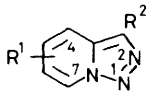
Triazolopyridines. Part 6.[1] Ring Opening Reactions of Triazolopyridines

Gurnos Jones*, Deborah J. Mouat, and Daryl J. Tonkinson
Department of Chemistry, University of Keele, Keele, Staffordshire, ST5 5BG, England.

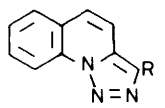
The triazole ring in 1,2,3-triazolo[1,5-*a*]-pyridines and -quinolines, and in 1,2,3-triazolo[5,1-*a*]isoquinolines can be opened with loss of nitrogen. The reagents described are bromine, aqueous sulphuric acid, glacial acetic acid, and selenium dioxide; the products from the triazolopyridines are dibromomethyl, hydroxymethyl, acetoxymethyl, and acyl derivatives of pyridine. The generality of the reactions is discussed. The first reported reaction in which the six-membered ring of a 1,2,3-triazolo[1,5-*a*]pyridine is opened, by hydride reduction, gives a triazolylbutadiene.

We have reported in previous parts of this series that the triazolopyridine (**1a**), triazoloquinolines (**2**) and (**3**), and triazoloisoquinoline (**4**) undergo directed lithiation which can lead to regiospecific substitution on the six membered rings. When this type of substitution can be combined with a good procedure for opening the triazole ring, with loss of nitrogen, we have syntheses of 2,6-disubstituted pyridines,[2-4] of 2,3-disubstituted quinolines,[1,5] and of 1,3-disubstituted isoquinolines.[1] Most of our syntheses have involved the use of bromine for the ring opening, giving for example 2-dibromomethylpyridine (**6a**) which was easily converted into pyridine-2-carbaldehyde,[6] but restrictions with this reaction led us to study other ring opening procedures. This study has much widened

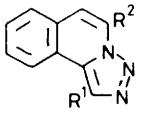


(1)

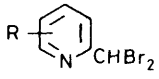
a; R^1 = H, R^2 = H
b; R^1 = H, R^2 = Me
c; R^1 = 4-Me, R^2 = H
d; R^1 = 5-MeO, R^2 = H
e; R^1 = 7-Me, R^2 = H
f; R^1 = H, R^2 = $CONEt_2$
g; R^1 = 7-(7-Triazolopyridyl-CH_2CH_2-), R^2 = H
h; R^1 = 7-(*p*-$MeOC_6H_4CHOH$), R^2 = Me
i; R^1 = 7-CH_2OH, R^2 = H



(2) R = H
(3) R = $CONEt_2$

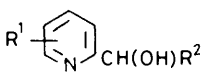


(4) R^1 = R^2 = H
(5) R^1 = Br, R^2 = H
(16) R^1 = H, R^2 = *p*-$MeOC_6H_4CHOH$



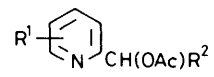
(6)

a; R = H
c; R = 3-Me
d; R = 4-MeO[a]



(7)

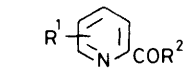
a; R^1 = R^2 = H
b; R^1 = H, R^2 = Me
d; R^1 = 4-MeO, R^2 = H
e; R^1 = 6-Me, R^2 = H
f; R^1 = H, R^2 = $CONEt_2$
h; R^1 = 6-ArCHOH[b], R^2 = Me



(8)

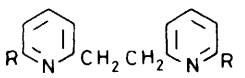
a; R^1 = R^2 = H
b; R^1 = H, R^2 = Me
e; R^1 = 6-Me, R^2 = H
f; R^1 = H, R^2 = $CONEt_2$
h; R^1 = 6-ArCHOH[b], R^2 = Me

[a] Plus some 3-bromo-5-methoxytriazolopyridine. [b] Ar = *p*-$MeOC_6H_4$.

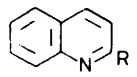


(9)

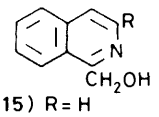
a; R^1 = R^2 = H
b; R^1 = H, R^2 = Me
c; R^1 = 6-Me, R^2 = H
f; R^1 = H, R^2 = $CONEt_2$
h; R^1 = 6-ArCO[b], R^2 = Me
i; R^1 = 6-CHO, R^2 = H



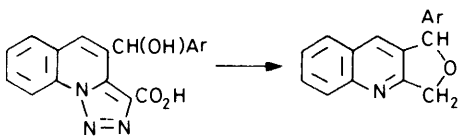
(10) R = CH_2OH
(11) R = CH_2OAc
(12) R = CHO



(13) R = $CHBr_2$
(14) R = CH_2OH



(15) R = H
(17) R = ArCHOH[b]
(18) R = ArCHOMe[b]



(19) (20)

the scope of our syntheses of disubstituted heterocycles, and has led to the discovery of an entirely new reaction.

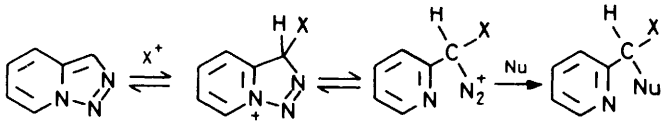
We have already reported [1,4,5] that the heterocycles (**1d**), (**2**), and (**4**), react with hot aqueous sulphuric acid to give the hydroxymethyl derivatives (**7d**), (**14**), and (**15**) respectively. Other examples are given in the Table in which are presented all our ring opening reactions. The yields of the aqueous acid procedure are in general very good, the procedure is simple, and the only side reaction observed was partial dehydration of a substituent tertiary aliphatic alcohol.[1] A related procedure is based on Boyer and Wolford's discovery [7] that triazolopyridines react with loss of nitrogen and formation of 2-acyloxy- or 2-aroyloxypyridines when treated with hot carboxylic acids. The yield reported for the reaction between triazolopyridine (**1a**) and glacial acetic acid was low,[7] but we have found that lengthening the reaction time produces dramatic increases in the yields of 2-acetoxymethylpyridines [entries (**8a**), (**8b**), (**8e**), (**8f**), and (**8h**)]. The glacial acetic acid procedure is the most generally successful. Aqueous acid and glacial acetic acid both react with 3-substituted triazolopyridines, which are not readily opened by bromine, but glacial acetic acid provides the only procedure for converting the disubstituted triazoloquinoline (**19**) into a 2,3-disubstituted quinoline (**20**).[1] We believe that all three reactions so far described proceed by attack by an electrophile (a proton or bromine) on the carbon atom of the

Table. Yields and conditions for triazolopyridine ring-opening reactions

Compd.	Reagent	Temp. (°C)	Time (h)	Solvent	Product	Yield (%)
(**1a**)	Br_2	0—5	1	CCl_4	(**6a**)	80
	H_2SO_4(2.5M)	95	5	H_2O	(**7a**)	78
	AcOH	118	2	AcOH	(**8a**)	70
	SeO_2	80	82	D	(**9a**)	89
	SeO_2	132	6	CB	(**9a**)	92
	SeO_2	140	8	X	(**9a**)	80
(**1b**)	H_2SO_4(2.5M)	95	48	H_2O	(**7b**)	69
	AcOH	118	2	AcOH	(**8b**)	98
	SeO_2	80	24	D	(**9b**)	13
	SeO_2	132	10	CB	(**9b**)	84
	SeO_2	140	24	X	(**9b**)	53
(**1c**)	Br_2	0—5	1	CCl_4	(**6c**)	58
(**1d**)	Br_2	Room	1	CH_2Cl_2	(**6d**)	30[a]
	H_2SO_4(1M)	95	1	H_2O	(**7d**)	78
(**1e**)	H_2SO_4(2.5M)	95	5	H_2O	(**7e**)	80
	AcOH	118	2	AcOH	(**8e**)	98
	SeO_2	80	24	D	(**9e**)	Poor
		140	24	X	(**9e**)	100
(**1f**)	H_2SO_4(2.5M)	95	5	H_2O	(**7f**)	70
	AcOH	118	2	AcOH	(**8f**)	73
	SeO_2	140	96	X	(**9f**)	80
(**1g**)	H_2SO_4(2.5M)	95	24	H_2O	(**10**)	70
	AcOH	118	2	AcOH	(**11**)	91
	SeO_2	140	24	X	(**12**)	44
(**1h**)	H_2SO_4(2.5M)	95	5	H_2O	(**7h**)	87
	AcOH	118	2	AcOH	(**8h**)	60
	SeO_2	140	24	X	(**9h**)	50
(**1k**)	SeO_2	140	24	X	(**9k**)	50
(**2**)	Br_2	Room	1	CH_2Cl_2	(**13**)	71
	H_2SO_4(1M)	100	1	H_2O	(**14**)	89
(**4**)	Br_2	Room or 70	Various	CH_2Cl_2 or CCl_4	None	0[b]
	H_2SO_4(1M)	100	3	H_2O	(**15**)	64
	SeO_2	80—100	Various	D or X	None	0
(**16**)	H_2SO_4(1M)	100	5	CH_3OH–H_2O	(**17**)	52
					(**18**)	15

D = dioxane, CB = chlorobenzene, X = xylene.

[a] Some 3-Bromo-5-methoxy[1,2,3]triazolo[1,5-*a*]pyridine was obtained.[4] [b] The product was 1-bromo[1,2,3]triazolo[5,1-*a*]isoquinoline (**5**).[1]

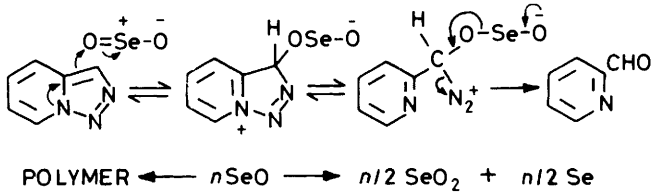


Scheme 1. X = H or Br; Nu = Br^-, H_2O, AcO^-

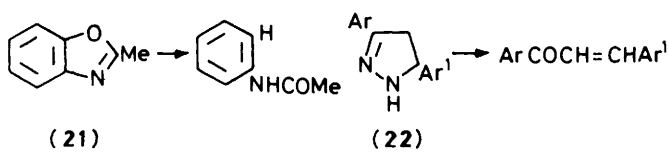
five-membered ring, with ring opening to the diazoalkane and subsequent attack by a nucleophile (bromide ion, water, or acetate) to give nitrogen and a pyridine (Scheme 1).

Our most interesting discovery is that the five-membered ring of triazolopyridines is opened smoothly by selenium dioxide, providing pyridine-2-carbaldehydes or 2-acylpyridines. We have used boiling dioxane, xylene, or chlorobenzene as the solvent, and the reaction proceeds particularly well in chlorobenzene. Again, 3-substituted triazolopyridines can be oxidized, but any substituent primary or secondary alcohols are also oxidized. Thus, 7-hydroxymethyltriazolopyridine (**1i**) gave pyridine-2,6-dicarbaldehyde (**9i**) and the alcohol (**1h**) gave a 2-acetyl-6-aroylpyridine (**9h**). Another notable reaction converted the bis(triazolopyridyl)ethane (**1g**) into 1,2-bis(6-formyl-2-pyridyl)ethane (**12**). Selenium dioxide failed to react with triazoloisoquinoline (**4**) under any of the standard conditions.

Oxidation by selenium dioxide is commonly supposed[8] to be due to selenious acid, formed by traces of water, and water is often added to the solvent. In our case the oxidation of the triazolopyridine (**1a**) was retarded by addition of traces of water, and we have consistently used anhydrous solvents and sublimed selenium dioxide. We suggest that selenium dioxide acts as an electrophile, attacking position 3. A mechanism similar to that proposed for electrophilic attack in general, with elimination of nitrogen and selenium monoxide (which would instantly disproportionate to selenium and selenium dioxide, or polymerize) is shown in Scheme 2.



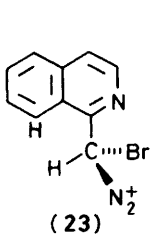
Scheme 2.



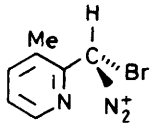
(**21**) (**22**)

We have found only two reported reactions in which selenium dioxide causes the opening of a five-membered heterocyclic ring, involving the benzoxazole (**21**)[9] and the dihydropyrazole (**22**).[10] The former reaction was performed with selenium dioxide in aqueous dioxane, and could be a simple hydrolysis, particularly since the corresponding benzthiazole was not reactive. The latter reaction could also be hydrolytic opening followed by elimination of hydrazine, but could possibly be an oxidation followed by ring opening of the pyrazole. It has also been reported[11] that 1,2,4-triazolo[4,3-*a*]pyrazines are oxidized to triazolopyrazinones by selenium dioxide, and a mechanism similar to that shown in Scheme 2 could apply to this oxidation.

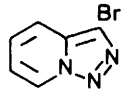
Our discovery[1] that the triazoloisoquinoline (**4**) does not undergo ring opening by bromine, instead giving the 1-bromo derivative (**5**), led us to reconsider our proposed mechanism[6] for the reaction of triazolopyridines with halogens. The most obvious explanation for the difference between the triazoloquinoline (**2**) and the triazoloisoquinoline (**4**) is in the poor accessibility of the proposed intermediate (**23**) towards S_N2 attack by the nucleophilic bromide ion. As a test for this hypothesis, we synthesized 4-methyl[1,2,3]triazolo[1,5-*a*]pyridine (**1c**) by a standard route, and treated it with bromine at 5 °C. The only isolated product was 2-dibromomethyl-3-methylpyridine (**6c**). Since the intermediate (**24**) appears to be at least as hindered as intermediate (**23**) it seems that steric hindrance is not the cause of the difference in reaction of compound (**4**) from that of other triazolopyridines and triazoloquinolines. A suggestion of inherent instability of the 3-bromotriazolopyridine (**25**) can now also be discounted; we have isolated small quantities of 3-bromotriazolopyridine (**25**) from large scale preparations of compound (**6a**) and can record that it is stable.



(**23**)



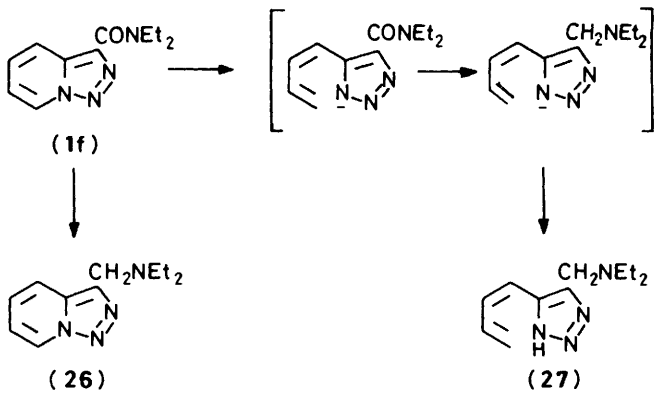
(**24**)



(**25**)

In summary, the scope of our synthesis of substituted pyridines, quinolines, and isoquinolines has been considerably extended, most notably by the discovery of routes to open 3-substituted triazolopyridines with concomitant loss of nitrogen. Thus, the 2-pyridylglycolamide (**7f**) and its acetyl derivative (**8f**) are not otherwise available, and we have shown elsewhere[4] the difficulty of obtaining derivatives of 2-pyridylglyoxylic acid, such as the amide (**9f**). These examples illustrate a further advantage, that the pyridines obtained are in either of two oxidation levels (two routes to aldehydes, one to ketones, and two to hydroxymethyl derivatives). As an example, the 3,7-disubstituted triazolopyridine (**1h**) can be converted into the 2-hydroxymethylpyridine (**7h**) in 87% yield or into the 2-acetylpyridine (**9h**), in 50% yield (this latter yield might be bettered by using a higher ratio of selenium dioxide to substrate). Overall, these two reactions represent the conversion of 2-acetylpyridine into the 6-substituted derivatives (**7h**) or (**9h**), a conversion impossible by any other reported route.

In all of our experiments to date, the triazolopyridines have proved resistant to nucleophiles, and the six-membered ring has remained intact. We attempted to prepare 3-diethylaminomethyltriazolopyridine (**26**) by reduction of the amide (**1f**) using lithium aluminium hydride. Two products were isolated in varying proportions, the first being identified by analysis and spectra as the desired amine (**26**). The second product,



Scheme 3.

$C_{11}H_{18}N_4$, was formally a dihydro derivative of compound (**26**), but the presence of a triazole NH in the ^1H n.m.r. and the i.r. spectrum indicated that the pyridine ring had been opened. The other new signals were in a multiplet from δ 5.0—7.7 and were readily identifed as a buta-1,3-dienyl residue. Hence the new product is the triazole (**27**) formed as shown in Scheme 3. Ring opening of triazolopyridium salts by nucleophiles has been reported[12,13] but this is the first such reaction for the unquaternized system. Attempts to reduce the parent (**1a**) using lithium aluminium hydride gave only polymeric products.

Experimental

M.p.s were determined on a Kofler heated stage, and are uncorrected. N.m.r. spectra were performed with $CDCl_3$ solutions, unless otherwise stated. Selenium dioxide was freshly sublimed, and was used with anhydrous solvents.

4-*Methyl*[1,2,3]*triazolo*[1,5-a]*pyridine* (**1c**).—(*a*) A solution of 3-methylpyridine-2-carbaldehyde (6 g) (prepared by oxidation of 3-methyl-2-pyridylmethanol by manganese dioxide)[14] and hydrazine hydrate (14 ml) in aqueous sodium hydroxide (4.2 g in 14 ml H_2O) was mixed and heated at 95 °C (0.5 h). The cooled mixture was treated with 30% sodium hydroxide (14 ml), extracted with CH_2Cl_2, and the organic solvent was dried and evaporated to give the crude hydrazone (4.8 g, 72%).

(*b*) The hydrazone (4.8 g) was added slowly to water (185 ml) containing sodium hydrogen carbonate (8 g) and potassium ferricyanide (30 g) at 100 °C, and the mixture was stirred and heated in a boiling water-bath (0.75 h). The cooled mixture was treated with aqueous sodium hydroxide (30%; 20 ml), extracted with dichloromethane, and the solution dried ($MgSO_4$) and evaporated to give a crude product. Purification by Chromatotron (eluant chloroform) gave the 4-*methyltriazolopyridine* (**1c**), m.p. 46—47 °C (3.67 g, 77%) (Found: C, 63.2; H, 5.5; N, 31.85. $C_7H_7N_3$ requires C, 63.15; H, 5.25; N, 31.6%); $\lambda_{max.}$ (95% EtOH) 282 nm ($\log_{10}$ ε 3.83); *m/z* 133 (M^+, 68%), 105 ($M^+ - N_2$, 82) and 104 [($M^+ - 1$) − N_2, 100]; δ 2.5 (3 H, s), 6.6—6.8 (2 H, m), 7.95 (1 H, s, 3-H), and 8.5—8.6 (1 H, br d, 7-H).

2-*Dibromomethyl*-3-*methylpyridine* (**6c**).—Prepared as described for 2-dibromomethylpyridine[6] in 58% yield, the *dibromomethyl compound* (**6c**) had m.p. 41—42 °C (Found: C, 31.9; H, 2.65; N, 5.4. $C_7H_7Br_2N$ requires C, 31.7; H, 2.65; N, 5.3%); $\lambda_{max.}$ (95% EtOH) 274 nm ($\log_{10}$ ε 3.56); $\nu_{max.}$($CHCl_3$) 680 cm^{-1}; δ 2.5 (3 H, s), 6.8 (1 H, s, $CHBr_2$), 6.95—7.5 (2 H, m, 4- and 5-H), and 8.3—8.4 (1 H, br d, 6-H); *m/z* 267 ($M^+ + 4$), 265 ($M^+ + 2$), 263 (M^+), 186 [($M^+ + 2$) − Br, 98%], 184 (M^+ − Br, 100), and 105 ($M^+ - 2$ Br, 80).

3-*Bromo*[1,2,3]*triazolo*[1,5-a]*pyridine* (**25**).—During large scale preparations of 2-dibromomethylpyridine an impurity was noted, and isolated using a Chromatotron [eluant: light petroleum–$CHCl_3$, (1:1)]. Recrystallized from light petroleum (40—60 °C b.p.) the *bromotriazolopyridine* (**25**) had m.p. 91 °C (Found: C, 36.55; H, 1.9; N, 21.35. $C_5H_4BrN_3$ requires C, 36.35; H, 2.0; N, 21.2%). $\lambda_{max.}$ (95% EtOH) 286 nm ($\log_{10}$ ε 3.79); *m/z* 199 (M^+ + 2, 7%), 197 (M^+, 8%), 171 [(M^+ + 2) − N_2, 22), and 169 (M^+ − N_2, 17); δ 6.8—7.3 (2 H, m, 5- and 6-H), 7.5—7.6 (1 H, d, 4-H), and 8.5—8.6 (1 H, br d, 7-H).

General Procedure for Sulphuric Acid Hydrolyses.—A solution of the triazolopyridine (*ca.* 1 g) in 2.5M-sulphuric acid (25—30 ml) was heated on a boiling water-bath; progress of the reaction was monitored by working up a small sample for t.l.c. The cooled solution was neutralized with saturated aqueous sodium hydrogen carbonate, extracted with dichloromethane, and the organic extracts were dried ($MgSO_4$), filtered, and evaporated. Purification procedures are given for each product; when a Chromatotron was used the eluants were mixtures of light petroleum and ethyl acetate, proportions given thus (8:2).

2-*Pyridylmethanol* (**7a**). Isolated almost pure, b.p. 107—109 °C/12 mmHg identical with a commercial sample (lit.,[7] b.p. 107—109 °C/12 mmHg).

1-(2-*Pyridyl*)*ethanol* (**7b**). Purified by Chromatotron (9:1), the alcohol (**7b**) had b.p. 145—150 °C/20 mmHg (lit.,[15] b.p. 150 °C/20 mmHg); δ 1.5 (3 H, d), 4.9 (1 H, q), 5.5 (1 H, br s, exch. D_2O), 6.9—7.7 (3 H, m), and 8.5 (1 H, d, 6-H).

6-*Methyl*-2-*pyridylmethanol* (**7e**). Purified by Chromatotron (8:2) the alcohol (**7c**) had b.p. 78—82 °C/1 mmHg (lit.,[16] b.p. 80 °C/3 mmHg) δ 2.4 (3 H, s), 4.6 (2 H, s), 5.1 (1 H, s, exch. D_2O), 6.9—7.2 (2 H, m, 3- and 5-H), and 7.5 (1 H, t, 4-H).

N,N-*Diethyl*-2-*pyridylglycolamide* (**7f**). Purified by Chromatotron (8:2), the *hydroxyamide* (**7f**) had b.p. 135 °C/0.2 mmHg (bulb tube) (Found: C, 63.35; H, 8.0; N, 13.2. $C_{11}H_{16}N_2O_2$ requires C, 63.45; H, 7.75; N, 13.45%); $\lambda_{max.}$ (95% EtOH) 265 nm ($\log_{10}$ ε 3.86); $\nu_{max.}$($CHCl_3$) 3 420 and 1 600 cm^{-1}; *m/z* 208 (M^+, 70%) and 130 [M^+ − (2-pyridyl), 100]; δ 1.2 (6 H, m), 3.3 (4 H, m), 5.4 (1 H, br s, OH), 6.6 (1 H, s, C*H*OH), 7.1 (1 H, m, 5-H), 7.5 (2 H, m, 3- and 4-H), and 8.4 (1 H, d, 6-H).

1-[6-(α-*Hydroxy*-4-*methoxybenzyl*)-2-*pyridyl*]*ethanol* (**7h**). Evaporation of the solvent gave almost pure *diol* (**7h**), m.p. 98—101 °C (Found: C, 69.85; H, 6.75; N, 5.25. $C_{15}H_{17}NO_3$ requires C, 69.45; H, 6.6; N, 5.4%); δ 1.5 (3 H, d, *Me*CH), 3.5 (3 H, s, OMe), 4.49 (1 H, br s, CHOH), 5.4 (1 H, s, OH), 6.7 (1 H, d, C*H*OH), 6.7 (2 H, d, 2′-, 6′-H), 7.1—7.5 (3 H, m, 2-, 3-, and 4-H) and 7.8 (2 H, d, 3′-, 5′-H).

1,2-*Bis*(6-*hydroxymethyl*-2-*pyridyl*)*ethane* (**10**). Evaporation of the solvent gave almost pure dipyridylethane (**10**), m.p. 156—158 °C (lit.,[17] m.p. 157—159 °C); δ 3.2 (4 H, s, CH_2CH_2), 4.7 (4 H, s, 2 × CH_2OH), 6.9 (4 H, d, 3-, 3′-, 5-, and 5′-H), and 7.5 (2 H, t, 4-, 4′-H).

General Procedure for Reactions in Boiling Glacial Acetic Acid.—A solution of the triazolopyridine (0.5—1.0 g) in glacial acetic acid (20 ml) was boiled (2 h): nitrogen evolution was observed. Evaporation under reduced pressure was followed by treatment with saturated aqueous sodium hydrogen carbonate and subsequently as for the sulphuric acid reactions.

2-*Acetoxymethylpyridine* (**8a**). Purified by Chromatotron (9:1) the acetate (**8a**) had b.p. 105—107 °C/12 mmHg (lit.,[17] b.p. 120—121 °C/ 23 mmHg).

2-(1-*Acetoxyethyl*)*pyridine* (**8b**). Purified by Chromatotron (9:1) the acetate (**8b**) had b.p. 60 °C/0.5 mmHg (bulb tube), (lit.,[18] b.p. 109—111 °C/16 mmHg); δ 1.7 (3 H, d), 2.1 (3 H, s), 6.0 (1 H, q), 7.0—7.7 (3 H, m), and 8.5 (1 H, dd, *J* 1 and 5 Hz, 6-H).

2-*Acetoxymethyl*-6-*methylpyridine* (**8e**).—Purified by Chromatotron (8:2), the acetate had b.p. 120—123 °C/20 mmHg (lit.,[18] b.p. 110—114 °C/15 mmHg); δ 2.1 (3 H, s), 2.5 (3 H, s, 6-Me), 5.1 (2 H, s), 6.9—7.1 (2 H, m, 3- and 5-H), and 7.5 (1 H, t, 4-H).

O-*Acetyl*-N,N-*diethyl*-2-*pyridylglycolamide* (**8f**). Purified by Chromatotron (9:1) the *acetoxy amide* (**8f**) had m.p. 83—84 °C (cyclohexane) (Found: C, 62.4; H, 7.6; N, 11.5. $C_{13}H_{18}N_2O_3$ requires C, 62.4; H, 7.25; N, 11.2%); $\lambda_{max.}$ (95% EtOH) 275 nm ($\log_{10}$ ε 3.61); $\nu_{max.}$($CHCl_3$) 1 610 cm^{-1}; *m/z* 250 (M^+, 70%); δ 0.9—1.4 (6 H, m), 2.2 (3 H, s, COMe), 3.0—3.7 (4 H, m), 6.3 [1 H, s, C*H*(OAc)CONEt$_2$], 7.2 (1 H, m, 5-H), 7.5 (2 H, m, 3- and 4-H), and 8.5 (1 H, d, 6-H).

1,2-*Bis*(2-*acetoxymethyl*-6-*pyridyl*)*ethane* (**11**). Evaporation gave virtually pure diacetoxypyridylethane (**11**), m.p. 133—134 °C, identical with a specimen obtained by the acetylation of compound (**10**), δ 2.2 (6 H, s, MeCO), 3.3 (4 H, s, CH_2CH_2), 5.2 (4 H, s, 2 × CH_2O), 7.0 (4 H, m, 3- and 5-H), and 7.4 (2 H, m, 4-H).

General Procedure for Selenium Dioxide Ring Opening of Triazolopyridines.—A solution of the triazolopyridine (0.5—1.0 g) in the anhydrous solvent (see Table) was added to freshly sublimed selenium dioxide (1.1—2.1 mol equiv., depending on the number of oxidizable groups present) and the suspension was boiled; the progress of the reaction was monitored by t.l.c. When the reaction was complete the suspension was filtered. The precipitate was washed with water and the latter was extracted with dichloromethane. The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, and the organic layers were dried ($MgSO_4$), filtered, and evaporated. Further purification procedures are given for each product.

Pyridine-2-*carbaldehyde* (**9a**). Purified by Chromatotron (light petroleum), the aldehyde (**9a**) was identical with a commercial specimen.

2-*Acetylpyridine* (**9b**). Purified by Chromatotron, (light petroleum) the ketone (**9b**) had b.p. 188—192 °C/750 mmHg. (lit.,[19] b.p. 188—189 °C/760 mmHg) and was identical with a commercial specimen.

6-*Methylpyridine*-2-*carbaldehyde* (**9e**).—Purified by Chromatotron (7:3), the aldehyde (**9e**) was identical with a synthetic specimen.[20]

N,N-*Diethyl*-2-*Pyridylglyoxylamide* (**9f**). Purified by distillation, the *amide* (**9f**) had b.p. 130 °C/0.01 mmHg (bulb tube) (Found: C, 63.8; H, 6.95; N, 13.5. $C_{11}H_{14}N_2O_2$ requires C, 64.05; H, 6.85; N, 13.6%); $\lambda_{max.}$ (95% EtOH) 280 nm ($\log_{10}$ ε 3.83); $\nu_{max.}$(film) 1 710 and 1 650 cm^{-1}; *m/z* 206 (M^+, 15%), 177 (M^+ − C_2H_5, 32), 106 ($C_5H_4N{\cdot}CO^+$, 80), and 100 (Et_2NCO^+, 73); δ 1.2 (6 H, m), 3.5 (4 H, m) 7.4 (1 H, m, 5-H), 7.9 (2 H, m, 3- and 4-H), and 8.5 (1 H, d, 6-H).

2-*Acetyl*-6-(4-*methoxybenzoyl*)*pyridine* (**9h**). Purification by Chromatotron (7:3) gave the *diketone* (**9h**) (Found: C, 67.9; H, 5.25, N, 5.2. $C_{15}H_{13}NO_3{\cdot}0.5\ H_2O$ requires C, 67.9; H, 5.3, N, 5.3%); $\nu_{max.}$($CHCl_3$) 1 710 and 1 650 cm^{-1}; δ 2.7 (3 H, s, MeCO), 3.9 (3 H, s, OMe), 7.0 (2 H, d, 3′- and 5′-H), and 7.9—8.3 (5 H, m).

Pyridine-2,6-*dicarbaldehyde* (**9i**). Evaporation of the solvent gave almost pure dicarbaldehyde (**9i**), m.p. 123—125 °C (lit.,[21] m.p. 124 °C); δ 7.9—8.2 (3 H, m) and 10.1 (2 H, s, 2 × CHO).

1,2-*Bis*(6-*formyl*-2-*pyridyl*)*ethane* (**12**). Evaporation gave a solid purified by Chromatotron (ethyl acetate) to give the *dicarbaldehyde* (**12**), m.p. 181—183 °C (from benzene) (Found: C, 70.0; H, 5.0; N, 11.75. $C_{14}H_{12}N_2O_2$ requires C, 70.0; H, 5.0; N, 11.65%); δ 3.3 (4 H, s, CH_2), 7.0—7.3 (2 H, m, 5-H), 7.6—7.8 (2 H, d, 3- and 4-H), and 10.0 (2 H, s, CHO).

Reduction of the Amide (**1f**) *by Lithium Aluminium Hydride.*—A suspension of the amide (**1f**) in anhydrous THF (50 ml) was added slowly, with vigorous stirring, to a cooled (10 °C) solution of lithium aluminium hydride (1.16 g) in THF (150 ml). The mixture was boiled under reflux (18 h), cooled, and treated with ethyl acetate, and then ice-water. The mixture was filtered, and the solids retained. The filtrate was extracted with dichloromethane and the organic solution was dried ($MgSO_4$), filtered, and evaporated to give a yellow oil (1.4 g). The solids were extracted (Soxhlet, THF, 24 h, then CH_2Cl_2, 18 h). The residues from the Soxhlet extracts (4.8 g) were combined with the earlier residue and chromatographed on an alumina column (210 g, activity 4). Gradient elution with light petroleum (b.p. 60—80 °C)–ethyl acetate gave first unchanged amide (0.6 g), then 3-*diethylaminomethyl*[1,2,3]*triazolo*[1,5-a]*pyridine* (**26**) (1.5 g, 24%), b.p. 103 °C/0.01 mmHg (Found: C, 64.65; H, 8.15; N, 27.2. $C_{11}H_{16}N_4$ requires C, 64.7; H, 7.85; N, 27.45%); $\lambda_{max.}$ (95% EtOH) 245 nm ($\log_{10}\varepsilon$ 3.89); δ 1.1 (6 H, t), 2.5 (4 H, q), 3.9 (2 H, s), 6.7—7.2 (2 H, m, 5- and 6-H), 7.7 (1 H, d, *J* 9 Hz, 4-H), and 8.5 (1 H, d, *J* 6 Hz, 7-H); *m/z* 204 (M^+, 8%), 133 ($M^+ - C_4H_9N$, 71), 106 (53), 105 (54), and 104 (C_7H_6N, 100). Further elution gave the *butadienyltriazole* (**27**), b.p. 100 °C/0.01 mmHg (4 g, 60%) (Found: C, 64.15; H, 9.05; N, 26.95. $C_{11}H_{18}N_4$ requires C, 64.05; H, 8.75; N, 27.2%); $\nu_{max.}$($CHCl_3$) 3 010 cm^{-1}; $\lambda_{max.}$ (95% EtOH) 230 nm ($\log_{10}\varepsilon$ 2.85); δ 1.1 (6 H, t), 2.5 (4 H, q), 3.7 (2 H, s), 5.0—5.4 (2 H, m), 6.1 (2 H, dd), 7.0—7.7 (1 H, m), and 11.3 (1 H, br s, NH); δ_C 11.1 (q), 45.9 (t), 46.5 (t), 115.6 (d), 120.3 (t), 132 (d), 134.3 (d), 139.4 (s), and 142.2 (s); *m/z* 206 (M^+, 58%), 191 ($M^+ - 15$, 100), 134 ($M^+ - Et_2N$, 30), 106 (30), 86 (35), 79 (56), 77 (42), 72 (55), and 58 (63).

Acknowledgements

Our thanks are due to the S.E.R.C. for a studentship (D. J. M.), to the University of Keele for a studentship (D. J. T.), and to Mr. J. Clews for skilled technical assistance.

References

1 Part 5, B. Abarca, R. Ballesteros, E. Gomez-Aldaravi, and G. Jones, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1897.
2 G. Jones and D. R. Sliskovic, *Tetrahedron Lett.*, 1980, **21**.
3 G. Jones and D. R. Sliskovic, *J. Chem. Soc., Perkin Trans. 1*, 1982, 967.
4 B. Abarca, D. J. Hayles, G. Jones, and D. R. Sliskovic, *J. Chem. Res.* (*S*), 1983, 144; (*M*), 1341—1350.
5 B. Abarca, E. Gomez-Aldaravi, and G. Jones, *J. Chem. Res.* (*S*), 1984, 140; (*M*), 1430—1440.
6 G. Jones, D. R. Sliskovic, B. Foster, J. Rogers, A. K. Smith, M. Y. Wong, and A. C. Yarham, *J. Chem. Soc., Perkin Trans. 1*, 1981, 78.
7 J. H. Boyer and L. T. Wolford, *J. Am. Chem. Soc.*, 1958, **80**, 2741.
8 See N. Rabjohn, *Org. React.*, **24**, ch. 4, 261.
9 M. Seyhan and S. Avan, *Rec. Fac. Sci. Univ. Istanbul*, 1951, **16A**, 30 (*Chem. Abstr.*, 1952, **46**, 8090).
10 D. D. Berge and A. V. Kale, *Chem. Ind.* (*London*), 1979, 662.
11 M. Iwao and T. Kuraishi, *J. Heterocycl. Chem.*, 1976, **13**, 639.
12 A. Gelleri and A. Messmer, *Tetrahedron Lett.*, 1973, 4395.
13 A. Gelleri, A. Messmer, S. Nagy, and L. Radics, *Tetrahedron Lett.*, 1980, **21**, 663.
14 J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1952, 1094.
15 M. Freifelder, *J. Org. Chem.*, 1964, **29**, 2895.
16 M. Tissier and C. Tissier, *Bull. Soc. Chim. Fr.*, 1967, 3155.
17 W. Baker, K. M. Buggle, J. F. W. McOmie, and D. A. M. Walker, *J. Chem. Soc.*, 1958, 3594.
18 V. Boekelheide and W. J. Linn, *J. Am. Chem. Soc.*, 1954, **76**, 1286.
19 Aldrich catalogue.
20 W. Mathes, W. Sauermilch, and T. Klein, *Chem. Ber.*, 1951, **84**, 452.
21 W. Mathes, W. Sauermilch, and T. Klein, *Chem. Ber.*, 1953, **86**, 584.

Received 7th May 1985; *Paper* 5/744