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Quinolizines. Part XIII.[1] Rearrangement of Quinolizinium-1-diazonium Salts into *v*-Triazolo[1,5-*a*]pyridines

By **L. S. Davies** and **Gurnos Jones,*** Department of Chemistry, University of Keele, Keele, Staffordshire ST5 5BG

A number of 1-aminoquinolizinium salts undergo rearrangement when treated with aqueous nitrous acid to give first the *cis*-3-(*v*-triazolo[1,5-*a*]-pyridyl)acraldehydes; these are readily isomerized to the *trans*-isomers. The structure of one pair of isomers has been established by oxidation to 3-formyl-*v*-triazolo[1,5-*a*]pyridine (12) which has been synthesized. The n.m.r. spectra of the triazolopyridines, and the mechanism of the rearrangement are discussed.

We have reported in previous parts [1-3] of this series on the properties of aminoquinolizinium salts. We have noted that 1-aminoquinolizinium salts (other than those bearing active methyl groups) react with aqueous nitrous acid to give neutral, apparently nonionic compounds to which we tentatively assigned structures such as (1), assuming initial *C*-nitrosation with subsequent cyclization. As we have briefly described,[4] these compounds are the products of a rearrangement are triazolopyridines. Evidence for this rearrangement and further examples are given in this paper.

Most of the exploratory work which has been on the rearrangement has used 1-amino-3-methylquinolizinium salts (2), which are most readily available. It had been noted [1] that treatment of the amine (2) with sodium nitrite in a weakly acidic solution gave a product, $C_{10}H_9N_3O$, which was rapidly converted by traces of acid (or base) into a higher melting, more-stable isomer. A re-examination of the original reaction [2] in which 1-aminoquinolizinium chlorides (3; X = Cl) had been used, showed that, in this case also, an initial product was isomerized to a more-stable isomer (which was the only isolated material under the original strongly acid conditions). The evidence below shows these isomers to be the *cis*-[compounds (4) and (5)] and *trans*-[compounds (6) and (7)] isomers of 3-(*v*-triazolo[1,5-*a*]pyridyl)-acraldehydes.

[1] Part XII, T. L. Hough and G. Jones, *J. Chem. Soc.* (*C*), 1968, 1088.
[2] A. R. Collicutt and G. Jones, *J. Chem. Soc.*, 1960, 4101.
[3] A. Fozard and G. Jones, *J. Chem. Soc.*, 1964, 2763.
[4] L. S. Davies and G. Jones, *Tetrahedron Letters*, 1969, 1549.

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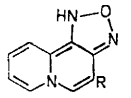
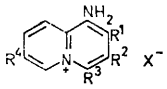
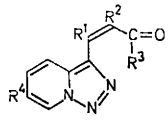


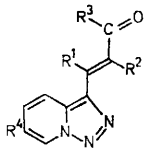
(1)



(2) $R^1 = R^3 = R^4 = H$, $R^2 = Me$
(3) $R^1 = R^2 = R^3 = R^4 = H$
(16) $R^1 = Br$, $R^2 = Me$, $R^3 = R^4 = H$
(19) $R^1 = R^3 = Br$, $R^2 = Me$, $R^4 = H$
(20) $R^1 = R^3 = D$, $R^2 = Me$, $R^4 = H$
(23) $R^1 = R^4 = H$, $R^2 = Me$, $R^3 = CO_2Et$
(28) $R^1 = R^3 = H$, $R^2 = R^4 = Me$



(4) $R^1 = R^2 = R^3 = R^4 = H$
(5) $R^1 = R^3 = R^4 = H$, $R^2 = Me$
(17) $R^1 = Br$, $R^2 = Me$, $R^3 = R^4 = H$
(21) $R^1 = R^3 = D$, $R^2 = Me$, $R^4 = H$
(26) $R^1 = R^4 = H$, $R^2 = Me$, $R^3 = CO_2Et$
(2b) $R^1 = R^3 = H$, $R^2 = R^4 = Me$

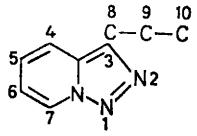


(6) $R^1 = R^2 = R^3 = R^4 = H$
(7) $R^1 = R^3 = R^4 = H$, $R^2 = Me$
(18) $R^1 = Br$, $R^2 = Me$, $R^3 = R^4 = H$
(22) $R^1 = R^3 = D$, $R^2 = Me$, $R^4 = H$
(27) $R^1 = R^4 = H$, $R^2 = Me$, $R^3 = CO_2Et$
(30) $R^1 = R^3 = H$, $R^2 = R^4 = Me$

The first evidence that the structures (1) were inadequate came from the mass spectra of compounds (5) and (7) which were identical. The major fragmentation showed loss of 28 units followed by 29 units (the detailed mass spectra will be discussed in a subsequent paper) and these have been shown to correspond to loss of N_2, CO, N_2H, and CHO. The 100 MHz n.m.r. spectra of compounds (4) and (5) showed a downfield 1H signal at δ 10·98 (d) and 10·9 (s) p.p.m.; in the corresponding *trans*-isomers (6) and (7) these were at δ 9·7 (d) and 9·6 p.p.m. (s) respectively. Spin-decoupling experiments on the parent compounds (4) and (6) revealed the sequence $\overset{\beta}{C}H=\overset{\alpha}{C}H-CH=O$ and the coupling constants $J_{\alpha,\beta}$ were 12 Hz in the *cis*- and 16 Hz in the *trans*-forms. The differing chemical shifts of the aldehyde proton in *cis*- and *trans*-forms is further discussed below.

The presence of the aldehyde function in compounds (5) and (7) was confirmed by borohydride reduction to give isomeric primary alcohols (8) and (9); acetylation gave acetates (10) and (11). The n.m.r. spectra of the alcohols (8) and (9) were more closely similar than those of the aldehydes (5) and (7), the major difference in the former being in the half width of the OH signal, [much larger in the *cis*-alcohol (8) than in the *trans*-alcohol (9)]. This indication of intramolecular hydrogen bonding in alcohol (8) was confirmed by an i.r. absorption at 3370 $cm.^{-1}$ (a plot of extinction coefficient against molar concentration gives a non-zero intercept when extrapolated to zero concentration [5]). Oxidation of the aldehydes (5) or (7) [or in better yield of the alcohols (8) and (9)] with periodate–permanganate [6] gave, in all cases, a crystalline formyl derivative (aldehyde absorption at δ 10·7 p.p.m.), identified as 3-formyl-*v*-triazolo[1,5-*a*]-pyridine (12). A poor yield of the same aldehyde was obtained by a Vilsmeier–Haack reaction on the parent *v*-triazolo[1,5-*a*]-pyridine (13); the specimens had identical melting points and spectra. An attempt to synthesize the acrolein (6) by an aldol condensation between

N.m.r. details of *v*-Triazolo[1,5-*a*]pyridines *



	Chemical shifts								
Cpd.	4-H	5-H	6-H	7-H	8-H	b-H	10-H	Other resonances	Coupling constants (in Hz)
(4)	7·78d	6·9—7·6		8·73d	6·9—7·6	6·12q	10·98d		$J_{4,5}$ 9; $J_{6,7}$ 8; $J_{8,9}$ 12; $J_{9,10}$ 7·5
(5)	7·78q	6·9—7·5		8·75d	6·9—7·5		10·9s	2·05s (Me)	$J_{4,5}$ 9, $J_{4,6}$ 1; $J_{6,7}$ 6; J_{8,CH_3} 1
(6)	7·78d	6·9—7·6		8·78d	6·9—7·6	6·99q	9·7d		$J_{4,5}$ 9; $J_{6,7}$ 7; $J_{8,9}$ 16; $J_{9,10}$ 7·5
(7)	7·78d	6·9—7·5		8·75d	6·9—7·5		9·6s	2·45s (Me)	$J_{4,5}$ 9; $J_{6,7}$ 6
(8)	7·84d	6·9—7·6		8·8d	6·58s		4·5d	4·8—5·4 (OH), 2·15d (Me)	$J_{4,5}$ 9; $J_{6,7}$ 8; J_{8,CH_3} 1·5
(9)	7·84d	6·9—7·6		8·8d	6·78		4·38s	3·48br,s (OH), 2·25s (Me)	$J_{4,5}$ 9; $J_{6,7}$ 8
(10)	7·9d	7·5m	7·2m	8·95d	6·7m		5·6s	2·1s, 2·25s (Me, Ac_3)	$J_{4,5}$ 9; $J_{6,7}$ 8
(11)	7·9d	7·5m	7·2m	8·95d	6·83m		4·95s	2·22s, 2·38s (Me, Ac_3)	$J_{4,5}$ 9; $J_{6,7}$ 8
(12)	8·65q	8·0m	7·58m	9·25d	10·7s				$J_{4,5}$ 8·5; $J_{4,6}$ 1; $J_{6,7}$ 6·5
(13)	7·95	7·45	7·17	9·0				8·3s (3-H)	$J_{4,5}$ 8·5; $J_{4,6}$ 1; $J_{6,7}$ 6·5
(14)	2·6—3·0	1·7—2·4m		4·5t	2·6—3·0	1·7—2·4	3·62d	4·3s (OH), 0·95s (Me)	$J_{9,10}$ 6; J_{9,CH_3} 6
(17)	8·04d	7·49t	7·13t	8·8d			9·67s	2·2s (Me)	$J_{4,5}$ 8; $J_{6,7}$ 6
(18)	8·04d	7·49t	7·13t	8·8d			9·9s	2·19s (Me)	$J_{4,5}$ 8; $J_{6,7}$ 6
(21)	7·8d	7·42t	7·07m	8·76d				2·05s (Me)	$J_{4,5}$ 9; $J_{6,7}$ 6
(22)	7·8d	7·42t	7·07m	8·76d				2·45s (Me)	$J_{4,5}$ 9; $J_{6,7}$ 6
(26)	7·75d	6·9—7·5m		8·63d	6·9—7·5			2·2d (Me), 4·13q (OCH_2), 1·23t (CH_2CH_3)	$J_{4,5}$ 9; $J_{6,7}$ 7
(27)	7·78d	6·9—7·5		8·75d	6·9—7·5			2·5s (Me), 4·42q (OCH_2), 1·4t (CH_2CH_3)	$J_{4,5}$ 9; $J_{6,7}$ 7
(29)	7·68d	7—7·5m		8·5s	7—7·5m		10·8s	2·4s (6-Me), 2·0s (9-Me)	$J_{4,5}$ 9
(30)	7·75d	7·1—7·5m		8·5s	7·1—7·5m		9·56s	2·4s (6-Me), 2·45s (9-Me)	$J_{4,5}$ 9

* All determined in $CDCl_3$. Values given are δ (p.p.m. from Me_4Si).

[5] M. Tichy, *Adv. Org. Chem.*, 1965, **5**, 121.
[6] J. H. Boyer and L. T. Wolford, *J. Amer. Chem. Soc.*, 1958, **80**, 2741.

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the 3-formyltriazolopyridine (12) and acetaldehyde was unsuccessful.

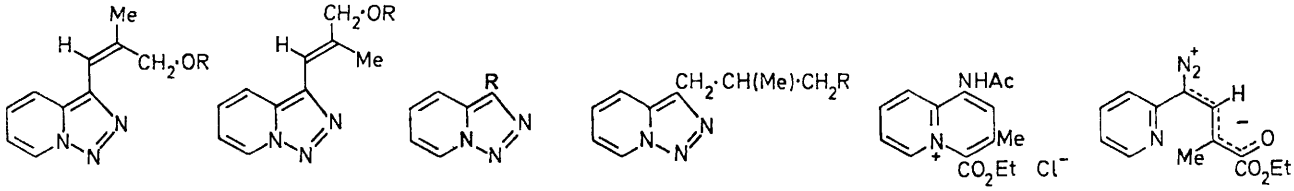
Catalytic reduction with palladium–charcoal of the aldehydes (5) or (7) was slow and gave mixtures. With Adams catalyst in glacial acetic acid at room temperature, or more easily by reduction of either alcohol (8) or (9) a primary alcohol was isolated. The u.v. absorption of the product ($\lambda_{max.}$ 225 nm.) showed the presence of a simple *v*-triazole and the structure was confirmed as (14) by n.m.r. spectroscopy (see Table). More violent reduction gave mixtures; the n.m.r. spectra indicated the presence of the deoxygenated material (15).

In an examination of the generality of the rearrangement we examined the reaction between other 1-aminoquinolizinium salts and aqueous nitrous acid. The 2-bromo-3-methyl derivative (16) [1] reacted in 2N-hydrochloric acid to give a mixture of *cis*- (17) and *trans*- (18) aldehydes. In nearly neutral medium almost pure *cis*-aldehyde (17) could be obtained; the *cis–trans* isomerization proved surprisingly difficult, requiring hot glacial acetic acid (1 hr. at 100°) to form the *trans*-aldehyde (18) (it is noteworthy that the parent *v*-triazolo[1,5-*a*]-pyridine (13) is decomposed under these conditions with loss of nitrogen [6]). The difficulty of isomerization we attribute to the nonplanarity of the side-chain and the triazolopyridine ring, discussed below. By contrast the 2,4-dibromo-derivative (19) failed to give either the triazolopyridine acrylic acid or the corresponding acid bromide when treated with aqueous nitrous acid.

Prolonged treatment of 1-amino-3-methylquinolizinium chloride (2) with D_2SO_4 at 150° led to replacement of the 2-H by D, and an 80% replacement of the 4-H by D; further heating resulted in replacement of the methyl H by D. By nitrous acid treatment of the predominantly 2,4-deuterioquinolizinium salt (20) a *cis*-aldehyde (21) and a *trans*-aldehyde (22) were obtained. In both retention of the deuterium appeared complete (estimated by n.m.r. and by mass spectral measurements) indicating that at no stage of the rearrangement are these atoms exchangeable with the aqueous solvent. Also of interest from the point of view of the mechanism proposed below, was the reaction of 1-amino-4-ethoxycarbonyl-3-methylquinolizinium chloride (23) [prepared by hydrolysis of the corresponding *N*-acetyl derivative (24) [1]] with nitrous acid. The crude product was a mixture showing a sharp absorption maximum at 2270 cm.$^{-1}$ which corresponds to that expected for the intermediate diazo-derivative (25). Recrystallization from methanol gave the pure *cis*-keto-ester (26), again easily isomerized to the *trans*-keto-ester (27). This increased stability of the intermediate monocyclic compound (25) (a vinylogous diazo-ketone) is in accord with the known greater stability of diazo-ketones over diazo-aldehydes. Finally, the dimethyl-1-aminoquinolizinium salt (28) was converted into the *cis*- (29) and the *trans*- (30) aldehydes.

N.m.r. Spectra.—The spectra are recorded in the Table. Generally, it is possible to distinguish the doublets due to the 4- and 7- protons (the latter being further downfield) and to derive $J_{4,5}$ and $J_{6,7}$; these are consistently in the region of 9 and 6—8 Hz respectively (very similar to those of indolizine [7]). The most interesting points of the side-chain absorptions are the downfield shifts shown by the *cis*-aldehyde in compounds (4), (5), and (29) relative to those of the *trans*-aldehydes (6), (7), and (30). These we attribute to the nitrogen lone-pair (N-2) and it is significant that the sole exception is the bromo-aldehyde (17); here a peri-interaction between bromine and the 4-H causes the side-chain to move out of the plane of the aromatic ring and hence removes the aldehyde from the vicinity of the nitrogen at the 2-position. This hypothesis is confirmed by the change in u.v. absorption of aldehydes (17) and (18) relative to the other examples (a hypsochromic shift) and by the considerably increased barrier to *cis–trans* isomerism mentioned above. The same effect is observed in the methylene protons of the acetates (10) and (11) although not in the alcohols (8) and (9). This is understandable since the *cis*-alcohol (8) is strongly hydrogen bonded to N-2 and hence the methylene protons are held away from the lone-pair—an effect which is lost on acetylation. A similar, but smaller, effect is shown by the methyl groups of the *trans*-aldehydes (7) and (30) which absorb approximately 0·4 p.p.m. downfield of the equivalent *cis*-aldehydes (5) and (29).

Mechanism.—The mechanism of the rearrangement is straightforward and must be similar to that by which 1-alkyl- or 1-aryl-3-aminopyridinium salts are converted into *v*-triazoles.[8,9] We suggest that initial diazotization leads to highly electron-deficient centres at C-2 and C-4 in the quinolizinium ring. Quinolizinium salts without additional activation can be attacked by nucleophiles



(8) R = H
(10) R = Ac

(9) R = H
(11) R = Ac

(12) R = CHO
(13) R = H

(14) R = OH
(15) R = H

(24)

(25)

[7] R. M. Acheson and D. A. Robinson, *J. Chem. Soc.* (*C*), 1968, 1633.

[8] W. König, M. Coenen, W. Lorenz, F. Bahr, and A. Bassl, *J. prakt. Chem.*, 1965, [4] **30**, 96.

[9] W. König, M. Coenen, F. Bahr, B. May, and A. Bassl, *J. prakt. Chem.*, 1966, [4] **33**, 54.

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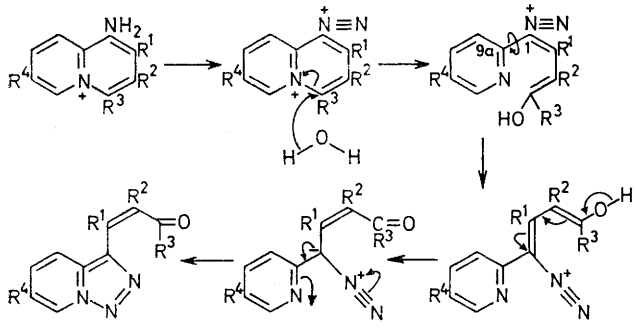
with ring opening (hydride,[10] Grignard reagents,[11] and even amines [12]); with the additional electron withdrawal due to the diazonium group, attack by solvent water at the 4-position leads to ring opening as shown in the Scheme. The most interesting point is that rotation around the C(1)–C(9a) bond occurs with retention of configuration since the *cis*-aldehyde is always obtained first under conditions which do not promote *cis–trans* isomerization. Evidence for an intermediate diazo-derivative was provided in the case of the amino-ester (23) as described. There is ample evidence for the cyclization stage in the work of Regitz.[13] All attempts to obtain the intermediate diazonium salt from compound (2) under nonaqueous conditions have been unsuccessful, although we were able to obtain the phenol (the 'normal' diazotization product) from the original 1-aminoquinolizinium salt (3).[2]



SCHEME

EXPERIMENTAL

All m.p.s were determined on a Kofler hot-stage and are uncorrected. N.m.r. spectra were determined on a Perkin-Elmer R10 60 MHz or a Varian 100 MHz spectrometer. I.r. spectra were determined a Perkin-Elmer 257 spectrometer (dilution experiments were performed with a Unicam SP 700 spectrometer). U.v. spectra were determined on a Unicam SP 800 spectrometer.

General Procedure for Diazotization of 1-*Aminoquinolizinium Salts*.—An excess of saturated aqueous sodium nitrite was added to a solution of 1-aminoquinolizinium chloride [2] (0·269 g.) in water (5 ml.) at −5°; on addition of two drops of N-hydrochloric acid a precipitate formed. Filtration gave *cis*-3-(3-*v-triazolo*[1,5-a]*pyridyl*)*acraldehyde* (4) (0·111 g., 43%), which recrystallized from 95% ethanol as needles, m.p. 162—163° (Found: C, 62·5; H, 3·75; N, 24·5. $C_9H_7N_3O$ requires C, 62·3; H, 4·1; N, 24·5%); $\nu_{max.}$ ($CHCl_3$) 1672 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 285, 350sh nm. [log ε 3·79, (−)].

cis-2-*Methyl*-3-(3-v-*triazolo*[1,5-a]*pyridyl*)*acraldehyde* (5).—This preparation is described in ref. 1; $\nu_{max.}$ ($CHCl_3$) 1672 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 224, 343 nm. ($\log_{10}$ ε 4·01, 4·19).

trans-3-(3-v-*Triazolo*[1,5-a]*pyridylacraldehyde* (6).—This was prepared both as described in ref. 2, and also by keeping a solution of the *cis*-acraldehyde (4) with piperidine in ethanol or chloroform for 1 hr. at room temperature; $\nu_{max.}$ (Nujol) 1666 cm.$^{-1}$; $\lambda_{max.}$ (H_2O) 345 nm. (log ε 4·25).

trans 2-*Methyl*-3-(3-v-*triazolo*[1,5-a]*pyridyl*)*acraldehyde* (7).—This was prepared as described in ref. 1; $\nu_{max.}$ ($CHCl_3$) 1669 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 224, 314sh, 336 nm. (log ε 3·98, (−), 4·18).

cis-2-*Methyl*-3-(3-v-*triazolo*[1,5-a]*pyridyl*)*allyl Alcohol* (8).—Sodium borohydride (0·11 g.) was added to an ethanolic solution of the *cis*-acraldehyde (5) (0·55 g.); after 3 hr. at room temperature the mixture was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was treated with dilute hydrochloric acid (20 ml.) and then extracted several times with chloroform. The chloroform extracts were dried (Na_2SO_4) and evaporated to dryness to give the *alcohol* (8) (0·449 g., 81%) which crystallized from aqueous ethanol as prisms, m.p. 113—114° (Found: C, 63·7; H, 6·15; N, 22·3. $C_{10}H_{11}N_3O$ requires C, 63·5; H, 5·85; N, 22·2%); $\nu_{max.}$ ($CHCl_3$) 3370; $\lambda_{max.}$ (EtOH) 224, 262, 293, 320sh nm. [log ε 4·23, 4·10, 3·97, (−)]. The acetyl derivative (10), prepared by action of acetic anhydride (3 hr., 100°) was a yellow *oil* (80%), b.p. 200—205°/0·4 mm. which solidified when cool, and crystallized from ether, m.p. 54—55° (Found: C, 62·4; H, 5·45; N, 18·1. $C_{12}H_{13}N_3O_2$ requires C, 62·3; H, 5·6; N, 18·2%); $\nu_{max.}$ ($CHCl_3$) 1735 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 221, 255sh, 264, 273sh, 292, 323sh nm. [log ε 4·24, (−), 4·08, (−), 3·95, (−)].

trans-2-*Methyl*-3-(3-*triazolo*[1,5-a]*pyridyl*)*allyl Alcohol* (9).—(*a*) This was prepared from the *trans*-acraldehyde (7) as described above, in 86% yield. The *alcohol* (9) crystallized from aqueous ethanol as needles, m.p. 130—131° (Found: C, 63·7; H, 5·8; N, 22·2. $C_{10}H_{11}N_3O$ requires C, 63·5; H, 5·8; N, 22·2%); $\nu_{max.}$ (Nujol) 3350; $\lambda_{max.}$ (EtOH) 224, 252sh, 259, 269, 293 nm. (log ε 4·22, 4·07, 4·08, 3·99, 3·92). The *acetyl* derivative (11), obtained in 69% yield as described for the *cis*-derivative (10), crystallized from ethanol–ether, m.p. 92—93° (Found: C, 61·9; H, 5·55; N, 18·0. $C_{12}H_{13}N_3O_2$ requires C, 62·3; H, 5·6; N, 18·2%); $\nu_{max.}$ ($CHCl_3$) 1734 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 221, 253sh, 261, 271sh, 291, 324sh nm. [log ε 4·22, (−), 4·095, (−), 3·94, (−)].

(*b*) A mixture of *trans*-alcohol (9) with *cis*-alcohol (8) was obtained when pure *cis*-alcohol was treated with 10% aqueous sodium hydroxide (1 hr., 100°).

3-*Formyl*-v-*triazolo*[1,5-a]*pyridine* (12).—(*a*) The *trans*-alcohol (9) (0·1 g.) was dissolved in water (80 ml.) and t-butyl alcohol (20 ml.) and the pH was adjusted to 7·8 by addition of solid sodium carbonate. A solution of oxidant (75 ml.) (containing 20·98 g. sodium metaperiodate and 167 ml. 0·1M-potassium permanganate per litre) was added slowly with stirring (0·5 hr.). Stirring was continued (1 hr.) and then the mixture was neutralized and filtered. The filtrate was extracted with chloroform and the extracts were dried (Na_2SO_4) and evaporated to dryness (68·1 mg., 87%). Sublimation at 120° 0·2 mm. gave the *aldehyde* (12), (38·4 mg., 49%), m.p. 147—148° (change of crystalline form, needles to rods, at 120—125°) (Found: C, 57·2; H, 3·3; N, 28·3. $C_7H_5N_3O$ requires C, 57·1; H, 3·4; N, 28·5%), $\nu_{max.}$ ($CHCl_3$) 1680 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 258, 290sh, 313 nm. [log ε 3·59, (−), 4·13].

(*b*) Similar oxidation of the *cis*-acraldehyde (5), the *trans*-acraldehyde (7), or the *cis*-alcohol (8) gave the aldehyde (12).

(*c*) Dimethylformamide (1·4 g.) and phosphoryl chloride (3 g.) were mixed under dry nitrogen; after 15 min., ethylene dichloride (13 g.) was added to the mixture which

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was then cooled to 0°. A solution of *v*-triazolo[1,5-*a*]-pyridine [14] (13) (1 g.) in ethylene dichloride was added dropwise to the mixture (below 10°), which was then stirred (1 hr., 0°). Finely divided calcium carbonate was added and the mixture was warmed until a violent reaction occurred; external cooling was required. The mixture was subsequently boiled (2 hr.), cooled, and poured into a mixture of sodium acetate (12·5 g.), water (12·5 ml.), and ice (2·5 g.). The resulting mixture was diluted with chloroform (50 ml.), filtered, and the organic layer separated off; the aqueous layer was extracted several times with chloroform. The combined organic layers were dried (Na_2SO_4), and the solvent was evaporated off, to leave an oil (0·45 g.); this was purified by preparative layer chromatography on Silica Gel Pf 254 and elution with chloroform–ether (1 : 1). From one band a gum was obtained (0·14 g.) which was purified by vacuum sublimation to give the aldehyde (12), m.p. 147—148° (95 mg., 8%), identical with that obtained as in (*a*) or (*b*).

3-(5,6,7,8-*Tetrahydro*-v-*triazolo*[1,5-a]*pyridyl*-3)-2-*methylpropanol* (14).—(*a*) A solution of the *trans*-alcohol (9) (0·385 g.) in 95% EtOH (50 ml.) with Adams catalyst (53 mg.) was hydrogenated at ambient temperature and pressure, absorption ceasing when 3 molar equivalents of hydrogen were absorbed. Filtration and evaporation of the filtrate gave the alcohol (14) as an oil (0·373 g., 94%), b.p. 178—185°/0·4 mm. (bulb tube) (Found: C, 61·3; H, 8·85; N, 21·3. $C_{10}H_{12}N_3O$ requires C, 61·5; H, 8·7; N, 21·5%); $\nu_{max.}$ (CCl_4) 3430 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 225 nm. ($\log_{10}$ ε 3·40). (*b*) The reduced alcohol (14) was similarly obtained by reduction of the *trans*-acrolein (7) in glacial acetic acid.

cis-3-*Bromo*-2-*methyl*-3-(3-v-*triazolo*[1,5-a]*pyridyl*)*acraldehyde* (17).—This was prepared as described above except that the mixture was allowed to come to room temperature after addition of the hydrochloric acid; the yield was 86%. The bromo-acraldehyde (17) crystallized from absolute ethanol as *needles*, m.p. 192—193° (Found: C, 45·0; H, 3·0; N, 15·7. $C_{10}H_8BrN_3O$ requires C, 45·1; H, 3·0; N, 15·9%); $\nu_{max.}$ ($CHCl_3$) 1667 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 232, 292, 320 nm. (log ε 4·43, 4·04, 4·03).

trans-3-*Bromo*-2-*methyl*-3-(3-v-*triazolo*[1,5-a]*pyridyl*)-*acraldehyde* (18).—A solution of the *cis*-bromo-compound (17) (0·3 g.) in glacial acetic acid was heated (1·5 hr., 100°). Evaporation under reduced pressure gave the *trans*-bromo acrolein (18) which crystallized from absolute ethanol as *rods*, m.p. 189—190° (0·25 g., 89%) (Found: C, 45·3; H, 3·3; N, 15·7. $C_{10}H_8BrN_3O$ requires C, 45·1; H, 3·0; N, 15·9%); $\nu_{max.}$ ($CHCl_3$) 1667 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 216, 253sh, 320 nm. [log ε 4·16, (—), 4·08].

1-*Amino*-4-*ethoxycarbonyl*-3-*methylquinolizinium Chloride* (23) *and Ethyl* cis-3-*Methyl*-2-*oxo*-4-(3-v-*triazolo*[1,5-a]-*pyridyl*)*but*-3-*enoate* (26).—A solution of 1-acetamido-4-ethoxycarbonyl-3-methylquinolizinium bromide (24) [1] (7 g.) in N-hydrochloric acid (50 ml.) was heated at 95—100° (1 hr.). Evaporation under reduced pressure, was followed by addition of absolute ethanol (25 ml.; repeated twice) and further evaporation. The black granular solid was extracted (Soxhlet, chloroform) to give a brown tar which on trituration with acetone gave the solid aminoquinolizinium bromide as a yellow powder (4·35 g., 70·5%); $\nu_{max.}$ (Nujol) 1710 cm.$^{-1}$; δ (D_2O) 1·3 (3H, t, CH_2CH_3), 2·1 (3H, s, CH_3), 4·4 (2H, q, CH_2CH_3), 6·7 (1H, s, 2-H), 7·7 (3H, m), 8·46 (1H, d, 6-H) p.p.m. The bromide (1 g.) in 95% ethanol (250 ml.) was percolated through Amberlite 1RA 400 (Cl^-); evaporation of the eluate gave the chloride (23) (0·825 g.). The chloride (23) in water (25 ml.) was treated with sodium nitrite and then N-hydrochloric acid as described above. The precipitate was filtered, washed with water, and dried to give the α-*keto-ester* (26) (0·7 g., 87%), which crystallized from methanol as yellow needles, m.p. 126—127° (Found: C, 60·6; H, 5·25; N, 16·5. $C_{13}H_{13}N_3O_3$ requires C, 60·2; H, 5·05; N, 16·2%); $\nu_{max.}$ ($CHCl_3$) 1730, 1673 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 221, 346 nm. (log ε 4·25, 4·15).

Ethyl trans-3-*Methyl*-2-*oxo*-4-(3-v-*triazolo*[1,5-a]*pyridyl*)-*but*-3-*enoate* (27).—A solution of *cis*-keto-ester (26) (0·2 g.) and piperidine (1 ml.) in chloroform (25 ml.) was evaporated after 1 hr. at room temperature to give the *trans* keto-ester (27) (0·19 g., 95%) which crystallized from methanol as *needles*, m.p. 170—171° (Found: C, 60·6; H, 5·2; N, 16·3. $C_{13}H_{13}N_3O_3$ requires C, 60·2; H, 5·05; N, 16·2%); $\nu_{max.}$ ($CHCl_3$) 1734, 1672 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 221, 349 nm. (log ε 4·13, 4·14).

2-*Aminomethyl*-5-*methylpyridine*.—A slurry of lithium aluminium hydride (18·4 g.) in dry ether (100 ml.) was added slowly to a stirred solution of 2-cyano-5-methylpyridine [15] (28·4 g.) in dry ether (225 ml.) at such a rate as to maintain gentle boiling. After complete addition the mixture was stirred (1 hr., room temperature), decomposed by careful addition of the minimum amount of water, and filtered. The solids were extracted with hot benzene (3 × 25 ml.); the combined organic solutions were dried (Na_2SO_4), the solvent was evaporated off, and the aminomethylmethylpyridine was distilled, b.p. 102—105°/12 mm. (11·2 g., 38%); the *picrate* had m.p. 187—188° (Found: C, 44·2; H, 3·55; N, 19·6. $C_{13}H_{13}N_5O_7$ requires C, 44·4; H, 3·7; N, 19·9%). Acetylation with acetic anhydride–glacial acetic acid mixture gave 2-acetamidomethyl-5-methylpyridine (12·9 g., 93%), b.p. 152—160°/0·2 mm., $\nu_{max.}$ (film) 1669 cm.$^{-1}$. The *picrate*, recrystallized from aqueous ethanol, had m.p. 179—180° (decomp.) (Found: C, 46·2; H, 3·8; N, 17·9. $C_{15}H_{15}N_5O_8$ requires C, 45·8; H, 3·8; N, 17·8%).

2-*Acetamidomethyl*-1-*ethoxycarbonylmethyl*-5-*methylpyridinium Bromide*.—A solution of 2-acetamido-5-methylpyridine (12·9 g.) and ethyl bromoacetate (19·8 g.) in sulpholane (130 ml.) was kept at 35° (3 days). Dilution with ethyl acetate precipitated a viscous oil the n.m.r. spectrum of which was consistent with it being a quaternary salt: δ(D_2O) 1·4 (3H, t), 2·2 (3H, s), 2·65 (3H, s), 4·45 (2H, q) 5·7 (2H, s, $COCH_2\overset{+}{N}$) 7·9—9 p.p.m. (3H, m). The oil was used without purification for the next stage.

1-*Acetamido*-4-*ethoxycarbonyl*-3,7-*dimethylquinolizinium Bromide*.—A solution of the crude quaternary bromide (see above) (2·3 g.), pyruvic aldehyde (1·9 ml., 40% aqueous solution), and di-n-butylamine (0·4 ml.) in ethanol (9 ml.) was boiled for 1 hr.; the mixture was evaporated to dryness and the residue was triturated with ethyl acetate–acetone to give a solid. Crystallization of this from methanol–acetone gave 1-*acetamido*-4-*ethoxycarbonyl*-3,7-*dimethylquinolizinium bromide*, m.p. 184—185° (0·8 g., 15·5% from 2-acetamido-5-methylpyridine) (Found: C, 52·6; H, 5·25; N, 7·6. $C_{16}H_{19}BrN_2O_3$ requires C, 52·3; H, 5·27; N, 7·6%); $\nu_{max.}$ (Nujol) 1720 and 1690 cm.$^{-1}$; δ (D_2O) 1·65 (3H, t), 2·55 (3H, s), 2·78br (6H, s), 4·82 (2H, m, obscured by HDO) 8·2—8·7 (3H, m; 2-H, 8-H, 9-H) 8·9 p.p.m. (1H, br, s, 6-H).

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1-*Amino*-3,7-*dimethylquinolizinium Bromide* (28; X = Br).—A solution of the acetamido-ester (5 g.) in 48% hydrobromic acid (100 ml.) was boiled for 1 hr.; the mixture was evaporated under reduced pressure, and the residue was treated with absolute ethanol (30 ml.) and again evaporated (twice). Trituration with ethyl acetate of the residue gave the aminoquinolizinium bromide (3·0 g., 87%), which crystallized from 95% ethanol as yellow *prisms*, m.p. >330° (Found: C, 52·3; H, 5·2; N, 10·9. $C_{11}H_{13}BrN_2$ requires C, 52·2; H, 5·15; N, 11·1%); δ (CF_3CO_2H) 2·68 (6H, s), 8·0—8·9 p.p.m. (5H, m).

cis-2-*Methyl*-3-(6-*methyl*-3-v-*triazolo*[1,5-a]*pyridyl*) *acraldehyde* (29).—Diazotization of the aminoquinolizinium chloride (28) (1·27 g.) as described above, gave the *cis*-acrolein (29), m.p. 150—151° (0·73 g., 60%) as *needles* from absolute ethanol (Found: C, 65·5; H, 5·55; N, 20·9. $C_{11}H_{11}N_3O$ requires C, 65·65; H, 5·45; N, 20·9%); $\nu_{max.}$ ($CHCl_3$) 1600 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 233·5, 297sh, 308sh, 343 nm. [log ε 4·17, (—), (—), 4·19].

trans-2-*Methyl*-3-(6-*methyl*-3-v-*triazolo*[1,5-a]*pyridyl*) *acrolein* (30).—The *cis*-isomer (29) was isomerized with piperidine in ethanol (1 hr., room temperature) (95% yield). The *trans*-acrolein (30), m.p. 165·5—167°, crystallized as needles from absolute ethanol (Found: C, 65·6; H, 5·55; N, 20·8. $C_{11}H_{11}N_3O$ requires C, 65·65; H, 5·45; N, 20·9%); $\nu_{max.}$ ($CHCl_3$) 1670 cm.$^{-1}$; $\lambda_{max.}$ (EtOH) 235, 296sh, 314sh, 343 nm. [log ε 4·19, (—), (—), 4·39].

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