Cytotoxic Compounds. Part XVI.[1] Reactions of the Bismethanesulphonates of 3-(*N*-Methylanilino)propane-1,2-diol and of 2-(*N*-Methylanilino)-propane-1,3-diol with Nucleophiles

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The products formed in the reactions of these bismethanesulphonates with various nucleophiles have been identified by n.m.r. spectroscopy. With methanol, both gave only the 1,2-dimethyl ether, but with sodium methoxide identical mixtures of the 1,2- and the 1,3-dimethyl ether were obtained from each. With potassium acetate, both gave identical mixtures of the 1,2- and the 1,3-diacetate. All these reactions proceeded under kinetic control, and the results reflect the variations in the preferred mode of attack on intermediate aziridinium ions. Reactions with sodium phenyl sulphide proceeded partly by direct displacement, not involving a cyclic ion.

THE reactions of isomeric pairs of bismethanesulphonates (1) and (2) towards a variety of nucleophiles have been shown [2,3] to proceed with differing degrees of rearrangement, according *inter alia* to the nature of the aryl group and the nucleophilicity of the reagent. To throw further light on the mode of action of alkylating agents of the aromatic nitrogen-mustard type,[4,5] some reactions of the nitrogenous bismethanesulphonates (4) and (10) have now been studied.

Diethyl *N*-methylanilinomalonate (14),[6] prepared by reaction of *N*-methylaniline with diethyl bromomalonate, could be distilled rapidly in small quantities, but prolonged heating during distillation (or heating a pure sample in boiling xylene or nitrobenzene) caused the deposition of a white solid, $C_{12}H_{13}NO_3$ (analysis and mass spectrum). The ^1H n.m.r. spectrum showed the presence of one ethoxy and one *N*-methyl group, a one-proton singlet at τ 1·30, and only four aromatic protons, and the i.r. spectrum showed two peaks in the carbonyl region. Blanc process were fruitless, a result which may be characteristic of *N*-substituted aminomalonates.[8] Reduction with lithium aluminium hydride gave the required diol (9), but in poor yield, a drawback which has been encountered also in similar reductions intended to give sulphur [2,9] and oxygen [9] analogues of this nitrogenous diol. For the sulphur compound the difficulty was surmounted [2] by the use of a new route involving the reaction of 1,3-*O*-benzylideneglycerol toluene-*p*-sulphonate with sodium phenyl sulphide, but *N*-methylaniline proved to be too weak a nucleophile to effect displacement with either this toluene-*p*-sulphonate or the 1,3-*O*-methylene analogue. Reaction of 1,3-*O*-methylene glycerol with thionyl chloride is reported [10] to give the chloride in low yield; a major product in our experiments was the corresponding sulphite, and the chloride was not obtained in sufficient quantity for its reactivity to be assessed. The only practicable route to the diol (9), in spite of the poor yield, was therefore the hydride

$ArS{\cdot}CH_2{\cdot}CH(O{\cdot}SO_2Me){\cdot}CH_2{\cdot}O{\cdot}SO_2Me$ (1)

$ArS{\cdot}CH(CH_2{\cdot}O{\cdot}SO_2Me)_2$ (2)

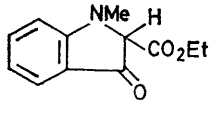
$PhNMe{\cdot}CH_2{\cdot}CHR{\cdot}CH_2R$

(3) R = OH
(4) R = $O{\cdot}SO_2Me$
(5) R = OMe
(6) R = OAc
(7) R = SPh
(8) R = Cl

$PhNMe{\cdot}CH(CH_2R)_2$

(9) R = OH
(10) R = $O{\cdot}SO_2Me$
(11) R = OMe
(12) R = OAc
(13) R = SPh

$PhNMe{\cdot}CH(CO_2Et)_2$ (14)



(15)

On this evidence the solid is formulated as 2-ethoxycarbonyl-*N*-methylindoxyl (15). Some analogous cyclisations of diethyl arylaminomalonates were reported 75 years ago, but this potentially useful route to the indoxyl system appears to have been used only once since that time.[7]

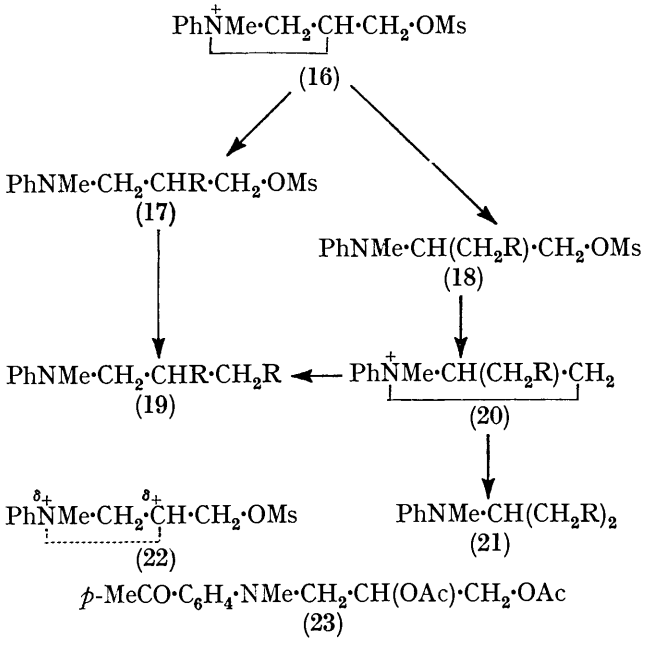
Attempts to reduce the ester (14) by the Bouveault–reduction of the ester (14). The 1,2-diol (3) is readily obtained [11] by reaction of *N*-methylaniline with glycidol (2,3-epoxypropan-1-ol).

The rather unstable bismethanesulphonates (4) and (10) were prepared from the diols under mild conditions. With more drastic treatment the 1,2-diol, heated with methanesulphonyl chloride and pyridine, gave the 1,2-dichloride (8). In contrast to the corresponding sulphur

[1] Part XV, M. S. Khan and L. N. Owen, *J.C.S. Perkin I*, 1972, 2067.
[2] M. V. A. Baig and L. N. Owen, *J. Chem. Soc.* (*C*), 1967, 1400.
[3] M. S. Khan and L. N. Owen, *J.C.S. Perkin I*, 1972, 2060.
[4] W. C. J. Ross, 'Biological Alkylating Agents,' Butterworths, London, 1962.
[5] M. H. Benn, P. Kazmaier, C. Watanatada, and L. N. Owen, *Chem. Comm.*, 1970, 1685.
[6] J. C. Nnadi and S. Y. Wang, *J. Amer. Chem. Soc.*, 1970, **92**, 4421.
[7] R. Blank, *Ber.*, 1898, **31**, 1812; G.P. 109,416; W. Borsche and B. Schacke, *Ber.*, 1923, **56**, 2498.
[8] *Cf.* E. R. H. Jones and W. Wilson, *J. Chem. Soc.*, 1949, 547.
[9] H. L. Yale, E. J. Pribyl, W. Braker, J. Bernstein, and W. A. Lott, *J. Amer. Chem. Soc.*, 1950, **72**, 3716.
[10] G. Tsatsas, *Ann. pharm. franç.*, 1950, **8**, 273.
[11] M. Malinovski and V. Perchik, *Zhur. obshchei Khim.*, 1957, **27**, 1591 (*Chem. Abs.*, 1958, **52**, 3721.)

compounds [3] neither of the two bismethanesulphonates (4) and (10) was isomerised by heating in boiling acetone. The dimethyl ethers (5) and (11), and the diacetates (6) and (12) were made from the diols to serve as authentic reference compounds for the identification of reaction mixtures. The *N*-methyl signals in the ^{1}H n.m.r. spectra (see Table) were well differentiated, being at higher field for all the 1,3-compounds in comparison with the 1,2-isomers, and the relative intensities of these signals in the spectra of products were used to determine the compositions mentioned later.

Rearrangement during nucleophilic displacement reactions on the bismethanesulphonates (4) and (10) would involve the aziridinium ion (16), from which the two products of partial replacement (17) and (18) can be derived. Whilst the former could, in principle, react further through an azetidinium ion, this four-membered



ring system is not readily formed, and can in any event be neglected because it would only give the same final product (19) as that produced by direct displacement on the intermediate (17). The other intermediate (18), however, can evidently give the aziridinium ion (20), from which both the 1,2- (19) and the 1,3-disubstituted compound (21) can be derived. It follows that if nucleophilic attack on both aziridinium ions were entirely unselective, these final products (provided that they are formed only under kinetic control) would be present in a ratio of 3 : 1.

Both bismethanesulphonates (4) and (10) reacted with methanol (buffered with calcium carbonate to prevent protonation of the amine function as solvolysis proceeded) to give exclusively the 1,2-dimethyl ether (5); this was not the result of thermodynamic control, since similar treatment of the 1,3-dimethyl ether (11) resulted in no isomerisation. Consequently, ring opening of the aziridinium ion (16) by the weakly nucleophilic methanol occurs solely by attack at the secondary position, and is thus controlled by polar rather than steric factors, dispersal of the positive charge on nitrogen forming an incipient secondary carbonium ion [*cf.* (22)] rather than a primary one.

In contrast, with sodium methoxide in methanol, both bismethanesulphonates gave mixtures, each consisting of about equal proportions of the 1,2- and the 1,3-dimethyl ether, indicating preferential reaction at the primary position in the aziridinium ions by sterically controlled S_N2-type attack. A similar but less marked preference occurred with potassium acetate in acetic anhydride, both bismethanesulphonates yielding a mixture of the 1,2- and the 1,3-diacetate in a ratio of 3 : 2, formed under kinetic control. A mixture of similar composition was obtained when the dichloride (8) was treated under the same conditions.

The 1,2-bismethanesulphonate reacted with sodium phenyl sulphide in methanol to give a 7 : 3 mixture of the 1,2- (7) and the 1,3-bisphenylthio-compound (13). These were separated by preparative t.l.c. and individually identified from their n.m.r. spectra (see Table). Under the same conditions the 1,3-bismethanesulphonate also gave a mixture of the two sulphides, but the proportions were now 2 : 3. Thus, with this powerful nucleophile, aziridinium intermediates are involved to only a limited extent, and a significant amount (50—60%) of direct S_N2 substitution must occur on the bismethanesulphonates to give unrearranged products.

The dependence of the mechanistic course on the character of the nucleophile, exemplified by these results, is broadly similar to that observed [2,3] for reactions on the sulphur analogues (1) and (2). However, judged from the amount of rearrangement occurring with sodium phenyl sulphide, the tendency for formation of the aziridinium ion is greater than that of the sulphonium ion; this is also indicated by the fact that the bismethanesulphonates (4) and (10), unlike the sulphur analogues, gave no olefinic products in their reactions with sodium methoxide. Elimination in the sulphur analogues is known [3] to proceed without the intervention of episulphonium ions.

When the 1,2-bismethanesulphonate (4) was solvolysed at 100° in acetic acid, containing a little acetic anhydride, the n.m.r. and i.r. spectra of the product indicated the presence of a methyl ketone. Separation of the mixture by t.l.c. gave the 1,2-diacetate (6) and the *p*-acetyl derivative (23). This unexpectedly easy nuclear acylation is presumably catalysed by the liberated methanesulphonic acid; aromatic tertiary amines have been acylated by acetic acid–phosphoric oxide, but only at much higher temperatures (170—200°).[12]

Kuwada [13] has reported the preparation of several 1,2-dichloro-3-dialkylaminopropanes and 1,3-dichloro-2-dialkylaminopropanes. Although he pointed out that the reactions of these compounds might proceed through

[12] A. W. Nineham, *J. Chem. Soc.*, 1952, 635.
[13] Y. Kuwada, *Chem. and Pharm. Bull.* (*Japan*), 1960, **8**, 807.

intermediate aziridinium ions, he did not consider the possibility that rearrangement (similar to that encountered [14] in the reaction of 2-dimethylaminopropanol with thionyl chloride) could occur during the preparation of the chlorides from the corresponding diols, and no rigid proof was provided of the constitution or the homogeneity of the dichlorides.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded for solutions in deuteriochloroform on a Varian A-60 instrument, and i.r. spectra for solutions in chloroform. Organic extracts were dried over magnesium sulphate. Petroleum refers to the fraction b.p. 60—80°. The absorbent for t.l.c. was Kieselgel GF_{254} (Merck). Chloroform used as a reaction solvent was free from ethanol. Products from the reactions of the methanesulphonates with nucleophiles were identified from the n.m.r. spectra.

2-(N-Methylanilino)propane-1,3-diol (*with* B. A. Bower).—A solution of diethyl *N*-methylanilinomalonate (15·5 g) in tetrahydrofuran (15 ml) was slowly added to a suspension of lithium aluminium hydride (3·2 g) in the same solvent (80 ml). The mixture was stirred and boiled under reflux for 3 days, then cautiously mixed with aqueous sodium hydroxide and extracted 5 times with chloroform to give an oil, which crystallised from benzene–petroleum to yield the *diol* (2·0 g), m.p. 62—64°, $\nu_{max.}$ 3200—3600 and 1600 cm^{-1} (Found: C, 66·6; H, 8·1; N, 7·9. $C_{10}H_{15}NO_2$ requires C, 66·4; H, 8·2; N, 7·7%).

Di-(1,3-dioxan-5-yl) Sulphite.—A mixture of 5-hydroxy-1,3-dioxan [16] (2·0 g) and pyridine (5 ml) was slowly added to a solution of thionyl chloride (2·1 g) in chloroform (30 ml). After being boiled under reflux for 30 min. the solution was cooled, washed successively with water, dilute hydrochloric acid, and aqueous sodium hydrogen carbonate, then dried and evaporated to give the *sulphite* (1·6 g), m.p. 104—105° (from benzene–petroleum), τ (CCl_4) 5·7—6·4 (4H, m, CH_2),

Chemical shifts (τ values) in $CDCl_3$

(i) PhNMe·CH_2·CHR·CH_2R

R	CHR	CH_2R	N·CH_2	N·CH_3	CH_3 in R
OH	6·1(m)	←6·6(m)→		7·10(s)	
O·SO_2Me	5·0(m)	5·6(m)	6·3(m)	←6·93(s), 7·00(s), 7·06(s)→	
OMe	←6·7(m)→			7·06(s)	6·65(s), 6·68(s)
OAc	4·7(m)	5·78(t)	6·50(q)	7·07(s)	7·92(s), 8·05(s)
SPh	←5·9—6·9(m)→			7·00(s)	
Cl	5·8(m)	←6·4(m)→		7·10(s)	

(ii) PhNMe·$CH(CH_2R)_2$

R	CH_2R	N·CH	N·CH_3	CH_3 in R
OH	←6·2(m)→		7·20(s)	
O·SO_2Me	5·55(s)	6·28(s)	7·11(s)	7·04(s)
OMe	6·41(d)	5·85(quint)	7·15(s)	6·67(s)
OAc	←5·7(m)→		7·16(s)	8·03(s)
SPh	6·75(m)	5·95(m)	7·26(s)	

Diethyl N-Methylanilinomalonate.—A solution of *N*-methylaniline (22 g) and diethyl bromomalonate [15] (24 g) in ethanol (150 ml) was boiled under reflux for 12 h, then concentrated, diluted with water, and extracted with chloroform to give the product (17 g), b.p. 116—122° at 10^{-4} mmHg, $\nu_{max.}$ 1725 cm^{-1}, τ 8·71 (6H, t, CH_3), 6·91 (3H, s, NCH_3), 5·70 (4H, q, CH_2), 4·83 (1H, s, NCH) and 2·6—3·3 (5H, m, aromatic) (Found: M^+, 265. Calc. for $C_{14}H_{19}NO_4$: *M*, 265). It failed to crystallise, though Nnadi and Wang [6] record m.p. 105—106°.

2-Ethoxycarbonyl-N-methylindoxyl.—(i) When distillation of the preceding ester was unduly prolonged the product was contaminated with a white solid. This was collected and recrystalllised from petroleum to give the *indoxyl*, m.p. 94—95°, $\nu_{max.}$ 1700 and 1650 cm^{-1}, τ (CCl_4) 8·58 (3H, t, CH_3), 6·22 (3H, s, NCH_3), 5·61 (2H, q, CH_2), 2·1—3·1 (4H, m, aromatic), and 1·30 (1H, s, NCH) (Found: C, 65·4; H, 5·9; N, 6·3%; M^+, 219. $C_{12}H_{13}NO_3$ requires C, 65·7; H, 6·0; N, 6·4%; *M*, 219).

(ii) The malonate (570 mg) was heated in boiling nitrobenzene (1 ml) for 30 min. Chromatography of the product, in benzene–ether, gave a fraction which when recrystallised from petroleum was identified as the indoxyl (130 mg), m.p. and mixed m.p. 94—95°.

[14] W. R. Brode and M. W. Hill, *J. Amer. Chem. Soc.*, 1947, **69**, 724; E. M. Schultz and J. M. Sprague, *ibid.*, 1948, **70**, 48; *cf.* N. H. Cromwell and A. Hassner, *ibid.*, 1955, **77**, 1568.

[15] C. S. Palmer and P. W. McWherter, *Org. Synth.*, 1941, Coll. Vol. I, 2nd edn., p. 245.

5·4 (1H, m, CH), and 5·21 (2H, s, O·CH_2·O) (Found: C, 38·15; H, 5·9; S, 12·4. $C_8H_{14}O_7S$ requires C, 37·8; H, 5·55; S, 12·6%).

1,3-Dioxan-5-yl Toluene-p-sulphonate.—(i) Reaction of 5-hydroxy-1,3-dioxan with toluene-*p*-sulphonyl chloride in pyridine gave the ester, m.p. 90—91° (from chloroform–petroleum). In the n.m.r. spectrum the methylenedioxy-group appeared as a two-proton singlet at τ 5·22, but when measured in CCl_4 the signal was an AB quartet centred at τ 5·36 (*J* 6 Hz). The compound has been mentioned previously [17] but not adequately described.

(ii) A mixture [16] of 5-hydroxy-1,3-dioxan and 1,3-dioxolan-4-methanol (15 g) was treated with toluene-*p*-sulphonyl chloride (34 g) in pyridine (100 ml). The mixture of esters so obtained was dissolved in warm chloroform and diluted with petroleum to give a crop of crystals (11 g), m.p. and mixed m.p. 91—92°, spectroscopically identical with the 1,3-dioxan-5-yl derivative.

The toluene-*p*-sulphonate (1·1 g) was unchanged (t.l.c. and spectrum) after being heated with *N*-methylaniline (1·0 g) in dimethylformamide for 10 h at 105°.

3-(N-Methylanilino)propane-1,2-diyl Bismethanesulphonate.—A solution of 3-(*N*-methylanilino)propane-1,2-diol [11] (4 g) and triethylamine (4·85 g) in chloroform (50 ml) was

[16] H. Hibbert and N. M. Carter, *J. Amer. Chem. Soc.*, 1928, **50**, 3120.

[17] T. A. Crabb and R. C. Cookson, *Tetrahedror Letters*, 1964, 679.

added dropwise to a cooled solution of methanesulphonyl chloride (5·3 g) in chloroform (20 ml). The mixture was set aside at *ca.* 0° for 12 h, then washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water. Evaporation of the dried solution under reduced pressure gave the *bismethanesulphonate* as an oil (7·7 g), $\nu_{max.}$ 1370 and 1180 cm^{-1} (Found: C, 42·1; H, 5·7; N, 4·0. $C_{12}H_{19}NO_6S_2$ requires C, 42·7; H, 5·7; N, 4·15%).

2-(N-*Methylanilino*)*propane*-1,3-*diyl Bismethanesulphonate*.—Similar treatment of the 1,3-diol (190 mg), but in dichloromethane instead of chloroform, gave the *bismethanesulphonate* (310 mg), $\nu_{max.}$ 1370 and 1180 cm^{-1} (Found: C, 41·8; H, 5·7; N, 4·0%). The low carbon content of this, and of the above isomer, is probably due to retention of traces of solvent. Both derivatives gave satisfactory n.m.r. spectra (see Table), and neither derivative was isomerised to the other when heated in boiling acetone for 6 h (n.m.r. spectra).

1,2-*Dichloro*-3-(N-*methylanilino*)*propane*.—A mixture of 3-(*N*-methylanilino)propane-1,2-diol (1·0 g), methanesulphonyl chloride (1·4 g), and pyridine (10 ml) was kept at 100° for 30 min, then cooled and diluted with chloroform. The washed and dried solution was evaporated to give the *dichloride* (0·25 g), b.p. 82° at 10^{-4} mmHg, n_D^{14} 1·5745 (Found: C, 55·3; H, 6·1; Cl, 32·4. $C_{10}H_{13}Cl_2N$ requires C, 55·1; H, 6·0; Cl, 32·5%).

1,2-*Dimethoxy*-3-(N-*methylanilino*)*propane*.—Sodium (0·5 g) was added to a boiling solution of the 1,2-diol (4·0 g) in benzene (20 ml), followed after 30 min by methyl iodide (3·2 g). The mixture was boiled under reflux for 2 h and treated again with the same quantities of sodium and methyl iodide. Finally the cooled and filtered solution was washed, dried, and evaporated to give the *dimethyl ether* (2·3 g), b.p. 104—106° at 0·5 mmHg, n_D^{27} 1·5269 (Found: C, 69·0; H, 9·2. $C_{12}H_{19}NO_2$ requires C, 68·9; H, 9·3%).

1,3-*Dimethoxy*-2-(N-*methylanilino*)*propane*.—A mixture of the 1,3-diol (0·18 g), dimethyl sulphate (0·40 g), powdered sodium hydroxide (0·26 g), and tetrahydrofuran (5 ml) was stirred for 12 h at ambient temperature, then diluted with water and extracted with benzene. Evaporation of the washed and dried extract gave an oil (0·19 g) which on purification by t.l.c. (chloroform) furnished the *dimethyl ether* (0·14 g), n_D^{18} 1·5294 (Found: C, 69·1; H, 9·3; N, 6·55. $C_{12}H_{19}NO_2$ requires C, 68·9; H, 9·3; N, 6·7%).

The 1,3-dimethyl ether (35 mg), calcium carbonate (100 mg), and methanol (5 ml) were boiled together under reflux for 6 h. The recovered dimethyl ether was unchanged (n.m.r. spectrum).

3-(N-*Methylanilino*)*propane*-1,2-*diyl Diacetate*.—Acetylation of the 1,2-diol with acetic anhydride and sodium acetate (1 h at 100°) gave the 1,2-diacetate, b.p. 129—130° at 0·3 mmHg, n_D^{19} 1·5189 (Found: C, 63·1; H, 7·0; N, 5·2. Calc. for $C_{14}H_{19}NO_4$: C, 63·4; H, 7·2; N, 5·3%).

The diacetate (70 mg) and potassium acetate (400 mg) in acetic anhydride (10 ml) were heated at 100° for 2 h. The recovered diacetate was unchanged (n.m.r. spectrum).

2-(N-*Methylanilino*)*propane*-1,3-*diyl Diacetate*.—Acetylation of the 1,3-diol (110 mg) with acetic anhydride in pyridine gave the 1,3-*diacetate* (150 mg), purified by t.l.c. (chloroform), n_D^{19} 1·5165, $\nu_{max.}$ 1735 cm^{-1} (Found: C, 63·4; H, 7·2; N, 5·1%).

Reactions of the Bismethanesulphonates with Nucleophiles.—The sulphonates were freshly prepared and the purity was checked from the n.m.r. spectra.

(i) *With methanol*. A solution of the 1,2-bismethanesulphonate (300 mg) in dry methanol (25 ml) containing calcium carbonate (1 g) was boiled under reflux for 12 h, then concentrated under reduced pressure, diluted with water (100 ml), and extracted thrice with chloroform to give the 1,2-dimethyl ether (150 mg), b.p. 84—85° at 0·2 mmHg.

The 1,3-bismethanesulphonate (30 mg) under the same conditions also gave only the 1,2-dimethyl ether (17 mg).

(ii) *With sodium methoxide*. The 1,2-bismethanesulphonate (1·0 g) was added to a solution prepared from sodium (0·27 g) and dry methanol (50 ml). The mixture was boiled under reflux for 2 h, then set aside overnight. After dilution with water it was extracted with chloroform to give a 1 : 1 mixture (0·55 g) of the 1,2- and the 1,3-dimethyl ether, b.p. 75—77° at 0·25 mmHg.

Similar treatment of the 1,3-dimethanesulphonate (for 4 h under reflux) gave an identical mixture.

(iii) *With potassium acetate*. A solution of the 1,2-bismethanesulphonate (0·6 g) and potassium acetate (1·1 g) in acetic anhydride (20 ml) was kept at 100° (oil-bath) for 2 h, then cooled, diluted with water, and extracted with chloroform. The extract was washed with aqueous sodium hydrogen carbonate and with water, then dried and evaporated to give a 3 : 2 mixture (0·35 g) of the 1,2- and the 1,3-diacetate, b.p. 106—108° at 10^{-2} mmHg.

The 1,3-bismethanesulphonate (0·6 g), similarly treated, gave an identical mixture (0·34 g).

(iv) *With sodium phenyl sulphide*. The 1,2-bismethanesulphonate (0·5 g) was added to a solution prepared from sodium (0·10 g), benzenethiol (0·51 g), and dry methanol (40 ml). The mixture was boiled under reflux for 5 h in an atmosphere of nitrogen, and was then diluted with water and extracted with chloroform. The extract was washed with aqueous sodium hydroxide and with water, then dried and evaporated to an oil (0·36 g), which was a 7 : 3 mixture of the 1,2- and the 1,3-products. These were separated by preparative t.l.c. (ether–petroleum, 1 : 20) to give 3-(N-*methylanilino*)-1,2-*bisphenylthiopropane* (0·10 g), R_F 0·3 (Found: C, 72·2; H, 6·3; N, 3·8. $C_{22}H_{23}NS_2$ requires C, 72·2; H, 6·3; N, 3·8%), and 2-(N-*methylanilino*)-1,3-*bisphenylthiopropane* (0·04 g), R_F 0·25 (Found: C, 72·2; H, 6·3; N, 3·7%).

Similar treatment of the 1,3-bismethanesulphonate (0·24 g), for 2·5 h, gave a 2 : 3 mixture (0·2 g) of the 1,2- and the 1,3-bisphenylthio-compounds.

(v) *With acetic acid*. A solution of the 1,2-bismethanesulphonate (0·35 g) in acetic acid (9 ml) and acetic anhydride (2 ml) was kept at 110° for 6 h, then cooled, diluted with water (50 ml), and neutralised with sodium hydrogen carbonate. Extraction with chloroform gave a red oil (0·23 g) which was separated by t.l.c. (ether) into the 1,2-diacetate (90 mg) and 3-(p-*acetyl*-N-*methylanilino*)*propane*-1,2-*diyl diacetate* (50 mg), which after sublimation at 90° and 10^{-2} mmHg had m.p. 122—123°, $\nu_{max.}$ 1740 and 1670 cm^{-1}, τ 7·58 (3H, s, $ArCOCH_3$), 6·98 (3H, s, NCH_3), 3·31 and 2·23 (4H, two d of ABq, J 9·0 Hz, aromatic), and resonances of other functional groups; the latter compound gave a positive iodoform test.

Reaction of 1,2-*Dichloro*-3-(N-*methylanilino*)*propane with Potassium Acetate*.—The dichloride (2·0 g), under the conditions described for the similar reaction on the 1,2-bismethanesulphonate, but with heating for 6 h, gave a 3 : 2 mixture (0·9 g) of the 1,2- and the 1,3-diacetate, b.p. 130—132° at 0·2 mmHg, n_D^{20} 1·5180.

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