboxylates. Similar treatment of *N*-methoxycarbonylmethyl-3-(phenylpropynoyloxymethyl)pyridinium salt again failed to give the intramolecular cycloaddition product. In contrast, the 3-[2-(phenylpropynoyloxy)ethyl], 3-[3-(phenylpropynoyloxy)propyl], and 3-[4-(phenylpropynoyloxy)butyl] analogues underwent smooth intramolecular 1,3-dipolar cycloaddition to yield the tricyclic pyrazolo[1,5-*a*]pyridine and indolizine derivatives containing seven-, eight-, and nine-membered lactone rings.

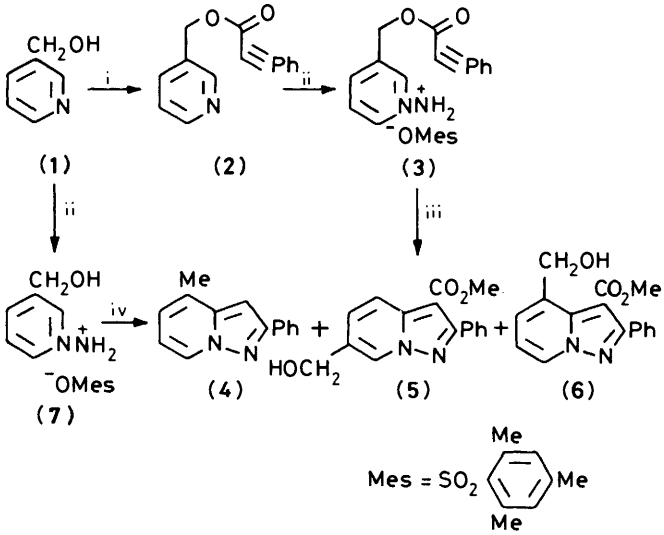
1,3-Dipolar cycloaddition reactions of pyridine *N*-methanides and *N*-imides with acetylenic esters have been extensively studied because they provide particularly ready access to indolizine and azaindolizine systems.[1,2] In connection with our interest in the chemistry of heterocycles with bridgehead nitrogen atoms,[3] we have investigated intramolecular 1,3-dipolar cycloadditions in order to develop a new synthetic route to peri-fused indolizines and azaindolizines. In this paper we describe the results of the reaction of *N*-amino- and *N*-alkoxycarbonylmethyl-3-(phenylpropynoyloxyalkyl)pyridinium salts with base.[4]

The desired ester (**2**) was prepared in 72% yield by the reaction of 3-pyridylmethanol (**1**) with phenylpropynoic acid in the presence of dicyclohexylcarbodi-imide (DCC) at −10 °C (Scheme 1). The ester (**2**) was aminated with *O*-mesitylenesulphonylhydroxylamine (MSH)[5] to give the *N*-amine salt (**3**) in quantitative yield. Treatment of the salt (**3**) with potassium carbonate in various solvents (*e.g.*, dimethylformamide, tetrahydrofuran, acetonitrile, and chloroform) resulted in the formation of complex mixtures. However, when the reaction was carried out in methanol, it gave unexpectedly 4-methyl-2-phenylpyrazolo[1,5-*a*]pyridine (**4**) and methyl 6- and 4-hydroxymethyl-2-phenylpyrazolo[1,5-*a*]pyridine-3-carboxylates (**5**) and (**6**) in 19, 12, and <1% yields, respectively. The structures of compounds (**4**)—(**6**) were readily assigned on the basis of the spectroscopic evidence (see Experimental section).

A mechanistic rationalisation of the formation of compounds (**4**)—(**6**) involves the assumption that the initially formed *N*-amide (**8**) undergoes methanolysis to give 3-hydroxymethylpyridine *N*-imide (**9**) and methyl phenylpropynoate (**10**). Intermolecular 1,3-dipolar cycloaddition between compounds (**9**) and (**10**) followed by rearomatisation leads to the products (**5**) and (**6**), while the formation of compound (**4**) involves the lactonisation of the intermediate (**11**), followed by tautomerisation, decarboxylation, and a 1,3-proton or -hydride shift (Scheme 2).

In order to confirm this mechanistic scheme, the *N*-amino-3-hydroxymethylpyridinium salt (**7**) and methyl phenylpropynoate (**10**) were allowed to react in methanol in the presence of potassium carbonate to give the products (**4**)—(**6**) in 23, 16, and 3% yields, respectively, essentially the same ratio as that obtained from compound (**3**). When treated under the same conditions as those used for compound (**3**), the pyrazolopyridine (**6**) was recovered unchanged, thus showing that it is not an intermediate in the formation of (**4**).

The closely related compound *N*-methoxycarbonylmethyl-

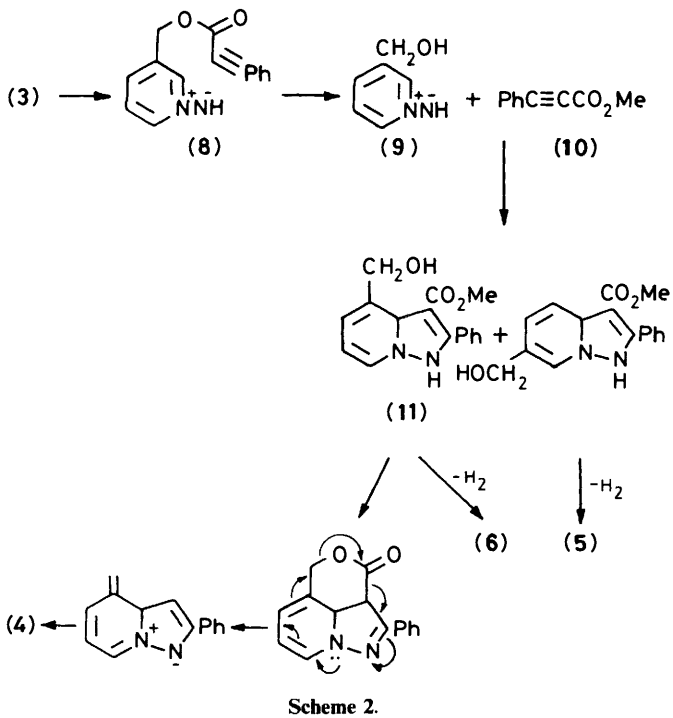


Scheme 1. *Reagents:* i, $PhC{\equiv}CCO_2H$, DCC; ii, NH_2OMes; iii, K_2CO_3 in MeOH; iv, $PhC{\equiv}CCO_2Me$, K_2CO_3 in MeOH

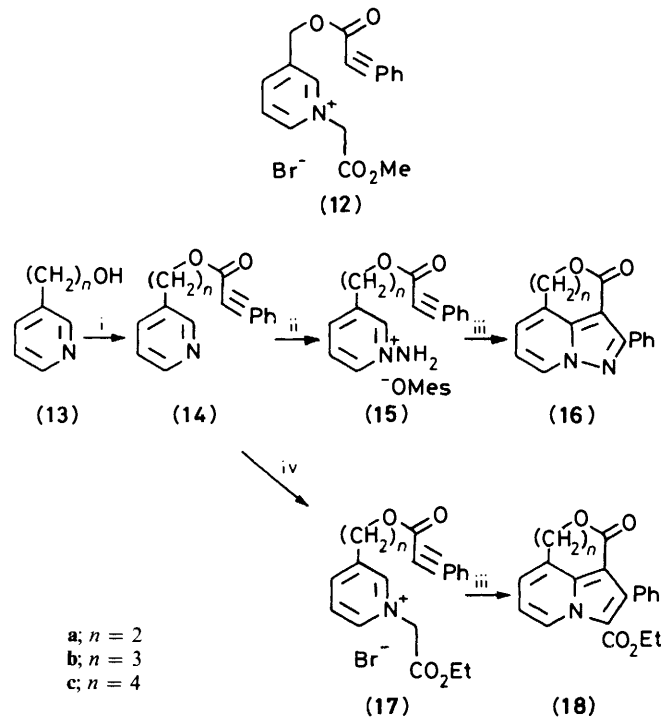
pyridinium bromide (**12**), prepared from compound (**2**) and methyl bromoacetate, again failed to undergo intramolecular 1,3-dipolar cycloaddition under various conditions. At an early stage of the reaction carried out in methanol in the presence of potassium carbonate, the methanolysis product (**10**) was detected by t.l.c., but no adducts were isolated.

The failure of compounds (**3**) and (**12**) to undergo intramolecular cycloaddition is probably due to an insufficient overlap of the orbitals of the 1,3-dipole (pyridine *N*-imide or *N*-methanide) and the dipolarophile (acetylenic group) in the transition state, as suggested by an examination of molecular models; thus other competing reactions such as methanolysis are favoured. We therefore examined the possibility of intramolecular cycloaddition in a homologous series of 3-(phenylpropynoyloxyalkyl)pyridine derivatives (**15a—c**) and (**17a—c**).

The starting propynoyl esters (**14a—c**) of 2-(3-pyridyl)ethanol (**13a**), 3-(3-pyridyl)propanol (**13b**), and 4-(3-pyridyl)butanol (**13c**) were prepared in a similar manner to that used for the preparation of (**2**). The *N*-amination and *N*-quaternisation of the esters with MSH and ethyl bromoacetate gave the corresponding salts (**15a—c**) and (**17a—c**) in high yields



Scheme 2.



Scheme 3. *Reagents:* i, $PhC{\equiv}CCO_2H$, DCC; ii, NH_2OMes; iii, K_2CO_3 in MeCN; iv, $BrCH_2CO_2Et$

(Scheme 3). Treatment of the *N*-amine salt (**15a**) with potassium carbonate in acetonitrile at room temperature gave a seven-membered lactone (**16a**) in 26% yield. The structure of compound (**16a**) was confirmed by the spectroscopic evidence; its i.r. spectrum shows a carbonyl group at 1 685 cm^{-1} and the n.m.r. spectrum reveals two multiplets due to two methylene groups at δ 3.3—3.4 (2 H) and 4.6—4.7 (2 H), a triplet at δ 6.92 (1 H, *J* 7 Hz, 9-H), a doublet of doublets at δ 7.18 (1 H, *J* 7 and 1 Hz, 10-H), a broad doublet at δ 8.45 (1 H, *J* 7 Hz, 8-H), and a multiplet in the aromatic region at δ 7.4—7.9 (5 H). In a similar manner, the *N*-amine salts (**15b**) and (**15c**) gave the eight- and nine-membered lactones (**16b**) and (**16c**) in 32 and 48% yields, respectively. The *N*-methoxycarbonylmethyl derivatives (**17a—c**) also gave the corresponding lactones (**18a—c**) in 13, 32, and 26% yields, respectively. It is of interest to note that even eight- and nine-membered lactones are relatively easily formed without the use of a special technique such as a high-dilution method. This is probably because the ylide intermediates are formed slowly under the reaction conditions used, producing the same effect as a high-dilution technique.

Experimental

N.m.r. spectra were determined with a JEOL FX200 spectrometer (200 MHz; $SiMe_4$ as internal standard). I.r. spectra were recorded with a Hitachi EPI-G2 spectrophotometer. Mass spectra were recorded on a Hitachi M-70 spectrometer at 70 eV. Ether refers to diethyl ether.

3-Pyridylmethanol (**1**) and 3-(3-pyridyl)propanol (**13b**) were obtained commercially. 2-(3-Pyridyl)ethanol (**13a**) was prepared according to the literature.[6]

4-(3-*Pyridyl*)*butanol* (**13c**).—To an ice-cooled suspension of 3-hydroxypropylphosphonium bromide[7] (8.78 g, 22 mmol) in dry tetrahydrofuran (80 ml) was added a 15% hexane solution of n-butyl-lithium (25.6 ml, 20 mmol) under argon, and the mixture stirred at room temperature for 30 min. A solution of pyridine-3-carbaldehyde (2.14 g, 20 mmol) in dry tetrahydrofuran (30 ml) was added to the reaction mixture at −10 °C and stirred at the same temperature for 1 h. Insoluble material was then filtered off, the filtrate was concentrated, the residue was dissolved in chloroform, and the solution was extracted three times with 10% hydrochloric acid. The aqueous solution was made alkaline with powdered K_2CO_3, and then extracted with chloroform. The extract was washed with brine, dried ($MgSO_4$), and concentrated to give an oil. Distillation with a Kugelrohr apparatus at 125—135 °C (0.6 mmHg) afforded 4-(3-pyridyl)but-3-en-1-ol [1.77 g, 59% as a mixture of (*E*)- and (*Z*)-isomers]. A solution of the butenol (230 mg) in ethanol (5 ml) was stirred with platinum oxide (20 mg) under hydrogen for 70 h. The mixture was filtered and the filtrate was concentrated to give an oil which was distilled with a Kugelrohr apparatus at 115—125 °C (0.5 mmHg) to give the butanol (**13c**) (150 mg, 64%) [lit.,[8] b.p. 125 °C (0.2 mmHg)].

General Procedure for the Synthesis of 3-*Pyridylalkyl Phenylpropynoates* (**2**) *and* (**14a—c**).—To a cold (−10 °C) stirred mixture of the 3-pyridylalkanol (9 mmol) and phenylpropynoic acid (9 mmol) in dry tetrahydrofuran (25 ml) was added a solution of dicyclohexylcarbodi-imide (DCC) (9 mmol) in dry tetrahydrofuran (15 ml). After the reaction mixture had been stirred at −10 °C for 2 h and then at room temperature overnight, the precipitates were filtered off and the filtrate was concentrated to yield a brown oil, which was dissolved in chloroform. The chloroform solution was washed with 10% K_2CO_3 solution, dried ($MgSO_4$), and concentrated. The pure compound was obtained by passing the crude product through a silica gel column (benzene–ethyl acetate). The following were obtained: 3-*pyridylmethyl phenylpropynoate* (**2**) (71.5%) as an oil; $\nu_{max.}$(film) 2 150 and 1 670 cm^{-1}; δ($CDCl_3$) 5.28 (2 H, s, $ArCH_2O$), 7.2—7.7 (6 H, m, 5-H and aromatic), 7.76 (1 H, ddd, *J* 8, 2, and 1.5 Hz, 4-H), 8.62 (1 H, dd, *J* 5 and 1.5 Hz, 6-H), and 8.68 (1 H, d, *J* 2 Hz, 2-H); its *picrate* had m.p. 142—143 °C (from ethanol) (Found: C, 54.3; H, 3.0; N, 12.05. $C_{21}H_{14}N_4O_9$ requires C, 54.1; H, 3.0; N, 12.0%). 2-(3-*Pyridyl*)*ethyl phenylpropynoate* (**14a**) (94%) as an oil; $\nu_{max.}$(film)

2 170 and 1 700 cm^{-1}; δ($CDCl_3$) 3.03 (2 H, t, *J* 7 Hz, CH_2CH_2OCO), 4.40 (2 H, t, *J* Hz, CH_2CH_2OCO), 7.2—7.7 (7 H, m, 4- and 5-H, and aromatic), and 8.52 (2 H, m, 2- and 6-H); its *picrate* had m.p. 120—122 °C (from ethanol) (Found: C, 55.3; H, 3.2; N, 11.6. $C_{22}H_{16}N_4O_9$ requires C, 55.0; H, 3.4; N, 11.7%). 3-(3-*Pyridyl*)*propyl phenylpropynoate* (**14b**) (85%) as an oil; $\nu_{max.}$ (film) 2 150 and 1 700 cm^{-1}; δ($CDCl_3$) 1.9—2.1 (2 H, m, $CH_2CH_2CH_2$), 2.7—2.8 (2 H, m, $ArCH_2$), 4.26 (2 H, t, *J* 7 Hz, CH_2OCO), 7.22 (1 H, ddd, *J* 8, 5, and 1 Hz, 5-H), 7.3—7.7 (5 H, m, aromatic), 7.53 (1 H, ddd, *J* 8, 2.5, and 2 Hz, 4-H), 8.46 (1 H, dd, *J* 5 and 2 Hz, 6-H), and 8.49 (1 H, br d, *J* 2.5 Hz, 2-H); its *picrate* had m.p. 105—107 °C (from ethanol) (Found: C, 56.2; H, 3.45; N, 11.5. $C_{23}H_{18}N_4O_9$ requires C, 55.9; H, 3.7; N, 11.2%). 4-(3-*Pyridyl*)*butyl phenylpropynoate* (**14c**) (88%) as an oil; $\nu_{max.}$ (film) 2 150 and 1 705 cm^{-1}; δ($CDCl_3$) 1.6—1.9 (4 H, m, $CH_2CH_2CH_2CH_2$), 2.6—2.8 (2 H, m, $ArCH_2$), 4.2—4.3 (2 H, m, CH_2OCO), 7.20 (1 H, ddd, *J* 8, 5, and 1 Hz, 5-H), 7.3—7.6 (5 H, m, aromatic), 7.50 (1 H, ddd, *J* 8, 2.5, and 2 Hz, 4-H), 8.44 (1 H, dd, *J* 5 and 2 Hz, 6-H), and 8.46 (1 H, br d, *J* 2.5 Hz, 2-H); its *picrate* had m.p. 111—112 °C (from ethanol) (Found: C, 56.8; H, 4.0; N, 10.9. $C_{24}H_{20}N_4O_9$ requires C, 56.7; H, 4.0; N, 11.0%).

General Procedure for the N-*Amination of Compounds* (**1**), (**2**), *and* (**14a—c**).—To an ice-cooled stirred solution of the pyridine (10 mmol) in methylene dichloride (20 ml) was added dropwise a solution of *O*-mesitylenesulphonylhydroxylamine (MSH) (10 mmol) in methylene dichloride (20 ml). The reaction mixture was left at room temperature for 1 h. After the addition of ether, the separated oil was washed with ether and dried under reduced pressure. The crude products were used for the next reaction without further purification. The yields were 87% for the salt (**3**), 87% for (**7**), 99% for (**15a**), 98% for (**15b**), and 97% for (**15c**).

4-*Methyl*-2-*phenylpyrazolo*[1,5-a]*pyridine* (**4**), *and Methyl* 6- *and* 4-*Hydroxymethyl*-2-*phenylpyrazolo*[1,5-a]*pyridine*-3-*carboxylates* (**5**) *and* (**6**).—(*a*) *From the pyridinium salt* (**3**). A mixture of compound (**3**) (1.0 g, 2.2 mmol) and K_2CO_3 (0.92 g, 6.6 mmol) in methanol (10 ml) was stirred under reflux for 5 h. After the reaction mixture had been cooled, the solvent was removed under reduced pressure, the residue was dissolved in chloroform, and the chloroform solution was washed with water, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography on alumina. Elution with benzene afforded the *pyrazolopyridine* (**4**) (79 mg, 19%): m.p. 77—78 °C (from n-hexane) (Found: C, 80.9; H, 5.8; N, 13.45. $C_{14}H_{12}N_2$ requires C, 80.7; H, 5.8; N, 13.45%); δ($CDCl_3$) 2.49 (3 H, s, CH_3), 6.65 (1 H, t, *J* 7 Hz, 6-H), 6.77 (1 H, d, *J* 1 Hz, 1-H), 6.86 (1 H, dd, *J* 7 and 1 Hz, 7-H), 7.3—7.5 (3 H, m, aromatic), 7.9—8.1 (2 H, m, aromatic), and 8.34 (1 H, br d, *J* 7 Hz, 5-H).

Further elution with benzene–ethyl acetate (1:1) afforded a mixture of products (**5**) and (**6**); this was separated by preparative t.l.c. (alumina, benzene–ethyl acetate, 10:1) to give the esters (**5**) (74 mg, 12%) and (**6**) (5 mg, 0.8%). *Compound* (**5**) had m.p. 128—129 °C (from benzene–n-hexane) (Found: C, 68.2; H, 4.95; N, 9.9. $C_{16}H_{14}N_2O_3$ requires C, 68.1; H, 5.0; N, 9.9%); $\nu_{max.}$(KCl) 3 300 and 1 695 cm^{-1}; δ($CDCl_3$) 2.50 (1 H,br s, OH), 3.83 (3 H, s, OCH_3), 4.69 (2 H, s, CH_2OH), 7.35 (1 H, dd, *J* 9 and 1 Hz, 7-H), 7.4—7.5 (3 H, m, aromatic), 7.7—7.8 (2 H, m, aromatic), 8.10 (1 H, d, *J* 9 Hz, 8-H), and 8.47 (1 H, s, 5-H).

Compound (**6**) had m.p. 113—114 °C (from benzene–n-hexane) (Found: C, 68.3; H, 4.9; N, 9.9%); $\nu_{max.}$(KCl) 3 400 and 1 680 cm^{-1}; δ($CDCl_3$) 3.68 (3 H, s, OCH_3), 4.90 (3 H, s, CH_2OH and OH), 6.94 (1 H, t, *J* 7 Hz, 6-H), 7.35 (1 H, dd, *J* 7 and 1 Hz, 7-H), 7.4—7.6 (5 H, m, aromatic), and 8.48 (1 H, dd, *J* 7 and 1 Hz, 5-H).

(*b*) *From compound* (**7**). To a stirred solution of compounds (**7**) (1.0 g, 3.1 mmol) and (**10**) (500 mg, 3.1 mmol) in methanol (20 ml) was added K_2CO_3 (1.3 g, 9.2 mmol). After the reaction mixture had been stirred at room temperature for 12 h, the solvent was evaporated off. The residue was dissolved in water and extracted with chloroform. The extract was dried ($MgSO_4$), and concentrated. Work-up as described above gave products (**4**) (136 mg, 23%), (**5**) (133 mg, 16%), and (**6**) (26 mg, 3%).

General Procedure for the Intramolecular Cycloaddition of the N-*Amine Salts* (**15a—c**).—To a stirred solution of the *N*-amine salt (1 mmol) in acetonitrile (10 ml) was added K_2CO_3 (1.5 mmol). The reaction mixture was stirred at room temperature overnight [in the case of (**15c**), then refluxed for 0.5 h]. After the insoluble material had been filtered off, the filtrate was concentrated. The residue was chromatographed on silica gel (benzene–ethyl acetate) to give the corresponding lactones. The products were obtained as follows. 5,6-*Dihydro*-2-*phenyl*-3H-*oxepino*[5,4,3-cd]*pyrazolo*[1,5-a]*pyridin*-3-*one* (**16a**) (26%) had m.p. 200—201 °C (from benzene) (Found: C, 72.8; H, 4.7; N, 10.4. $C_{16}H_{12}N_2O_2$ requires C, 72.7; H, 4.6; N, 10.6%); $\nu_{max.}$ (Nujol) 1 685 cm^{-1}; δ($CDCl_3$) 3.3—3.4 (2 H, m, $ArCH_2$), 4.6—4.7 (2 H, m, CH_2OCO), 6.92 (1 H, t, *J* 7 Hz, 9-H), 7.18 (1 H, dd, *J* 7 and 1 Hz, 10-H), 7.4—7.5 (3 H, m, aromatic), 7.7—7.9 (2 H, m, aromatic), and 8.45 (1 H, br d, *J* 7 Hz, 8-H). 6,7-*Dihydro*-2-*phenyl*-3H,5H-*oxocino*[5,4,3-cd]*pyrazolo*[1,5-a]*pyridin*-3-*one* (**16b**) (32%) had m.p. 194—195 °C (from ethyl acetate) (Found: C, 73.5; H, 5.2; N, 10.0. $C_{17}H_{14}N_2O_2$ requires C, 73.4; H, 5.1; N, 10.1%); $\nu_{max.}$(Nujol) 1 700 cm^{-1}; δ($CDCl_3$) 1.7—2.5 (2 H, br s, $CH_2CH_2CH_2$), 2.8—3.3 (2 H, br s, $ArCH_2$), 4.4—4.6 (2 H, m, CH_2OCO), 6.85 (1 H, t, *J* 7 Hz, 10-H), 7.10 (1 H, dd, *J* 7 and 1 Hz, 11-H), 7.3—7.5 (3 H, m, aromatic), 7.7—7.8 (2 H, m, aromatic), and 8.40 (1 H, dd, *J* 7 and 1 Hz, 9-H). 5,6,7,8-*Tetrahydro*-2-*phenyl*-3H-*oxocino*[5,4,3-cd]*pyrazolo*[1,5-a]*pyridin*-3-*one* (**16c**) (48%) had m.p. 158—159 °C (from ethyl acetate) (Found: C, 73.8; H, 5.3; N, 9.6. $C_{18}H_{16}N_2O_2$ requires C, 73.95; H, 5.2; N, 9.6%); $\nu_{max.}$(Nujol) 1 690 cm^{-1}; δ($CDCl_3$) 1.7—2.0 (4 H, m, $CH_2CH_2CH_2CH_2$), 3.12 (2 H, t, *J* 6 Hz, $ArCH_2$), 4.66 (2 H, t, *J* 6 Hz, CH_2OCO), 6.81 (1 H, t, *J* 7 Hz, 11-H), 7.11 (1 H, dd, *J* 7 and 1 Hz, 12-H), 7.3—7.5 (3 H, m, aromatic), 7.8—7.9 (2 H, m, aromatic), and 8.42 (1 H, dd, *J* 7 and 1 Hz, 10-H).

General Procedure for the N-*Quaternisation to give Compounds* (**12**) *and* (**17a—c**).—A mixture of the pyridine (5 mmol) and ethyl bromoacetate or methyl bromoacetate (5 mmol) in dry acetone (5 ml) was left at room temperature overnight. Ether was added to the reaction mixture, and the precipitated oil was washed several times with ether and dried *in vacuo* to give hygroscopic crystals which were used for the next reaction without further purification. The yields were 85% for (**12**), 99% for (**17a**), 98% for (**17b**), and 98% for (**17c**).

General Procedure for the Intramolecular Cycloaddition of Compounds (**17a—c**).—A solution of the quaternary salt (0.9 mmol) and K_2CO_3 (195 mg, 1.4 mmol) in acetonitrile (9 ml) was stirred at room temperature overnight. The reaction mixture was filtered and the filtrate was concentrated. The residue was chromatographed (silica gel: benzene–ethyl acetate, 1:1) to give a crystalline product. The following were obtained. *Ethyl* 1,2-*dihydro*-4-*oxo*-6-*phenyl*-4H-*oxepino*[5,4,3-hi]*indolizine*-6-*carboxylate* (**18a**) (13%) had m.p. 184—185 °C (from ethyl acetate) (Found: C, 71.5; H, 5.1; N, 4.25. $C_{20}H_{17}NO_4$ requires C, 71.6; H, 5.1; N, 4.2%); $\nu_{max.}$(Nujol) 1 690 and 1 675 cm^{-1}; δ($CDCl_3$) 0.84 (3 H, t, *J* 7 Hz, OCH_2CH_3), 3.3—3.4 (2 H, m, $ArCH_2$), 4.04 (2 H, q, *J* 7 Hz, OCH_2CH_3), 4.5—4.7 (2 H, m, CH_2OCO), 6.94 (1 H, t, *J* 7 Hz, 9-H), 7.08 (1 H, dd, *J* 7 and 1 Hz, 10-H), 7.2—7.4 (5 H, m, aromatic), and 9.52 (1 H, dd, *J* 7 and 1 Hz, 8-H). *Ethyl* 1,2-*dihydro*-5-*oxo*-6-*phenyl*-3H,5H-*oxocino*[5,4,3-hi]*indolizine*-7-*carboxylate* (**18b**) (32%) had m.p. 175—177 °C (from ethyl acetate) (Found: C, 72.3; H, 5.3; N, 4.0. $C_{21}H_{19}NO_4$ requires C,

72.2; H, 5.5; N, 4.0%); $\nu_{max.}$(Nujol) 1 700 and 1 680 cm^{-1}; δ ($CDCl_3$) 0.88 (3 H, t, *J* 7 Hz, OCH_2CH_3), 1.6—1.9 and 2.3—2.5 (1 H each, m, $CH_2CH_2CH_2$), 2.7—2.9 and 3.1—3.3 (1 H each, m, $ArCH_2$), 4.06 (2 H, q, *J* 7 Hz, OCH_2CH_3), 4.2—4.6 (2 H, m, CH_2OCO), 6.88 (1 H, t, *J* 7 Hz, 10-H), 7.02 (1 H, dd, *J* 7 and 1 Hz, 11-H), 7.2—7.4 (5 H, m, aromatic), and 9.50 (1 H, dd, *J* 7 and 1 Hz, 9-H). *Ethyl* 6-*oxo*-7-*phenyl*-1,2,3,4-*tetrahydro*-6H-*oxocino*[5,4,3-hi]*indolizine*-8-*carboxylate* (**18c**) (26%) had m.p. 116—117 °C (from n-hexane–ethyl acetate) (Found: C, 72.5; H, 5.8; N, 3.9. $C_{22}H_{21}NO_4$ requires C, 72.7; H, 5.8; N, 3.85%); $\nu_{max.}$ (Nujol) 1 715 and 1 675 cm^{-1}; δ($CDCl_3$) 0.90 (3 H, t, *J* 7 Hz, OCH_2CH_3), 1.8—2.0 (4 H, m, $CH_2CH_2CH_2CH_2$), 2.8—3.0 (2 H, m, $ArCH_2$), 4.06 (2 H, q, *J* 7 Hz, OCH_2CH_3), 4.4—4.6 (2 H, m, CH_2OCO), 6.84 (1 H, t, *J* 7 Hz, 11-H), 7.02 (1 H, dd, *J* 7 and 1 Hz, 12-H), 7.3—7.5 (5 H, m, aromatic), and 9.52 (1 H, dd, *J* 7 and 1 Hz, 10-H).

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Received 11*th June* 1984; Paper 4/965