Heterocyclic Compounds with Bridgehead Nitrogen Atoms. Part 10.[1] Synthesis in the Pyrrolo[2,1,5-*de*]quinolizine Series ([2.3.3]Cyclazinones and [2.3.3]Cyclazinylium Salts) starting from Quinolizines

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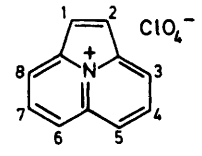
Ethyl 1-oxo-1*H*-pyrrolo[2,1,5-*de*]quinolizine-2-carboxylate was obtained by thermal cyclisation of diethyl quinolizin-4-ylidenemalonate and the corresponding 3-oxo-3*H*-1-carboxylate by reaction of 3-hydroxyquinolizinylium bromide with sodium carbonate and ethyl propynoate in boiling nitrobenzene. These isomeric esters were hydrolysed and decarboxylated to give 1*H*- and 3*H*-pyrrolo[2,1,5-*de*]quinolizin-1- and -3-ones and were converted into various pyrrolo[2,1,5-*de*]quinolizinylium salts, including the parent compound. The n.m.r. spectra and chemical properties of the pyrrolo[2,1,5-*de*]quinolizinylium ion are consistent, for the most part, with a structure in which the 1,2-bond is part of the aromatic system. Nucleophilic attack on this ion occurs at C-3 and, to a lesser extent, at C-5. Among the compounds obtained by such reactions was 5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-one, thus leaving the corresponding 4-oxo-4*H*-compound as the only member of this isomeric series that remains unknown.

In principle, derivatives of [2.3.3]cyclazine† should be accessible either from indolizines or from quinolizines. Various syntheses based on the indolizine pathway were described in Part 9[1] but yields were low in the absence of aryl substituents. We now describe the synthesis of [2.3.3]cyclazines from quinolizines by two independent routes, both of which provide access to salts of the parent [2.3.3]cyclazinylium ion (**1a**).

Synthesis

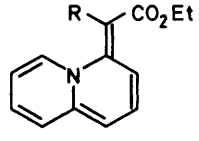
Route (i).—The first of these synthetic routes became possible after the unexpected discovery that diethyl quinolizin-4-ylidenemalonate (**2a**)[2] may be converted (>80%) into 2-ethoxycarbonyl-1*H*-[2.3.3]cyclazin-1-one (**3b**) by heating under reflux in nitrobenzene or 1,2,4-trichlorobenzene. The structure of this bright orange compound followed from its ^{1}H n.m.r. spectrum (Table 1) which, when compared with that of the precursor (**2a**), showed the disappearance of one set of OEt resonances and of the high frequency resonance (δ 9.06) due to the α-pyridine proton [6-H in (**2a**)]; at 360 MHz, the remaining six-proton multiplet was seen to comprise two AMX spin systems. Under the same reaction conditions, the quinolizinylidenecyanoacetate (**2b**) gave the cyanocyclazinone (**3c**). The cyclazinones (**3b** and **c**) showed i.r. absorptions (*ca.* 1 620 cm^{-1}) characteristic of a highly polarised carbonyl group and this structural feature was presumed to be responsible also for the water solubility of the compounds and for their tendency to crystallise as hydrates. The anhydrous compounds, obtained by drying *in vacuo* or by vacuum sublimation, were highly hygroscopic.

The intramolecular acylation leading to these cyclazinones invites mechanistic speculation since, assuming a high degree of polarisation in the starting material [canonical structure (**2c**)], it would seem to involve electrophilic attack at a position of relatively low π-electron density. A possible explanation of this apparent anomaly is shown in Scheme 1. It is suggested that the



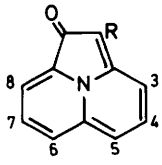
(1)

a; parent
b; 1-OH
c; 1-OMe
d; 1-OEt
e; 1-CO_2Et,2-Cl
f; 1-CO_2Et,2-Br
g; 1-CO_2Et
h; 1-SMe
i; 1-CO_2Et, 2-SMe
j; 3-OH
k; 3-Cl
m; 3-Br
n; 3-SMe



(2)

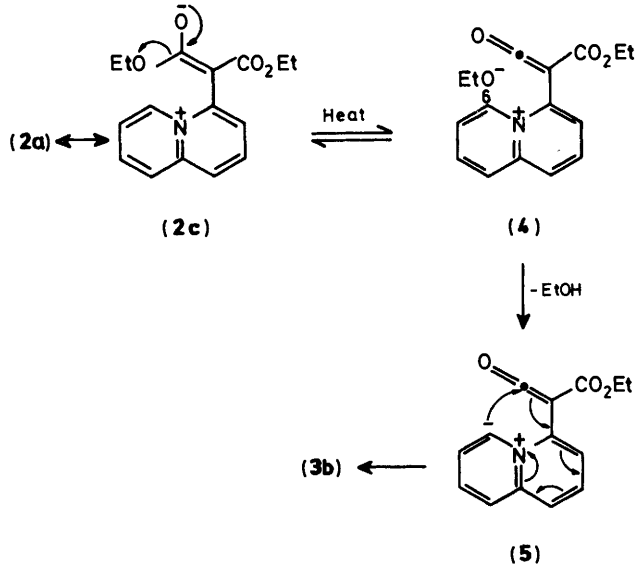
a; R=CO_2Et
b; R=CN



(3)

a; R=H
b; R=CO_2Et
c; R=CN

† See footnote in Part 9[1] for an outline of nomenclature. Cyclazine names are used for convenience in the discussion and IUPAC names with identifying formula numbers in the Experimental section.



Scheme 1.

Table 1. ^{1}H N.m.r. data[a] (360 MHz) of pyrrolo[2,1,5-*de*]quinolizinones (δ/p.p.m. from $SiMe_4$)

Compd.	δ_1	δ_2	δ_3	δ_4	δ_5	δ_6	δ_7	δ_8	*J*/Hz[b]
(**3a**)		5.90 (s)	7.43 (d)	7.88 (t)	7.52 (d)	8.13	8.11	8.33 (d)	$J_{3,4} \simeq J_{4,5}$ 8.1
(**3b**)			8.35 (d)	8.09 (t)	7.74 (d)	8.26 (dd)	8.17 (dd)	8.37 (dd)	$J_{3,4} \simeq J_{4,5}$ 8.2, $J_{6,7}$ 8.5, $J_{7,8}$ 7.1
(**3c**)			7.83 (dd)	8.22 (t)	7.82 (dd)	8.33	8.30	8.53 (dd)	$J_{3,4} = J_{4,5}$ 8.2, $J_{7,8}$ 6.5, $J_{6,8}$ 1.8
(**9a**)	7.25 (d)	8.05 (d)		7.47 (d)	7.94 (d)	7.80 (dd)	7.67 (dd)	8.12 (dd)	$J_{1,2}$ 4.9, $J_{4,5}$ 9.7, $J_{6,7}$ 7.4, $J_{7,8}$ 8.3
(**9b**)		8.47 (s)		7.37 (d)	7.95 (d)	7.8	7.8	8.80 (dd)	$J_{4,5}$ 9.8
(**9f**)		7.45 (s)		7.52 (d)	7.93 (d)	7.84 (d)	7.60 (t)	8.20 (d)	$J_{4,5}$ 9.8
(**16a**)	7.29 (d)	7.57 (d)	8.10 (d)	7.16 (d)		8.64 (dd)	7.81 (t)	8.24 (dd)	$J_{1,2}$ 4.8, $J_{3,4}$ 9.6, $J_{6,7}$ 8.0, $J_{7,8}$ 8.2
(**16b**)		7.98 (s)	8.09 (d)	7.20 (d)		8.55 (dd)	7.92 (t)	8.85 (dd)	$J_{3,4}$ 9.7, $J_{6,7}$ 7.7, $J_{7,8}$ 8.5
(**16c**)[c]	6.45 (s)		8.10 (d)	7.09 (d)		8.48 (dd)	7.75 (t)	7.94 (dd)	$J_{3,4}$ 9.5, $J_{6,7}$ 7.9, $J_{7,8}$ 8.1

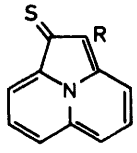
[a] In $CDCl_3$. [b] Only those coupling constants reliably measurable to ±0.1 Hz are reported; for (**3b**), (**9a**) and (**16a**, **b**, and **c**) $J_{6,8}$ *ca.* 1 Hz. [c] N.O.e. difference spectroscopy showed an enhancement (2.3%) of the δ7.94 resonance when the singlet at δ6.54 was irradiated.

precursor, already highly polarised, dissociates at high temperature to form an ion-pair (**4**), the cation of which contains a ketene group; the ethoxide ion then abstracts a proton from C-6 [*cf.* acidity of the α-protons in the parent quinolizinylium ion (**6a**)[3]] to give a zwitterion (**5**) which contains a σ-carbanion site for electrophilic attack by the ketene.

De-ethoxycarbonylation of the ethoxycarbonylcyclazinone (**3b**), besides occurring to a minor extent during the initial formation of (**3b**), was effected in good yield (85%) by heating

(**6**)

a ; parent
b ; 3-OH



(**7**)

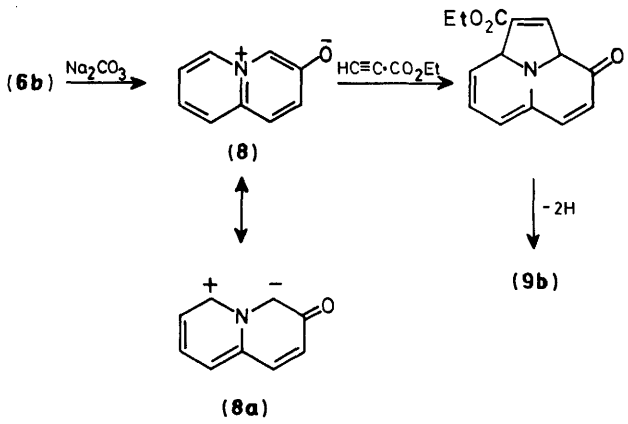
a ; R = H
b ; R = CO_2Et

with aqueous hydrochloric acid. The resulting bright red, highly water-soluble 1*H*-[2.3.3]cyclazin-1-one (**3a**) could not be obtained anhydrous but was readily converted, for analytical purposes, into the 1-hydroxycyclazinylium salts (**1b**) and, after treatment with methyl fluorosulphonate or triethyloxonium tetrafluoroborate, into the corresponding 1-alkoxy-salts (**1c** and **d**). Attempts to prepare 1-halogenocyclazinylium salts by treatment of the cyclazinone (**3a**) with phosphoryl chloride or bromide failed; work-up after a short reaction time gave the 1-hydroxy salt and longer reaction times led to intractable dark products. In contrast, the 2-ethoxycarbonylcyclazinone (**3b**) was readily converted into the corresponding chloro- and bromo-cyclazinylium salts (**1e** and **f**).

The 2-bromo-1-ethoxycarbonylcyclazinylium salt (**1f**) was at first regarded as a potential precursor of the parent salt (**1a**). Removal of bromine was effected by catalytic hydrogenolysis (1 atm H_2; Pd-C) but, owing to rapid loss of catalyst activity, it was necessary to carry out the reaction in two stages and the final yield of the 1-ethoxycarbonylcyclazinylium salt (**1g**) was insufficient to justify the search for a method of decarboxylation. Attention was turned instead to the 1-methylthiocyclazinylium salt (**1h**) as a possible precursor of the parent compound. The salt (**1h**) was first obtained from the parent cyclazin-1-one (**3a**) by treatment with phosphorus pentasulphide and methylation of the resulting deep purple thione (**7a**); this, however, was highly light-sensitive and formed in poor yield. A better yield of the methylthio salt was obtained, from the ethoxycarbonylcyclazinone (**3b**), by delaying decarboxylation until the final stage: conversion into the thione (**7b**) and methylation gave the 1-ethoxycarbonyl-2-methylthiocyclazinylium salt (**1i**) (82%), hydrolysis was carried out in aqueous hydrochloric acid, and decarboxylation[4] (59%) by heating with copper(I) oxide in *N*,*N*-dimethylacetamide. Conversion (52%) into the parent cyclazinylium salt (**1a**) was effected by heating the methylthio compound (**1h**) in ethanol with Raney nickel.

This route to the parent salt (**1a**), though satisfactory for small-scale preparations, suffered from the disadvantage that the conditions for efficient C–S bond hydrogenolysis were not easily reproducible owing to the variable and age-dependent activity of the Raney nickel.

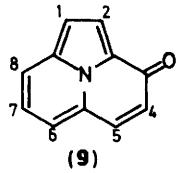
Route (*ii*).—The second, and more satisfactory, route to the [2.3.3]cyclazinylium ion was based on the use of 3-hydroxyquinolizinylium bromide (**6b**) as starting material. This compound, readily obtainable[5] from pyridine-2-carbaldehyde, gives rise to a mesoionic betaine (**8**) which may be expected to show 1,3-dipolar reactivity [canonical structure (**8a**)]. Accordingly, the salt (**6b**) was heated under reflux with ethyl propynoate and anhydrous sodium carbonate in nitrobenzene, a solvent selected for its expected ability[2] to dehydrogenate the initial adduct (Scheme 2). Despite considerable darkening, the resulting bright



Scheme 2.

yellow 1-ethoxycarbonyl-3*H*-[2.3.3]cyclazin-3-one (**9b**) was isolated chromatographically in good yield (75%). Its ^{1}H n.m.r. spectrum (Table 1) showed that one proton in the unsubstituted six-membered ring was strongly deshielded (δ 8.80, dd, 8-H), thus locating the ethoxycarbonyl group at C-1 rather than at C-2. A similar reaction of the bromide (**6b**) with dimethyl butynedioate gave the 1,2-di(methoxycarbonyl)cyclazinone (**9c**) (41%) which was converted, by boiling with aqueous hydrochloric acid, into the 1-carboxylic acid (**9d**), identical with the acid obtained by hydrolysis of the monoester (**9b**).

The acid (**9d**) was decarboxylated by heating it under vacuum with dry copper(I) oxide, the resulting 3*H*-[2.3.3]cyclazin-3-one (**9a**) (84%) being collected as a deep yellow sublimate. Like the isomeric 1*H*-cyclazin-1-one (**3a**), this compound was very hygroscopic and, for elemental analysis, it was converted into 3-hydroxy[2.3.3]cyclazinylium perchlorate (**1j**). The ^{1}H n.m.r.



(**9**)

a; parent
b; 1-CO_2Et
c; 1,2-$(CO_2Me)_2$
d; 1-CO_2H
e; 1-CO_2Me
f; 1-OMe

spectrum (Table 1) of the cyclazinone (**9a**) showed the expected AMX and two AX spin systems; the i.r. spectrum showed the presence of a highly polarised carbonyl group (ν 1 590 cm^{-1}); and the u.v.–visible spectrum was quite similar to those of the substituted 3*H*-[2.3.3]cyclazin-3-ones described in Part 9.[1] Treatment of the cyclazinone (**9a**) with phosphoryl chloride or bromide gave the corresponding 3-halogeno[2.3.3]cyclazinylium salts in high yield, and catalytic hydrogenolysis (1 atm H_2; Pd–C) of the 3-bromo-salt (**1m**) yielded the parent cyclazinylium salt (**1a**) (74%), identical with the product obtained by route (i).

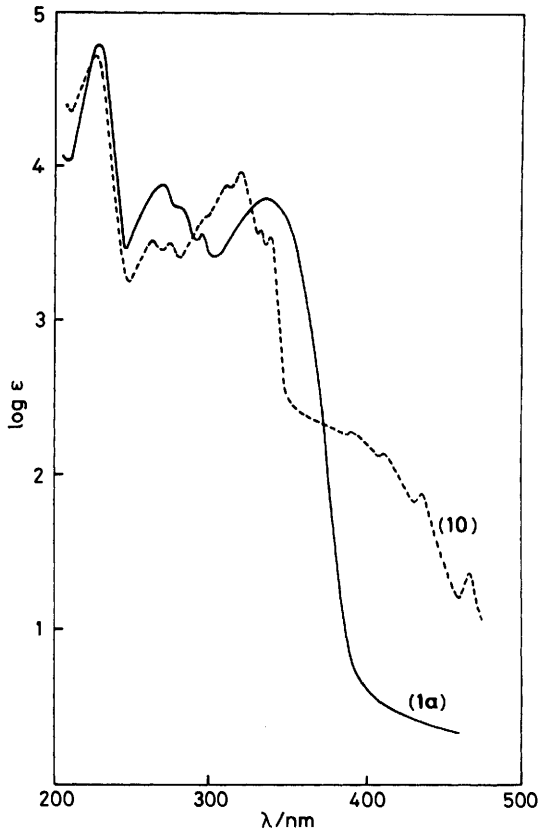


Figure 2. Electronic spectra of pyrrolo[2,1,5-*de*]quinolizinylium perchlorate (**1a**) and acenaphthylene (**10**) in ethanol

Structure and Properties

(a) *Introduction.*—The [2.3.3]cyclazinylium ion is formally isoelectronic with the hydrocarbon acenaphthylene (**10**), for the ground state of which the π-electron densities and bond orders shown in Figure 1a have been calculated.[6] It is noteworthy that first electronic transition[7] of acenaphthylene (and responsible for the yellow colour of that hydrocarbon) is either absent or hypsochromically shifted.

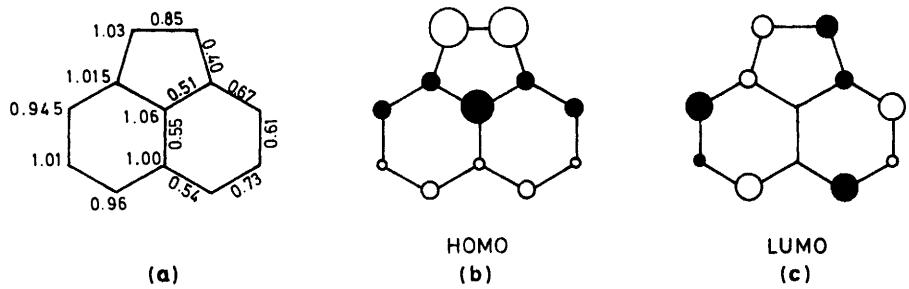


Figure 1. Molecular diagrams (LCI–SCF) for acenaphthylene (**10**); (a) π-electron densities (left) and bond orders (right) for the ground state; (b) the distribution of an electron in the highest occupied molecular orbital; (c) the distribution of an electron in the lowest unoccupied molecular orbital. The radii of circles are approximately proportional to the absolute values of expansion coefficients; the relative signs of coefficients are indicated by open and filled circles

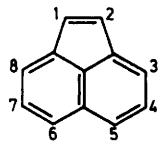
the highest electron density occurs at the internal carbon atom (C-8b) and that a concentration of charge at this point is also a feature of the highest occupied molecular orbital (HOMO) (Figure 1b). It is to be expected, therefore, that replacement of the central carbon by the more electronegative nitrogen will stabilise the ground state and, in particular, will lower the energy of the HOMO; the energy of the LUMO (Figure 1c) will be only slightly affected since the central atom lies on a node. The resulting increase in the HOMO-LUMO separation is apparent in the u.v. spectrum of the cyclazinylium ion (Figure 2) in which a low intensity absorption band corresponding to the

A further consequence of the introduction of nitrogen will be to perturb the molecular orbitals of the ground state in such a way that π-electron density is increased at the nitrogen and depleted at the periphery of the molecule. To the extent that this effect occurs, the molecule will become more like an [11] annulenylium ion σ-bonded to an internal neutral nitrogen [formula (**11**)]. HMO Calculations for the cyclazinylium ion (**1a**) (carried out by Professor W. Flitsch[8]) lend support to this suggestion in showing, compared with acenaphthylene, lower bond orders at the 1,2-bond and at the bonds to the central atom, and higher bond orders at the 1,8a- and 2,2a-bonds; other

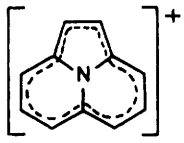
calculated bond orders were little affected by 8b-aza-substitution.

We turn now to discuss the extent to which the above predictions are borne out in experimental observation.

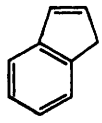
(b) *N.M.R. Chemical Shifts.*—Referring to Table 2, we note first that 3-, 4-, and 5-H of acenaphthylene (**10**) are shielded by 0.1—0.3 p.p.m. relative to the corresponding protons of naphthalene and we interpret this relatively minor shift as an indication that the naphthalene moiety of (**10**) suffers little electronic perturbation by the *peri*-bridging double bond. Turning next to the cyclazinylium ion (**1a**), we note a marked contrast, in that the corresponding resonance shifts of 3-, 4-, and 5-H relative to 3-, 2-, and 1-H (respectively) of the



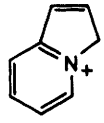
(**10**)



(**11**)



(**12**)



(**13**)

quinolizinylium ion (**6a**), are deshielding and quite large (0.6—1.1 p.p.m.); the 1-, 2-H resonance of (**1a**), at δ 8.64, is also well within the range normally associated with the protons of heteroaromatic cations. Evidently, therefore, the ethylenoid and naphthalenoid moieties are more strongly coupled in (**1a**) than in (**10**) and it might seem valid to interpret the strong proton deshielding in (**1a**) as due to a high positive charge density at the periphery—the result of a substantial contribution from the delocalised structure (**11**). However, we are obliged to reject this explanation on the evidence of the ^{13}C chemical shifts of the cyclazinylium ion; in particular we note that the average ^{13}C shift (131.7 p.p.m.) for C-3, -4, -5 and -5a differs little from the average (132.4 p.p.m.) for the correspondingly situated carbon atoms (C-1, -2, -3, and -9a) in the quinolizinylium ion. There is, however, some indication from the smaller spread of ^{13}C resonances, that positive charge is distributed somewhat more evenly in the cyclazinylium ion than in the quinolizinylium ion. We suggest, therefore, that the contribution from the delocalised structure (**11**) is small but sufficient to establish a peripheral diamagnetic ring-current pathway, not present in (**6a**) or in acenaphthylene, and that the observed proton deshielding in (**1a**) is due to this additional ring current, the effect of increased ring size[9] compensating for the small participation of the peripherally conjugated structure.

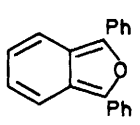
The ^{15}N n.m.r. spectra show that the nitrogen of the cyclazinylium ion is more shielded than that of the quinolizinylium ion to the extent of 22.3 p.p.m., a shift similar in magnitude to the shielding effect of a 4-methoxy group on the ^{15}N resonance of the *N*-methylpyridinium ion ($\Delta\delta$ = 199.4 − 178.1 = 21.3 p.p.m.).[10] In view of the ^{13}C evidence, however, it seems likely that only a small part of this shift could be due to increased electron density at nitrogen. A peripheral ring current could perhaps be responsible but such effects are not well documented for ^{15}N.

(c) *N.M.R. Coupling Constants.*—We had initially hoped that the vicinal H–H coupling constant ($^3J_{1,2}$) would provide evidence relating to the nature of the 1,2-bond in the cyclazinylium ion (**1a**). Unfortunately, the known[11] linear relationship of $^3J_{HH}$ to carbon–carbon bond order for rings of a given size has been established only for carbocyclic rings. An estimate is therefore required of the expected effect (other than that due to bond order change) of the positively charged nitrogen on $^3J_{1,2}$. Such an estimate may be obtained by subtracting $^3J_{HH}$ (5.6 Hz)[12] for the double bond of indene (**12**) from $^3J_{HH}$ (6.3 Hz)[13] for the presumably similar double bond of 3*H*-indolizinium (**13**), yielding an increment, ΔJ = +0.7 Hz, due to replacement of C by N^+. Since the value of $^3J_{1,2}$ for acenaphthylene[14] is 5.2 Hz, a reference value of 5.9 Hz may be estimated for a hypothetical cyclazinylium ion in which the 1,2-bond order is the same as that in acenaphthylene. The experimental value, obtained from the line separation of the ^{13}C side bands of the 1-, 2-H resonance of (**1a**), was 5.7 ± 0.1 Hz. In view of implicit assumptions and the possible accumulation of errors in the estimation of the reference value, this marginally lower figure cannot be said to indicate any significant lowering of the 1,2-bond order in (**1a**) relative to acenaphthylene.

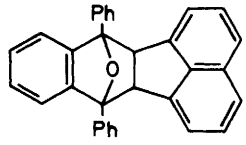
A more reliable indicator of π-electron delocalisation is the ratio of H–H coupling constants ($^3J_{3,4}$:$^3J_{4,5}$) which is expected to be closer to unity, the smaller the degree of bond alternation.[15] The value of this ratio for the cyclazinylium ion (**1a**) was 0.91 which is appreciably greater than the corresponding value ($^3J_{2,3}$:$^3J_{1,2}$ = 0.85) for the quinolizinylium ion (**6a**), indicating less bond alternation (*i.e.* a more delocalised structure) for (**1a**) than for (**6a**). In comparison, the corresponding *J* ratios for acenaphthylene (0.83) and naphthalene (0.82) are essentially equal confirming once again that the naphthalene moiety of (**10**) is not appreciably perturbed by the *peri*-bridging double bond.

(d) *Chemical Reactivity.*—In seeking chemical evidence for or against a delocalised peripheral π-system in the cyclazinylium ion (**1a**) we considered the reactivity of the 1,2-bond to be of prime importance. The resistance of this bond to catalytic hydrogenation first became apparent during the preparation of (**1a**) by hydrogenolysis of its 3-bromo derivative (**1m**). Since this apparent lack of olefinic character was in direct contrast to the reported behaviour of acenaphthylene (**10**), we carried out a competitive hydrogenation in a solution containing millimolar quantities of both (**1a**) and (**10**). Absorption of hydrogen ceased when 1 mmol of H_2 had been consumed and work-up then showed that only the hydrocarbon had been hydrogenated (to acenaphthene).

A further comparison of the cyclazinylium ion with acenaphthylene was centred on the dienophilic reactivity of the 1,2-bond. It has been reported[16] that acenaphthylene reacts with 1,3-diphenylisobenzofuran (**14**) to give the Diels–Alder adduct



(**14**)



(**15**)

(**15**) and we have confirmed this reaction, obtaining the adduct (61%) by conducting the reaction at 140 °C in benzonitrile, a solvent chosen for its ability to dissolve both (**10**) and (**1a**) while being unlikely to influence selectively the reactivity of either compound. Since the diene (**14**) is electron-rich it might be expected, other things being equal (*e.g.* 1,2-bond order), to react

Table 2. N.m.r. data of pyrrolo[2,1,5-*de*]quinolizinylium perchlorate and selected reference compounds (δ/p.p.m.; J/Hz)

A Pyrrolo[2,1,5-*de*]quinolizinylium perchlorate (**1a**)

Position:	1	2a	3		4		5	5a	N
δ_H[a]	8.64		9.35		9.11		9.39		
$^3J_{HH}$[a]	5.7			7.75		8.5			
δ_C[b,c]	127.5	141.1	126.2		136.1		128.1	136.4	
$^1J_{CH}$[b,c]	184.8		175.5		172.5		175.7		
δ_N[d]									184.4

B Quinolizinylium perchlorate (**6a**)

Position:	4	3		2		1	9a	N
δ_H[a]	9.46	8.14		8.43		8.69		
$^3J_{HH}$[a]			7.2		8.5			
δ_C[e]	136.7	123.7		136.8		126.9	142.4	
δ_N[d]								207.1

C Acenaphthylene (**10**)

Position:	1	2a	3		4		5	5a	8b
δ_H[f]	6.88		7.41		7.28		7.53		
$^3J_{HH}$	5.2[h]			6.9[f]		8.3[f]			
δ_C[b,g]	129.4	139.2	124.5		127.9		127.3	127.7	127.8
$^1J_{CH}$[b]	169.4		160.5		160.0		161.7		

D Naphthalene

Position:	3		2		1
δ_H[i]			7.32		7.67
$^3J_{HH}$[i]		6.8		8.3	

[a] At 360 MHz in $(CD_3)_2CO$. [b] At 25.2 MHz in $(CD_3)_2SO$. [c] ^{13}C Assignments for (**1a**) are based on a comparison of its fully proton-coupled spectrum with that of (**10**), corresponding carbon resonances showing the same long-range splitting patterns in both spectra. [d] At 36.5 MHz in $(CD_3)_2SO$; δ/p.p.m. downfield from external anhydrous ammonia. [e] At 90.6 MHz in $(CD_3)_2SO$. [f] At 60 MHz in CCl_4 (M. J. S. Dewar and R. C. Fahey, *J. Am. Chem. Soc.*, 1963, **85**, 2704). [g] ^{13}C Assignments for (**10**) are based on correlations with the ^1H resonances according to the method of ref. 20; they are in agreement with the assignments reported previously for solutions of (**10**) in CS_2 (A. J. Jones, T. D. Alger, D. M. Grant, and W. M. Litchman, *J. Am. Chem. Soc.*, 1970, **92**, 2386). [h] Ref. 14. [i] At 60 MHz in CCl_4 (M. A. Cooper and S. L. Manatt, *J. Am. Chem. Soc.*, 1969, **91**, 6325).

even more readily with the positive ion (**1a**) than with the neutral hydrocarbon (**10**). In fact, however, no cycloaddition was observed at 140 °C in benzonitrile, both the cyclazinylium salt and the diene being recovered (93 and 78% respectively). We conclude from these experiments that the 1,2-bond in the cyclazinylium ion is not olefinic in character.

Another important objective of our investigation of reactivity in the cyclazinylium ion was to determine the preferred position(s) for attack by nucleophiles. Reaction of the salt (**1a**) with sodium sulphide in *N,N*-dimethylformamide gave a deep purple, highly light-sensitive cyclazinethione, the product of a formal displacement of H^- by S^{2-}. Such oxidative substitutions have been reported[17] previously in alkoxyphenalenium ions and related cationic systems. In view of its instability to light and air, the thione was converted, by methylation, into the corresponding methylthiocyclazinylium perchlorate which was identical with the compound (**1n**) obtained from the 3-chlorocyclazinylium salt (**1k**) by treatment with sodium sulphide and methylation of the derived thione. Nucleophilic attack by sulphide ion had therefore taken place mainly at C-3 of the cation (**1a**) but, since the resulting thione had shown a slight colour gradation in its single t.l.c. spot, the presence of an isomeric product was suspected.

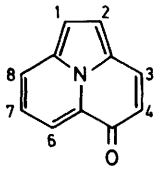
Accordingly, a fresh sample of the thione was allowed to become oxidised in sunlight and the resulting mixture was separated, by p.l.c., into the 3*H*-cyclazin-3-one (**9a**), identical with the specimen obtained previously, and a smaller amount of the 5*H*-cyclazin-5-one (**16**).* The latter was identified by its ^1H n.m.r. spectrum (Table 1) which, though quite distinct from that of (**9a**), likewise showed the presence of one AMX and two AX spin systems. With the isolation of compound (**16a**), three (1-, 3-, and 5-oxo-) of the four possible oxo[2.3.3]cyclazines are now known.

N-Alkyl-2-pyridones and their benzo-derivatives are obtained in good yield from the corresponding *N*-alkylpyridinium ions by reaction with hydroxide in the presence of ferricyanide.[18] When applied to the cyclazinylium salt (**1a**), however, this procedure gave only a very low yield (6%) of the 3*H*-cyclazin-3-one (**9a**). The conjugate bases of malononitrile and ethyl cyanoacetate reacted with the cyclazinylium salt (**1a**), in the same way as sulphide ion, to give the 3-methylene-3*H*-cyclazines (**17a** and **b**), identical with authentic specimens synthesised from the 3-chlorocyclazinylium salt (**1k**).

That C-3 and C-5 (β-pyridine positions) of the cyclazinylium ion should be the preferred sites for nucleophilic substitution is not unexpected since this allows the intermediate adduct [*e.g.* (**18**)] to retain an aromatic indolizine moiety. Again, however, this is a result that highlights the importance of the fused five-membered ring in modifying the properties of the quinolizinylium system, the parent bicyclic form of which is attacked by nucleophiles at the α- and γ-pyridine positions.[19]

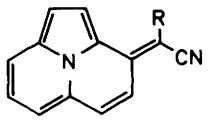
The reactions of 1-methoxy- and 1-ethoxycarbonyl-cyclazinylium salts with sodium sulphide were also investigated in order to determine the directing effects of these substituents. 1-

* In view of the very low conversion of cyclazinethiones into cyclazinones, the relative yields of the latter are not considered to represent the true substitution ratio for attack by sulphide on cyclazinylium cations.



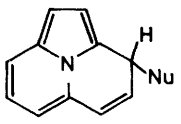
(16)

a; parent
b; 1-CO_2Et
c; 2-OMe

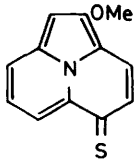


(17)

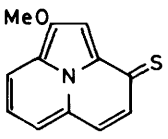
a; R = CN
b; R = CO_2Et



(18)



(19)



(20)

(21)

Methoxycyclazinylium perchlorate (**1c**) gave a mixture of two inseparable thiones, (**19**) and (**20**), in the approximate ratio 5:1 (measured by integration of the respective pyrrole ring ^1H resonances). For identification purposes, the mixed thiones were converted, by oxidation in air and sunlight, into the corresponding cyclazinones (low yield)* which were separated by p.l.c. The structures assigned to these oxo- and thioxo-compounds rest on the following ^1H n.m.r. evidence.

(i) The thiocarbonyl group of the major cyclazinethione was evidently at C-5 since it caused strong deshielding of one of the protons in the unsubstituted six-membered ring (δ 9.02, dd, 6-H). (ii) Irradiation of the singlet resonance (δ 6.56) in the spectrum (Table 1) of the major cyclazinone caused a nuclear Overhauser enhancement (2.3%) of the 8-H resonance (δ 7.94, dd) thus showing that the singlet was due to 1-H and that this compound was the 2-methoxycyclazin-5-one (**16c**); the methoxy-group caused shielding (Δδ 0.75 p.p.m.) of 1-H relative to 1-H in the parent cyclazin-5-one (**16a**). (iii) The minor cyclazinone was identified as 1-methoxycyclazin-3-one (**9f**) since its spectrum (Table 1) was closely similar to that of the parent cyclazin-3-one (**9a**) except that the 2-H resonance (δ 7.45) was more shielded (Δδ 0.6 p.p.m.) owing to the electron-releasing effect of the methoxy-group; had the methoxy-group been present at C-2, the remaining pyrrole-ring proton (1-H) would have been more shielded than 1-H (δ 7.25) in the parent compound (**9a**).

1-Ethoxycarbonylcyclazinylium perchlorate (**1g**) reacted with sodium sulphide to give a mixture of unstable thiones which, as before, were identified after photo-oxidation to the corresponding cyclazinones.* Separation of the cyclazinones by p.l.c. gave the 1-ethoxycarbonylcyclazin-3-one (**9b**), identical with the specimen prepared previously, and the 1-ethoxycarbonylcyclazin-5-one (**16b**), identified by its ^1H n.m.r. spectrum (Table 1) which showed the presence of two deshielded protons (6- and 8-H) in the unsubstituted six-membered ring.

Despite our inability to measure accurate product ratios in these nucleophilic substitution reactions of 1-substituted cyclazinylium ions (**21**), we believe that one significant result emerges—namely, that a 1-ethoxycarbonyl group (X = CO_2Et) directs the nucleophile into the more remote six-membered ring (B), whereas a 1-methoxy group (X = OMe) directs it mainly into the less remote ring (C). This result may be attributed to maximisation of stability in the intermediate adduct [*cf.* formula (**18**)], the residual indolizine moiety tending to retain electron-withdrawing substituents (X) at the more electron-rich position (C-1) and electron-releasing substituents (X) at the less electron-rich position (C-2).

Experimental

Unless otherwise stated, ^1H n.m.r. data were obtained at 100 MHz. For compounds (**3a**), (**9a**), and (**9e**), the non-quaternary ^{13}C resonances (90.6 MHz) were assigned partly by correlation with the 360 MHz ^1H resonances, according to the method of Feeny and his co-workers,[20] and partly on the basis of their multiplicities in fully proton-coupled spectra (stated, for example, as Dd, upper case letters referring to one-bond coupling and lower case letters to longer-range coupling). I.r. data refer to Nujol mulls and u.v. data to ethanolic solutions. Alumina for chromatography was Laporte Type H or UG deactivated by treatment with 10% aqueous acetic acid (0.1 cm^3 per g alumina). Silica for t.l.c. and p.l.c. was Merck Kieselgel G and alumina for p.l.c. was Merck Aluminiumoxid 60 G neutral (Type E). Unless otherwise indicated, glassware for preparation and manipulation of cyclazinethiones was wrapped with aluminium foil to protect the contents from bright light. Extracts were dried over magnesium sulphate and evaporated under reduced pressure. Ether refers to diethyl ether.

Ethyl 1-*Oxo*-1H-*pyrrolo*[2,1,5-de]*quinolizine*-2-*carboxylate* (**3b**).—A solution of diethyl quinolizin-4-ylidenemalonate[2] (3.4 g) in nitrobenzene (120 cm^3) was heated under reflux for 1 h. The solution was evaporated to dryness and the residue was chromatographed on alumina. Elution with chloroform yielded (i) the title *ester monohydrate* (2.3 g, 75%) as orange–yellow prisms, m.p. 188—189 °C (from benzene) (Found: C, 65.3; H, 4.9; N, 5.4. $C_{14}H_{11}NO_3 \cdot H_2O$ requires C, 64.9; H, 5.1; N, 5.4%) which was converted, by sublimation at 180 °C and 0.1 mmHg, into the anhydrous *ester*, an orange solid (Found: C, 69.7; H, 4.5, N, 5.8. $C_{14}H_{11}NO_3$ requires C, 69.7; H, 4.6; N, 5.8%); ν_{max} 1 620 (CO) and 1 660 cm^{-1} (ester CO); $\lambda_{max.}$ 219, 273, 287sh, 298sh, 380, and 454 nm (log ε 4.56, 4.35, 4.05, 3.89, 3.60, and 3.65); and (ii) 1*H*-pyrrolo[2,1,5-*de*]quinolizin-1-one (0.18 g, 9%) as red needles (from benzene–ethanol), i.r. spectrum identical with that of the product obtained by hydrolysis and decarboxylation of the ester (**3b**).

Repetition of this reaction in 1,2,4-trichlorobenzene gave the same products in 85 and 6% yield, respectively.

2-*Cyano*-1H-*pyrrolo*[2,1,5-de]*quinolizin*-1-*one* (**3c**).—Ethyl quinolizin-4-ylidenecyanoacetate (0.5 g), treated as in the foregoing experiment, yielded the *cyano-compound* (0.24 g, 60%) as orange needles, m.p. 262—264 °C (from benzene–methanol), obtained anhydrous by sublimation at 240 °C and 0.1 mmHg (Found: C, 73.05; H, 3.2; N, 14.5. $C_{12}H_6N_2O$ requires C, 73.0; H, 3.3; N, 14.5%); ν_{max} 1 600 (CO) and 2 250 cm^{-1} (CN).

1H-*Pyrrolo*[2,1,5-de]*quinolizin*-1-*one* (**3a**).—The ester (**3b**) (4.82 g) was heated under reflux in 6M-aqueous hydrochloric

* In view of the very low conversion of cyclazinethiones into cyclazinones, the relative yields of the latter are not considered to represent the true substitution ratio for attack by sulphide on cyclazinylium cations.

acid (160 cm^3) for 75 min and the solution was evaporated to dryness. The residual pale yellow solid was dissolved in water (60 cm^3) and treated, at 5 °C, with an excess of 2M-aqueous sodium hydroxide. Continuous extraction with chloroform for 30 h gave a red solution which was dried and evaporated. The residual red oil was triturated with ether to give the *pyrroloquinolizinone* (2.88 g, 85%) as red needles, m.p. 186—192 °C (from benzene–ethanol) which could not be obtained anhydrous; λ_{max} 222, 255, 293, 304, 400sh, and 485 nm; $\delta_C(CDCl_3)$ 91.5 (D, C-2), 111.7 (Ddd, C-5), 112.2 (Dd, C-8), 116.7 (Dd, C-3), 125.3 (Ddd, C-6), 131.7 (D, C-4), 134.3 (D, C-7), 136.2 (m), 139.6 (m), 149.5 (m), and 172.7 (C-1). For analysis, the pyrroloquinolizinone was converted, by treatment with perchloric acid in acetic acid and precipitation with ether, into 1-*hydroxypyrrolo*[2,1,5-de]*quinolizinylium perchlorate* (**1b**), yellow needles, decomp. *ca.* 270 °C darkening from 250 °C (from acetic acid containing a trace of $HClO_4$) (Found: C, 49.1; H, 3.0; N, 5.1. $C_{11}H_8ClNO_5$ requires C, 49.0; H, 3.0; N, 5.2%); ν_{max} 3 150 cm^{-1} (OH); $\delta_H(CF_3CO_2H)$ 7.35 (1 H, s, 2-H) and 8.5—9.2 (6 H, m).

1-*Methoxypyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1c**).—A solution of the cyclazinone (**3a**) (0.24 g) and methyl fluorosulphonate (excess) in chloroform (30 cm^3) was heated under reflux for 15 min during which the 1-methoxypyrroloquinolizinylium fluorosulphonate (0.39 g, 98%) was deposited. Treatment of this product, in ethanol, with perchloric acid and precipitation with ether gave the *perchlorate* (**1c**), m.p. 185—186 °C (Found: C, 50.8; H, 3.6; N, 5.0. $C_{12}H_{10}ClNO_5$ requires C, 50.8; H, 3.5; N, 4.8%); $\delta_H(CF_3CO_2H)$ 4.40 (3 H, s, OMe), 7.32 (1 H, s, 2-H), and 8.6—9.1 (6 H, m).

1-*Ethoxypyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1d**).—The cyclazinone (**3a**) (3.6 g) was dried *in vacuo* as thoroughly as possible and dissolved in dry dichloromethane (25 cm^3). Triethyloxonium tetrafluoroborate (4 g) in dry dichloromethane (10 cm^3) was added dropwise with stirring and, after 15 min, the solution was evaporated. The residue was dissolved in methanol (15 cm^3) and treated with 70% perchloric acid (1.2 cm^3). Ether was added and the resulting yellow precipitate was filtered off and recrystallised from ethanol containing a trace of $HClO_4$ to yield the *perchlorate* (3.93 g, 62%), m.p. 162—163 °C (Found: C, 52.7; H, 4.1; N, 4.7. $C_{13}H_{12}ClNO_5$ requires C, 52.4; H, 4.0; N, 4.7%); $\delta_H(CF_3CO_2H)$ 1.75 (3 H, t, OEt), 4.70 (2 H, q, OEt), 7.30 (1 H, s, 2-H), and 8.6—9.1 (6 H, m).

2-*Chloro*-1-*ethoxycarbonylpyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1e**).—The cyclazinone (**3b**) (0.2 g) (dried *in vacuo* at 100 °C) was heated with phosphoryl chloride (0.5 cm^3) at 90 °C for 10 min. After being cooled, the solution was diluted with ether (10 cm^3) and a few drops of perchloric acid were added. The resulting precipitate was filtered off and recrystallised from ethanol containing a trace of $HClO_4$ to give the *perchlorate* (0.25 g, 84%), pale grey prisms, m.p. 170—171 °C (Found: C, 46.8; H, 3.0; N, 3.7. $C_{14}H_{11}Cl_2NO_6$ requires C, 46.7; H, 3.1; N, 3.9%); $\delta_H[(CD_3)_2SO]$ 1.48 (3 H, t, OEt), 4.59 (2 H, q, OEt), 8.9—9.15 (2 H, m), and 9.3—9.55 (4 H, m).

2-*Bromo*-1-*ethoxycarbonylpyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1f**).—The dry cyclazinone (**3b**) (0.69 g) was heated with phosphoryl bromide (2.6 g) at 110 °C for 1 h and acetic acid (5 cm^3) was added. Dilution with ether yielded a grey solid (1.07 g) which was dissolved in hot acetic acid and treated with 70% perchloric acid (0.5 cm^3) to give the *perchlorate* (0.88 g, 76%) as pale grey needles, m.p. 180—182 °C (from acetic acid) (Found: C, 41.4; H, 2.7; N, 3.4. $C_{14}H_{11}BrClNO_6$ requires C, 41.6; H, 2.7; N, 3.5%), ^1H n.m.r. spectrum as for (**1e**).

1-*Ethoxycarbonylpyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1g**).—The bromo-salt (**1f**) (0.86 g) was hydrogenated at atmospheric pressure in acetic acid (300 cm^3) in the presence of 5% palladium-on-carbon catalyst (0.2 g). Uptake of hydrogen ceased after 3.5 h, at which time the salt was recovered and shown by n.m.r. to contain starting material. Continued hydrogenation in acetic acid (250 cm^3)–water (2 cm^3) over fresh catalyst (0.2 g) ceased after 3 h and the n.m.r. spectrum of recovered salt then showed absence of starting material. Recrystallisation from acetic acid–ethanol gave the *ethoxycarbonylpyrroloquinolizinylium perchlorate* (0.37 g, 54%) as pale grey plates, m.p. 186—187 °C (Found: C, 51.7; H, 3.7; N, 4.2. $C_{14}H_{12}ClNO_6$ requires C, 51.5; H, 3.7; N, 4.3%); $\delta_H[(CD_3)_2SO]$ 1.48, (3 H, t, OEt), 4.58 (2 H, q, OEt), 8.95—9.2 (3 H, m), and 9.25—9.6 (4 H, m).

1-*Ethoxycarbonyl*-2-*methylthiopyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1i**).—A solution of the cyclazinone (**3b**) (2.0 g) in chloroform (150 cm^3) was stirred with phosphorus pentasulphide (3.0 g) at 40 °C. After 20 min, more phosphorus pentasulphide (2.0 g) was added and stirring was continued at 40 °C for 30 min. The resulting deep blue solution, containing cyclazinethione, was decanted from a brown gum and the latter was dissolved in 0.4M-aqueous sodium sulphide (100 cm^3). The aqueous solution was extracted with chloroform (5 × 100 cm^3) and the extract, combined with the original thione solution, was evaporated to a small volume and chromatographed on alumina. Elution with chloroform gave a deep blue eluate which was evaporated to dryness. The residue, dissolved in benzene (300 cm^3), was heated with an excess of methyl iodide at 30—35 °C for 4 h, and the solution (containing a precipitate) was evaporated to 50 cm^3. Ether (100 cm^3) was added and the brown methiodide (2.2 g) was filtered off. Treatment of the methiodide, in hot acetic acid (50 cm^3), with perchloric acid, and precipitation with ether (100 cm^3) gave the *perchlorate* (2.03 g, 82%) as orange-brown needles, m.p. 234—237 °C (from ethanol containing a trace of perchloric acid) (Found: C, 48.6; H, 3.9; N, 3.8. $C_{15}H_{14}ClNO_6S$ requires C, 48.5; H, 3.9; N, 3.8%); $\delta_H(CF_3CO_2H)$ 1.67 (3 H, t, OEt), 3.14 (3 H, s, SMe), 4.79 (2 H, q, OEt), and 8.8—9.45 (6 H, m).

1-*Carboxy*-2-*methylthiopyrrolo*[2,1,5-de]*quinolizinylium Perchlorate*.—The foregoing ester perchlorate (3.9 g) was heated under reflux with 6M-hydrochloric acid (200 cm^3) for 1.25 h and the solution was evaporated to dryness. The residue was dissolved in hot acetic acid (50 cm^3), reprecipitated with ether (150 cm^3), and recrystallised from ethanol containing a trace of perchloric acid to give the *acid perchlorate* (2.8 g, 78%) as yellow needles, m.p. 223—226 °C (Found: C, 45.3; H, 2.9; N, 4.2. $C_{13}H_{10}ClNO_6S$ requires C, 45.4; H, 2.9; N, 4.1%).

1-*Methylthiopyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1h**).—Dry, redistilled *N,N*-dimethylacetamide (200 cm^3) was heated briefly under reflux in a stream of nitrogen and allowed to cool under nitrogen. The foregoing acid perchlorate (3.4 g) and freshly prepared copper(I) oxide (2 g) were added and the solution was heated under nitrogen, with stirring, and held at reflux for 8 min. The solution was filtered and evaporated to dryness, and the residue was recrystallised from ethanol containing a trace of $HClO_4$ to give the *methylthio compound* (1.74 g, 54%) as greenish yellow needles, m.p. 225—227 °C (Found: C, 48.0; H, 3.4; N, 4.9. $C_{12}H_{10}ClNO_4S$ requires C, 48.1; H, 3.3; N, 4.7%); λ_{max} (EtOH–2% $HClO_4$) 226, 300, 319sh, 347sh, and 428nm (log ε 4.66, 3.88, 3.69, 3.50, and 3.79); $\delta_H(CF_3CO_2H)$ 2.92 (3 H, s, SMe), 7.81 (1 H, s, 2-H), and 8.6—9.05 (6 H, m).

Ethyl 3-*Oxo*-3H-*pyrrolo*[2,1,5-de]*quinolizine*-1-*carboxylate* (**9b**).—3-Hydroxyquinolizinylium bromide[5] (4.2 g), ethyl propynoate (2.3 g, 1.5 equiv.), and anhydrous sodium carbonate (4.2 g) were heated under reflux in nitrobenzene (125 cm^3) for 30 *min*. The solution was filtered and evaporated and the residue, in chloroform, was chromatographed on alumina. Elution with chloroform gave the *ester* (3.5 g, 75%) as yellow needles, m.p. 166—167 °C (from ethyl acetate) (Found: C, 69.8; H, 4.6; N, 5.7. $C_{14}H_{11}NO_3$ requires C, 69.7; H, 4.6; N, 5.8%); λ_{max} 252, 269, 302, 314, 318, 329, 392sh, 412, and 434nm (log ε 4.52, 4.59, 3.51, 3.67, 3.68, 3.65, 3.79, 4.09, and 4.14).

3H-*Pyrrolo*[2,1,5-de]*quinolizin*-3-*one* (**9a**).—The ester (**9b**) (1.0 g) was heated under reflux with 6M-aqueous hydrochloric acid (25 cm^3) for 4 h, after which the solution was cooled, neutralised with sodium hydrogen carbonate, and readjusted to pH 4 by the addition of dilute HCl. The resulting yellow precipitate of 3-oxo-3*H*-pyrrolo[2,1,5-*de*]quinolizine-1-carboxylic acid (**9d**) (0.85 g) was filtered off and dried. The acid (0.45 g) was intimately mixed, by grinding in a mortar, with copper(I) oxide (0.45 g) and the mixture was spread thinly over the base of a large cold-finger sublimation apparatus. Heating of the latter for 5 h at 230 °C and 0.05 mmHg caused decarboxylation and the product that collected on the cold finger, after resublimation at 140 °C and 0.05 mmHg, yielded the *pyrroloquinolizinone* (0.3 g, 84%) as deep yellow needles, m.p. 165—167 °C; ν_{max} 1 590 cm^{-1} (C=O); λ_{max} 257, 268sh, 314, 414, and 433 nm (log ε 4.61, 4.43, 3.67, 3.96, and 3.99); $\delta_C(CDCl_3)$ 110.4 (D, C-1), 118.9 (Ddd, C-6), 120.5 (Dd, C-2), 120.8 (Dd, C-8), 123.1 (D, C-7), 128.4 (m), 128.9 (Dd, C-5), 134.5 (D, C-4) 135.8 (m), and 170.8 (d, C-3). For analysis, the highly hygroscopic pyrroloquinolizinone was converted, by treatment with perchloric acid in acetic acid and precipitation with ether, into 3-*hydroxypyrrolo*[2,1,5-de]*quinolizinylium perchlorate* (**1j**), yellow needles, m.p. 270—280 °C, softening and darkening from 250 °C (Found: C, 49.0; H, 3.0; N, 5.2. $C_{11}H_8ClNO_5$ requires C, 49.0; H, 3.0; N, 5.2%).

Dimethyl 3-*Oxo*-3H-*pyrrolo*[2,1,5-de]*quinolizine*-1,2-*dicarboxylate* (**9c**).—3-Hydroxyquinolizinylium bromide[5] (5.0 g), dimethyl butynedioate (4.1 g, 1.5 equiv.), and anhydrous sodium carbonate (5.0 g) were heated under reflux in nitrobenzene (125 cm^3) for 15 min. The solution was filtered and evaporated, and the residue, in ether, was chromatographed on alumina. Elution with chloroform gave the *diester* (2.6 g, 41%) as yellow needles, m.p. 225 °C (from ethyl acetate) (Found: C, 62.9; H, 3.9; N, 5.0. $C_{15}H_{11}NO_5$ requires C, 63.1; H, 3.9; N, 4.9%); $\delta_H(CDCl_3)$ 3.95 (3 H, s, OMe), 4.05 (3 H, s, OMe), 7.20 (1 H, d, 4-H), 7.8 (3 H, m, 5-, 6-, and 7-H), and 8.60 (1 H, dd, 8-H). Hydrolysis of the diester (**9c**), as described for the monoester (**9b**) gave a monocarboxylic acid which, when treated with ethereal diazomethane, yielded *methyl* 3-*oxo*-3H-*pyrrolo*[2,1,5-de]-*quinolizine*-1-*carboxylate* (**9e**), m.p. 206—207 °C (Found: C, 68.6; H, 4.0; N, 6.2. $C_{13}H_9NO_3$ requires C, 68.7; H, 4.0; N, 6.2%); $\delta_C(CDCl_3)$ 51.6 (Q, Me), 112.4 (s, C-1), 119.1 (Dddd, C-6), 121.5 (Ddd, C-8), 122.0 (D, C-2), 125.4 (D, C-7), 126.9 (dd), 128.6 (m), 130.2 (Dd, C-5), 134.6 (D, C-4), 135.0 (m), 163.9 (m, ester C=O), and 172.5 (d, C-3), identical with the methyl ester of the acid (**9d**) obtained from (**9b**).

3-*Halogenopyrrolo*[2,1,5-de]*quinolizinylium Perchlorates* (**1k**) *and* (**1m**).—(*a*) The cyclazinone (**9a**) (0.45 g) was heated with phosphoryl chloride (2 cm^3) at 90 °C for 20 min. The solution was then diluted with hot acetic acid (20 cm^3), treated with a slight excess of perchloric acid, cooled, and diluted with ether. The resulting precipitate was filtered off and recrystallised from acetic acid containing a trace of perchloric acid to give 3-*chloropyrrolo*[2,1,5-de]*quinolizinylium perchlorate* (**1k**) (0.55 g, 91%) as needles, m.p. 244—246 °C (Found: C, 45.85; H, 2.5; N, 4.7. $C_{11}H_7Cl_2NO_4$ requires C, 45.8; H, 2.4; N, 4.8%); δ [360 MHz; $(CD_3)_2SO$] 8.62 (2 H, AB, 1- and 2-H), 8.98 (1 H, t, 7-H), 9.08 (1 H, d, 4-H), and 9.27—9.31 (3 H, m, 5-, 6-, and 8-H).

(*b*) Treatment of the cyclazinone (**9a**) (0.8 g) with phosphoryl bromide (1.6 g) at 100 °C for 1 h, and work-up as in (*a*) gave 3-*bromopyrrolo*[2,1,5-de]*quinolizinylium perchlorate* (**1m**) (1.1 g, 70%) as needles, m.p. 237—240 °C (Found: C, 39.7; H, 2.1; N, 4.2. $C_{11}H_7BrClNO_4$ requires C, 39.7; H, 2.1; N, 4.2%).

Pyrrolo[2,1,5-de]*quinolizinylium Perchlorate* (**1a**).—(*a*) W-2 Raney nickel (*ca.* 2 g), which had been kept under ethanol for not more than 4 days at −5 °C, was heated under reflux in acetone for 1 h. After decantation of acetone, the nickel was washed three times with ethanol by decantation and left under ethanol (50 cm^3). The 1-methylthiopyrroloquinolizinylium salt (**1h**) (0.2 g) was added and the solution was stirred and heated under reflux until the initial yellow-green colour changed to pale green or grey (10—15 min). A few drops of perchloric acid were added, the warm solution was filtered, and the residual nickel was washed with acetone. The filtrate and washings were evaporated and the recovered salt was recrystallised from acetic acid to yield *pyrrolo*[2,1,5-de]*quinolizinylium perchlorate* (0.091 g, 52%) as needles, m.p. 284—285 °C (Found: C, 51.9; H, 3.1; N, 5.5. $C_{11}H_8ClNO_4$ requires C, 52.1; N, 3.2; N, 5.5%); λ_{max} 229, 269, 282sh, 295, and 332 nm (log ε 4.81, 3.89, 3.74, 3.58, and 3.79).

(*b*) The 3-bromopyrroloquinolizinylium salt (**1m**) (0.3 g) was hydrogenated at atmospheric pressure in 50% aqueous acetic acid (50 cm^3) in the presence of 10% palladium on carbon catalyst (0.03 g). After 1 equiv. of H_2 (20.5 cm^3) had been absorbed, the catalyst was filtered off, the filtrate was evaporated, and the residue was recrystallised from acetic acid to yield the perchlorate (**1a**) (0.17 g, 74%), m.p. 283—285 °C, i.r. and ^1H n.m.r. spectra identical with those of the specimen prepared by method (*a*).

Hydrogenation of Acenaphthylene in the Presence of Pyrrolo[2,1,5-de]*quinolizinylium Perchlorate*.—A solution of acenaphthylene (0.15 g, 1 mmol) and the salt (**1a**) (0.23 g, 0.9 mmol) in acetic acid (45 cm^3)–water (5 cm^3) was hydrogenated at atmospheric pressure in the presence of 5% palladium on carbon catalyst (0.015 g). Uptake of hydrogen ceased after 3 h when 22 cm^3 of H_2 had been absorbed. The solution was filtered and evaporated, and the residue was extracted with ether (100 cm^3)–methanol (3 cm^3) to yield the salt (**1a**) (0.215 g, 93%) as an insoluble residue (i.r. and n.m.r. spectra identical with those of the starting material). The ethereal solution was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to yield acenaphthene (0.13 g, 85%), m.p. 94—95 °C (lit., m.p. 96 °C), i.r. spectrum identical with that of an authentic specimen.

Diels–Alder Reaction of Acenaphthylene with 1,3-*Diphenylisobenzofuran*.—A solution of acenaphthylene (0.12 g, 0.8 mmol) in benzonitrile (15 cm^3) was deoxygenated by heating at reflux under nitrogen for 15 min. The solution was cooled, 1,3-diphenylisobenzofuran (0.23 g, 0.85 mmol) was added, and heating was resumed, at 140 °C for 7 h under nitrogen and with exclusion of bright light. The solution was evaporated and the residual gum was triturated with ether to yield a buff solid. Recrystallisation from ethanol yielded the adduct (0.21 g, 60%) as yellow needles, m.p. 205—207 °C (lit.,[16] m.p. 208 °C).

Attempted Reaction of Pyrrolo[2,1,5-de]*quinolizinylium Perchlorate* (**1a**) *with* 1,3-*Diphenylisobenzofuran*.—The salt (**1a**) (0.30 g, 1.2 mmol) and the furan (0.32 g, 1.2 mmol) were heated at 140 °C in benzonitrile (25 cm^3) under the conditions described for the foregoing experiment. After 7 h, the solution was cooled and diluted with ether and the resulting precipitate

was filtered off, washed with ether, and dried to yield the salt (**1a**) (0.28 g, 93% recovery), m.p. and i.r. spectrum identical with those of the starting material. The filtrate was evaporated and the residue was chromatographed on alumina to yield 1,3-diphenylisobenzofuran (0.25 g, 78% recovery). Immobile dark material remained on the column.

Reaction of Pyrrolo[2,1,5-de]*quinolizinylium Perchlorate with Sodium Sulphide.*—(*a*) The salt (**1a**) (0.21 g) in *N,N*-dimethylformamide (15 cm^3) was treated with a solution of sodium sulphide nonahydrate (1 g) in water (15 cm^3). The solution was stirred for 90 min, diluted with water (150 cm^3), and extracted with chloroform (3 × 100 cm^3). The extract was washed with water, dried, evaporated to 10 cm^3, and applied to a column of alumina. Elution with chloroform, collection of a deep purple eluate, and evaporation of the latter yielded the crude thione (0.1 g, 65%) as a dark purple solid. The thione and an excess of methyl iodide were allowed to react in chloroform (25 cm^3) at room temperature for 16 h and the resulting yellow solution was evaporated. The solid residue was dissolved in acetic acid and treated with a slight excess of perchloric acid. Dilution with ether gave 3-*methylthiopyrrolo*[2,1,5-de]*quinolizinylium perchlorate* (**1n**) (0.11 g, 44%) as yellow needles, m.p. 204—206 °C (from acetic acid) (Found: C, 48.3; H, 3.3; N, 4.7. $C_{12}H_{10}ClNO_4S$ requires C, 48.1; H, 3.3; N, 4.7%) δ_H[360 MHz; $(CD_3)_2CO$] 3.12 (3 H, s, SMe), 8.49 (1 H, d, *J* 5.6 Hz, 1-H), 8.56 (1 H, d, *J* 5.6 Hz, 2-H), 8.90 (1 H, dd, 7-H), 8.96 (1 H, d, 4-H), and 9.20—9.24 (3 H, m, 5-, 6-, and 8-H).

The same compound (73%) was obtained, under identical conditions, from the 3-chloropyrroloquinolizinylium salt (**1k**).

(*b*) The salt (**1a**) (0.22 g) in *N,N*-dimethylformamide (10 cm^3) was treated with a solution of sodium sulphide nonahydrate (1 g) in water (2 cm^3). The solution was stirred for 2 h, diluted with water (100 cm^3), and extracted with dichloromethane (3 × 50 cm^3). The extract was dried and exposed to strong daylight in air until its purple colour had changed to yellow. Evaporation of the solution and p.l.c. of the residue on alumina in ethyl acetate–ethanol (100 : 7) gave two yellow bands, the recovered materials from which were sublimed at 120—140 °C and 0.1 mmHg to yield (i) 5H-*pyrrolo*[2,1,5-de]*quinolizin-5-one* (**16a**) (0.0019 g) as a deep yellow solid, m.p. 180—182 °C (Found: M^+, 169.0527. $C_{11}H_7NO$ requires *M*, 169.0528); λ_{max} 212, 232, 279, 297, 356, 451sh, 468sh, and 475 nm (log ε 4.09, 4.07, 3.76, 3.76, 3.30, 3.72, 3.82, and 3.83), and (ii) 3*H*-pyrrolo[2,1,5-*de*]-quinolizin-3-one (**9a**) (0.0033 g), m.p. 164—167 °C, ^1H n.m.r. spectrum identical with that of the specimen described previously.

Reaction of Pyrrolo[2,1,5-de]*quinolizinylium Perchlorate* (**1a**) *with Hydroxide Ion.*—The procedure was adapted from that of Fargher and Furness.[18]

Solutions of (i) the salt (**1a**) (0.25 g, 1 mmol) in water (50 cm^3) and (ii) potassium hydroxide (0.13 g, 2.3 mmol) in water (10 cm^3) were added dropwise and simultaneously to a cooled (0 °C), stirred solution of potassium ferricyanide (0.52 g, 2.0 mmol) in water (10 cm^3). Stirring was continued for a further 1 h after which the solution was filtered and the filtrate extracted continuously with chloroform for 12 h. The extract was dried, evaporated to a small volume, and applied to a column of alumina. Elution with chloroform yielded 3*H*-pyrrolo[2,1,5-*de*]quinolizin-3-one (0.01 g, 6%), i.r. spectrum identical with that of the specimen obtained previously. A similar yield of the same product was obtained in the absence of ferricyanide.

3H-*Pyrrolo*[2,1,5-de]*quinolizin*-3-*ylidenepropanedinitrile* (**17a**).—A solution of malononitrile (0.1 g, 1.5 mmol) in *N,N*-dimethylformamide (25 cm^3) was treated with dry, freshly prepared sodium ethoxide (0.1 g, 1.5 mmol) and, when the ethoxide had dissolved, the salt (**1a**) (0.25 g, 1.0 mmol) was added. After 18 h, the solution was diluted with water (150 cm^3) and extracted several times with ether. The extract was washed with water, dried, and evaporated, and the residue was chromatographed on alumina. Elution with chloroform and vacuum sublimation of the recovered purple material yielded the *dinitrile* (0.18 g, 84%) as a red–purple solid, subliming at 190—200 °C (Found: C, 77.2; H, 3.2; N, 19.0. $C_{14}H_{11}N_3$ requires C, 77.4; H, 3.2; N, 19.3%), identical in all respects with the compound obtained by reaction of the 3-chloro salt (**1k**) with sodiomalononitrile.

Ethyl 3H-*Pyrrolo*[2,1,5-de]*quinolizin*-3-*ylidenecyanoacetate* (**17b**).—Repetition of the foregoing reaction with ethyl cyanoacetate in place of malononitrile yielded the cyanoacetate (81%) as a red–purple solid, m.p. 153—155 °C (Found: C, 72.45; H, 4.6; N, 10.6. $C_{16}H_{12}N_2O_2$ requires C, 72.7; H, 4.6; N, 10.6%), identical in all respects with a specimen prepared from the 3-chloro-salt (**1k**).

Reaction of 1-*Methoxypyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1c**) *with Sodium Sulphide.*—(*a*) The salt (**1c**) (0.9 g) in *N,N*-dimethylformamide (50 cm^3) was treated with an excess of aqueous sodium sulphide. The solution was stirred for 24 h, diluted with water, and extracted with chloroform (×3). The extract was washed with water, dried, and evaporated, and the residue was chromatographed on alumina. Elution with dichloromethane gave a red-purple eluate which upon evaporation yielded a red-purple solid (0.21 g, 32%), homogeneous by t.l.c. but believed to be a mixture of 2-methoxy-5*H*-pyrrolo[2,1,5-*de*]quinolizine-5-thione (**19**) (*ca.* 5 parts) and 1-methoxy-3*H*-pyrrolo[2,1,5-*de*]quinolizine-3-thione (**20**) (*ca.* 1 part); $\delta_H(CDCl_3)$ 4.11 (s, OMe), 6.56 [s, 1-H (**19**)], 7.50 [s, 2-H (**20**)], 7.62 [d, 4-H (**20**)], 7.73 [d, 3-H (**19**)], 7.7—8.05 [m, 7- and 8-H (**19**) and 6-, 7-, and 8-H (**20**)], 8.20 [d, 5-H (**20**)], 8.26 [d, 3-H (**19**)], and 9.02 [dd, 6-H (**19**)]. Recrystallisation of the mixed thiones from cyclohexane–ethanol yielded red–purple prisms, m.p. 157—160 °C (Found: C, 67.2; H, 4.2; N, 6.6. $C_{12}H_9NOS$ requires C, 66.9; H, 4.2; N, 6.5%).

(*b*) The salt (**1c**) (0.07 g) was treated with sodium sulphide, as in (*a*), and the resulting thiones were extracted into dichloromethane. The extract was dried and exposed to strong daylight in air until its purple colour had changed to yellow. Evaporation of the solution and p.l.c. of the residue on alumina in ethyl acetate–ethanol (10:1) gave two yellow bands, the recovered materials from which were sublimed at 120—140 °C and 0.1 mmHg to yield (i) 2-*methoxy*-5H-*pyrrolo*[2,1,5-de]*quinolizin-5-one* (**16c**) (0.0027 g), yellow needles, m.p. 186—187 °C (Found: M^+, 199.0633. $C_{12}H_9NO_2$ requires *M*, 199.0633) and (ii) 1-*methoxy*-3H-*pyrrolo*[2,1,5-de]*quinolizin*-3-*one* (**9f**) (0.0012 g), orange needles, m.p. 173—174 °C (Found: M^+, 199.0635).

Reaction of 1-*Ethoxycarbonylpyrrolo*[2,1,5-de]*quinolizinylium Perchlorate* (**1g**) *with Sodium Sulphide.*—The salt (**1g**) (0.34 g) in *N,N*-dimethylformamide (20 cm^3) was treated with a solution of sodium sulphide nonahydrate (1 g) in water (2 cm^3). The solution was stirred for 3.75 h, diluted with water (100 cm^3), and extracted with dichloromethane (×4). The extract was dried and exposed to strong daylight in air until its blue colour had changed to yellow–brown. Evaporation of the solution and p.l.c. of the residue on silica in ethyl acetate gave two main bands, the recovered materials from which were sublimed at 180 °C and 0.01 mmHg to yield (i) *ethyl* 5-*oxo*-5H-*pyrrolo*[2,1,5-de]*quinolizine*-1-*carboxylate* (**16b**) (0.004 g) as orange–yellow needles, m.p. 167—168 °C (from ethyl acetate) (Found: C, 69.6; H, 4.55; N, 5.65. $C_{14}H_{11}NO_3$ requires C, 69.7; H, 4.6; N, 5.8%); λ_{max} 225, 240, 280, 296sh, 341sh, 353, 442, and 470 nm (log ε 4.26, 4.28, 4.37, 4.19, 3.48, 3.55, 4.14, and 4.45), and (ii) the

corresponding 3-oxo-3*H*-compound (**9b**) (0.002 g), m.p. 166—167 °C, ^{1}H n.m.r. spectrum identical with that of the specimen described previously.

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