337. *Amino-oxy-derivatives. Part V.*[1] *Some O-Ethers of 2-Substituted 4,6-Diamino-1,2-dihydro-1-hydroxy-1,3,5-triazines*

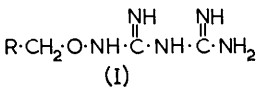
By P. MAMALIS, J. GREEN, D. J. OUTRED, and M. J. RIX

Some new *O*-ethers of 4,6-diamino-1,2-dihydro-1-hydroxy-1,3,5-triazines have been prepared by cyclisation of the corresponding diguanides with carbonyl compounds and by a novel *O*-alkylation of the corresponding 1-hydroxydihydrotriazines.

EARLIER Communications described the preparation and some properties of a number of alkyloxy- and arylalkyloxy-diguanides [2,3] (I) and dihydrotriazines [1,4] (II), many of which exhibit marked *in vitro* microbiological properties. One of the more active compounds (II; R = C_9H_{19}, R′ = R″ = Me) was comparable in topical antibacterial action with the bisdiguanide derivative chlorhexidine [5] and with some more-recently described bisguanidine derivatives.[6] A number of new dihydrotriazines are now described which show interesting microbiological properties, details of which are being published elsewhere.

[1] Part IV, S. A. Price, L. Jeffries, J. Green, D. J. Outred, M. J. Rix, and P. Mamalis, *J. Medicin. Chem.*, to be published.
[2] P. Mamalis, J. Green, and D. McHale, *J.*, 1960, 229.
[3] S. A. Price, P. Mamalis, D. McHale, and J. Green, *Brit. J. Pharmacol.*, 1960, **15**, 243.
[4] P. Mamalis, J. Green, D. J. Outred, and M. J. Rix, *J.*, 1962, 3915.
[5] G. E. Davies, J. Francis, A. R. Martin, F. L. Rose, and G. Swain, *Brit. J. Pharmacol.*, 1954, **9**, 192.
[6] A. F. McKay and D. L. Garmaise, B.P. 935,614; A. F. McKay, D. L. Garmaise, H. A. Baker, L. R. Hawkins, V. Falta, R. Gaudry, and G. Y. Paris, *J. Medicin. Chem.*, 1963, **6**, 587.

Furukawa *et al.*[7a] showed that, whilst aryldiguanides cyclise readily under acidic conditions with a wide variety of carbonyl compounds to give dihydrotriazines, alkyldiguanides fail to react. Recently, however, Lombardino [7b] showed that, under rigorous conditions, it is possible to obtain dihydrotriazines in poor to moderate yield from alkyl- and phenethyl-diguanides with aldehydes or with acetone. The diguanide ethers (I) were more reactive, and both alkoxy- and arylmethoxy-diguanides reacted under similar conditions with a restricted number of carbonyl compounds to give the corresponding triazines.[4] Thus, ethyl methyl ketone reacted with diguanides (I) in ethanol in the presence of hydrochloric acid at room temperature to give rather poor yields of dihydrotriazines, whilst cyclohexanone, benzaldehyde, and *p*-methoxybenzaldehyde gave better yields under the same conditions. This type of reaction has now been extended to include 4-methylcyclohexanone, cyclopentanone, *o*-methoxybenzaldehyde, cinnamaldehyde, and propionaldehyde, which gave variable yields: no dihydrotriazines could be isolated when using *o*-chloro- or *o*-bromo-benzaldehyde, octanal, or chloroacetone.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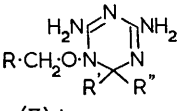
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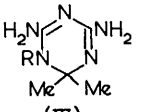
(IIa) hydrochloride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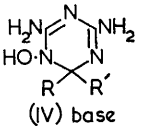
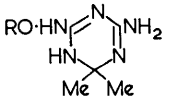
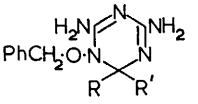

(IV) base

(IVa) hydrochloride


(V)


(VI)

Compounds of the oxy-series differ from those of the non-oxygenated series in a further respect: the " three-component " synthesis of dihydrotriazines [8] from arylmethoxyamines, dicyandiamide, and acetone, fails to take place,[9] stable oxime *O*-ethers being formed.[4] In the arylamine series, this one-stage synthesis of dihydrotriazines occasionally fails under reflux conditions, as was found by Modest and Levine [10] in attempts to prepare 4,6-diamino-1,2-dihydro-2,2-dimethyl-1-*p*-nitrophenyl-1,3,5-triazine (III; R = *p*-$C_6H_4{\cdot}NO_2$). We encountered similar difficulties during abortive attempts to prepare the 3,5-dichlorophenyltriazine (III; R = $C_6H_3{\cdot}3,5\text{-}Cl_2$) by heating a mixture of 3,5-dichloroaniline, hydrochloric acid, acetone, and dicyandiamide. Contrary to the work of Crowther,[9] refluxing a mixture of 3,5-dichlorophenyldiguanide hydrochloride, acetone, and hydrochloric acid failed to afford any of the desired product. Both reactions, however, gave good yields when carried out at room temperature.

The ready formation of the *N*-hydroxydihydrotriazine (IV) by hydrogenation of *O*-arylmethyl derivatives [4] suggested that the compound might be a useful intermediate for the synthesis of alkylated dihydrotriazines. The *N*-hydroxydihydrotriazine (IV) can be regarded as a cyclic *NN*-disubstituted hydroxylamine containing two amino-substituents in the ring. As with the 4,6-diaminopyrimidines, prototropic shifts are possible, and ready *N*-alkylation is therefore unlikely to take place.[11] This is also indicated by the small amount of published data referring to the acetylation of substituted diaminopyrimidines. For example, it has been reported that 4- and 6-aminopyrimidines are relatively slowly acetylated.[11b]

[7] (*a*) M. Furukawa, Y. Seto, and S. Toyoshima, *Chem. and Pharm. Bull.* (*Japan*), 1961, **9**, 914; (*b*) L. Lombardino, *J. Medicin. Chem.*, 1963, **6**, 213.
[8] E. J. Modest, *J. Org. Chem.*, 1956, **21**, 1.
[9] A. F. Crowther, B.P. 709,906.
[10] E. J. Modest and P. Levine, *J. Org. Chem.*, 1956, **21**, 14.
[11] (*a*) J. Baddiley, B. Lythgoe, and A. R. Todd, *J.*, 1943, 571; (*b*) G. W. Kenner and A. R. Todd, in "Heterocyclic Compounds," ed. R. C. Elderfield, John Wiley & Sons Inc., New York, 1957, Vol. 6, pp. 271, 307.

Few examples of the alkylation of *NN*-dialkylhydroxylamines have been described. Butyl iodide and two equivalents of *NN*-dimethylhydroxylamine were found to give *O*-butyl-*NN*-dimethylhydroxylamine,[12] whilst bromoacetic acid and the same hydroxylamine in the presence of sodium hydroxide gave *O*-carboxymethyl-*NN*-dimethylhydroxylamine.[13] Other alkylations of simple *NN*-disubstituted derivatives were carried out mainly on disodium hydroxylamine disulphonate which *O*-alkylated smoothly in aqueous solution.[14] In contrast to the apparently simple alkylation of *NN*-dialkylhydroxylamines, *NN*-dibenzylhydroxylamine reacted with ethyl iodide in the presence of one equivalent of sodium methoxide, giving *NN*-dibenzylethylamine with loss of the oxygen atom.[15] A similar loss of oxygen accompanied the Michael addition of *N*-hydroxypiperidines to vinylpyridines giving pyridylethylpiperidines.[16,17] In contrast, acrylates added normally to *N*-hydroxypiperidine giving ethers with no loss of oxygen.[18] Behrend and Leuchs [19] found that benzylation of *NN*-dibenzylhydroxylamine gave products, the nature of which varied with the presence or absence of extra base. At 120—130° with benzyl chloride in the absence of base, much dibenzylhydroxylamine was recovered, together with lesser amounts of di- and tri-benzylamines. Tribenzylhydroxylamine, the expected product, was isolated only in very low yield. In ethanol, with sodium carbonate, none of the trisubstituted hydroxylamine was formed.

We have examined the action of benzyl bromide on *NN*-diethylhydroxylamine in dimethylformamide in three series of experiments, employing molar ratios of (*a*) 1 : 1, (*b*) 1 : 1·75—1 : 2, and (*c*) 1 : 1 in the presence of sodium hydroxide (1 mol.). In all experiments, yields of products were very low, the main component being the oxygen-free *NN*-diethylbenzylamine, a product analogous to the *NN*-dibenzylethylamine obtained by Walder from *NN*-dibenzylhydroxylamine and ethyl iodide. This product was usually accompanied by a small amount of benzyl alcohol. *O*-Benzyl-*NN*-diethylhydroxylamine was detected in very small quantities in the experiments employing one equivalent of sodium hydroxide. Even smaller amounts were isolated from experiments using two moles of *NN*-diethylhydroxylamine but none from reactions using equimolecular amounts of *NN*-diethylhydroxylamine and benzyl bromide.

Despite the inconsistent results of the *NN*-disubstituted hydroxylamine alkylations, it was considered worth while to attempt the *O*-alkylation of *N*-hydroxydihydrotriazines. In our initial experiments, the hydroxytriazine base (IV) was heated in ethanol containing sodium with the halogenoarylmethyl compound in equimolar proportions. It was soon apparent that the major products from these reactions were not always the dihydrotriazines (II). In three out of seven preparations of this type, only rearranged dihydrotriazines (V) could be isolated, either as bases or as picrates from which the bases were subsequently recovered. In the other four preparations dihydrotriazine hydrochlorides (IIa) were obtained in variable yield. The structure of these was confirmed by a comparison of melting points and infrared spectra with those obtained from authentic triazines prepared from diguanides. Confirmation of the structures also followed from hydrogenation studies of the products. Rapid uptake of 1 mole of hydrogen occurred with cleavage of the C–O bond to give the original hydroxydihydrotriazine hydrochloride (IVa) and a hydrocarbon. In no case were crystalline hydrochlorides obtained from rearranged triazines. This agreed with our previous observation [4] that hydrochlorides of such bases

[12] W. B. Hardy, U.S.P. 2,649,484.
[13] E. L. Schumann, L. A. Paquette, R. V. Heinzelman, D. P. Wallach, J. P. DaVanzo, and M. E. Greig, *J. Med. Pharm. Chem.*, 1962, **5**, 464.
[14] See, *e.g.*, F. Winternitz and R. Lachazette, *Bull. Soc. chim. France*, 1958, 664; B.P. 914,459; 930,389; 935,389; G.P. 1,112,082.
[15] F. Walder, *Ber.*, 1897, **20**, 1751.
[16] J. Thesing and W. Sirrenberg, *Chem. Ber.*, 1959, **92**, 1748.
[17] L. A. Paquette, *J. Org. Chem.*, 1962, **27**, 2870.
[18] G. Zinner, *Angew. Chem.*, 1959, **71**, 311.
[19] R. Behrend and K. Leuchs, *Annalen*, 1890, **257**, 203.

could be obtained crystalline only with considerable difficulty, even when pure bases were employed.

Later work established that the reaction proceeded more cleanly and in better yield if the reactants were heated in a suitable medium in the absence of extraneous base. Under these conditions, the hydrohalide of the dihydrotriazine was formed directly and could be isolated merely by concentration and crystallisation. Suitable solvents were dimethyl sulphoxide and dimethylformamide; formamide and ethanol were less satisfactory. It was not necessary to isolate the pure hydroxytriazine base (IV) before reaction: the hydrochloride could be neutralised *in situ* with strong aqueous sodium hydroxide and the normal procedure followed. Since the salt of the substituted triazine is formed during the course of this reaction, there is little possibility of isomerisation to the rearranged triazine (V). We observed that hydroxytriazines (IV) could not be made to rearrange under these conditions.

Whilst *N*-hydroxydihydrotriazine bases reacted smoothly with reactive halides, the hydroxytriazine salts did not react, even under vigorous conditions.

Alkyl bromides and iodides gave reasonable yields of dihydrotriazines as did arylmethyl chlorides and bromides. Diphenylbromomethane, however, failed to give the required product, giving rise to diphenylmethanol and the hydrobromide of the hydroxytriazine (IV). Aryl derivatives with longer side-chains, such as phenethyl and 3-phenylpropyl bromide, reacted normally. In contrast, 1-(2-chloroethoxy)naphthalene did not react under our conditions. Dimethyl sulphate and ethyl toluene-*p*-sulphonate also gave alkylated triazines with (IV; R = R′ = Me). Salts of some of the triazines were prepared by treatment with organic acids.

Whilst alkylation of *N*-hydroxytriazines (IV) proceeded readily, alkylation of 2-amino-5,6-dihydro-4-hydroxyamino-6,6-dimethyl-1,3,5-triazine (V; R = H) did not appear to take place. Thus, in one experiment, heating the rearranged hydroxytriazine with benzyl bromide in dimethylformamide gave, as sole crystalline product, the crude hydrobromide of the unchanged triazine.

The scope of the reaction was extended by the use of a number of 1-hydroxydiamino-dihydrotriazines bearing different 2-substituents (IV), prepared by catalytic hydrogenation of the triazines obtained by cyclisation of benzyloxydiguanide, with benzaldehyde, *o*-methoxybenzaldehyde, cyclohexanone, and 4-methylcyclohexanone giving (VI; R = H, R′ = Ph; R = H, R′ = *o*-C_6H_4·OMe; RR′ = $-[CH_2]_5-$; and RR′ = $-[CH_2]_2$·CHMe·$[CH_2]_2-$, respectively).

Intermediate arylmethylhalides required for this work were prepared either by halogenation of the arylalkanes with *N*-bromosuccinimide or by treatment of the arylcarbinols with hydrogen bromide or chloride.

9-Bromomethylanthracene was prepared by treatment of 9-methylanthracene with one mole of *N*-bromosuccinimide in dry carbon tetrachloride. In an experiment in which two moles of reagent were used, a product was isolated containing two bromine atoms and tentatively formulated as 9-bromo-10-bromomethylanthracene since it melted only a few degrees lower than the compound of this structure described by Barnett and Matthews.[20] Subsequent attempts to prepare this material failed unless the mixture was treated with a trace of water, when rapid reaction to give the dibromo-compound took place. The structure of the dibromo-compound was confirmed by heating it with aqueous ethanolic calcium carbonate. No 9-anthraldehyde could be detected in the product by thin-layer chromatography, indicating the absence of 9-dibromomethylanthracene. Chromatography of the product on alumina gave a solid, which, from its melting point and analysis, was probably 9-bromo-10-hydroxymethylanthracene. 2-Bromomethylphenanthrene, obtained by bromination of 2-methylphenanthrene with *N*-bromosuccinimide, melted several degrees lower than the product [21] obtained from 2-hydroxymethylphenanthrene and hydrogen

[20] E. de B. Barnett and M. A. Matthews, *Ber.*, 1926, **59**, 1429.
[21] E. Mossetig and J. van de Kamp, *J. Amer. Chem. Soc.*, 1933, **55**, 2995.

bromide. It was purified by conversion into the 2-hydroxymethyl derivative (which analysed correctly although melting 10° lower than the literature figure) and treatment with hydrogen bromide in benzene.

The carbinols were obtained either by reduction of the corresponding aryl aldehydes with sodium borohydride or lithium aluminium hydride or by reduction of the corresponding esters with lithium aluminium hydride. On distillation of crude methyl *o*-bromomethyl benzoate at reduced pressure, considerable quantities of phthalide were formed, presumably by elimination of methyl bromide. This occurred to a lesser extent when a higher vacuum was used.

Attempts to prepare 1-cyanomethyl-4-methylnaphthalene by reaction of 1-chloromethyl-4-methylnaphthalene with ethanolic potassium cyanide gave only 1-ethoxymethyl-4-methylnaphthalene. This is in contrast to the work of Kubiczek and Neugebauer,[22] who found that 1-bromomethylnaphthalene readily gave the substituted acetonitrile under the same conditions.

$Ar\cdot[CH_2]_2O\cdot NH_2,HCl$	$Ph\cdot CHMe\cdot CH_2\cdot O\cdot NHMe,HCl$	$Ph\cdot CH_2\cdot CHMe\cdot O\cdot NMe_2,HCl$
(VII)	(VIII)	(IX)

Since the completion of much of the work described above, Nicolaus *et al.*[23] have described the interesting properties of some phenethyloxyamines (VII) which contain one more carbon atom in the chain than the arylmethoxyamines. Although the bases (VII) appeared to be stable compounds, the hydrochlorides underwent spontaneous decomposition after a relatively short induction period. Arylmethoxyamine hydrochlorides proved to be stable in our laboratories for several years at room temperature as was 3-phenylpropyloxyamine hydrochloride, which contains a third carbon atom in the chain. Earlier, Major and Ohly [24] noted the decomposition of compounds of type (VII) but did not characterise the decomposition products, now known to be ammonium chloride and carbonyl derivatives. Kinetic decomposition products were also obtained from compounds (VIII) and (IX).[20]

Experimental

1-Benzyloxy-4,6-diamino-1,2-dihydro-1,3,5-triazine-2-spirocyclohexane Hydrochloride (IIa; R = Ph, R′R″ = $-[CH_2]_5-$).—Benzyloxydiguanide dihydrochloride (55 g.), cyclohexanone (40 ml.), and methanol (400 ml.) were set aside overnight at room temperature when solid separated (34·4 g.); concentration of the liquors gave a further 6·5 g. Recrystallisation of the combined solids from methanol gave the *triazine hydrochloride* (32·3 g.), m. p. 230—232° (Found: C, 55·4; H, 7·2; N, 21·8. $C_{15}H_{22}ClN_5O$ requires C, 55·6; H, 6·85; N, 21·6%). Other *triazines* similarly prepared are described in Table 1.

4,6-Diamino-1-(3,5-dichlorophenyl)-1,2-dihydro-2,2-dimethyl-1,3,5-triazine Hydrochloride.—(III; R = 3,5-$C_6H_3\cdot Cl_2$) (*a*) A mixture of 3,5-dichloroaniline (16·2 g.), powdered dicyandiamide (8·4 g.), acetone (120 ml.), ethanol (30 ml.), and concentrated hydrochloric acid (9·0 ml.) was stirred at room temperature. The solution cleared after 2 hr. then solid began to separate. After 6½ hr. this was collected (1·55 g.), m. p. 250—255°, and identified as crude 3,5-dichlorophenyldiguanide hydrochloride (grey precipitate with ammoniacal copper sulphate solution). From the filtrate was obtained the triazine hydrochloride (18·0 g.), m. p. 198—200° (Found: C, 40·85; H, 4·9; N, 21·3. Calc. for $C_{11}H_{14}Cl_3N_5$: C, 40·9; H, 4·4; N, 21·7%) which crystallised from ethanol as prisms, m. p. 190—192° (Found: C, 40·75; H, 4·5; N, 21·9%).

(*b*) A mixture of 3,5-dichlorophenyldiguanide hydrochloride (10·0 g.), methanol (20 ml.), acetone (50 ml.), and concentrated hydrochloric acid (1·5 ml.) was stirred at room temperature for 5 hr. and concentrated to give the triazine hydrochloride (9·2 g.), m. p. 198—200°.

2-Amino-4-(3,5-dichloroanilino)-5,6-dihydro-6,6-dimethyl-1,3,5-triazine.—The foregoing triazine hydrochloride (0·5 g.), 4N-sodium hydroxide (3 ml.), and ethanol (10 ml.) were refluxed for 3 hr. The rearranged *triazine base* formed needles, m. p. 196—198° (from ethanol) (Found: C, 46·2; H, 4·6; N, 23·8. $C_{11}H_{13}Cl_2N_5$ requires C, 46·1; H, 4·55; N, 24·5%). Similarly

[22] G. Kubiczek and L. Neugebauer, *Monatsh.*, 1950, **81**, 917.
[23] B. J. R. Nicolaus, G. Pagani, and E. Testa, *Helv. Chim. Acta*, 1962, **45**, 1381.
[24] R. T. Major and K. W. Ohly, *J. Med. Pharm. Chem.*, 1961, **4**, 51.

TABLE 1

Dihydrotriazines (II) prepared from diguanides

R and deriv.	R′	R″	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
Nonyl, HCl	Me	H	208—209° [a,c]	$C_{14}H_{30}ClN_5O$	52·8	9·4	22·0	52·7	9·4	21·9
Nonyl, HCl	CH_2·CHPh	H	210 [b]	$C_{21}H_{34}ClN_5O$	61·2	8·4		61·8	8·3	
Nonyl, HCl	−[CH_2]$_5$−		225—227 [a,e]	$C_{18}H_{36}ClN_5O$	58·2	9·95	18·3	57·8	9·7	18·7
Nonyl	−[CH_2]$_5$−		118 [a,d]	$C_{18}H_{35}N_5O$	63·4	10·2	20·2	64·1	10·5	20·8
Nonyl, HCl	−CH_2·CH_2·CHMe·CH_2·CH_2−		219—220 [a,c]	$C_{19}H_{38}ClN_5O$	59·3	10·0	18·15	58·8	9·9	18·05
Nonyl, H_2O	−CH_2·CH_2·CHMe·CH_2·CH_2−		90—92 [a,c]	$C_{19}H_{37}N_5O,H_2O$	62·3	10·7	19·6	61·8	10·6	19·0
Phenyl, HCl	Ph	H	249—250 [a,d]	$C_{16}H_{18}ClN_5O$	58·8	5·5	20·9	58·0	5·5	21·1
Phenyl, HCl	*o*-C_6H_4·OMe	H	221—223 [a,d]	$C_{17}H_{20}ClN_5O_2$	56·1	5·4	18·8	56·5	5·6	19·4
Phenyl, HCl	*p*-C_6H_4·OMe	H	258—259 [a,e]	$C_{17}H_{20}ClN_5O_2$	56·6	5·8	19·1	56·5	5·6	19·4
Phenyl, HCl	−CH_2·CH_2·CHMe·CH_2·CH_2−		223—224 [a,d]	$C_{16}H_{24}ClN_5O$	56·4	7·4	20·9	56·8	7·2	20·7
3,4-Dichlorophenyl, HCl	Me	H	224—225 [a,f]	$C_{11}H_{14}Cl_3N_5O$	38·9	4·1	20·3	38·8	4·1	20·6
3,4-Dichlorophenyl, HCl	Et	H	224—225 [a,f]	$C_{12}H_{16}Cl_3N_5O$	40·1	4·5	20·3	40·5	4·55	19·8
3,4-Dichlorophenyl, HCl	−[CH_2]$_5$−		220 [b,f]	$C_{15}H_{20}Cl_3N_5O$	45·5	5·4	17·1	45·8	5·3	17·7
1-Naphthyl, HCl	Me	H	221 [a,f]	$C_{15}H_{18}ClN_5O$	56·1	5·9	22·2	56·3	5·6	21·9
1-Naphthyl, HCl	Et	H	214—216 [b,f]	$C_{16}H_{20}ClN_5O$	57·1	5·6	21·0	57·5	6·0	21·0
1-Naphthyl, HCl	Et	Me	207—208 [a,f]	$C_{17}H_{22}ClN_5O$	58·8	6·5	19·8	58·6	6·4	20·1
1-Naphthyl, saccharinate	Et	Me	190—191 [b,d]	$C_{24}H_{26}N_6O_4S$	58·3	5·4	16·7	58·4	5·3	17·0
1-Naphthyl, dipicrate	CH_2NEt_2	Me	226 [a,e]	$C_{32}H_{34}N_{12}O_{15}$	46·0	4·0	19·7	46·5	4·1	20·3
1-Naphthyl, HCl, $2H_2O$	*o*-C_6H_4·OMe	H	218—220 [a,c]	$C_{21}H_{22}ClN_5O,2H_2O$	56·2	6·0	16·3	56·2	5·85	15·6
1-Naphthyl, HCl	CH:CHPh	H	218 [a,g]	$C_{22}H_{22}ClN_5O$	64·3	5·6	17·5	64·7	5·4	17·2
1-Naphthyl, HCl	−[CH_2]$_4$−		213—217 [a,c]	$C_{18}H_{22}ClN_5O$	60·6	6·4	19·6	60·2	6·1	19·5
1-Naphthyl, HCl	−[CH_2]$_5$−		218—220 [a,h]	$C_{19}H_{24}ClN_5O$	60·6	6·6	18·8	61·0	6·5	18·7
1-Naphthyl, saccharinate	−[CH_2]$_5$−		201 [a,h]	$C_{26}H_{28}N_6O_4S$	59·7	5·6	16·3	60·0	5·4	16·1
1-Naphthyl, HCl	−CF_3·CH_2·CHMe·CH_2·CH_2−		228—230 [a,c]	$C_{20}H_{26}ClN_5O$	61·5	7·1	18·4	61·9	6·7	18·1
1-Methyl-4-naphthyl, HCl	*o*-Cl_6H_4·OMe	H	199—200 [a,f]	$C_{22}H_{24}ClN_5O$	61·4	5·8	16·8	61·9	5·7	16·45
1-Methyl-4-naphthyl, HCl	−[CH_2]$_5$−		241—242 [a,c]	$C_{20}H_{26}ClN_5O$	62·2	6·9	18·15	62·4	6·75	18·05
1-Bromo-2-naphthyl, HCl, H_2O	Et	Me	170—172 [a,c]	$C_{17}H_{21}BrClN_5O,H_2O$	46·2	5·4	15·5	46·0	5·2	15·7

[a] Needles. [b] Prisms. Recryst. from [c] ethanol, [d] aqueous ethanol, [e] aqueous methanol, [f] ethanol–ether, [g] ethanol–acetone, [h] methanol.

TABLE 2

Dihydrotriazines (II; R′ = R″ = Me)

R and deriv.	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
o-Fluorophenyl, HBr	216° [a,d]	$C_{12}H_{17}BrFN_5O$	42·0	5·2	19·7	41·6	5·0	20·2
o-Chlorophenyl, HBr	217 [a,e]	$C_{12}H_{17}BrClN_5O$	40·1	5·0	19·7	39·7	4·7	19·3
p-Chlorophenyl, HBr	222 [b,f]	$C_{12}H_{17}BrClN_5O$	40·2	4·7	19·7	39·7	4·7	19·3
,, saccharinate	175—177 [a,f]	$C_{19}H_{21}ClN_6O_4S$	48·9	4·2	18·4	49·0	4·5	18·1
o-Bromophenyl, HBr	230 [a,g]	$C_{12}H_{17}Br_2N_5O$	35·7	4·4	16·9	35·4	4·2	17·2
2,4-Dichlorophenyl, HBr	209 [a,f]	$C_{12}H_{16}BrCl_2N_5O$	36·1	4·3	17·2	36·3	4·1	17·6
3,5-Dichlorophenyl, HCl	221—223 [a,h]	$C_{12}H_{16}Cl_3N_5O$	40·8	4·6	19·8	40·9	4·6	19·9
p-Sulphamoylphenyl, HBr	196—198 [a,i]	$C_{12}H_{19}BrN_6O_3S$	35·7	4·9	20·4	35·4	4·7	20·6
o-Methoxycarbonylphenyl, HBr	225—228 [a,j]	$C_{14}H_{20}BrN_5O_3$	43·3	5·0	18·4	43·5	5·2	18·1
o-Carboxyphenyl, HBr, H_2O	210—211 [a,k]	$C_{13}H_{18}BrN_5O_3,H_2O$	40·2	5·6	17·5	40·0	5·2	17·9

TABLE 2 (*Continued*)

R and deriv.	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
p-Methoxycarbonylphenyl, HBr	219·5—220·5 [c,g]	$C_{14}H_{20}BrN_5O_3$	43·6	5·1	18·3	43·5	5·2	18·1
p-Ethoxyphenyl, HBr	213—214 [a,f]	$C_{14}H_{22}BrN_5O_2$	45·6	6·1	18·9	45·2	6·0	18·8
o-Ethoxyphenyl, HBr	214—215 [a,d]	$C_{14}H_{22}BrN_5O_2$	44·95	6·0	18·7	45·2	6·0	18·8
p-Propyloxyphenyl, HBr	211—213 [a,f]	$C_{15}H_{24}BrN_5O_2$	46·8	6·1	18·9	46·7	6·3	18·15
o-Propyloxyphenyl, HBr	215 [a,f]	$C_{15}H_{24}BrN_5O_2$	47·3	5·9	18·3	46·7	6·3	18·15
p-Butyloxyphenyl, HBr	207—208 [a]	$C_{16}H_{26}BrN_5O_2$	47·9	6·5	17·8	48·0	6·6	17·5
,, saccharinate	182·5—184 [a,i]	$C_{23}H_{30}N_6O_5S$	54·5	5·9	16·5	54·9	6·0	16·7
o-Butyloxyphenyl, HBr	216—217 [a,f]	$C_{16}H_{26}BrN_5O_2$	47·8	6·6	17·4	48·0	6·6	17·5
p-Pentyloxyphenyl, HBr	197—199 [a,d,l]	$C_{17}H_{28}BrN_5O_2$	49·8	6·9	16·6	49·3	6·8	16·9
p-Isopentyloxyphenyl, HBr	210—211 [a,d,l]	$C_{17}H_{28}BrN_5O_2$	49·7	6·8	17·0	49·3	6·8	16·9
p-Hexyloxyphenyl, HBr	193—195 [a,d]	$C_{18}H_{30}BrN_5O_2$	50·2	7·0	16·8	50·5	7·1	16·4
o-Hexyloxyphenyl, HBr	174—176 [a,d]	$C_{18}H_{30}BrN_5O_2$	50·9	6·9	16·1	50·5	7·1	16·4
p-Octyloxyphenyl, HBr	192 [a,d]	$C_{20}H_{34}BrN_5O_2$	52·4	7·4	15·65	52·6	7·5	15·35
p-Decyloxyphenyl, HBr	184 [a,d,l]	$C_{22}H_{38}BrN_5O_2$	54·9	7·9	14·4	54·55	7·9	14·5
3,4-Dimethoxyphenyl, HCl	212—214 [a,f]	$C_{14}H_{22}ClN_5O_3$	48·9	6·6	20·1	48·9	6·45	20·4
3,5-Dimethoxyphenyl, HCl	217—219 [a,f]	$C_{14}H_{22}ClN_5O_3$	48·95	6·45	20·2	48·9	6·45	20·4
2,6-Dimethoxyphenyl, HCl	242—243 [a,f]	$C_{14}H_{22}ClN_5O_3$	49·3	6·8	19·8	48·9	6·45	20·4
3,4-Methylenedioxyphenyl, HBr	217 [a,d]	$C_{13}H_{18}BrN_5O_3$	42·1	4·8	19·2	41·8	4·9	18·8
3,4,5-Trimethoxyphenyl, HCl	231—232 [a,f]	$C_{15}H_{24}ClN_5O_4$	48·3	6·5	18·5	48·2	6·5	18·7
Styryl, HBr	217—218 [a,f]	$C_{14}H_{20}BrN_5O$	47·2	5·5	19·8	47·5	5·65	19·8
1-Naphthyl, HBr	218—220 [a,f,m]	$C_{16}H_{20}BrN_5O$	51·1	5·5	18·8	50·8	5·3	18·5
,, mandelate	182—183 [a,f]	$C_{24}H_{27}N_5O_4$	64·0	5·8	15·9	64·0	6·05	15·6
,, saccharinate	208—209 [a,i]	$C_{23}H_{24}N_6O_4S$	57·4	5·1	17·1	57·5	5·0	17·5
1-Chloro-2-naphthyl, HBr	223—224 [a,f]	$C_{16}H_{19}BrClN_5O$	46·6	4·6	17·2	46·6	4·6	16·95
1-Bromo-2-naphthyl, HBr	217 [a,d]	$C_{16}H_{19}Br_2N_5O$	42·7	4·4	15·8	42·1	4·2	15·3
1-Methyl-4-naphthyl, HCl	234 [a,f]	$C_{17}H_{22}ClN_5O$	58·5	6·5	20·2	58·8	6·3	20·2
2-Pyridyl, C_2H_5OH	203 [b,f]	$C_{13}H_{22}N_6O_2$	52·9	7·5	28·6	53·0	7·5	28·6
2-Quinolyl, HCl, H_2O	193—194 [a]	$C_{15}H_{19}ClN_6O,H_2O$	50·3	6·1	23·4	51·0	6·0	23·7
,, HBr, H_2O	186—187 [a,f]	$C_{15}H_{19}BrN_6O,H_2O$	45·4	5·5	20·8	45·4	5·3	21·2
6-Chloro-1,3-benzodioxan-8-yl, HCl	245—246 [a,f,n]	—	—	—	—	—	—	—
,, saccharinate	206—207 [a,i]	$C_{21}H_{23}ClN_6O_6S$	48·2	4·2	16·5	48·2	4·4	16·1
1,4-Benzodioxan-2-yl, HBr	224—225 [a,d]	$C_{14}H_{20}BrN_5O_3$	44·0	5·2	18·1	43·5	5·2	18·1
5-Methoxycarbonyl-2-furyl, HCl	192—198 [a,d,o]	$C_{13}H_{20}ClN_5O_4$	45·4	5·9	20·4	45·2	5·8	20·3
4-Diphenylyl, HCl, H_2O	228 [a,g]	$C_{18}H_{22}ClN_5O,H_2O$	57·3	6·2	18·65	57·3	6·4	18·5
4-Phenoxyphenyl, HCl, $0·5H_2O$	222 [a,g]	$C_{18}H_{22}ClN_5O_2,0·5H_2O$	56·5	6·3	17·5	56·3	6·0	18·2
9-Anthryl, HBr	218—219 [a,f]	$C_{20}H_{22}BrN_5O$	56·0	5·6	16·7	56·1	5·2	16·3
,, H_2O	233 [b,f]	$C_{20}H_{21}N_5O,H_2O$	66·15	6·8		65·8	6·4	
,, saccharinate	160 [a,i]	$C_{27}H_{26}N_6O_4S$	61·3	5·2	15·6	61·1	4·9	15·9
9-Bromo-10-anthryl, HBr	219—219·5 [a,d]	$C_{20}H_{21}Br_2N_5O$	47·4	4·4	13·8	47·3	4·2	13·8
2-Phenanthryl, HBr	222—223 [a,d]	$C_{20}H_{22}BrN_5O$	56·1	5·4	16·5	56·1	5·2	16·3
3-Phenanthryl, HBr	230 [a,f]	$C_{20}H_{22}BrN_5O$	56·2	5·4	16·35	56·1	5·2	16·3
,, saccharinate	186—188 [a,i]	$C_{27}H_{26}N_6O_4S$	61·2	4·8	15·7	61·2	4·95	15·8
3-Pyrenyl, HBr	238—239 [a]	$C_{22}H_{22}BrN_5O$	58·7	5·1	15·8	58·4	4·9	15·5

[a] Needles. [b] Leaflets. [c] Prisms. Recryst. from [d] ethanol–ether, [e] methanol–ether, [f] ethanol, [g] methanol, [h] propan-2-ol–ethanol, [i] aqueous ethanol, [j] dimethylformamide–ether. [k] Purified by dissolving in aqueous sodium hydrogen carbonate and precipitating with acetic acid. [l] Addition of hydrogen bromide in ethanol or aqueous hydrogen bromide was necessary to prevent partial loss of HBr as indicated by low m. p. and poor analysis. [m] Identical with the hydrobromide (m. p. 219°) obtained from 4,6-diamino-1,2-dihydro-2,2-dimethyl-1-(1-naphthylmethoxy)-1,3,5-triazine hydrochloride by way of the base. [n] Lit.,[4] m. p. 247°. [o] With addition of a trace of ethanolic hydrogen chloride.

prepared were 2-*amino*-4-(3,4-*dichloroanilino*)-5,6-*dihydro*-6,6-*dimethyl*-1,3,5-*triazine*, needles, m. p. 202° (from methanol) (Found: C, 46·0; H, 4·6; N, 24·9%), which could also be prepared by heating the *unrearranged base* [(III; R = 3,4-$C_6H_3 \cdot Cl_2$), needles, m. p. 144—146° (from aqueous methanol) (Found: C, 45·8; H, 4·3; N, 24·9. $C_{11}H_{13}Cl_2N_5$ requires C, 46·1; H, 4·55; N, 24·5%)] in aqueous suspension for 3 hr., and 2-*amino*-4-(1-*naphthylamino*)-5,6-*dihydro*-6,6-*dimethyl*-1,3,5-*triazine monohydrate*, needles, m. p. 234° (from ethanol) (Found: C, 63·2; H, 7·0; N, 24·2. $C_{15}H_{17}N_5,H_2O$ requires C, 63·3; H, 6·7; N, 24·6%).

Reaction of NN-*Diethylhydroxylamine with Benzyl Bromide.*—A mixture of the hydroxylamine, benzyl bromide, dimethylformamide and, in one series of experiments, sodium hydroxide, was heated at 85—95° for 1 hr. The cooled solution was acidified with dilute hydrochloric acid, evaporated at reduced pressure, basified, and extracted with ether. Evaporation of the ethereal extract left an oil which was analysed semi-quantitatively by gas-phase and thin-layer chromatography. Quantities of reactants and results of three such experiments are summarised below:

Et_2NOH (g.)	$PhCH_2Br$ (g.)	NaOH (g.)	Ether-soluble products (g.)	Components
1·1 (1 equiv.)	2·1 (1 equiv.)	—	0·66	*NN*-Diethylbenzylamine * Benzyl alcohol †
1·1 (1 equiv.)	2·1 (1 equiv.)	1·11 (2 equiv.)	0·3	*NN*-Diethylbenzylamine * *O*-Benzyl-*NN*-diethylhydroxylamine ‡
1·3 (1 equiv.)	1·45 (1·75 equiv.)	—	0·25	*NN*-Diethylbenzylamine * *O*-Benzyl-*NN*-diethylhydroxylamine ‡ Benzyl alcohol †

* Major component. † Minor component. ‡ Trace.

2-*Amino*-4-*benzyloxyamino*-5,6-*dihydro*-6,6-*dimethyl*-1,3,5-*triazine* (V; R = $CH_2 \cdot Ph$).—To sodium (0·46 g.) in ethanol (5 ml.) was added the *N*-hydroxytriazine hydrochloride (IVa; R = R′ = Me) (1·94 g.) in ethanol (20 ml.), followed by benzyl bromide (1·7 g.), and the mixture refluxed for 2 hr. The solvent was removed, the residual solid treated with water, and the product collected (1·9 g., 77%). Crystallisation from ethanol gave needles, m. p. 218°, not depressed on admixture with the authentic substance,[4] m. p. 220°.

2-*Amino*-4-p-*t*-*butylbenzyloxyamino*-5,6-*dihydro*-6,6-*dimethyl*-1,3,5-*triazine* (V; R = *p*-$C_6H_4 \cdot Bu^t$).—To a solution of the *N*-hydroxytriazine hydrochloride (IVa; R = R′ = Me) (1·94 g.) in ethanol (25 ml.) containing sodium (0·46 g.) was added *p*-t-butylbenzyl bromide (2·3 g.) and the mixture refluxed for 2 hr. The cooled mixture was filtered to remove insoluble inorganic material, the filtrate evaporated, and the residual oil treated with a slight excess of 10% ethanolic hydrogen chloride and ether to give an oily product which was converted into the picrate (3·15 g.). Crystallisation from acetone–light petroleum and then from aqueous ethanol gave needles of the pure *picrate* of the rearranged triazine, m. p. 240° (Found: C, 50·1; H, 5·5; N, 20·7. $C_{22}H_{28}N_8O_8$ requires C, 49·6; H, 5·3; N, 21·1%). Treatment of the picrate with N-sodium hydroxide gave the *rearranged base*, leaflets, m. p. 246° (from aqueous ethanol) (Found: C, 63·3; H, 8·4; N, 23·6. $C_{16}H_{25}N_5O$ requires C, 63·4; H, 8·3; N, 23·1%).

4,6-*Diamino*-1(1-*chloro*-2-*naphthylmethoxy*)-2,2-*dimethyl*-1,3,5-*triazine Hydrochloride* (IIa; R = 1-chloro-2-naphthyl, R′ = R″ = Me).—By repeating the foregoing experiment, using 2-bromomethyl-1-chloronaphthalene (2·56 g.) as alkylating agent, there was obtained the triazine hydrochloride (0·95 g.), m. p. 207°, forming leaflets, m. p. 218° (from ethanol–acetone) (lit.,[4] 221°) (Found: C, 52·5; H, 5·3; N, 18·7. Calc. for $C_{16}H_{19}Cl_2N_5O$: C, 52·3; H, 5·2; N, 19·0%), The *saccharinate* formed prisms, m. p. 185—186° (from ethanol–ether) (Found: C, 53·5; H. 4·4; N, 16·6. $C_{23}H_{23}ClN_6O_4$ requires C, 53·75; H, 4·5; N, 16·35%).

4,6-*Diamino*-1-(1-*bromo*-4-*naphthylmethoxy*)-2,2-*dimethyl*-1,3,5-*triazine Hydrochloride* (IIa; R = 1-bromo-4-naphthyl, R′ = R″ = Me).—Prepared by the same method from 1-bromo-4-bromomethylnaphthalene (3·0 g.), the triazine hydrochloride (1·45 g.) formed prismatic needles, m. p. 225° (from ethanol–ether) (lit.,[4] 227°) (Found: C, 46·4; H, 4·7; N, 16·5. Calc. for $C_{16}H_{19}BrClN_5O$: C, 46·5; H, 4·6; N, 16·95%). The 1-(1-bromo-2-naphthylmethoxy)-isomer, prepared similarly (49%), had m. p. 215—217° (lit.,[4] 217°).

2-*Amino*-5,6-*dihydro*-4-(1-*methoxycarbonyl*-2-*naphthylmethoxyamino*)-6,6-*dimethyl*-1,3,5-*triazine* (V; R = 1-methoxycarbonyl-2-naphthylmethyl) *Picrate.*—A mixture of sodium (0·155 g.) in ethanol (25 ml.) and the *N*-hydroxytriazine hydrochloride (0·65 g.) was treated with methyl 2-bromomethyl-1-naphthoate (0·94 g.) and stirred for 3 hr., then heated under reflux for 1 hr. A crystalline hydrochloride could not be obtained and the oily product was converted into the

picrate, needles (0·23 g.), m. p. 240—241° (from acetone–light petroleum) (Found: C, 49·3; H, 4·6; N, 19·5. $C_{24}H_{24}N_8O_{10}$ requires C, 49·4; H, 4·15; N, 19·2%).

4,6-*Diamino*-1,2-*dihydro*-2,2-*dimethyl*-1-(8-*quinolylmethoxy*)-1,3,5-*triazine* (II; R = 8-quinolylmethyl, R′ = R″ = Me) *Dihydrochloride*.—Made similarly to the foregoing triazine, the product formed a *dihydrochloride* separating from ethanol–ether as small needles, m. p. 242° (Found: C, 47·8; H, 5·7; N, 22·2. $C_{15}H_{20}Cl_2N_6O$ requires C, 48·5; H, 5·45; N, 22·6%). The *monosaccharinate* formed needles, m. p. 234—235° (from aqueous ethanol) (Found: C, 54·1; H, 4·7; N, 19·9. $C_{22}H_{23}N_7O_4S$ requires C, 54·9; H, 4·8; N, 20·2%). The *base monohydrate* prepared by treatment of an ethanolic solution with aqueous sodium hydroxide and precipitation with water, formed needles, m. p. 178° (from methanol–ether) (Found: C, 57·4; H, 6·4; N, 25·2. $C_{15}H_{18}N_6O,H_2O$ requires C, 57·0; H, 6·35; N, 25·5%).

Reduction of 2-*Amino*-5,6-*dihydro*-6,6-*dimethyl*-4-(2-*naphthylmethoxyamino*-1,3,5-*triazine* (V; R = 1-naphthylmethyl) *in Acid Solution*.—The base (0·65 g.) in ethanol (15 ml.) containing 20% ethanolic hydrogen chloride (0·4 ml.) was shaken with hydrogen and 10% palladised charcoal until uptake ceased. The catalyst was filtered off and the solvent removed, leaving an oil which was extracted with light petroleum (b. p. 60—80°). From the extracts was isolated 2-methylnaphthalene (0·23 g.), m. p. 33—34°. The insoluble solid (0·36 g.), m. p. 184—185°, was crystallised twice from ethanol–ether to give needles of 2-*amino*-5,6-*dihydro*-4-*hydroxyamino*-6,6-*dimethyl*-1,3,5-*triazine hydrochloride*, m. p. 202—204° (Found: C, 31·35; H, 6·4; N, 36·1. $C_5H_{12}ClN_5O$ requires C, 31·0; H, 6·2; N, 36·2%).

Reduction of 2-*Amino*-4-*benzyloxyamino*-5,6-*dihydro*-6,6-*dimethyl*-1,3,5-*triazine* (V; R = CH_2·Ph).—The rearranged base (2·0 g.), dissolved in ethanol (40 ml.), was shaken with hydrogen and 10% palladised charcoal until uptake ceased. Evaporation of the filtered mixture gave a solid (1·23 g.), m. p. 263—273°. Three crystallisations from aqueous ethanol gave 2-*amino*-5,6-*dihydro*-4-*hydroxyamino*-6,6-*dimethyl*-1,3,5-*triazine sesquihydrate* (0·35 g.), m. p. 285°, from which the anhydrous triazine could not be obtained on drying at 78°/1 mm. (Found: C, 32·25; H, 7·7; N, 37·5. $C_5H_{11}N_5O,1\frac{1}{2}H_2O$ requires C, 32·6; H, 7·6; N, 38·0%).

4,6-*Diamino*-1,2-*dihydro*-2,2-*dimethyl*-1-(1-*naphthylmethoxy*)-1,3,5-*triazine* (II; R = 1-naphthylmethyl, R′ = R″ = Me) *Hydrobromide*.—Sodium hydroxide (4·0 g.) in ethanol (400 ml.) was added to a warm solution of the hydroxytriazine hydrochloride (IVa; R = R′ = Me) (19·4 g.) in ethanol (400 ml.). The salt which separated was filtered off and the filtrate evaporated and dried azeotropically with benzene–ethanol. The residual solid, suspended in dimethylformamide (150 ml.), was stirred with 1-bromomethylnaphthalene (22·1 g.). Mild heating initiated an exothermic reaction and the solid dissolved to give a yellow solution. After heating for 30 min. on a steam-bath, the solvent was evaporated under reduced pressure, the residue stirred with ether, and the product collected (31·0 g., 82%), m. p. 199—200°. Further purification by extraction with cold water to remove traces of inorganic material, and crystallisation from ethanol gave the pure *dihydrotriazine hydrobromide* as prismatic needles, m. p. 214° (Found: C, 51·1; H, 5·7; N, 18·7. $C_{16}H_{20}BrN_5O$ requires C, 50·8; H, 5·3; N, 18·5%).

4,6-*Diamino*-1,2-*dihydro*-2,2-*dimethyl*-1-(2-*pyridylmethoxy*)-1,3,5-*triazin* (IIa; R = 2-pyridyl, R′ = R″ = Me) *Hydrochloride*.—To the hydroxytriazine hydrochloride (IVa; R = R′ = Me) (19·4 g.) dissolved in warm dimethyl sulphoxide (200 ml.) was added a solution of sodium hydroxide (8·0 g.) in water (20 ml.). 2-Chloromethylpyridine hydrochloride (16·4 g.) in water (20 ml.). 2-Chloromethylpyridine hydrochloride (16·4 g.) was added and the mixture heated with stirring on a steam-bath for 1 hr. After cooling, inorganic material was removed by filtration and the clear filtrate evaporated under reduced pressure. The residual solid was triturated with acetone, collected (21 g.), and crystallised from ethanol, giving the *triazine hydrochloride* as needles (15·2 g.), m. p. 195—196° (Found: C, 45·9; H, 6·2; N, 30·0. $C_{11}H_{17}ClN_6O$ requires C, 46·3; H, 6·0; N, 29·5%). In a similar manner to the foregoing two examples, the *dihydrotriazines* recorded in Table 2 were prepared. In general, heating was carried out for 15—60 min.

Effect of Solvent on the Formation of 4,6-*Diamino*-1,2-*dihydro*-2,2-*dimethyl*-1-(1-*naphthylmethoxy*)-1,3,5-*triazine Hydrochloride*.—Under identical conditions and on the same scale as in the foregoing experiment, but using 1-chloromethylnaphthalene (17·6 g.), the following yields of triazine hydrochloride, m. p. 210—212°, were obtained using the solvent stated: dimethylsulphoxide (66%), dimethylformamide (51%), ethanol (43%), and formamide (38·5%). Comparative yields using 1-bromomethylnaphthalene were: dimethylformamide (82%), ethanol (45%).

4,6-*Diamino*-1,2-*dihydro*-1-*methoxy*-2,2-*dimethyl*-1,3,5-*triazine* (II; R = H, R′ = R″ = Me)

Hydriodide.—The hydroxytriazine (IV; R = R′ = Me) from the hydrochloride (1·94 g.) in dimethylformamide (20 ml.) was stirred with iodomethane (1·7 g.) at room temperature for 1 hr., then refluxed for 1 hr. The solid remaining after evaporation was washed with cold water and crystallised twice from ethanol–ether, giving the *product* as needles (1·4 g.), m. p. 217—218·5° (Found: C, 24·4; H, 4·7; N, 23·9. $C_6H_{14}IN_5O$ requires C, 24·3; H, 4·75; N, 23·4%).

4,6-*Diamino*-1-*decyloxy*-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine* (II; R = C_9H_{19}, R′ = R″ = Me), *hydrobromide*, prepared similarly, formed needles, m. p. 193—194° (from ethanol–ether containing a small amount of hydrogen bromide) (Found: C, 47·5; H, 8·3; N, 18·9. $C_{15}H_{32}BrN_5O$ requires C, 47·6; H, 8·5; N, 18·5%). The *triazine base* crystallised from aqueous ethanol as needles, m. p. 126—127° (Found: C, 59·9; H, 10·5; N, 23·8. $C_{15}H_{31}N_5O$ requires C, 60·6; H, 10·5; N, 23·6%). Heating of the base in aqueous ethanol for 2½ hr. gave 2-*amino*-4-*decyloxyamino*-5,6-*dihydro*-6,6-*dimethyl*-1,3,5-*triazine* (V; R = $C_{10}H_{21}$), needles, m. p. 174—176° (Found: C, 61·0; H, 10·1; N, 24·0%).

4,6-*Diamino*-1-*carboxymethoxy*-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine Hydrochloride* (IIa; R = CO_2H, R′ = R″ = Me).—To a suspension of the hydroxytriazine (IV; R = R′ = Me) (6·3 g.) in dimethylformamide (30 ml.) was added chloroacetic acid (3·8 g.) and the mixture stirred on a steam-bath for 10 min. Solvent was removed at reduced pressure and the residual gum triturated with ether to give a solid (7·8 g.), m. p. 191—193° (shrinking from 180°). Two crystallisations from aqueous ethanol gave the *product* as needles, m. p. 193° (Found: C, 33·7; H, 5·4; N, 27·4. $C_7H_{14}ClN_5O_3$ requires C, 33·4; H, 5·6; N, 27·8%). The *free base*, obtained with aqueous sodium hydroxide, formed needles, m. p. 246—248° (Found: C, 38·75; H, 6·0; N, 32·3. $C_7H_{13}N_5O_3$ requires C, 39·05; H, 6·1; N, 32·8%).

4,6-*Diamino*-1-(α-*chlorocarboxymethoxy*)-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine* (III; R = O·CHCl·CO_2H) *hydrochloride*, prepared from dichloroacetic acid, formed needles, m. p. 196° (from ethanol–ether) (Found: C, 29·55; H, 4·6; N, 24·7. $C_7H_{13}Cl_2N_5O_3$ requires C, 29·4; H, 4·6; N, 24·9%). 1-*Allyloxy*-4,6-*diamino*-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine* (II; R = CH_2·CH:CH_2, R′ = R″ = Me) *hydrobromide*, prepared at room temperature, formed needles, m. p. 192—193° (from propan-2-ol) (Found: C, 34·6; H, 6·05; N, 25·25. $C_8H_{16}BrN_5O$ requires C, 34·6; H, 5·8; N, 25·2%). When the hydroxytriazine was reacted with chloroacetamide, a gummy product was obtained which could not be induced to crystallise. Treatment with lithium picrate gave 4,6-*diamino*-1-*carboxyamidomethoxy*-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine picrate*, needles, m. p. 282—283° (from aqueous ethanol) (Found: C, 35·7; H, 3·8; N, 28·4. $C_{13}H_{17}N_9O_9$ requires C, 35·2; H, 3·8; N, 28·4%).

4,6-*Diamino*-1,2-*dihydro*-2,2-*dimethyl*-1-(1-*phenylethoxy*)-, needles, m. p. 211—212° (from ethanol) (Found: C, 45·6; H, 5·6; N, 20·3. $C_{13}H_{20}BrN_5O$ requires C, 45·6; H, 5·85; N, 20·5%); -1-*phenethyloxy*-, needles, m. p. 218—220° (Found: C, 45·6; H, 5·9; N, 21·0%); -1-(3-*phenylpropoxy*)-, needles, m. p. 201—203° (from ethanol) (Found: C, 47·8; H, 6·4; N, 19·6. $C_{14}H_{22}BrN_5O$ requires C, 47·2; H, 6·2; N, 19·7%); and -1-(2-*methyl*-1-*naphthylethoxy*)-1,3,5-*triazine hydrobromide*, needles, m. p. 256—257° (from aqueous ethanol) (Found: C, 52·8; H, 5·8; N, 17·0. $C_{18}H_{24}BrN_5O$ requires C, 53·2; H, 5·8; N, 17·2%) were similarly prepared in dimethyl sulphoxide from the requisite bromides.

Reaction between Benzhydryl Bromide and 4,6-*Diamino*-1,2-*dihydro*-1-*hydroxy*-2,2-*dimethyl*-1,3,5-*triazine*.—A suspension of the hydroxytriazine, prepared *in situ* from the hydrochloride (1·57 g.) and aqueous sodium hydroxide in dimethylformamide (30 ml.), was treated with benzhydryl bromide (2·0 g.) and heated on a steam-bath for 1 hr. The clear solution was evaporated and the residual oily solid extracted with several portions of ether. Evaporation of the ether layer gave a semi-solid which after crystallisation from aqueous ethanol gave diphenylmethanol (0·75 g.). The ether-insoluble material was extracted with ethanol, giving a crude sample of the hydrobromide, m. p. 230—231°, of the starting hydroxytriazine. When compared with an authentic sample prepared from the hydroxytriazine base and hydrogen bromide, the infrared spectra were almost indistinguishable; the pure *hydrobromide* formed needles, m. p. 241—242° (from ethanol) (Found: C, 25·4; H, 4·8; Br, 33·25; N, 29·3. $C_5H_{12}BrN_5O$ requires C, 25·2; H, 5·1; Br, 33·6; N, 29·4%). When the hydroxytriazine (from 19·4 g. hydrochloride) was similarly treated with benzhydryl chloride (20·25 g.) there was obtained diphenylmethanol (14·1 g.) and 4,6-diamino-1,2-dihydro-1-hydroxy-2,2-dimethyl-1,3,5-triazine hydrochloride (9·5 g.), m. p. 238°.

4,6-*Diamino*-1,2-*dihydro*-1-*methoxy*-2,2-*dimethyl*-1,3,5-*triazine Picrate*.—To the hydroxytriazine (IV; R = R′ = Me) (from 9·7 g. hydrochloride) in dimethylformamide (50 ml.) was

added dimethyl sulphate (8·4 ml.) and the mixture stirred on a steam-bath for 30 min. Working up gave a gummy product which was dissolved in water and treated with lithium picrate. The *triazine picrate* formed needles, m. p. 240° (from acetic acid) (Found: C, 36·0; H, 4·3; N, 27·5. $C_{12}H_{16}N_8O_8$ requires C, 36·0; H, 4·0; N, 28·0%).

4,6-*Diamino*-1-*ethoxy*-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine Toluene*-p-*sulphonate*.—The hydroxytriazine (from 9·7 g. hydrochloride), dimethylformamide (60 ml.), and ethyl toluene-*p*-sulphonate (10 g.) were stirred on a steam-bath for 30 min., then evaporated at reduced pressure to give a solid. This was stirred with a little cold water and crystallised from aqueous ethanol, giving the *product*, m. p. 190—193° (Found: C, 46·4; H, 6·6; N, 19·6. $C_{14}H_{23}N_5O_4S$ requires C, 46·8; H, 6·45; N, 19·6%).

A number of *dihydrotriazine salts*, prepared by standard methods, are listed in Table 3.

Reaction of Acetic Acid with 4,6-*Diamino*-1-*decyloxy*-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine*.—The base (3·0 g.) was dissolved in warm acetic acid (15 ml.) and the solvent removed to give a gum which was dissolved in warm water (30 ml.) and set aside. Prisms separated (2·5 g.) and were recrystallised from water to give the *acetate monohydrate*, m. p. 174—176° (Found: C, 54·0; H, 9·7; N, 18·5. $C_{17}H_{35}N_5O_3,H_2O$ requires C, 54·3; H, 9·9; N, 18·8%). Treatment of aqueous solutions of the salt with aqueous hydrochloric or nitric acid gave the hydrochloride, m. p. 202—204° and nitrate, m. p. 179—180°, respectively.

4,6-*Diamino*-1-*o*-*carboxybenzyloxy*-1,2-*dihydro*-2,2-*dimethyl*-1,3,5-*triazine* (II; R = *o*-C_6H_4·CO_2H, R′ = R″ = Me) *Hydrobromide*.—The ester hydrobromide (II; R = *o*-C_6H_4·CO_2Me, R′ = R″ = Me) (3·8 g.) and sodium hydroxide (1·0 g.) in 50% aqueous ethanol (20 ml.) were set aside for 4 hr. at 20°, then made acid with acetic acid. A solid (1·76 g.) separated, which contained bromide. Purification was effected by dissolving the material in aqueous sodium hydrogen carbonate and precipitating with acetic acid giving the *hydrobromide monohydrate*, m. p. 210—211° (Found: C, 40·2; H, 5·6; N, 17·5. $C_{13}H_{18}BrN_5O_3,H_2O$ requires C, 40·0; H, 5·2; N, 17·9%).

Reaction of Iodomethane with 4,6-*Diamino*-1,2-*dihydro*-2,2-*dimethyl*-1-(2-*pyridylmethoxy*)-1,3,5-*triazine*.—A mixture of the triazine (1·0 g.), iodomethane (10 ml.), and dimethylformamide (20 ml.) was set aside for 3 days. Addition of ether gave a tan solid which was crystallised from ethanol–ether to give a *dimethiodide*, m. p. 131° (Found: C, 29·8; H, 4·4; N, 16·0. $C_{13}H_{22}I_2N_6O$ requires C, 29·3; H, 4·2; N, 15·8%). Similarly, 4,6-*diamino*-1,2-*dihydro*-2,2-*dimethyl*-1-(2-*quinolylmethoxy*)-1,3,5-*triazine methiodide monohydrate* was obtained as needles, m. p. 198° (from ethanol) (Found: C, 41·6; H, 5·1; I, 28·4; N, 18·9. $C_{16}H_{21}IN_6O,H_2O$ requires C, 41·8; H, 5·0; I, 27·8; N, 18·4%).

4,6-*Diamino*-1,2-*dihydro*-1-*hydroxy*-2,2-*dimethyl*-1,3,5-*triazine* (IV; R = R′ = Me) was prepared by percolating a solution of the hydrochloride (IVa; R = R′ = Me) (1·0 g.) in water through a Deacidite FF ion-exchange column and evaporating the halogen-free eluate to give the triazine base (0·5 g.), m. p. 199—200° (from ethanol–ether) (lit.,[4] 197—198°) (Found: C, 38·2; H, 7·3; N, 44·2. Calc. for $C_5H_{11}N_5O$: C, 38·2; H, 7·0; N, 44·5%). A number of *salts* prepared from this triazine are described in Table 4. All were crystallised from ethanol or aqueous ethanol as needles or prisms.

4,6-*Diamino*-1,2-*dihydro*-1-*hydroxy*-1,3,5-*triazine*-2-*spirocyclohexane Hydrochloride* (IVa; RR′ = $-[CH_2]_5-$).—4,6-Diamino-1-benzyloxy-1,2-dihydro-1,3,5-triazine-2-spirocyclohexane hydrochloride (3·24 g.) in 50% aqueous methanol (50 ml.) was shaken with hydrogen and 10% palladised charcoal until uptake ceased. After filtration, the solvents were removed and the residual solid crystallised from ethanol, giving the *product* as needles (2·17 g., 93%), m. p. 239—240° (Found: C, 41·6; H, 7·1; N, 29·8. $C_8H_{16}ClN_5O$ requires C, 41·0; H, 6·9; N, 30·0%). Similarly were prepared the *hydrochlorides* of the following 2-*substituted* 1-*hydroxytriazines*: 2-*spiro*-(4-*methylcyclohexane*) (IVa; RR′ = $-[CH_2]_2$·CHMe·$[CH_2]_2-$), needles, m. p. 252·5—253° (from ethanol) (Found: C, 44·0; H, 7·2; N, 28·4. $C_9H_{18}ClN_5O$ requires C, 43·6; H, 7·3; N, 28·3%); 2-*phenyl* (IVa; R = Ph, R′ = H), needles, m. p. 216—218° (from ethanol) (Found: C, 45·4; H, 4·9. $C_9H_{12}ClN_5O$ requires C, 44·7; H, 5·0%) and 2-*o*-methoxyphenyl (IVa; R = *o*-C_6H_4·OMe, R′ = H), which formed a *hydrochloride dihydrate*, m. p. 216° from aqueous ethanol (Found: C, 39·7; H, 5·9; N, 21·9. $C_{10}H_{14}ClN_5O,2H_2O$ requires C, 39·2; H, 5·9; N, 22·8%). Drying at 78° over P_2O_5 at 0·2 mm. gave the *anhydrous hydrochloride* (Found: C, 43·9; H, 5·6; N, 25·9. $C_{10}H_{14}ClN_5O$ requires C, 44·2; H, 5·2; N, 25·8%. Loss in wt.: Found, 11·8: requires 12·05%).

Some of the new 2-*substituted dihydrotriazines* were prepared from the corresponding hydroxytriazines by the methods described earlier and are listed in Table 5.

TABLE 3

Dihydrotriazine salts (II; R′ = R″ = Me)

R	Salt	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
Nonyl	Lactate	98—100° [a,c]	$C_{18}H_{37}N_5O_4$	55·6	9·6	18·6	55·8	9·5	18·1
Nonyl	Acid maleate	196 [a,d]	$C_{19}H_{35}N_5O_5$	55·6	8·6	16·5	55·3	8·5	16·9
Nonyl	Nitrate	181 [a,e]	$C_{15}H_{32}N_6O_4$	50·2	9·1	22·9	50·0	8·9	23·3
Nonyl	*p*-Dipropylsulphamoyl benzoate, H_2O	138 [a,e]	$C_{28}H_{50}N_6O_5S,H_2O$	56·2	8·9	14·1	56·0	8·7	14·0
Nonyl	Saccharinate	181 [b,e]	$C_{22}H_{36}N_6O_4S$	55·1	7·6	17·5	55·0	7·5	17·5
3,4-Dichlorophenyl	Saccharinate	183 [a,d]	$C_{19}H_{20}Cl_2N_6O_4S$	45·6	4·1	17·0	45·7	4·0	16·8
1-Naphthyl	Chloroacetate	170—172 [a,f]	$C_{18}H_{22}ClN_5O_3$	55·1	5·8	17·7	55·1	5·65	17·8
1-Naphthyl	Laurate	151—152 [a,g]	$C_{28}H_{43}N_5O_3$	67·5	8·5	14·5	67·5	8·7	14·0
1-Naphthyl	Stearate	149—150 [a,e]	$C_{34}H_{55}N_5O_3$	70·7	9·0	12·0	70·2	9·55	12·0
1-Naphthyl	Mandelate	151—152 [a,h]	$C_{24}H_{27}N_5O_4$	64·5	6·0	15·4	64·0	6·05	15·55
1-Naphthyl	2,4-Dichlorobenzoate	172 [b,e]	$C_{23}H_{23}Cl_2N_5O_3$	56·4	4·7	14·2	56·5	4·7	14·3
1-Naphthyl	3,4-Dichlorobenzoate	196 [a,e]	$C_{23}H_{23}Cl_2N_5O_3$	56·7	4·6	14·8	56·5	4·7	14·3
1-Naphthyl	2,4,5-Trichlorophenol, C_2H_5OH	115 [a,d]	$C_{22}H_{22}Cl_3N_5O_2,C_2H_6O$	53·4	5·8	12·7	53·3	5·2	12·9
1-Naphthyl	*p*-Dipropylsulphamoyl benzoate	194—196 [b,d]	$C_{29}H_{38}N_6O_5S$	59·6	6·8	14·0	59·7	6·5	14·4
1-Naphthyl	Phthalimide	162—164 [a,e]	$C_{24}H_{24}N_6O_3$	64·7	5·7	19·0	64·8	5·4	18·9
1-Naphthyl	Saccharinate	207 [b,d]	$C_{23}H_{24}N_6O_4S$	57·5	4·9	17·4	57·5	5·0	17·5
1-Naphthyl	3-Cyano-6-methoxy-methyl-4-methyl-2-pyridone	170—171 [a,d]	$C_{25}H_{29}N_7O_3$	63·4	6·4	20·2	63·1	6·2	20·6
1-Bromo-2-naphthyl	Chloroacetate	173 [b,f]	$C_{18}H_{21}BrClN_5O_3$	46·1	4·6	14·7	45·7	4·5	14·85
1-Bromo-2-naphthyl	Propionate	171—172 [a,h]	$C_{19}H_{24}BrN_5O_3$	50·6	5·4	15·0	50·6	5·4	15·55

[a] Needles. [b] Prisms. Recryst. from [c] ethanol–ether, [d] ethanol, [e] aqueous ethanol, [f] ethanol–light petroleum (b. p. 60—80°), [g] ethyl acetate, [h] propan-2-ol–ether.

TABLE 5

Dihydrotriazine salts (II)

R and deriv.	R′	R″	Recryst. from *	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
Nonyl, HBr	$-[CH_2]_5-$		EtOH †	223—226°	$C_{18}H_{36}BrN_5O$	52·2	8·9	16·5	51·7	8·7	16·7
Nonyl, picrate	o-C_6H_4·OMe	H	EtOH	160—162	$C_{26}H_{36}N_6O_9$	51·7	6·4	18·9	51·6	6·0	18·5
1-Naphthyl, HBr	$-[CH_2]_5-$		EtOH–H_2O	227—229	$C_{19}H_{24}BrN_5O$	54·1	5·8	17·05	54·5	5·8	16·8
1-Methyl-4-naphthyl, HCl	$-[CH_2]_5-$		EtOH	241—242	$C_{20}H_{26}ClN_5O$	62·2	6·9	18·15	62·4	6·75	18·05
1-Methyl-4-naphthyl, HCl	$-[CH_2]_2$·CHMe·$[CH_2]_2-$		EtOH–H_2O	239—241	$C_{21}H_{28}ClN_5O$	62·9	7·3	17·1	62·9	7·05	17·5
1-Methyl-4-naphthyl, HCl	o-C_6H_4·OMe	H	EtOH–Et_2O	199—200	$C_{22}H_{24}ClN_5O_2$	61·4	5·8	16·8	61·9	5·7	16·45
1-Bromo-4-naphthyl, HBr	$-[CH_2]_5-$		EtOH–H_2O	240—242	$C_{19}H_{23}Br_2N_5O$	46·4	4·7	14·6	46·0	4·7	14·1
1-Bromo-4-naphthyl, HBr	$-[CH_2]_2$·CHMe·$[CH_2]_2-$		EtOH–H_2O	235—236	$C_{20}H_{25}Br_2N_5O$	47·2	4·6	14·15	47·0	4·9	13·7
9-Phenanthryl, HCl	$-[CH_2]_2$·CHMe·$[CH_2]_2-$		DMF	262—264	$C_{24}H_{28}ClN_5O$	66·1	6·8	15·8	65·7	6·4	16·0

* All crystallised as needles. † Containing a trace of hydrogen bromide.

TABLE 4

Hydroxydihydrotriazine salts (IV; R = R′ = Me)

Salt	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
Stearate	163—164°	$C_{23}H_{47}N_5O_3$	62·2	11·0	16·0	62·4	10·7	15·8
p-Toluate	214	$C_{13}H_{19}N_5O_3$	53·0	6·6	24·0	53·3	6·55	23·9
p-Nitrobenzoate.....	207—208	$C_{12}H_{16}N_6O_5$	44·2	5·4	26·3	44·5	5·0	25·9
2,4-Dichlorobenzoate	188—189	$C_{12}H_{15}Cl_2N_5O_3$	41·5	4·5	19·6	41·5	4·3	20·1
3,4-Dichlorobenzoate	232	$C_{12}H_{15}Cl_2N_5O_3$	41·8	4·6	20·5	41·5	4·3	20·1
3,5-Dichlorobenzoate	216—217	$C_{12}H_{15}Cl_2N_5O_3$	41·7	4·5	20·0	41·5	4·3	20·1
N-Acetylglycinate ...	203—205	$C_9H_{18}N_6O_4$	39·7	6·6	30·2	39·4	6·65	30·6
Saccharinate, H_2O ...	200—201	$C_{12}H_{16}N_6O_4S,H_2O$	40·1	5·0	23·6	40·3	5·0	23·5

2-Amino-4-benzyloxyamino-5,6-dihydro-1,3,5-triazine-2-spirocyclohexane.—4,6-Diamino-1-benzyloxy-1,2-dihydro-2,2-dimethyl-1,3,5-triazine hydrochloride (2·0 g.) and 2N-sodium hydroxide (25 ml.) were refluxed for 3 hr. After cooling, the solid which separated (1·7 g.) was crystallised from ethanol to give needles of the *rearranged triazine* (1·4 g.), m. p. 225—227° (Found: C, 62·65; H, 7·0; N, 24·2. $C_{15}H_{21}N_5O$ requires C, 62·6; H, 7·4; N, 24·2%). The *2-spiro-(4-methylcyclohexane) analogue*, similarly prepared, formed needles, m. p. 228—230° (Found: C, 63·8; H, 7·6; N, 23·2. $C_{16}H_{23}N_5O$ requires C, 63·7; H, 7·7; N, 23·2%).

Substituted Benzaldehydes.—Alkylation of *o*- and *p*-hydroxybenzaldehydes with alkyl iodides or bromides in ethanolic potassium hydroxide proceeded normally, giving the alkoxybenzaldehydes, most of which have been previously described. *o*-Propoxybenzaldehyde was prepared both by alkylation and by catalytic reduction of *o*-allyloxybenzaldehyde in ethanol in the presence of 10% palladised charcoal. A number of previously undescribed derivatives are listed in Table 6.

TABLE 6

Derivatives of *o*- and *p*-alkyloxybenzaldehydes, R·C_6H_4·CHO

R	Derivative	M. p.*	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
p-OCH_2·CH:CH_2	Semicarbazone	188—189°	$C_{11}H_{13}N_3O_2$	59·9	5·9	19·7	60·3	6·0	19·2
p-OC_3H_7	Semicarbazone	187—188	$C_{11}H_{15}N_3O_2$	59·6	6·6	19·5	59·8	6·8	19·0
p-OC_4H_9	Semicarbazone	191—192	$C_{12}H_{17}N_3O_2$	61·7	7·2	18·1	61·3	7·3	17·9
p-OC_5H_{11}	Semicarbazone	188—189	$C_{13}H_{19}N_3O_2$	62·5	7·2	17·05	62·7	7·7	16·85
p-OC_6H_{13}	Semicarbazone	191—192	$C_{14}H_{21}N_3O_2$	64·2	7·95	16·3	64·0	8·1	16·0
o-OCH_2·CH:CH_2	Semicarbazone	167—168 †	$C_{11}H_{13}N_3O_2$	60·0	6·25	19·2	60·0	6·0	19·2
o-OC_4H_9	Semicarbazone	179—180 †	$C_{12}H_{17}N_3O_2$	61·2	7·1	18·1	61·3	7·3	17·9
o-OC_4H_9	2,4-Dinitrophenylhydrazone	192 ‡	$C_{17}H_{18}N_4O_5$	57·3	5·1	15·9	57·0	5·1	15·6

* All recrystallised from ethanol as colourless leaflets unless otherwise stated. † Colourless needles. ‡ Red needles.

p-*Hexyloxybenzyl Alcohol.*—To a solution of potassium hydroxide (31·5 g.) in methanol (37 ml.) was slowly added a solution of 36% formalin (23 ml.) and *p*-hexyloxybenzaldehyde (38·55 g.) in methanol (35 ml.) with stirring at 60—70°. After a further 2 hr. at this temperature, the methanol was removed, water added, and the product extracted into ether. The *product* was isolated as a colourless oil (31·3 g.), b. p. 136—142°/0·2 mm., which solidified, m. p. 31—32° (Found: C, 75·0; H, 9·4. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·7%).

1-(2-*Hydroxyethyl*)-2-*methylnaphthalene.*—A solution of ethyl (2-methyl-1-naphthyl)acetate (4·85 g.) in dry ether (40 ml.) was added with stirring to lithium aluminium hydride (1·05 g.) so as to maintain gentle reflux. After working up in the usual manner, there was obtained an oil (4·0 g.) which still contained unchanged ester. The latter was eliminated by treatment with alkali in aqueous ethanol and the product isolated as an oil (3·05 g.), b. p. 140°/0·1 mm. which crystallised, m. p. 35° (lit.,[25] 36—36·5°) (Found: C, 84·1; H, 7·3. Calc. for $C_{13}H_{14}O$: C, 84·0; H, 7·6%).

p-*Decyloxybenzyl Alcohol.*—*p*-Decyloxybenzaldehyde (17·4 g.) in dry ether (30 ml.) was slowly added to lithium aluminium hydride (0·85 g.) in dry ether (70 ml.) under gentle reflux. After 1 hr., working up gave the *product* as leaflets (16·0 g.), m. p. 51—52° [from ether–light petroleum (b. p. 40—60°)] (Found: C, 76·8; H, 10·9. $C_{17}H_{28}O_2$ requires C, 77·2; H, 10·7%).

[25] P. Cagniant and P. Cagniant, *Bull. Soc. chim. France*, 1952, 970.

Other previously undescribed carbinols made by the above methods were: *p*-allyloxybenzyl alcohol, b. p. 142—146°/0·5 mm.; *p*-isopentyloxybenzyl alcohol, b. p. 132—134°/0·4 mm.; *o*-hexyloxybenzyl alcohol, b. p. 137—140°/0·3 mm.; *o*-decyloxybenzyl alcohol, b. p. 145—153°/0·2 mm., *3,5-dinitrobenzoate*, m. p. 72—73° (from ethanol) (Found: C, 62·5; H, 6·0; N, 5·9. $C_{24}H_{30}N_2O_7$ requires C, 62·8; H, 6·6; N, 6·1%); and *o*-fluorobenzyl alcohol, b. p. 94—96°/14 mm. This last compound was prepared by Shoesmith and Slater,[26] who gave no physical properties.

β-p-*Propoxyphenylpropionic Acid.*—A solution of diethyl malonate (2·9 g.) in methanol (20 ml.) containing sodium (0·42 g.) was evaporated to dryness and the residual solid dissolved in dimethylformamide (15 ml.). *p*-Propoxybenzyl bromide (3·75 g.) was added and the mixture refluxed for 2½ hr. Working up gave an oily product which was heated with 30% aqueous potassium hydroxide (50 ml.) on a steam-bath for 4 hr. The clear solution was treated with 30% sulphuric acid (100 ml.) and refluxed for 4 hr. Cooling gave an oil which was extracted into benzene, washed, dried, and evaporated to give a solid (1·4 g.). Crystallisation from aqueous ethanol gave the *product* as needles (0·9 g.), m. p. 97—98° (Found: C, 69·0; H, 7·5. $C_{12}H_{16}O_3$ requires C, 69·0; H, 7·7%). Similarly prepared were β-p-*butoxyphenylpropionic acid*, m. p. 85—86·5° (Found: C, 69·7; H, 7·8. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·1%); and o-*propoxybenzylmalonic acid*, m. p. 156°, which could not be decarboxylated (Found: C, 62·3; H, 6·4. $C_{13}H_{16}O_5$ requires C, 62·0; H, 6·4%). By a similar reaction, 1-bromomethylnaphthalene and diethyl malonate gave a mixture of β-(1-naphthyl)propionic acid, m. p. 151° (Found: C, 77·8; H, 6·2. Calc. for $C_{13}H_{12}O_2$: C, 78·0; H, 6·0%) and *di-(1-naphthylmethylacetic acid*, m p. 174° (Found: C, 85·0; H, 6·0. $C_{24}H_{20}O_2$ requires C, 84·7; H, 5·9%).

Aralkyl bromides.—Method (A). A mixture of 3-methylpyrene (10 g.), *N*-bromosuccinimide (8·25 g.) and αα′-azobisisobutyronitrile (100 mg.) in carbon tetrachloride (70 ml.) was refluxed for 2½ hr. After cooling, the solid was filtered off, the filtrate evaporated, and the residual solid crystallised from benzene, giving needles of *3-bromomethylpyrene* (10·4 g.), m. p. 145—146° (Found: C, 68·9; H, 3·85. $C_{17}H_{11}Br$ requires C, 69·1; H, 3·8%).

Method (B). *p*-Decyloxybenzyl alcohol (11·0 g.) in dry benzene (50 ml.) was treated with a rapid stream of dry hydrogen bromide for 20 min. at 0—5°. The solution was poured into ice–water, extracted with chloroform, and the extract washed with aqueous sodium hydrogen carbonate and with water. Evaporation of the dried extracts gave an oil from which *p*-decyloxybenzyl bromide (8·3 g.), b. p. 182—184°/0·45 mm. was obtained. This, and a number of other

TABLE 7

Substituted bromides, Ar·CH_2Br

Ar	M. p.[a] or b. p./mm.	Method	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
o-Fluorophenyl	82—86°/14[b]	B					
p-Methoxycarbonylphenyl	50—52°[c]	A					
o-Methoxycarbonylphenyl	114°/0·44[d]	A	$C_9H_9BrO_2$	47·0	4·1	47·2	4·0
1-Methoxycarbonyl-4-naphthyl	75—76°	A	$C_{13}H_{11}BrO_2$	56·5	4·1	56·1	4·0
1-Methoxycarbonyl-2-naphthyl	68°	A	$C_{13}H_{11}BrO_2$	56·3	3·6	56·1	4·0
9-Anthryl	143—144·5°[e]	A	$C_{15}H_{11}Br$	66·95	4·0	66·5	4·1
p-Ethoxyphenyl	134—136°/15	B					
p-Propoxyphenyl	102—106°/0·25	B					
p-Butoxyphenyl	108—112°/0·25	B					
p-Pentyloxyphenyl	126—128°/0·25	B					
p-Isopentyloxyphenyl	130—132°/0·5	B					
p-Hexyloxyphenyl	136—140°/0·25	B					
p-Octyloxyphenyl	161°/0·45	B					
o-Ethoxyphenyl	84—86°/0·3	B					
o-Propoxyphenyl	87—90°/0·2	B					
o-Butoxyphenyl	93—97°/0·2	B					
o-Hexyloxyphenyl	118—122°/0·45	B					
3,4-Methylenedioxyphenyl	48°[f]						
	101—103°/0·15	B					

[a] Solid bromides were crystallised from light petroleum (b. p. 60—80°). [b] G. Olah, A. Pavlath, J. A. Olah, and F. Herr (*J. Org. Chem.*, 1957, **22**, 879) give b. p. 195—200°. [c] Yu. S. Salkind (*J. Russ. Phys. Chem. Soc.*, 1914, **46**, 510) gives m. p. 53°. [d] When distilled at 18 mm. a considerable residue of phthalide was obtained. [e] J. Romo and A. Romo de Vivar (*Bol. Inst. Quím. Univ. nac. auton. México*, 1956, **8**, 10) give m. p. 140—142°. [f] R. Robinson and G. M. Robinson (*J.*, 1914, **105**, 1463) give m. p. 49°.

[26] J. B. Shoesmith and R. H. Slater, *J.*, 1926, 220.

alkoxybenzyl bromides, have not been previously described. They were converted into triazines without further purification. *Bromides* prepared by methods (A) and (B) are given in Table 7.

9-*Methylanthracene*.—Wolff–Kishner reduction of 9-anthraldehyde (44·7 g.) with hydrazine hydrate (28·5 g.) and potassium hydroxide (38·7 g.) in triethylene glycol (260 ml.) gave, after chromatography on alumina, anthracene (2·0 g.), m. p. 213—215° (benzene eluate) and 9-methylanthracene (15·0 g.), m. p. 76—77° (benzene then benzene–ethanol). It was confirmed that the anthracene was not present in the 9-anthraldehyde used.

9-*Bromo*-10-*bromomethylanthracene*.—A mixture of 9-methylanthracene (2·0 g.), *N*-bromosuccinimide (3·92 g.), α,α′-azobisisobutyronitrile (50 mg.), carbon tetrachloride (20 ml.), and a drop of water was refluxed for 1½ hr. and the mixture filtered hot. From the cooled filtrate a yellow solid separated (2·1 g.). Crystallisation from benzene gave the product (1·05 g.), m. p. 195—197° (lit.,[20] 200°) (Found: C, 51·0; H, 2·8. Calc. for $C_{15}H_{10}Br_2$: C, 51·5; H, 2·9%).

Hydrolysis of 9-*Bromo*-10-*bromomethylanthracene*.—A mixture of the above dibromide (0·5 g.), water (10 ml.), calcium carbonate (2 g.), and ethanol (3 ml.) was refluxed for 5 hr., cooled, and extracted with ethyl acetate to give a yellow solid (0·4 g.), m. p. 165—226° containing no carbonyl group (thin-layer chromatography and absence of C=O band in infrared). Chromatography on alumina gave unchanged dibromide and a solid (0·1 g.), m. p. 226°, apparently 9-bromo-10-hydroxymethylanthracene (evidence of OH peak in infrared spectra run in Nujol mull and carbon disulphide solution) (lit., m. p. 229°) (Found: C, 63·1; H, 3·9. Calc. for $C_{15}H_{11}BrO$: C, 62·7; H, 3·8%).

2-*Bromomethylphenanthrene*.—A mixture of 2-methylphenanthrene (12 g.), *N*-bromosuccinimide (11·2 g.), αα′-azobisisobutyronitrile (50 m.g), and carbon tetrachloride was refluxed for 2 hr., filtered, and evaporated. Several crystallisations of the residual solid (13·5 g.) from chloroform–light petroleum (b. p. 60—80°) gave needles, m. p. 107—108° (lit.,[21] 111—111·5°, indicating that our compound may have contained some dibrominated derivative) (Found: C, 61·3; H, 3·8. Calc. for $C_{15}H_{11}Br$: C, 66·5; H, 4·1%).

2-*Hydroxymethylphenanthrene*.—The foregoing bromide (13 g.), anhydrous sodium acetate (7·2 g.), and acetic acid were refluxed for 2 hr., concentrated, and partitioned between water and ethyl acetate. Evaporation of the organic layer gave crude 2-acetoxymethylphenanthrene which was warmed with 4N-sodium hydroxide (50 ml.) and methanol (50 ml.) for 1 hr. to give the carbinol (8·25 g.). Crystallisation from aqueous ethanol gave needles, m. p. 114—116° (lit.,[21] 125—125·5°) (Found: C, 86·6; H, 5·6. Calc. for $C_{15}H_{12}O$: C, 86·6; H, 5·8%).

Reaction of 2-*Hydroxymethylphenanthrene with Hydrogen Bromide*.—The hydroxymethyl compound (3·5 g.), dissolved in benzene (20 ml.), was treated with hydrogen bromide at room temperature for 30 min. After washing with water until free from acid, the dried solution was evaporated to give 2-bromomethylphenanthrene, needles, m. p. 109—111° [from chloroform–light petroleum (b. p. 40—60°)] (Found: C, 67·0; H, 4·1%).

1-(2-*Bromoethyl*)-2-*methylnaphthalene*, prepared by treatment of 1-(2-hydroxyethyl)-2-methylnaphthalene with phosphorus tribromide in ether under reflux, had b. p. 128°/0·3 mm. (lit.,[25] 181°/15 mm.) (Found: C, 63·1; H, 5·1. Calc. for $C_{13}H_{13}Br$: C, 62·75; H, 5·3%).

2,6-, 3,4-, and 3,5-Dimethoxybenzyl chlorides and 3,4,5-trimethoxybenzyl chloride were made by the method of Adams *et al.*[27] and used without purification: all have previously been prepared (refs. 28, 29, 27, and 30, respectively).

1-*Ethoxymethyl*-4-*methylnaphthalene*.—A mixture of 1-chloromethyl-4-methylnaphthalene (15·0 g.) and potassium cyanide (5·15 g.) in ethanol (75 ml.) was refluxed for 8 hr. and the oil obtained on working up distilled to give the *ether*, b. p. 84°/0·03 mm., n_D^{24} 1·5838 (Found: C, 84·4; H, 8·2. $C_{14}H_{16}O$ requires C, 84·1; H, 8·0%). There was no absorption due to C≡N in the infrared spectrum.

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