Cytotoxic Compounds. Part 23.[1] Reactions of the Methanesulphonates of 2-(*N*-Aryl-*N*-methylamino)propan-1-ols and of 1-(*N*-Aryl-*N*-methylamino)propan-2-ols with Nucleophiles

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Syntheses of the primary alcohols *p*-RC_6H_4·NMe·CHMe·CH_2·OH (from ethyl 2-bromopropanoate) and of the secondary isomers *p*-RC_6H_4·NMe·CH_2·CHMe·OH (from propylene oxide) are described (R = H, Cl, OMe, or NO_2). In solution, the primary methanesulphonates rearrange to the secondary isomers, a process facilitated by an electron-donating aryl substituent. Reactions of the primary and the secondary methanesulphonates with methanol, sodium methoxide, acetic acid, potassium acetate, tetramethylammonium acetate, sodium phenyl sulphide, sodium benzyl sulphide, lithium bromide, and sodium azide show that with weak nucleophiles the intermediate aziridinium ion is opened almost exclusively to give the secondary substitution product; with more powerful nucleophiles some sterically-controlled opening occurs to give also some primary product. When the formation of the aziridinium ion is retarded by the presence of an electron-attracting aryl substituent, strong nucleophiles can effect direct S_N2 substitution on the methanesulphonates to give unrearranged products. The *N*-methyl resonances in the ^1H n.m.r. spectra of the primary compounds are consistently at higher field than those of the secondary isomers.

An earlier Part [2] described the reactions of the bismethane sulphonates (1) and (2) with a variety of nucleophiles, the objective being to provide more information on the mode of action of alkylating agents of the nitrogen mustard type.[3] Interpretation of the results from such bifunctional compounds is complicated by the fact that successive displacements of two leaving groups are involved, and we have therefore turned to a study of some monofunctional analogues.

$PhNMe \cdot CH(CH_2 \cdot O \cdot SO_2Me)_2$

(1)

$PhNMe \cdot CH_2 \cdot CH(O \cdot SO_2Me) \cdot CH_2 \cdot O \cdot SO_2Me$

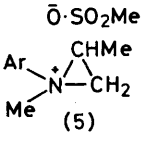
(2)

p-$RC_6H_4 \cdot S \cdot CHMe \cdot CH_2 \cdot O \cdot SO_2Me$

(3)

p-$RC_6H_4 \cdot S \cdot CH_2 \cdot CHMe \cdot O \cdot SO_2Me$

(4)



(5)

p-$RC_6H_4\ S \cdot CH(CH_2 \cdot O \cdot SO_2Me)_2$

(6)

p-$RC_6H_4 \cdot S \cdot CH_2 \cdot CH(O \cdot SO_2Me) \cdot CH_2 \cdot O \cdot SO_2Me$

(7)

p-Methoxy- and *p*-chloro-*N*-methylaniline were prepared by methylation and subsequent hydrolysis of the *p*-substituted acetanilide,[4] but *p*-nitroacetanilide gave unsatisfactory results by this procedure [5] and *N*-methyl-*p*-nitroaniline was therefore obtained by direct monomethylation of *p*-nitroaniline with trioxan and sulphuric acid.[6] Reaction of *N*-methylaniline, and of the *p*-methoxy-, *p*-chloro-, and *p*-nitro-compounds, severally, with ethyl 2-bromopropanoate,† followed by reduction with lithium aluminium hydride [7] (lithium borohydride for the nitro-compound), gave the 2-(*N*-methylanilino)-propan-1-ols (8)—(11) (Table 1). The secondary alcohols (38)—(41) were prepared by reaction of the same *N*-methylanilines with propylene oxide in aqueous acetic acid; the ring opening was not completely regiospecific,[3] traces of the primary isomers being detected (^1H n.m.r. spectra) in the crude products.

The methanesulphonates (20)—(23) and (50)—(53) were prepared from the alcohols by reaction with methanesulphonyl chloride in the presence of triethylamine, temperature control being very important for the primary derivatives because of their tendency to isomerise in solution to the secondary compounds; indeed, the best recrystallised samples which could be obtained of the primary methanesulphonates in the unsubstituted and in the *p*-methoxy-series always contained *ca.* 20% of the secondary isomers. ^1H N.m.r. spectroscopy showed that, in deuteriochloroform, rearrangement of the primary *p*-methoxy-compound. (21) was 50% complete in 8 min at 38 °C, whereas the primary *p*-nitro-compound (23) was 50% isomerised in 3 days at 60 °C, clearly illustrating the differing effects of the aryl substituents on the ease of formation of the intermediate aziridinium methanesulphonate ion-pair (5). The 1,3-bismethanesulphonate (1) was *not* converted into the 1,2-isomer (2), even in boiling acetone,[2] an evident consequence of the electron-withdrawing nature of a methylsulphonyloxymethyl group compared with the *C*-methyl group in the present series. It is also interesting that the thio-compounds (3; R = OMe, H, and Cl) were even more unstable than the nitrogen analogues, all attempts to prepare them from the primary alcohols giving only the secondary methanesulphonates (4); [8] furthermore, the 1,3-bismethanesulphonates (6; R = H or Cl) were converted into the 1,2-isomers (7) in boiling acetone,

† Differences in the nucleophilic reactivities of the various *N*-methylanilines towards the bromo-ester necessitated considerable variations in the conditions used to effect displacement (see Experimental section).

and attempts to prepare the *p*-methoxy-derivative (6; R = OMe) gave only the 1,2-isomer.[9]

The *N*-methyl signals are at higher field for all the primary compounds compared with their secondary isomers,

TABLE 1

Chemical shifts (τ values) for solutions in deuteriochloroform (aromatic, *p*-methoxy, and hydroxy protons omitted)

No.	R^1	R^2	Chemical shift: CH	CH_2	NMe	CMe	Me in R^2
(i) Compounds *p*-$R^1C_6H_4$·NMe·CHMe·CH_2R^2							
(8)	H	OH	5.9 (m)	6.40(d)	7.31 (s)	8.98 (d)	
(9)	OMe	OH	5.8—6.7 (m)		7.32 (s)	9.08 (d)	
(10)	Cl	OH	5.8—6.6 (m)		7.30 (s)	8.97 (d)	
(11)	NO_2	OH	5.8 (m)	6.30 (d)	7.10 (s)	8.84 (d)	
(12)	H	OAc	5.5—6.1 (m)		7.23 (s)	8.80 (d)	8.07 (s)
(13)	OMe	OAc	5.6—6.1 (m)		7.28 (s)	8.86 (d)	8.06 (s)
(14)	Cl	OAc	5.6—6.1 (m)		7.26 (s)	8.82 (d)	8.06 (s)
(15)	NO_2	OAc	5.3—6.0 (m)		7.09 (s)	8.72 (d)	8.07 (s)
(16)	H	OMe	5.9 (m)	6.6 (m)	7.24 (s)	8.86 (d)	6.67 (s)
(17)	OMe	OMe	6.1 (m)	6.6 (m)	7.28 (s)	8.85 (d)	6.63 (s)
(18)	Cl	OMe	5.9 (m)	6.5 (m)	7.25 (s)	8.85 (d)	6.65 (s)
(19)	NO_2	OMe	5.7 (m)	6.5 (m)	7.06 (s)	8.77 (d)	6.66 (s)
(20)	H	O·SO_2Me	5.4—6.0 (m)		7.20 (s)	8.73 (d)	7.10 (s)
(21)	OMe	O·SO_2Me	5.6—6.1 (m)		7.30 (s)	8.80 (d)	7.09 (s)
(22)	Cl	O·SO_2Me	5.6—5.8 (m)		7.20 (s)	8.75 (d)	7.07 (s)
(23)	NO_2	O·SO_2Me	5.3—5.8 (m)		7.04 (s)	8.64 (d)	7.04 (s)
(24)	H	SPh	6.0 (m)	7.0 (m)	7.27 (s)	8.75 (d)	
(25)	OMe	SPh	6.1 (m)	6.9 (m)	7.31 (s)	8.75 (d)	
(26)	Cl	SPh	6.0 (m)	7.0 (m)	7.28 (s)	8.76 (d)	
(27)	H	S·CH_2Ph	6.0 (m)	7.5 (m)	7.37 (s)	8.88 (d)	6.34 (s) *
(28)	OMe	S·CH_2Ph	6.1 (m)	7.4 (m)	7.37 (s)	8.89 (d)	6.29 (s) *
(29)	Cl	S·CH_2Ph	6.1 (m)	7.4 (m)	7.33 (s)	8.84 (d)	6.31 (s) *
(30)	H	Br			7.24 (s)		
(31)	OMe	Br			7.30 (s)		
(32)	Cl	Br			7.26 (s)		
(33)	NO_2	Br	5.6 (m)	6.51 (d)	7.06 (s)	8.58 (d)	
(34)	H	N_3	5.8 (m)	6.6 (m)	7.23 (s)	8.80 (d)	
(35)	OMe	N_3	6.1 (m)	6.7 (m)	7.30 (s)	8.87 (d)	
(36)	Cl	N_3	5.9 (m)	6.6 (m)	7.23 (s)	8.80 (d)	
(37)	NO_2	N_3	5.7 (m)	6.5 (m)	7.08 (s)	8.71 (d)	
(ii) Compounds *p*-$R^1C_6H_4$·NMe·CH_2·CHR^2Me							
(38)	H	OH	5.8 (m)	6.78 (d)	7.05 (s)	8.78 (d)	
(39)	OMe	OH	6.0 (m)	6.95 (d)	7.18 (s)	8.82 (d)	
(40)	Cl	OH	5.9 (m)	6.80 (d)	7.08 (s)	8.80 (d)	
(41)	NO_2	OH	5.8 (m)	6.57 (d)	6.85 (s)	8.73 (d)	
(42)	H	OAc	4.7 (m)	6.6 (m)	7.03 (s)	8.75 (d)	8.10 (s)
(43)	OMe	OAc	4.8 (m)	6.6 (m)	7.07 (s)	8.75 (d)	8.04 (s)
(44)	Cl	OAc	4.8 (m)	6.6 (m)	7.06 (s)	8.77 (d)	8.07 (s)
(45)	NO_2	OAc	4.7 (m)	6.4 (m)	6.91 (s)	8.72 (d)	8.09 (s)
(46)	H	OMe	6.2—6.8 (m)		7.00 (s)	8.85 (d)	6.63 (s)
(47)	OMe	OMe	6.4—6.9 (m)		7.07 (s)	8.86 (d)	6.65 (s)
(48)	Cl	OMe	5.9—6.7 (m)		7.00 (s)	8.85 (d)	6.64 (s)
(49)	NO_2	OMe	6.2—6.6 (m)		6.85 (s)	8.82 (d)	6.67 (s)
(50)	H	O·SO_2Me	5.0 (m)	6.5 (m)	7.00 (s)	8.58 (d)	7.24 (s)
(51)	OMe	O·SO_2Me	5.0 (m)	6.5 (m)	7.18 (s)	8.56 (d)	7.03 (s)
(52)	Cl	O·SO_2Me	5.0 (m)	6.4 (m)	6.96 (s)	8.55 (d)	7.17 (s)
(53)	NO_2	O·SO_2Me	4.9 (m)	6.3 (m)	6.83 (s)	8.51 (d)	7.13 (s)
(54)	H	SPh	6.3—6.9 (m)		7.07 (s)	8.70 (d)	
(55)	OMe	SPh	6.3—6.8 (m)		7.08 (s)	8.69 (d)	
(56)	Cl	SPh	6.3—6.9 (m)		7.06 (s)	8.72 (d)	
(57)	H	S·CH_2Ph	6.3—7.2 (m)		7.07 (s)	8.75 (d)	6.20 (s) *
(58)	OMe	S·CH_2Ph	6.5—6.9 (m)		7.12 (s)	8.76 (d)	6.18 (s) *
(59)	Cl	S·CH_2Ph	6.5—6.7 (m)		7.08 (s)	8.77 (d)	6.20 (s) *
(60)	H	Br	5.7 (m)	6.4 (m)	6.97 (s)	8.30 (d)	
(61)	OMe	Br	5.7 (m)	6.4 (m)	7.03 (s)	8.30 (d)	
(62)	Cl	Br	5.7 (m)	6.4 (m)	6.99 (s)	8.32 (d)	
(63)	NO_2	Br	5.6 (m)	6.2 (m)	6.80 (s)	8.25 (d)	
(64)	H	N_3	6.2 (m)	6.7 (m)	7.00 (s)	8.79 (d)	
(65)	OMe	N_3	6.2 (m)	6.77 (dd)	7.05 (s)	8.77 (d)	
(66)	Cl	N_3	6.2 (m)	6.78 (d)	7.05 (s)	8.85 (d)	
(67)	NO_2	N_3	6.1 (m)	6.5 (m)	6.84 (s)	8.68 (d)	

* S·CH_2 resonance.

The more important ^{1}H n.m.r. parameters of the *N*-methylanilinopropanols, their acetates, their methyl ethers (prepared as authentic reference compounds), and their methanesulphonates, are recorded in Table 1. and this criterion was used to differentiate between primary and secondary compounds, obtained by nucleophilic displacements on the sulphonates, when authentic materials (azides, bromides, *etc.*) were not available. The

relative intensities of these signals were used to determine the ratio of primary to secondary substitution product in all reaction mixtures obtained by nucleophilic displacement, the results (expressed as percentage of secondary product) being summarised in Table 2.

TABLE 2

Secondary substitution product (%) in primary–secondary mixtures formed by reaction of *p*-RC_6H_4·NMe·CHMe·CH_2·O·SO_2Me and *p*-RC_6H_4·NMe·CH_2·CHMe·O·SO_2Me with nucleophiles

		Reagent								
R	Methanesulphonate	MeOH	NaOMe	AcOH	KOAc	Me_4NOAc	PhSNa	$PhCH_2SNa$	LiBr	NaN_3
OMe	Primary *	>98	53	91	65	62	49	31	>98	75
OMe	Secondary	>98	79	91	67	65	57	45	>98	77
H	Primary *	96	65	90	72	62	50	28	>98	69
H	Secondary	>98	75	95	80	70	51	38	>98	84
Cl	Primary	>98	54	91	73	61	50	25	>98	66
Cl	Secondary	>98	74	93	75	79	57	40	>98	91
NO_2	Primary	93	52	91	62	<2			36	<2
NO_2	Secondary	>98	67	>98	87	89			88	>98

* Containing *ca.* 20% of secondary isomer.

Solvolysis of the eight methanesulphonates in boiling methanol gave, almost exclusively, the secondary methyl ethers; only very weak resonances for the primary ethers were present in the ^{1}H n.m.r. spectra of the products. Control experiments established that the authentic primary ethers were not isomerised under the experimental conditions, and therefore the products are the result of kinetically controlled fission of the aziridinium ion (5), essentially by attack at the more substituted carbon atom, this being the site at which stabilisation of an incipient carbonium ion would be more favoured.[10,*] With sodium methoxide in methanol, however, significant amounts of the primary methyl ethers were always formed, indicating the occurrence of S_N2-type sterically controlled attack on the aziridinium ions by the more nucleophilic methoxide anion. Furthermore, the formation of a higher proportion of primary ether from the primary than from the secondary methanesulphonates shows that *direct* substitution (not involving an aziridinium ion) must be occurring to some extent.

Solvolysis in boiling acetic acid in all cases gave mainly the secondary acetate by kinetic control (the authentic primary acetates were not isomerised in control experiments), but reactions with potassium acetate, like those with sodium methoxide (and for the same reason), led to the formation of significant proportions of primary product; for the *p*-nitro-compounds the much greater amount of primary acetate from the primary methanesulphonate, compared with that from the secondary methanesulphonate, again indicates that some degree of direct substitution is occurring. This effect was even more striking when tetramethylammonium acetate was used, the primary *p*-nitro-compound giving almost pure primary acetate whilst the secondary isomer gave a very high proportion of secondary acetate.

Excluding the two nitro-compounds (23) and (53), which would probably have failed to react smoothly,[11] the methanesulphonates were treated with sodium phenyl sulphide in boiling methanol to give mixtures (each *ca.* 1 : 1) of the primary and the secondary phenylthio-derivatives (24), (54); (25), (55); and (26), (56). Each mixture was separated by t.l.c. and constitutions were assigned to the individual compounds on the basis of the chemical shift of the *N*-methyl resonance in the ^{1}H n.m.r. spectrum. The same method was used to identify the six benzylthio-derivatives obtained in similar reactions with sodium benzyl sulphide; with this more powerful nucleophile a predominance of primary product was formed in each reaction, indicating the preponderance of sterically controlled S_N2 attack on the aziridinium ions, but inspection of the results for any isomeric pair reveals the occurrence also of some direct S_N2 displacement on the methanesulphonates, a greater amount of primary product being produced from the primary than from the secondary methanesulphonate.

On reaction with lithium bromide in acetone, the same six methanesulphonates gave products which were composed almost entirely of the corresponding secondary bromides; the traces of primary bromides, detected by the very weak *N*-methyl resonances at higher field, could not be isolated. Because bromide ion is a good leaving group, the primary and secondary bromide can evidently become equilibrated (thermodynamic control), so that even if the primary methanesulphonates underwent significant direct S_N2 attack this would not be revealed from the composition of the products. However, the *p*-nitro-compounds (23) and (53) behaved differently, the primary and the secondary methanesulphonate each giving a considerable preponderance of unrearranged bromide (kinetic control), direct attack clearly being involved to a considerable extent.

The reactions of all eight methanesulphonates with sodium azide in dimethylformamide showed an increasing tendency for direct substitution to occur as the electron-withdrawing power of the aryl substituent became greater, the product from each nitro-compound containing virtually no rearranged azide.

In general, therefore, the nature of the products obtained depends on the type of nucleophilic reagent and on the electronic effect of the substituent in the aryl ring. With weak nucleophiles (methanol, acetic acid) reaction proceeds through the aziridinium ion, which is

* In addition to the electronic factor, steric crowding between the *C*-methyl and (depending on the configuration adopted) the *N*-methyl or *N*-aryl group would also favour fission of the more highly substituted bond in the aziridinium ring.

opened almost exclusively at the more substituted carbon atom, but with more powerful nucleophiles some sterically controlled attack at the less substituted position becomes evident. Furthermore, when the tendency to form an aziridinium ion is diminished by the presence of an electron-withdrawing aryl group, these more powerful nucleophiles can attack the methanesulphonate in a direct S_N2 displacement, a process which becomes completely dominant in the reaction of azide ion with the *p*-nitro-compounds. Qualitatively, somewhat similar results have been reported [11] for reactions of the same range of nucleophiles with some thio-analogues (3) and (4) but a major difference between compounds of the sulphur mustard and the nitrogen mustard type is that no elimination products have been encountered in reactions of the latter (see also ref. 2), whereas with comparable mono- and bis-methanesulphonates of the sulphur mustard type the occurrence of competitive elimination (which did not involve an intermediate episulphonium ion) was a significant feature of reactions with the more basic nucleophiles.[10-12]

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded for solutions in deuteriochloroform on a Varian T-60 instrument, and reaction products were identified, qualitatively and quantitatively, from their spectra. Routine recordings of i.r. spectra were made, and were in accord with structural assignments, but the absorptions are not cited. Kieselgel GF_{254} (Merck) was used for t.l.c., and plates were developed with dichloromethane, unless otherwise specified. Petroleum refers to the fraction of b.p. 40—60 °C.

N-Methylanilines.—(i) *N*-Acetyl-*p*-anisidine (78 g) was added to sodium powder (11.5 g) under xylene (300 ml), and the mixture was stirred and boiled under reflux for 2 h. Heating was then discontinued, and a solution of dimethyl sulphate (32 ml) in xylene (60 ml) was added at a rate sufficient to maintain gentle boiling. Heating was then continued for 2 h, and the xylene was then distilled off under reduced pressure. A solution of potassium hydroxide (70 g) in ethanol (250 ml) and water (25 ml) was added to the residue, and the mixture was boiled under reflux for 60 h, then concentrated, diluted with water, and extracted with ether to give an oil. This was distilled to give a fraction, b.p. 45—47° at 0.1 mmHg, which solidified. Recrystallisation from dichloromethane–petroleum gave *N*-methyl-*p*-anisidine (14.3 g), m.p. 35° (lit.,[13] 35—36°).

(ii) Similarly, *p*-chloroacetanilide (97 g) gave *N*-methyl-*p*-chloroaniline (81 g), b.p. 70° at 0.15 mmHg (lit.,[14] 239—240° at 764 mmHg), τ 2.89 (2 H, d), 3.52 (2 H, d), 6.37br (1 H, NH), and 7.23 (3 H, s, NMe).

(iii) Trioxan (40 g) was added in portions to a solution of *p*-nitroaniline (27 g) in sulphuric acid (400 g) at 100°. Heating was continued for a further 2 h, after which the cooled mixture was poured onto crushed ice (200 g) and neutralised with ammonia. The precipitate was collected and recrystallised from ethanol to give *N*-methyl-*p*-nitroaniline (18 g), m.p. 150° (lit.,[14] 152°).

Ethyl 2-(N-*Methylanilino*)*propanoates.*—(i) A mixture of ethyl 2-bromopropanoate (9.0 g), *N*-methylanisidine (6.8 g), and pyridine (5 ml) was heated at 120 °C for 46 h under nitrogen, and then distilled. The main fraction, b.p. 90° at 0.15 mmHg, was purified by t.l.c. to give *ethyl* 2-(p-*methoxy*-N-*methylanilino*)*propanoate* (2.5 g), n_D^{19} 1.521 2, τ 3.13 (4 H, s), 5.4—6.0 (3 H, m, C*H*Me and C*H*$_2$Me), 6.23 (3 H, s, OMe), 7.14 (3 H, s, NMe), 8.57 (3 H, d, CH*Me*), and 8.78 (3 H, t, CH$_2$*Me*) (Found: C, 65.7; H, 8.0; N, 6.0. $C_{13}H_{19}NO_3$ requires C, 65.8; H, 8.1; N, 5.9%).

(ii) A mixture of ethyl 2-bromopropanoate (18.1 g), *N*-methylaniline (10.7 g), and sodium acetate (9.0 g) was heated under nitrogen for 30 h at 120 °C, then cooled and partitioned between ether and water. Distillation of the washed and dried ether layer gave ethyl 2-(*N*-methylanilino)propanoate (17.4 g), b.p. 76° at 0.1 mmHg, n_D^{18} 1.523 8 (lit.,[7] n_D^{25} 1.5190), τ 2.5—3.4 (5 H, m), 5.3—6.0 (3 H, m, C*H*Me and C*H*$_2$Me), 7.10 (3 H, s, NMe), 8.53 (3 H, d, CH*Me*), and 8.77 (3 H, t, CH$_2$*Me*).

(iii) A mixture of ethyl 2-bromopropanoate (41.7 g), *p*-chloro-*N*-methylaniline (14.1 g), sodium acetate (9.0 g), sodium iodide (1.5 g), and pyridine (12 ml) was heated for 50 h at 115 °C, then fractionally distilled to give *ethyl* 2-(p-*chloro*-N-*methylanilino*)*propanoate* (9.0 g), b.p. 105° at 0.25 mmHg, n_D^{24} 1.537 2, τ 2.76 (2 H, d), 3.26 (2 H, d), 5.60 (1 H, m, C*H*Me), 5.80 (2 H, q, C*H*$_2$Me), 7.12 (3 H, s, NMe), 8.53 (3 H, d, CH*Me*), and 8.80 (3 H, t, CH$_2$*Me*) (Found: C, 59.5; H, 6.7; N, 5.6. $C_{12}H_{16}ClNO_2$ requires C, 59.6; H, 6.7; N, 5.8%).

(iv) A mixture of ethyl 2-bromopropanoate (13.6 g), *N*-methyl-*p*-nitroaniline (11.4 g), sodium acetate (6.8 g), sodium iodide (0.2 g), and dimethylformamide (25 ml) was heated at 135° for 10 days, then cooled, filtered, and concentrated under reduced pressure. The residue was purified by t.l.c. (petroleum–dichloromethane, 2 : 1) to give *ethyl* 2-(N-*methyl*-p-*nitroanilino*)*propanoate* (5.4 g), an oil, τ 1.80 (2 H, d), 3.25 (2 H, d), 5.37 (1 H, q, C*H*Me), 5.78 (2 H, q, C*H*$_2$Me), 6.97 (3 H, s, NMe), 8.45 (3 H, d, CH*Me*), and 8.76 (3 H, t, CH$_2$*Me*) (Found: C, 57.3; H, 6.6; N, 10.9. $C_{12}H_{16}N_2O_4$ requires C, 57.1; H, 6.4; N, 11.1%).

2-(N-*Methylanilino*)*propan*-1-*ols.*—(i) A solution of ethyl 2-(*p*-methoxy-*N*-methylanilino)propanoate (2.5 g) in ether (50 ml) was added to a stirred suspension of lithium aluminium hydride (0.38 g) in ether (12 ml), and the mixture was stirred and boiled under reflux for 17 h. After addition of water, followed by 10% aqueous sodium hydroxide, the ethereal layer was separated, dried, and evaporated to give 2-(p-*methoxy*-N-*methylanilino*)*propan*-1-*ol* (9) (1.8 g), an oil, n_D^{18} 1.549 6 (Found: C, 67.55; H, 8.6; N, 7.0. $C_{11}H_{17}NO_2$ requires C, 67.7; H, 8.8; N, 7.2%).

(ii) Similar reduction of ethyl 2-(*N*-methylanilino)propanoate (17.4 g) gave 2-(*N*-methylanilino)propan-1-ol (8) (10.2 g), b.p. 82° at 0.13 mmHg, n_D^{17} 1.559 7 (lit.,[7] n_D^{25} 1.557 9).

(iii) Under the same conditions, ethyl 2-(*p*-chloro-*N*-methylanilino)propanoate (7.2 g) gave 2-(p-*chloro*-N-*methylanilino*)*propan*-1-*ol* (10) (5.5 g), b.p. 114° at 0.5 mmHg, n_D^{24} 1.573 0 (Found: C, 60.1; H, 7.0; N, 7.2. $C_{10}H_{14}ClNO$ requires C, 60.2; H, 7.0; N, 7.0%).

(iv) A solution of lithium borohydride (0.9 g) in tetrahydrofuran (90 ml) was slowly added (30 min) to a solution of ethyl 2-(*N*-methyl-*p*-nitroanilino)propanoate (3.4 g) in tetrahydrofuran (12 ml) at 0 °C. The mixture was stirred at ambient temperature for 70 h, and then the excess of reagent was destroyed by addition of dilute aqueous acetic acid. The tetrahydrofuran was removed by distillation, and the residue was extracted with dichloromethane to give an oil, which crystallised after purification by t.l.c. Recrystallisation from dichloromethane–petroleum gave 2-(N-*methyl*-p-*nitroanilino*)*propan*-1-*ol* (11) (2.5 g), m.p. 62°

(Found: C, 57.05; H, 6.8; N, 13.1. $C_{10}H_{14}N_2O_3$ requires C, 57.1; H, 6.7; N, 13.3%).

1-(N-*Methylanilino*)*propan*-2-*ols*.—(i) A mixture of *N*-methyl-*p*-anisidine (5.6 g), propylene oxide (15 ml), acetic acid (2 ml), and water (35 ml) was stirred for 15 h at ambient temperature and then concentrated to remove excess of propylene oxide. The residue was neutralised with sodium carbonate and extracted with ether to give 1-(p-*methoxy*-N-*methylanilino*)*propan*-2-*ol* (39) (4.1 g), n_D^{18} 1.549 3 (Found: C, 67.7; H, 8.9; N, 7.0. $C_{11}H_{17}NO_2$ requires C, 67.7; H, 8.8; N, 7.2%). A very weak resonance at τ 7.32 indicated the presence of a trace of the primary isomer.

(ii) Similarly, a mixture of *N*-methylaniline (21.4 g), propylene oxide (20.3 g), acetic acid (60 g), and water (300 ml), stirred for 45 h, gave 1-(*N*-methylanilino)propan-2-ol (38) (24.5 g), b.p. 68° at 0.1 mmHg (lit.,[15] 100° at 1 mmHg), n_D^{17} 1.556 5 (lit.,[15] n_D^{25} 1.555 8).

(iii) Reaction of *p*-chloro-*N*-methylaniline (17.0 g) with propylene oxide (23 g) in acetic acid (145 g) and water (250 ml) for 70 h gave 1-(p-*chloro*-N-*methylanilino*)*propan*-2-*ol* (40) (14.0 g), b.p. 80° at 0.6 mmHg, n_D^{18} 1.564 5 (Found: C, 60.2; H, 7.1; Cl, 17.8; N, 6.9. $C_{10}H_{14}ClNO$ requires C, 60.2; H, 7.0; Cl, 17.8; N, 7.0%).

(iv) Propylene oxide (50 ml) was added to a solution of *N*-methyl-*p*-nitroaniline (0.7 g) in acetic acid (10 ml) and water (7 ml). The mixture was stirred for 4 days at ambient temperature and for a further 5 days at reflux temperature. Starting material was still present, but purification of the crude product by t.l.c. gave 1-(N-*methyl*-p-*nitroanilino*)-*propan*-2-*ol* (41) (0.4 g), m.p. 99° (from ether–petroleum) (Found: C, 57.0; H, 6.5; N, 13.1. $C_{10}H_{14}N_2O_3$ requires C, 57.1; H, 6.7; N, 13.3%).

Acetates.—Prepared by acetylation of the alcohol with acetic anhydride in pyridine at ambient temperature, and purified by t.l.c., 1-*acetoxy*-2-(N-*methylanilino*)*propane* (12) had n_D^{24} 1.525 8 (Found: C, 69.45; H, 8.2; N, 6.6. $C_{12}H_{18}NO_2$ requires C, 69.5; H, 8.3; N, 6.75%); 2-*acetoxy*-1-(N-*methylanilino*)*propane* (42) had n_D^{16} 1.524 8 (Found: C, 69.65; H, 8.5; N, 6.8%); 1-*acetoxy*-2-(p-*methoxy*-N-*methylanilino*)*propane* (13) had n_D^{24} 1.524 2 (Found: C, 65.8; H, 7.9; N, 5.9. $C_{13}H_{19}NO_3$ requires C, 65.8; H, 8.1; N, 5.9%); 2-*acetoxy*-1-(p-*methoxy*-N-*methylanilino*)*propane* (43) had n_D^{20} 1.521 3 (Found: C, 65.9; H, 8.1; N, 5.9%); 1-*acetoxy*-2-(p-*chloro*-N-*methylanilino*)*propane* (14) had n_D^{24} 1.541 7 (Found: C, 59.55; H, 6.7; N, 5.8. $C_{12}H_{16}ClNO_2$ requires C, 59.6; H, 6.7; H, 5.8%); and 2-*acetoxy*-1-(p-*chloro*-N-*methylanilino*)*propane* (44) had n_D^{24} 1.538 0 (Found: C, 59.4; H, 6.6; N, 5.6%).

^1H N.m.r. data for the nitro-compounds (15) and (45) were obtained from acetates formed by nucleophilic displacement reactions (see below).

Methyl Ethers.—A mixture of 2-(*N*-methylanilino)-propan-1-ol (165 mg), dimethyl sulphate (250 mg), powdered sodium hydroxide (150 mg), and tetrahydrofuran (5 ml) was stirred for 24 h at ambient temperature, then diluted with water (10 ml), and extracted with ether. Evaporation of the washed and dried extract, followed by t.l.c. (ether–petroleum, 1 : 20), gave 1-*methoxy*-2-(N-*methylanilino*)*propane* (16) (90 mg) (Found: C, 73.9; H, 9.4; N, 7.7. $C_{11}H_{17}NO$ requires C, 73.7; H, 9.55; N, 7.8%). Similarly prepared were 2-*methoxy*-1-(N-*methylanilino*)*propane* (46), n_D^{15} 1.531 5 (Found: C, 73.9; H, 9.4; N, 7.7%); 1-*methoxy*-2-(p-*methoxy*-N-*methylanilino*)*propane* (17), n_D^{19} 1.531 5 (Found: C, 69.1; H, 9.2; N, 6.6. $C_{12}H_{19}NO_2$ requires C, 68.9; H, 9.15; N, 6.7%); 2-*methoxy*-1-(p-*methoxy*-N-*methylanilino*)*propane* (47), n_D^{20} 1.528 8 (Found: C, 69.0; H, 9.0; N, 6.6%); 1-*methoxy*-2-(p-*chloro*-N-*methylanilino*)-*propane* (18), n_D^{24} 1.546 9 (Found: C, 61.8; H, 7.6; N, 6.5. $C_{11}H_{16}ClNO$ requires C, 61.8; H, 7.55; N, 6.55%); 2-*methoxy*-1-(p-*chloro*-N-*methylanilino*)*propane* (48), n_D^{24} 1.546 5 (Found: C, 61.9; H, 7.55; N, 6.6%); and 1-*methoxy*-2-(N-*methyl*-p-*nitroanilino*)*propane* (19) (t.l.c. in benzene–ethyl acetate, 9 : 1) (Found: C, 59.0; H, 7.1; N, 12.4. $C_{11}H_{16}N_2O_3$ requires C, 58.9; H, 7.2; N, 12.5%).

^1H N.m.r. parameters for the nitro-compound (49) were obtained from the product of a displacement reaction (see below).

Methanesulphonates.—(i) A solution of methanesulphonyl chloride (0.63 g) in dichloromethane (2 ml) was added slowly (1 h) to a stirred solution of 2-(*N*-methylanilino)-propan-1-ol (0.83 g) and triethylamine (0.5 g) in dichloromethane (5 ml) at 0 °C. After a further 30 min the mixture was filtered, and the filtrate was quickly washed successively with ice-cold 10% hydrochloric acid, aqueous sodium hydrogencarbonate, and water, and then evaporated under reduced pressure at 0 °C. Recrystallisation of the residue from dichloromethane gave 2-(N-*methylanilino*)-1-*methylsulphonyloxypropane* (20) (0.70 g), m.p. 40° (Found: C, 54.3; H, 7.0; N, 5.7; S, 13.1. $C_{11}H_{17}NO_3S$ requires C, 54.3; H, 7.0; N, 5.75; S, 13.2%), which contained *ca.* 20% of the secondary isomer (^1H n.m.r. spectrum).

(ii) By the same procedure, but at ambient temperature, 1-(*N*-methylanilino)propan-2-ol (4.9 g) gave 1-(N-*methylanilino*)-2-*methylsulphonyloxypropane* (50) (4.8 g), m.p. 39° (from ether–petroleum) (Found: C, 54.4; H, 6.9; N, 5.6%).

(iii) By reaction at 0 °C, 2-(*p*-methoxy-*N*-methylanilino)-propan-1-ol (0.97 g) gave 2-(p-*methoxy*-N-*methylanilino*-1-*methylsulphonyloxypropane* (21) (0.66 g), m.p. 45° (from ether) (Found: C, 52.8; H, 7.2; N, 5.0; S, 11.6. $C_{12}H_{19}NO_4S$ requires C, 52.7; H, 7.0; N, 5.1; S, 11.7%). The ^1H n.m.r. spectrum showed the presence of *ca.* 20% of the secondary isomer.

(iv) At ambient temperature, 1-(*p*-methoxy-*N*-methylanilino)propan-2-ol (1.95 g) gave 1-(p-*methoxy*-N-*methylanilino*)-2-*methylsulphonyloxypropane* (51) (1.35 g), m.p. 79—81° (from chloroform) (Found: C, 52.95; H, 7.1; N, 5.0; S, 11.7%).

(v) 2-(*p*-Chloro-*N*-methylanilino)propan-1-ol (1.0 g) at 0 °C gave 2-(p-*chloro*-N-*methylanilino*)-1-*methylsulphonyloxypropane* (22) (0.70 g), m.p. 47° (from dichloromethane–petroleum) (Found: C, 47.8; H, 5.8; N, 5.0; S, 11.8. $C_{11}H_{16}ClNO_3S$ requires, C, 47.6; H, 5.8; N, 5.0; S, 11.5%).

(vi) 1-(*p*-Chloro-*N*-methylanilino)propan-2-ol (10.0 g) at ambient temperature gave 1-(p-*chloro*-N-*methylanilino*)-2-*methylsulphonyloxypropane* (52) (9.5 g), m.p. 74° (from dichloromethane–petroleum) (Found: C, 47.3; H, 5.8; N, 4.8; S, 11.5%).

(vii) 2-(*N*-Methyl-*p*-nitroanilino)propan-1-ol (0.63 g) at 0 °C gave 2-(N-*methyl*-p-*nitroanilino*)-1-*methylsulphonyloxypropane* (23) (0.70 g), m.p. 103—105° (from ether–petroleum) (Found: C, 46.0; H, 5.6; N, 9.7; S, 10.9. $C_{11}H_{16}N_2O_5S$ requires C, 45.8; H, 5.6; N, 9.7; S, 11.1%).

(viii) 1-(*N*-Methyl-*p*-nitroanilino)propan-2-ol (1.2 g) at ambient temperature gave 1-(N-*methyl*-p-*nitroanilino*)-2-*methylsulphonyloxypropane* (53) (0.9 g), m.p. 150—151° (from dichloromethane–petroleum) (Found: C, 45.8; H, 5.4; N, 9.5; S, 10.9%).

Reactions with Nucleophiles.—The methanesulphonates were freshly prepared, and reactions with a particular nucleophile were carried out under identical conditions;

only typical examples are described below, but all results are summarised in Table 2. The proportions of primary and secondary compounds were determined from the ^{1}H n.m.r. spectra of the total reaction products.

(i) *With methanol.* (*a*) A solution of the methanesulphonate (20) (150 mg) in methanol (12 ml), containing calcium carbonate (250 mg), was boiled under reflux for 24 h, then filtered, and evaporated under reduced pressure. The residue was partitioned between water and dichloromethane, and the organic layer was dried and evaporated to an oil (96 mg); the ^{1}H n.m.r. spectrum showed that this was 2-methoxy-1-(*N*-methylanilino)propane containing 4% of 1-methoxy-2-(*N*-methylanilino)propane.

(*b*) The methanesulphonate (23) (80 mg) gave a mixture (62 mg) of primary (7%) and secondary methyl ether (93%), which on purification by t.l.c. (dichloromethane–benzene, 9 : 1) furnished 2-*methoxy*-1-(N-*methyl*-p-*nitroanilino*)*propane* (49) (Found: C, 58.8; H, 6.9; N, 12.3. $C_{11}H_{16}N_2O_3$ requires C, 58.9; H, 7.2; N, 12.5%).

(ii) *With sodium methoxide.* When the reaction of sodium (50 mg) with methanol (15 ml) was complete, the methanesulphonate (20) (150 mg) was added, and the solution was boiled under reflux for 2 h, then concentrated, diluted with water, and extracted with dichloromethane to give a mixture (85 mg) of primary (35%) and secondary (65%) methyl ether.

(iii) *With acetic acid.* (*a*) A solution of the methanesulphonate (20) (83 mg) in acetic acid (2.5 ml) and acetic anhydride (0.1 ml) was boiled gently under reflux for 8 h, then diluted with water, and extracted with ether. The extract was washed with dilute aqueous sodium hydroxide and with water, then dried and evaporated to give a mixture (51 mg) of 1-acetoxy-2-(*N*-methylanilino)propane (10%) and 2-acetoxy-1-(*N*-methylanilino)propane (90%).

(*b*) The methanesulphonate (23) (80 mg) gave a mixture (69 mg) of primary (9%) and secondary acetate (91%); purification by t.l.c. (dichloromethane–benzene, 20 : 1) gave 2-*acetoxy*-1-(N-*methyl*-p-*nitroanilino*)*propane* (45) (Found: C, 57.1; H, 6.5; N, 10.95. $C_{12}H_{16}N_2O_4$ requires C, 57.1; H, 6.4; N, 11.1%).

(iv) *With potassium acetate.* A mixture of the methanesulphonate (20) (120 mg), potassium acetate (150 mg), and acetic anhydride (2.0 ml) was stirred at 100° for 6 h, then cooled, diluted with water, and extracted with dichloromethane. Evaporation of the washed (aqueous sodium hydroxide) and dried extract gave a mixture (63 mg) of primary (28%) and secondary acetate (72%).

(v) *With tetramethylammonium acetate.* (*a*) The methanesulphonate (20) (80 mg) was added to a suspension of tetramethylammonium acetate [9] (185 mg) in acetone (3.5 ml), and the mixture was boiled under reflux for 6 h, then concentrated and extracted with dichloromethane. The extract was washed with water, then dried and evaporated to give a mixture (45 mg) of primary (38%) and secondary acetate (62%).

(*b*) The methanesulphonate (23) (80 mg) gave 1-*acetoxy*-2-(N-*methyl*-p-*nitroanilino*)*propane* (15) (65 mg), purified by t.l.c. (dichloromethane–benzene, 20 : 1) (Found: C, 57.1; H, 6.5; N, 10.95. $C_{12}H_{16}N_2O_4$ requires C, 57.1; H, 6.4; N, 11.1%). Before purification, the product contained 1—2% of the secondary isomer.

(vi) *With sodium phenyl sulphide.* (*a*) The methanesulphonate (20) (90 mg) was added to a solution prepared from sodium (25 mg), methanol (7 ml), and benzenethiol (120 mg). The mixture was boiled under reflux for 3 h (nitrogen atmosphere), then concentrated, diluted with water, and extracted with dichloromethane. The extract was washed with 2N-sodium hydroxide and with water, then dried and evaporated to give a mixture (87 mg) of 2-(N-*methylanilino*)-1-*phenylthiopropane* (24) (50%) (Found: C, 74.5; H, 7.45; N, 5.5. $C_{16}H_{19}NS$ requires C, 74.7; H, 7.4; N, 5.4%) and 1-(N-*methylanilino*)-2-*phenylthiopropane* (54) (50%) (Found: C, 74.9; H, 7.5; N, 5.4%); these were separated by t.l.c. (ether–petroleum, 1 : 20).

(*b*) Similar treatment of the methanesulphonate (21) (110 mg) gave a mixture (100 mg) of 2-(p-*methoxy*-N-*methylanilino*)-1-*phenylthiopropane* (25) (51%), n_D^{24} 1.594 8 (Found: C, 70.9; H, 7.1; N, 4.9. $C_{17}H_{21}NOS$ requires C, 71.0; H, 7.4; N, 4.9%) and 1-(p-*methoxy*-N-*methylanilino*)-2-*phenylthiopropane* (55) (49%), n_D^{24} 1.593 8 (Found: C, 71.1; H, 7.3; N, 4.8%) separated by t.l.c. (ether–petroleum, 1 : 20).

(*c*) The methanesulphonate (22) (90 mg) similarly gave a mixture (80 mg) of 2-(p-*chloro*-N-*methylanilino*)-1-*phenylthiopropane* (26) (50%), n_D^{22} 1.618 8 (Found: C, 66.0; H, 6.2; N, 4.8; S, 11.1. $C_{16}H_{18}ClNS$ requires C, 65.85; H, 6.2; N, 4.8; S, 11.0%), and 1-(p-*chloro*-N-*methylanilino*)-2-*phenylthiopropane* (56) (50%), n_D^{22} 1.616 1 (Found: C, 66.1; H, 6.3; N, 4.75; S, 11.2%), separated by t.l.c. (ether–petroleum, 1 : 20).

(vii) *With sodium benzyl sulphide.* (*a*) The methanesulphonate (20) (90 mg) was added to a solution prepared from sodium (20 mg), methanol (2 ml), and toluene-α-thiol (120 mg). The mixture was boiled under reflux (nitrogen atmosphere) for 6 h and worked up as described for the reaction with sodium phenyl sulphide to give a mixture (102 mg) of 1-*benzylthio*-2-(N-*methylanilino*)*propane* (27) (72%), n_D^{20} 1.601 8 (Found: C, 75.1; H, 7.6; N, 5.15; S, 11.9. $C_{17}H_{21}NS$ requires C, 75.2; H, 7.8; N, 5.2; S, 11.8%), and 2-*benzylthio*-1-(N-*methylanilino*)*propane* (57) (28%), n_D^{20} 1.603 7 (Found: C, 75.4; H, 7.7; N, 5.1; S, 11.8%), separated by t.l.c. (ether–petroleum, 1 : 20).

(*b*) The methanesulphonate (21) (110 mg) gave a mixture (120 mg) of 1-*benzylthio*-2-(p-*methoxy*-N-*methylanilino*)-*propane* (28) (69%), n_D^{24} 1.578 5 (Found: C, 71.75; H, 7.8; N, 4.5; S, 10.4. $C_{18}H_{23}NOS$ requires C, 71.7; H, 7.7; N, 4.65; S, 10.6%), and 2-*benzylthio*-1-(p-*methoxy*-N-*methylanilino*)*propane* (58) (31%), n_D^{24} 1.580 5 (Found: C, 71.8; H, 7.8; N, 4.45; S, 10.7%), separated by t.l.c. (ether–petroleum, 1 : 20).

(*c*) The methanesulphonate (22) (90 mg) gave a mixture (80 mg) of 1-*benzylthio*-2-(p-*chloro*-N-*methylanilino*)*propane* (29) (75%), n_D^{22} 1.608 4 (Found: C, 66.5; H, 6.4; N, 4.8; S, 10.7. $C_{17}H_{20}ClNS$ requires C, 66.8; H, 6.6; N, 4.6; S, 10.5%), and 2-*benzylthio*-1-(p-*chloro*-N-*methylanilino*)*propane* (59) (25%), n_D^{22} 1.606 5 (Found: C, 66.75; H, 6.4; N, 4.65; S, 10.7%), separated by t.l.c. (ether–petroleum, 1 : 20).

(viii) *With lithium bromide.* (*a*) The methanesulphonate (20) (90 mg), lithium bromide (320 mg), and acetone (2.5 ml) were heated together under reflux for 6 h. The solvent was removed under reduced pressure and the residue was extracted with ether. The extract was washed with water, then dried and evaporated to give an oil (37 mg) which contained a very small amount (<2%) of primary bromide (30) (τ 7.24) and consisted essentially of 2-*bromo*-1-(N-*methylanilino*)*propane* (60), n_D^{18} 1.576 0, after purification by t.l.c. (ether–petroleum, 1 : 20) (Found: C, 52.4; H, 6.0; N, 6.0. $C_{10}H_{14}BrN$ requires C, 52.65; H, 6.2; N, 6.1%).

(*b*) The methanesulphonate (21) (90 mg) gave 2-bromo-

1-(*p*-methoxy-*N*-methylanilino)propane (61) (45 mg) containing 1—2% of the primary isomer (31). Purification by t.l.c. failed because of decomposition on the plate.

(*c*) The methanesulphonate (22) (90 mg) gave an oil (66 mg) which contained 1—2% of primary bromide (32) but was essentially 2-*bromo*-1-(p-*chloro*-N-*methylanilino*)-*propane* (62), n_D^{22} 1.587 4, after purification by t.l.c. (ether–petroleum, 1 : 20) (Found: C, 45.75; H, 4.9; Br, 30.6; N, 5.3. $C_{10}H_{13}BrClN$ requires C, 45.7; H, 5.0; Br, 30.4; N, 5.3%).

(*d*) The methanesulphonate (53) (70 mg) gave a mixture (65 mg) of the primary bromide (33) and 2-*bromo*-1-(N-*methyl*-p-*nitroanilino*)*propane* (63); the latter compound, separated by t.l.c. (benzene–dichloromethane, 1 : 20) and recrystallised from dichloromethane–petroleum, had m.p. 97° (Found: C, 44.2; H, 5.1; Br, 29.1; N, 10.2. $C_{10}H_{13}BrN_2O_2$ requires C, 44.0; H, 4.8; Br, 29.3; N, 10.3%).

(ix) *With sodium azide.* (*a*) A solution of the methanesulphonate (20) (80 mg) and sodium azide (280 mg) in dimethylformamide (4 ml) was kept at 60 °C for 6 h, then cooled, diluted with water, and extracted with ether. The extract was washed with water, then dried and evaporated to give a mixture (48 mg) of primary (31%) and secondary azide (69%). Separation by t.l.c. (ether–petroleum, 1 : 20) gave 1-*azido*-2-(N-*methylanilino*)*propane* (34), n_D^{20} 1.558 0 (Found: C, 63.2; H, 7.4; N, 29.5. $C_{10}H_{14}N_4$ requires C, 63.1; H, 7.4; N, 29.45%), and 2-*azido*-1-(N-*methylanilino*)*propane* (64), n_D^{18} 1.556 4 (Found: C, 63.0; H, 7.3; N, 29.5%).

(*b*) The methanesulphonate (21) (200 mg) gave a mixture (160 mg) of primary (25%) and secondary azide (75%). Separation by t.l.c. (ether–petroleum, 1 : 20) gave 1-*azido*-2-(p-*methoxy*-N-*methylanilino*)*propane* (35), n_D^{24} 1.551 5 (Found: C, 59.8; H, 7.25; H, 25.45. $C_{11}N_{16}N_4O$ requires C, 60.0; H, 7.3; N, 25.4%), and 2-*azido*-1-(p-*methoxy*-N-*methylanilino*)*propane* (65), n_D^{24} 1.548 9 (Found: C, 60.25; H, 7.1; N, 25.6%).

(*c*) The methanesulphonate (22) (95 mg) gave a mixture (46 mg) of primary (34%) and secondary azide (66%), separated by t.l.c. into 1-azido-(2-*p*-chloro-*N*-methylanilino)propane (36) (which decomposed before analysis), and 2-*azido*-1-(p-*chloro*-N-*methylanilino*)*propane* (66), n_D^{20} 1.568 1 (Found: C, 53.3; H, 5.85; N, 24.9. $C_{10}H_{13}ClN_4$ requires C, 53.45; H, 5.8; N, 24.9%).

(*d*) The methanesulphonate (23) (52 mg) gave 1-*azido*-2-(N-*methyl*-p-*nitroanilino*)*propane* (37) (40 mg), purified by t.l.c. (benzene–dichloromethane, 1 : 20), n_D^{27} 1.698 9 (Found: C, 50.7; H, 5.5; N, 29.6. $C_{10}H_{13}N_5O_2$ requires C, 51.0; H, 5.6; N, 29.8%). Before purification it contained 1—2% of the secondary isomer.

(*e*) The methanesulphonate (53) (70 mg) gave 2-*azido*-1-(N-*methyl*-p-*nitroanilino*)*propane* (67) (50 mg), purified by t.l.c. (ether–petroleum, 1 : 9) (Found: C, 51.3; H, 5.6; N, 29.5%). The crude product contained a trace of primary azide.

Control Experiments.—(i) Typically, a solution of 1-acetoxy-2-(*p*-methoxy-*N*-methylanilino)propane (50 mg) and methanesulphonic acid (18 mg) in acetic acid (3 ml) and acetic anhydride (0.1 ml) was boiled under reflux for 8 h, and then worked up (as described for the solvolysis of the methanesulphonates) to give unchanged primary acetate (^{1}H n.m.r. spectrum).

(ii) Typically, a solution of 1-methoxy-2-(*p*-methoxy-*N*-methylanilino)propane (130 mg) and methanesulphonic acid (58 mg) in methanol (15 ml) containing calcium carbonate (300 mg) was boiled under reflux for 24 h. The mixture was worked up by the standard procedure to give unchanged primary methyl ether.

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