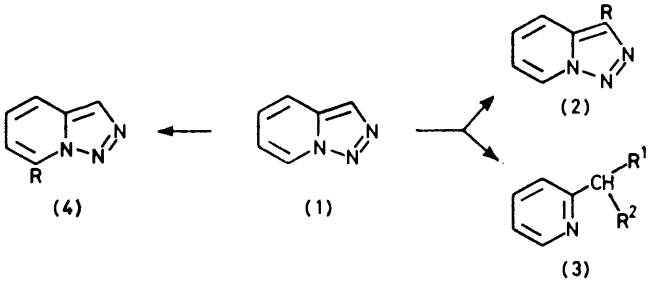
Triazolopyridines. Part 2.[1] Preparation of 7-Substituted Triazolo[1,5-*a*]pyridines by Directed Lithiation

By **Gurnos Jones** * and **D. Robert Sliskovic**, Department of Chemistry, University of Keele, Keele, Staffordshire ST5 5BG

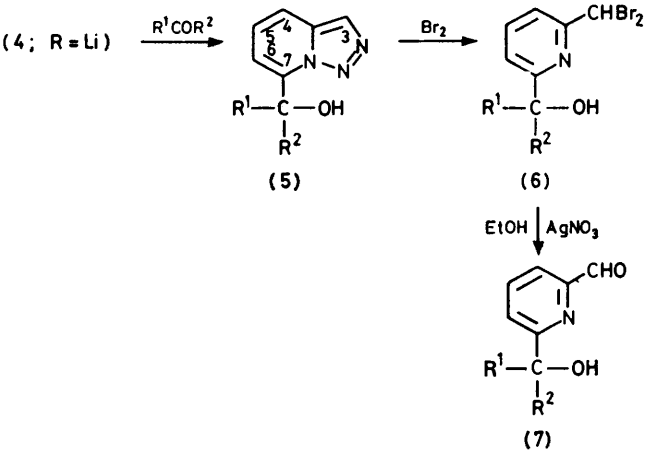
The lithiation reactions of 1,2,3-triazolo[1,5-*a*]pyridine (1) to give the 7-lithio-derivative (4; R = Li), and of its 7-methyl derivative (16) to give the 7-lithiomethyl compound, are described. These lithium derivatives react with electrophiles, notably aldehydes and ketones, to give triazolopyridin-7-yl derivatives (5a—h), (8), (10), (17), and 20). Selected 7-substituted triazolopyridines react with bromine to give 2-dibromomethylpyridines, and hence 6-substituted pyridine-2-carbaldehydes.

We have reported[1] that triazolo[1,5-*a*]pyridine (1) reacts with electrophiles in two modes. Simple electrophilic substitution at position 3 occurs in nitration and in formylation, giving compounds (2; R = NO_2 or CHO). With halogens or mercury(II) acetate, 2-methylpyridine derivatives are obtained (3; R^1 = R^2 = Cl; R^1 = R^2 = Br; R^1 = OAc, R^2 = HgOAc). If the 'pyridine' ring of triazolopyridine were functionalized, the second mode would provide a route to substituted 2-methylpyridines (or pyridine-2-carboxaldehydes); we report here that directed lithiation gives 7-substituted triazolopyridines (4), and thence 2,6-disubstituted pyridines.[2]



(4) (1) (2) (3)

When a solution of n-butyl-lithium in ether, at temperatures from −40 to −78 °C, was treated with the triazolopyridine (1), a brick red colour slowly developed. Quenching the mixture with deuterium oxide gave, after work-up, triazolopyridine which exhibited a much less intense 7-H signal in the ^1H n.m.r. spectrum. A number of experiments with various lithium reagents, solvents, and times of reaction showed that the exchange was slow; optimum yields of 7-deuteriotriazolopyridine (4; R = ^2H) were obtained using lithium di-isopropylamide at −40 °C in ether as solvent. We believe that this lithiation is directed by the *peri*-nitrogen atom, because deuterium exchange normally occurs first at position 3, under base catalysis.[3] Under these conditions, the 7-lithiotriazolopyridine (4; R = Li) was treated with various aldehydes and ketones chosen to provide a full range of reactivities. The triazolopyridin-7-ylmethanols (5) were obtained in yields ranging from 20 to 69%. This route could be used to prepare substituted pyridine-2-carbaldehydes; for example, compounds (5c and g) were treated with bromine in dichloromethane at 0—10 °C and the dibromomethylpyridines (6c and g), thus obtained in excellent yields, were treated with silver nitrate in ethanol to give the 6-substituted pyridine-2-carbaldehydes (7c and g).



(4; R = Li) → (5) → (6) → (7)

a; R^1 = H, R^2 = n-C_7H_{15}
b; R^1 = H, R^2 = Ph
c; R^1 = H, R^2 = 4-$MeOC_6H_4$
d; R^1 = H, R^2 = 4-$O_2NC_6H_4$
e; R^1 = Me, R^2 = 2-pyridyl
f; R^1R^2 = $[CH_2]_4$
g; R^1 = R^2 = Ph
h; R^1 = Me, R^2 = $CH{=}CH_2$

It was felt that the low yields of some carbinols might be improved if the lithium derivative could be converted into a Grignard reagent; the ethereal solution of 7-lithiotriazolopyridine was therefore treated with anhydrous magnesium bromide. Reaction with methyl vinyl ketone then gave the alcohol (5h), but in a yield little different from that obtained from the lithium derivative. An attempt was made also to generate the bis(triazolopyridin-7-yl)copper reagent. Addition of copper(I) bromide–dimethyl sulphide complex to the 7-lithiotriazolopyridine (4; R = Li) produced a change from brick red to yellow, but subsequent addition of methyl vinyl ketone gave only the 1,2-addition product (5h), with no 1,4-addition product.

Attempts to bring about reactions of the 7-lithiotriazolopyridine with electrophiles other than aldehydes or ketones met with mixed success. No alkylation was achieved with methyl iodide. With ethyl chloroformate the lithium derivative (4; R = Li) gave the bistri-

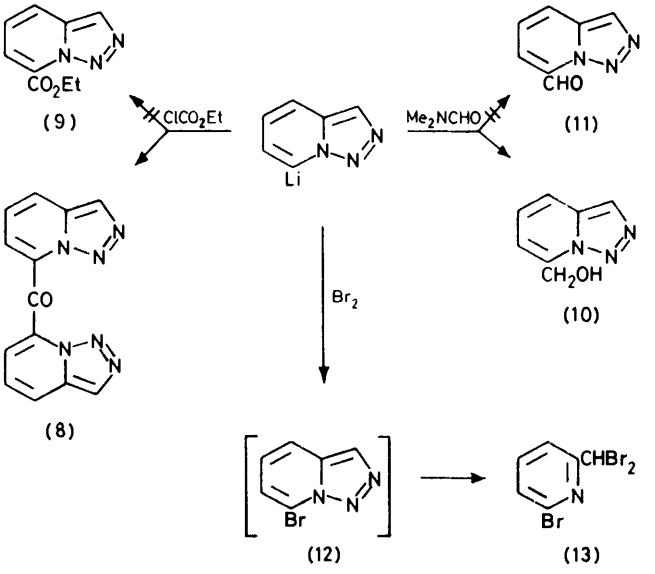
^{1}H N.m.r. signals (δ values; J in Hz) for triazolo[1,5-*a*]pyridines *

Compd.	R	H-3	H-4	H-5	H-6	Other	J
(4)	^{2}H	8.06 (s)	7.7 (d of d)	7.3 (d of d)	7.0 (d of d)		$J_{4,5}$ 9; $J_{4,6}$ 1; $J_{5,6}$ 7
(5a)	n-C_7H_{13}CH(OH)	8.0 (s)	7.6 (d of d)	7.2 (d of d)	6.95 (d of d)	0.75—2.3 (15 H. m), 4.0 (1 H, br, s, exch. D_2O) 5.35 (1 H, t, C*H*OH)	$J_{4,5}$ 9; $J_{4,6}$ 1: $J_{5,6}$ 7
(5b)	PhCH(OH)	8.1 (s)	7.69 (d of d)	7.3 (d of d)	6.72 (d of d)	4.69 (1 H, d, OH, exch.), 6.5 (1 H. d, CHOH), 7.36—7.62 (5 H, benzene)	$J_{4,5}$ 9; $J_{4,6}$ 1; $J_{5,6}$ 7; $J_{CH(OH)}$ 4.5
(5c)	4-$MeOC_6H_4$CH(OH)	8.12 (s)	7.7 (d of d)	7.24 (d of d)	6.73 (d of d)	3.82 (3 H, s, OMe), 4.49 (1 H, d, OH) 6.5 (1 H, d, CHOH), 6.93 (2 H, d, H-2′, -6′), 7.48 (2 H. d, H-3′, -5′)	$J_{4,5}$ 9; $J_{4,6}$ 1; $J_{5,6}$ 7; $J_{2',3'}$ 9
(5d)	4-$O_2NC_6H_4$CH(OH)	8.26 (s)	8.2 (d of d)	7.48 (d of d)	7.9 (d of d)	6.6 (1 H. s, C*H*OH). 6.9 (1 H, s. OH), 7.49—7.79 (4 H, m, benzene)	$J_{4,5}$ 9: $J_{4,6}$ 1.7: $J_{5,6}$ 8
(5e)	4-Pyridyl-CH(OH)Me	8.1 (s)	7.8 (d of d)	7.4 (d of d)	7.16 (d of d)	2.03 (3 H. s. Me), 6.03 (1 H, br. s, OH), 7.3 (4 H, m. pyridine)	$J_{4,5}$ 9; $J_{4,6}$ 1.3; $J_{5,6}$ 7
(5f)	$[CH_2]_5$	8.09 (s)	7.68 (d of d)	7.29 (d of d)	6.96 (d of d)	1.6—2.47 (10 H, m), 5.33 (1 H, br, OH)	$J_{4,5}$ 9; $J_{4,6}$ 1.3; $J_{5,6}$ 7
(5g)	Ph_2C(OH)	8.07 (s)	7.73 (d of d)	7.18 (d of d)	6.32 (d of d)	6.77 (1 H. br, OH). 7.3 (10 H, Ph)	$J_{4,5}$ 9; $J_{4,6}$ 1; $J_{5,6}$ 7
(5h)	CH_2=CHCMeOH	8.11 (s)	7.73 (d of d)	7.31 (d of d)	7.07 (d of d)	1.9 (3 H, s, Me), 5.2—6.4 (3 H, vinyl), 5.9 (1 H, br, OH)	$J_{4,5}$ 9; $J_{4,6}$ 1.2; $J_{5,6}$ 7
(8)	CO·TP †	8.29 (s)	8.32 (d of d)	7.62 (d of d)	7.87 (d of d)		$J_{4,5}$ 9.5; $J_{4,6}$ 1.4; $J_{5,6}$ 7
(10)	CH_2OH	8.5 (s)	7.87 (d of d)	7.44 (d of d)	7.23 (d of d)	5.19 (2 H, s. CH_2OH)	$J_{4,5}$ 9: $J_{4,6}$ 13: $J_{5,6}$ 7
(16)	CH_3	8.1 (s)	7.63 (d of d)	7.2 (d of d)	6.79 (d of d)	2.88 (3 H, s, Me)	
(17)	4-$MeOC_6H_4CH(OH)CH_2$	8.13 (s)	7.74 (d of d)	6.8–7.4 (m)		3.51 (2 H. m, H-β) 3.76 (3 H, s, Me) 5.35 (1 H, m, H-α)	$J_{4,5}$ 8.5; $J_{4,6}$ 1
(20)	CH_2CH_2TP †	8.1 (s)	7.6 (d of d)	7.1 (d of d)	6.7 (d of d)	3.95 (4 H, s, CH_2CH_2)	$J_{4,5}$ 9; $J_{4,6}$ 1: $J_{5,6}$ 7

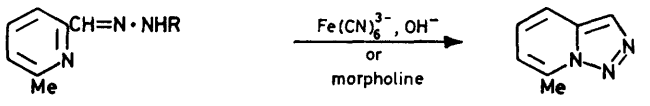
* Solutions in $CDCl_3$. † TP = triazolopyridin-7-yl.

azolopyridin-7-yl ketone (8), not the ester (9). More surprisingly, treatment of the lithium compound (4; R = Li) with dimethyl formamide gave the triazolopyridin-7-ylmethanol (10) rather than the aldehyde (11). Addition of bromine to the ethereal solution of 7-lithiotriazolopyridine at −40 °C gave as the only identified material, after warming to room temperature, 6-bromo-2-dibromomethylpyridine (13). It appears that the ring opening is sufficiently rapid, even at low temperatures, to compete with the electrophilic attack on the 7-position, and this can be confirmed by treatment of triazolopyridine itself with bromine at −40 °C. Thus some 7-bromotriazolopyridine (12) is formed, but it reacts with more bromine to give the bromo(dibromomethyl)pyridine (13). No identified products were obtained from the lithium compound (4; R = Li) with benzonitrile, nor with cyanogen bromide.

By oxidation of the hydrazone (14) of 6-methylpyridine-2-carbaldehyde, or by treatment of the tosylhydrazone (15) with morpholine, the 7-methyltriazolopyridine (16) was obtained. Experiments with lithium deuteroxide resulted in no deuterium exchange, and on treatment with sodamide followed by addition of benzyl bromide no alkylation was observed, showing that the methyl group in compound (16) had little if any activity of the type exhibited by 2-methylpyridine. However,



lithiation (presumably directed by the *peri*-nitrogen atom) proceeded normally at −40 °C (with lithium di-isopropylamide), and treatment of the 7-lithiomethyl intermediate with anisaldehyde gave the secondary alcohol (17) in 57% yield. The alcohol (17) reacted with bromine to give the dibromomethylpyridine (18) (87%), and this in turn, treated with alcoholic silver

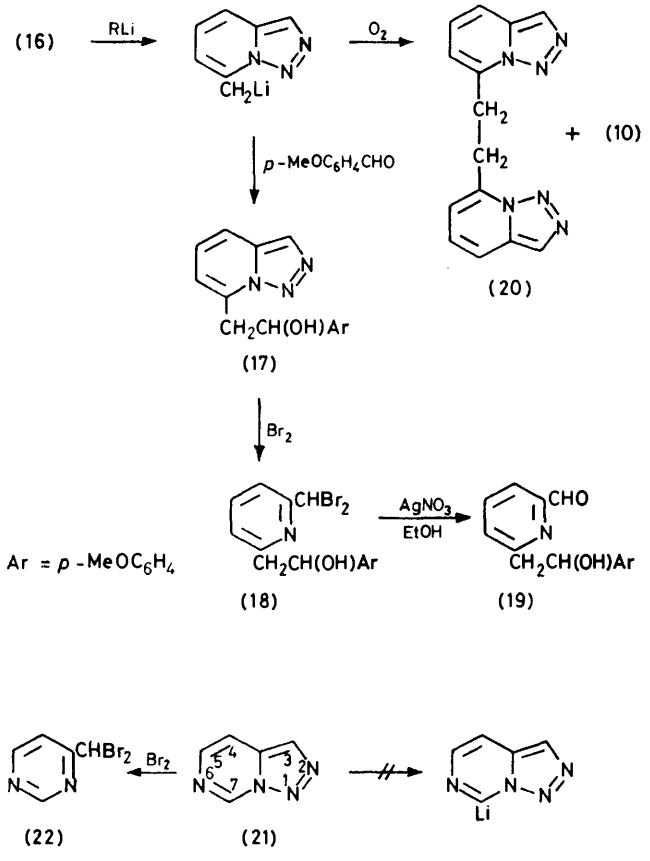


(14) R = H
(15) R = $SO_2C_6H_4Me$-*p*

(16)

nitrate, gave the pyridine-2-carbaldehyde (19) (68%). When nitrogen containing a small percentage of oxygen was used in the preparation of the 7-lithiomethyltriazolopyridine, or if air was passed through the solution of the lithium reagent, yields of up to 35% of the 7-hydroxymethyltriazolopyridine (10) could be obtained, together with very small amounts of 1,2-bis(triazolopyridin-7-yl)ethane (20).

Our first attempt to widen the scope of the synthesis has failed. Triazolo[1,5-*c*]pyrimidine (21), prepared by the method of Maury *et al.*,[4] reacted with bromine to give 4-dibromomethylpyrimidine (22). No evidence of lithiation was obtained under a variety of conditions;



thus functionalization of compound (21) at position 7 has not proved possible.

EXPERIMENTAL

All lithiation experiments were conducted under oxygen-free nitrogen [5] or argon atmosphere. Preparative layer chromatography was performed on silica gel plates (PF_{254}; 20 × 40 cm). Medium-pressure column chromatography was carried out on Kieselgel 60; the alumina used was from Woelm (activity shown in parentheses).

General Procedure for Lithiation of Triazolo[1,5-a]*pyridine.*—A solution of n-butyl-lithium (14.5 ml of 1.16M; 0.0168 mol) in hexane, was added to di-isopropylamine (0.0168 mol, freshly distilled from KOH) at −40 °C. A solution of triazolo[1,5-*a*]pyridine (1) (2 g, 0.0168 mol) in dry ether (80 ml) was added with stirring, which was continued at −40 °C (6 h) during which time a deep red colour developed. Addition of the carbonyl co-reactant (0.016 mol) caused a colour change to yellow; the mixture was allowed to come to room temperature and stirred overnight, then hydrolysed by a solution of ammonium chloride in ammonia (specific gravity 0.880). Purification procedures are given for each compound.

1-(*Triazolopyridin-7-yl*)*octan*-1-*ol* (5a).—The organic material obtained by extraction (CH_2Cl_2) after hydrolysis, was chromatographed on alumina (4) (120 g). Elution with petroleum (b.p. 60—80 °C) gave octanal (0.4 g) and with benzene–petroleum (1 : 1) gave triazolopyridine (0.3 g). Elution with dichloromethane–benzene (1 : 4) gave the *octanol* (5a), as an unstable oil (2.5 g, 56%) (Found: M^+, 247.168 47; $C_{14}H_{21}N_3O$ requires *M*, 247.1684); $\nu_{max.}$ ($CHCl_3$) 3 390br cm^{-1}.

α-(*Triazolopyridin-7-yl*)*benzyl Alcohol* (5b).—Extracted from the hydrolysed mixture and purified by medium-pressure chromatography [eluting solvent ethyl acetate–petroleum (b.p. 60—80 °C) (3 : 1)] the *alcohol* (5b) had m.p. 123.5—124.5 °C (cyclohexane) (yield 2.0 g, 53% based on benzaldehyde consumed) (Found: C, 69.6; H, 5.0; N, 19.0. $C_{13}H_{11}N_3O$ requires C, 69.3; H, 4.9; N, 18.65%); $\nu_{max.}$ ($CHCl_3$) 3 590 and 3 440br cm^{-1}; *m/z* 225 (M^+).

α-(*Triazolopyridin-7-yl*)-4-*methoxybenzyl Alcohol* (5c).—Separated as a yellow solid from the hydrolysed reaction mixture, the *alcohol* (5c) had m.p. 171—172 °C (benzene) (yield 2.77 g, 69%) (Found: C, 65.75; H, 5.05; N, 16.75%; M^+, 255.1000. $C_{14}H_{13}N_3O_2$ requires C, 65.85; H, 5.15; N, 16.45%; *M*, 255.1007); $\nu_{max.}$ ($CHCl_3$) 3 345br and 1 110 cm^{-1};

4-*Nitro*-α-(*triazolopyridin-7-yl*)*benzyl Alcohol* (5d).—Trituration with chloroform of the red oil obtained after hydrolysis gave the *benzyl alcohol* (5d), m.p. 180—182 °C (0.9 g, 20%) (Found: C, 57.9; H, 3.5; N, 20.75%; M^+, 270.0754. $C_{13}H_{10}N_4O_3$ requires C, 57.75; H, 3.75; N, 20.75%; *M*, 270.0753); $\nu_{max.}$ (Nujol) 3 300br, 1 520, and 1 350 cm^{-1}; $\lambda_{max.}$ (EtOH, 95%) 275 nm ($\log_{10}$ ε 4.08).

1-(2-*Pyridyl*)-1-(*triazolopyridin-7-yl*)*ethanol* (5e).—The material extracted from the hydrolysed mixture was chromatographed on a medium-pressure column; elution with ethyl acetate gave on oil, solidifying on trituration with petroleum. The *pyridylethanol* (5e) (1.6 g, 40% based on acetylpyridine consumed) had m.p. 125—126° (cyclohexane) (Found: C, 65.45; H, 5.2; N, 23.2. $C_{13}H_{12}N_4O$ requires C, 65.0; H, 5.05; N, 23.3%); $\nu_{max.}$ ($CHCl_3$) 3 430br cm^{-1}; *m/z* 240 (M^+).

1-(*Triazolopyridin-7-yl*)*cyclohexanol* (5f).—This was ex-

tracted from the crude hydrolysis mixture by dichloromethane, and purified by chromatography on alumina (4) (85 g). Elution with benzene–petroleum (3 : 7) gave cyclohexanone (0.3 g); elution with benzene–petroleum (1 : 1) gave triazolopyridine (0.5 g) and the *cyclohexanol* (5f), m.p. 100 °C (from petroleum, b.p. 60—80 °C) (yield 0.91 g, 30% based on cyclohexanone consumed) (Found: C, 66.45; H, 7.05; N, 19.65%: M^+, 217.1211. $C_{12}H_{15}N_3O$ requires C, 65.35; H, 6.96; N, 19.35%; *M*, 217.1215); $\nu_{max.}$ ($CHCl_3$) 3 470 cm^{-1}; $\lambda_{max.}$ (EtOH, 95%) 285 nm ($\log_{10}$ ε 3.62).

Diphenyl(triazolopyridin-7-yl)methanol (5g).—A yellow solid, isolated from the hydrolysed mixture, was almost pure *alcohol* (5g); recrystallised from cyclohexane it had m.p. 186.5—187.5 °C (yield 2.65 g, 52%) (Found: C, 75.65; H, 4.85; N, 13.95%; M^+, 301.1216. $C_{19}H_{15}N_3O$ requires C, 75.75; H, 5.0; N, 13.95%; *M*, 301.1215); $\nu_{max.}$ ($CHCl_3$) 3 430br cm^{-1}.

2-(*Triazolopyridin-7-yl*)*but-3-en-2-ol* (5h).—The organic extract from the hydrolysed mixture was purified by medium-pressure chromatography, eluting with ethyl acetate–petroleum (b.p. 60—80 °C) (3 : 1). The butenol (5h) was an unstable oil, $\nu_{max.}$ ($CHCl_3$) 3 420br, 1 660, 1 320, 1 220, 1 040, 980, and 930 cm^{-1}; *m/z* 189 (M^+). Analyses were inconsistent, even after repeated p.l.c.

Bis(triazolopyridin-7-yl) Ketone (8).—From the lithium derivative (4; R = Li) (from 2 g of triazolopyridine) and ethyl chloroformate (1.6 ml) was obtained, after hydrolysis, a crude product (3.3 g). Trituration with ether gave the *ketone* (0.85 g, 19%), m.p. indistinct, >290 °C (Found: C, 59.0; H, 2.9; N, 32.25. $C_{13}H_8N_6O$ requires C, 59.1; H, 3.05; N, 31.8%); $\nu_{max.}$ (Nujol) 1 666, 1 620, 1 325, 1 090, and 885 cm^{-1}; $\lambda_{max.}$ (95% EtOH) 238, 276, and 366 nm ($\log_{10}$ ε 4.31, 3.99, and 3.70); *m/z* 264 (6%), 263 (25), 236 (21), 179 (35), 159 (31), 132 (37), 130 (67), 106 (46), 93 (18), 86 (42), 63 (42), 51 (35), 44 (68), and 32 (100).

7-*Hydroxymethyltriazolopyridine* (10).—(*a*) To the lithium reagent from triazolopyridine (3 g) was added dry dimethylformamide (1.9 ml). The colour of the mixture changed to yellow. After stirring overnight, the mixture was hydrolysed with 2N-hydrochloric acid, and the deep red solution stirred (1 h). Separation, extraction, extraction of the aqueous layer with dichloromethane, drying of the combined organic layers ($MgSO_4$), and evaporation gave the crude product (1.5 g). Medium-pressure chromatography, eluting with ethyl acetate–petroleum (b.p. 60—80 °C) (1 : 1) gave 7-*hydroxymethyltriazolopyridine* (10), m.p. 127—129 °C (benzene) (1.1 g, 30%) (Found: C, 56.25; H, 4.6; N, 28.6. $C_7H_7N_3O$ requires C, 56.35; H, 4.75; N, 28.9%); $\nu_{max.}$ ($CHCl_3$) 3 420br cm^{-1}; $\lambda_{max.}$ (95% EtOH) 282 nm ($\log_{10}$ ε 3.51); *m/z* 149 (84%, M^+), 121 (18), 94 (20), 93 (100), 92 (60), 77 (22), 67 (34), 66 (100), 65 (84), 64 (76), 63 (56), 51 (30), and 39 (52).

(*b*) A solution of 7-lithiomethyltriazolopyridine [from 7-methyltriazolopyridine (3 g)], prepared as described below, was stirred at −40 °C while dry air was passed through; the colour changed from red to yellow. Work up as in (*a*), except that the ethereal solution was washed with $Fe^{II}SO_4$ and $NaHSO_4$ to remove peroxides, gave the hydroxymethyl compound (10) in 33% yield.

6-*Bromo-2-dibromomethylpyridine* (13).—To the lithium reagent from the triazolopyridine (1) at −40° was added bromine (2.68 g). Normal work-up gave a crude product (4.1 g) from which benzene extracted the *bromopyridine* (13), m.p. 131—133 °C (cyclohexane) (yield 1.1 g, 20%) (Found: C, 21.75; H, 1.15; N, 4.3. $C_6H_4Br_3N$ requires C, 21.85; H, 1.2; N, 4.25%); $\lambda_{max.}$ (95% EtOH) 277 nm ($\log_{10}$ ε 3.83); δ 6.55 (1 H, s, $CHBr_2$) and 7.2—7.85 (3 H, m).

7-*Methyltriazolo*[1,5-a]*pyridine* (16).—This was obtained from 6-methylpyridine-2-carbaldehyde, *via* the *hydrazone* (14), m.p. 80—82 °C [benzene–petroleum (b.p. 60—80 °C) (1 : 1)] (Found: C, 62.2; H, 6.7; N, 31.1. $C_7H_9N_3$ requires C, 62.15; H, 6.5; N, 30.3%), or *via* the p-*tolylsulphonylhydrazone* (15), m.p. 84—86 °C [petroleum (b.p. 40—60 °C)–dichloromethane (4 : 1)] (Found: C, 58.1; H, 5.25; N, 14.55. $C_{14}H_{15}N_3O_3S$ requires C. 57.35; H, 5.15; N, 14.15%).

(*a*) The hydrazone (14) (20 g) was heated in aqueous solution (800 ml) with potassium hexacyanoferrate(III) (107.3 g) and sodium hydrogen carbonate (27.4 g) on a boiling water-bath (30 min). Effervescence occurred and a black oil separated. The cooled mixture was made alkaline with 30% sodium hydroxide (70 ml) and extracted with dichloromethane (5 × 500 ml). The organic layer was dried ($MgSO_4$), filtered, and evaporated to give crude triazolopyridine (16) (12.2 g). Distillation gave pure 7-*methyltriazolopyridine* (16), b.p. 94 °C at 0.05 mmHg, m.p. 40—42 °C (9 g, 46%) (Found: C, 63.05; H, 5.15; N, 31.3. $C_7H_7N_3$ requires C, 63.15; H, 5.35; N, 31.55%); $\lambda_{max.}$ (95% EtOH) 281 nm ($\log_{10}$ ε 3.88).

1-(p-*Methoxyphenyl*)-2-(*triazolopyridin-7yl*)*ethanol* (17).—(*a*) A solution of 7-methyltriazolopyridine (16) (2 g) in dry ether (60 ml) was added at −40 °C to a mixture of n-butyllithium (10.5 ml; 1.43M in hexane) and di-isopropylamine (2.1 ml) in ether (20 ml). After 6 h at −40 °C an intense red colour had developed, changing instantly to yellow when anisaldehyde (1.83 ml) was added. The mixture was stirred overnight at room temperature, hydrolysed with ammonium chloride in ammonia (specific gravity 0.88) and separated. Extraction of the aqueous layer with dichloromethane, combination of the organic layers, drying ($MgSO_4$), and evaporation gave a crude product (4.1 g). Medium-pressure chromatography (elution with ethyl acetate–petroleum, 2 : 3) gave anisaldehyde (0.2 g), *p*-methoxybenzyl alcohol, and 7-methyltriazolopyridine; elution with an increased proportion of ethyl acetate gave the *methoxyphenylethanol* (17), m.p. 117—118 °C (benzene) (yield 2.3 g, 63% based on anisaldehyde consumed) (Found: C, 67.0; H, 5.55; N, 15.9. $C_{15}H_{15}N_3O_2$ requires C. 66.9; H, 5.6; N, 15.6%); $\nu_{max.}$ ($CHCl_3$) 3 400br cm^{-1}; $\lambda_{max.}$ (95% EtOH) 281 nm ($\log_{10}$ ε 3.54); *m/z* 269 (M^+). From subsequent fractions a small amount (0.3 g) of 7-hydroxymethyltriazolopyridine (10) was obtained.

(*b*) If the experiment was performed under 'oxygen-free' nitrogen without the usual oxygen-removing train, the major product was 7-hydroxymethyltriazolopyridine (10) (35%), and a small amount (2%) of 1,2-*bis(triazolopyridin-7-yl)ethane* (20), m.p. 211—212 °C (benzene), was isolated (Found: C, 62.95; H. 4.4; N, 32.0. $C_{14}H_{12}N_6$ requires C, 63.62; H, 4.6: N. 31.8%); $\lambda_{max.}$ (95% EtOH) 286 nm ($\log_{10}$ ε 4.25): *m/z* 264 (M^+).

General Procedure for Reactions between Triazolopyridines and Bromine.—The triazolopyridine was dissolved in dichloromethane (2 g in *ca.* 25 ml) and cooled to 0—5 °C, and bromine (1 mol equiv.) in dichloromethane was added dropwise. Vigorous gas evolution occurred and stirring was continued after addition was complete (1 h). The solution was shaken with aqueous sodium hydrogencarbonate, then water, and dried ($MgSO_4$). Evaporation gave the substantially pure dibromomethylpyridine.

(6-*Dibromomethylpyridin*-2-*yl*)-(p-*methoxyphenyl*)-*methanol* (6c).—Obtained in 98% yield, the *pyridylmethanol* (6c) was an oil (Found: C, 43.6; H, 3.5; N, 3.55. $C_{14}H_{13}Br_2NO_2$ requires C, 43.45; H, 3.35; N, 3.6%); $\nu_{max.}$ ($CHCl_3$) 3 300br cm^{-1}; $\lambda_{max.}$ 229 and 278 nm ($\log_{10}$ ε 4.04 and 3.96); δ 3.76 (3 H, s, OCH_3), 4.7 (1 H, br, s OH), 5.6 (1 H, br, s, C*H*–OH), 6.2 (1 H, s, $CHBr_2$), 6.94 (2 H, dd, *J* 9 and 2 Hz, H-3′, -5′), 7.37 (2 H, dd, *J* 9 and 2 Hz, H-2′, -6′), 7.1 (1 H, m, H-4), and 7.9—8.1 (2 H, m, H-3, -5).

Diphenyl-(6-*dibromomethylpyridin*-2-*yl*)*methanol* (6g).—Obtained in 76% yield from compound (5 g), the *pyridylmethanol* (6 g) had m.p. 118—120 °C (absolute EtOH) (Found: C, 53.0; H, 3.5; N, 3.35. $C_{19}H_{15}Br_2NO$ requires C, 52.7; H, 3.45; N, 3.25%); $\nu_{max.}$ ($CHCl_3$) 3 400br cm^{-1}; $\lambda_{max.}$ 274 nm ($\log_{10}$ ε 4.03); δ 5.87 (1 H, br, s, exch. D_2O, OH), 6.64 (1 H, s, $CHBr_2$), 7.04 (1 H, q, H-4), 7.28 (10 H, m), and 7.73 (2 H, m. H-5, -3).

2-(6-*Dibromomethylpyridin*-2-*yl*)-1-(p-*methoxyphenyl*)-*ethanol* (18).—Obtained in 87% yield from compound (17), the *pyridylethanol* (18) was an oil (Found: C, 44.6; H, 3.65; N, 3.5. $C_{15}H_{15}Br_2NO_2$ requires C, 44.9; H, 3.75; N, 3.5%); $\nu_{max.}$ (film) 3 400br cm^{-1}; $\lambda_{max.}$ (95% EtOH) 225 and 272 nm ($\log_{10}$ ε 4.4 and 3.98); δ 3.2 (2 H, d, CH_2CHOH) 3.8 (3 H, s, OCH_3), 5.2 (1 H. t, C*H*OH), 6.7 (1 H, s, $CHBr_2$), and 6.8—7.8 (7 H. m).

General Procedure for Conversion of 2-*Bromomethylpyridines into Pyridine*-2-*carbaldehydes*.—The dibromomethylpyridine (*ca.* 1.2 g in 25 ml of ethanol) was mixed with silver nitrate (2.1 mol equiv.) in hot water (7 ml). The mixture was boiled (15 min) then cooled, and concentrated hydrochloric acid (7 ml) added. The silver salts were removed by filtration, the filtrate was evaporated under reduced pressure, and the residue was treated with saturated aqueous sodium hydrogencarbonate. Extraction with dichloromethane, drying of the organic extracts ($MgSO_4$), and evaporation gave virtually pure pyridine-2-carbaldehyde.

α-(6-*Formylpyridin*-2-*yl*)-4-*methoxybenzyl Alcohol* (7c).—Obtained in 78% yield from compound (6c), the aldehyde (7c) was an oil, characterised as its 2,4-*dinitrophenylhydrazone*, m.p. 189—192 °C (absolute ethanol) (Found: C, 56.55; H, 3.85; N, 16.5. $C_{20}H_{17}N_5O_6$ requires C, 56.75; H, 4.05; N, 16.55%). The aldehyde (7c) had $\nu_{max.}$ ($CHCl_3$) 3 400br and 1 710 cm^{-1}; $\lambda_{max.}$ (95% EtOH) 272 nm ($\log_{10}$ ε 3.82); δ 3.7 (3 H, s, OCH_3), 4.75 (1 H, br, s, D_2O exch., OH), 5.75 (1 H, s, C*H*OH), 6.6—7.3 (4 H, H-2′, -3′, -5′, -6′), 7.5 (1 H, m, H-4), 7.8 (2 H, m, H-3, -5), and 9.9 (1 H, s, CHO).

Diphenyl-(6-*formylpyridin*-2-*yl*)*methanol* (7g).—Prepared from compound (6g) in quantitative yield, as an oil, the formylpyridine (7g) was characterised as its 2,4-*dinitrophenylhydrazone*, m.p. 197—199 °C (Found: C, 64.05; H, 3.95; N, 14.9. $C_{15}H_{19}N_5O_6$ requires C, 63.95; H, 4.1; N, 14.9%). The formylpyridine (7g) had $\lambda_{max.}$ 265 and 270sh nm ($\log_{10}$ ε 3.86, —); $\nu_{max.}$ ($CHCl_3$) 3 400br and 1 710 cm^{-1}; δ 5.9 (1 H, br, s, exch. D_2O, OH), 7.28 (10 H, br, s, benzene H), 7.3—7.8 (3 H, m, H-3, -4, -5), and 9.9 (1 H, s, CHO).

2-(6-*Formylpyridine*-2-*yl*)-1-(*p-methoxyphenyl*)*ethanol* (19).—Prepared from compound (18) in 68% yield, the *formylpyridine* (19) was purified by p.l.c.; m.p. 103—108 °C (Found: C, 70.1; H, 5.6; N, 5.2. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9; N, 5.45%); $\nu_{max.}$ 3 400 and 1 710 cm^{-1}; δ 3.8 (5 H, m, CH_2 and OCH_3), 6.9 (1 H, t, C*H*OH), 7.1—7.9 (7 H, benzene and pyridine H), and 10.1 (1 H, s, CHO).

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