755. *Some 1,2-Diaryl-4-dimethylamino-3-methylbutan-2-ols and Derivatives Related to Propoxyphene*

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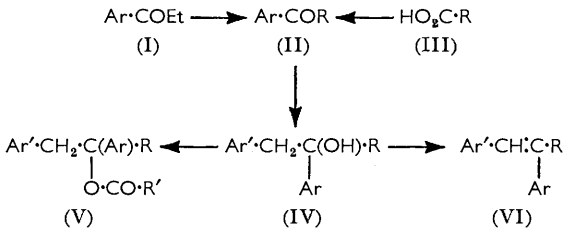
The synthesis, esterification, and dehydration of some 1,2-diaryl-4-dimethylamino-3-methylbutan-2-ols and related heterocyclic butanols are reported.

As part of a study of structure–activity relationships in compounds related to the analgesic propoxyphene (4-dimethylamino-3-methyl-1,2-diphenyl-2-propanoyloxybutane), the synthesis of a series of 1,2-diaryl-3-methylbutan-2-ols (IV) and derivatives was undertaken. The routes employed are shown below.



	Ar	Ar′		Ar	Ar′
a:	Ph	*o*-C_6H_4Me	g:	*o*-C_6H_4Me	Ph
b:	Ph	*p*-C_6H_4Me	h:	*p*-C_6H_4Me	Ph
c:	Ph	*m*-C_6H_4F	i:	2-Thienyl	Ph
d:	Ph	*p*-C_6H_4F	j:	2-Furyl	Ph
e:	Ph	*p*-C_6H_4OMe	k:	2-Thienyl	2-Pyridyl
f:	Ph	2-Pyridyl			

Most of the amino-ketones (II) were prepared by a Mannich reaction using an aryl ethyl ketone (I); two members (II; Ar = *o*- and *p*-C_6H_4Me) were made by treating 3-dimethylamino-2-methylpropanoic acid (III) with two moles of the appropriate aryl-lithium. The amino-acid (III) was conveniently prepared by the hydrolysis of methyl 3-dimethylamino-2-methylpropanoate under neutral conditions. Attempts to prepare the 2-pyridyl analogue (II; Ar = 2-pyridyl) by these methods were unsuccessful.

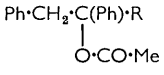
The aminobutanols (IVa—e) were prepared by reaction between the amino-ketone (II; Ar = Ph) and a substituted benzylmagnesium chloride [in one case, (IVf), the organometallic reagent was 2-picolyl-lithium]; the aminobutanols (IIg—j) were obtained by treating the appropriate amino-ketone (II; Ar ≠ Ph) with benzylmagnesium chloride [2-picolyl-lithium was used to prepare (IVk)]. The yield of the 2-thienyl member (IVi) was improved when the amino-ketone (II; Ar = 2-thienyl) hydrochloride rather than the free base was used, and was greater than that reported previously.[1,2] In the synthesis of the 2-furyl member (IVj), use of the amino-ketone hydrochloride was essential, no alcohol being isolated when the base was employed. The *p*-methoxyphenyl ketone (II; Ar = *p*-C_6H_4OMe) hydrochloride gave no isolable basic product after reaction with benzylmagnesium chloride. Isomers analogous to α- and β-4-dimethylamino-1,2-diphenyl-3-methylbutan-2-ol (IV; Ar = Ar′ = Ph) [3] were obtained only in the case of the 1-*o*-tolyl alcohol (IVa). Reaction between the amino-ketone (II; Ar = 2-thienyl) and 2-picolyllithium gave the mixed heterocyclic alcohol (IVk). With three exceptions the amino-alcohol (IV) hydrochlorides had absorption bands in the 2460—2680 and 3200—3350 cm.$^{-1}$ regions, characteristic of $^{+}$N–H and O–H stretching, respectively.[4,5] The

[1] W. G. Stoll, C. J. Morel, and C. Frey, *Helv. Chim. Acta*, 1950, **33**, 1194.
[2] F. C. Rogers and W. L. Nobles, *J. Pharm. Sci.*, 1962, **51**, 273.
[3] A. Pohland and H. R. Sullivan, *J. Amer. Chem. Soc.*, 1953, **75**, 4458.
[4] L. J. Bellamy, " The Infra-red Spectrum of Complex Molecules," Methuen, London, 1954.
[5] P. J. Stone, J. Cymerman Craig, and H. W. Thompson, *J.*, 1958, 52.

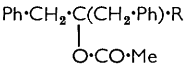
spectra of the hydrochlorides of the alcohols (IVc—e), however, exhibited no $^{+}N-H$ absorption band within the usual range of assignment but instead displayed two closely placed bands within the range 3025—3125 cm.$^{-1}$.

Esterification of the amino-alcohols (IV) was carried out by (*a*) heating the alcohol with an acid anhydride and pyridine, (*b*) stirring a cold solution of the alcohol and an acid chloride in chloroform with sodium carbonate, and (*c*) treating a metallic salt of the alcohol with an acid anhydride or acid chloride. 4-(2-Furyl)- and 4-(2-thienyl)-4-piperidinols undergo elimination when heated with acid anhydride–pyridine mixtures but may be esterified by method (*c*).[6] The lithium salt of the 2-thienyl alcohol (IVi), however, gave starting material and the corresponding elimination product (VIi) after treatment with propionyl chloride. This alkene is formulated as a but-1-ene since its n.m.r. spectrum shows signals due to vinylic hydrogen, and methyl linked to CH (structures absent in the corresponding but-2-ene). Method (*b*) caused both the 2-thienyl and 2-furyl analogues (IVi and j) to undergo elimination. In view of the significant analgesic activities of ethyl ethers of certain 4-piperidinols,[7] attempts were made to etherify the amino-alcohol (IV; Ar = Ar′ = Ph). Williamson procedures (*e.g.*, reaction between the lithium salt of the alcohol and methyl iodide or dimethyl sulphate) failed, probably because of the highly hindered nature of the nucleophile. Another attempt was modelled upon a method successfully applied to the methylation of 4-phenyl-4-piperidinols and esters.[6] This process, in which the ester (or alcohol) is heated with a methanol-concentrated sulphuric acid mixture, is considered to proceed by way of carbonium ions generated by alkyl-oxygen heterolysis. Evidence that esters of the amino-alcohol (IV; Ar = Ar′ = Ph) may undergo alkyl-oxygen fission is provided by the report of Pohland and Sullivan,[3] and presently confirmed, that the propionoxy-ester of the α-diastereoisomer of this alcohol is partly converted into the β-alcohol when heated in very dilute aqueous hydrochloric acid. Only unchanged ester was recovered, however, when water was replaced by methanol in this experiment. Use of higher acid concentrations gave the alkene (VI; Ar = Ar′ = Ph) rather than the desired ether.

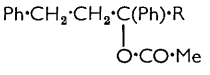
The analgesic properties of some of the amino-esters (V) were assessed in mice by the hot-plate or tail-pinch tests. The acetoxy-ester (VII) was 1·3 times as active as pethidine in the former test, all derivatives with aromatic substituents being less active. With *para*-substituents in the 1-phenyl ring, activity fell as the size of the substituent increased; hot-plate activities (pethidine = 1) were 0·4 for the *p*-fluoro (Vd; R′ = Me) and 0·2 for the *p*-methyl derivative (Vb; R′ = Me), whilst the *p*-methoxy-derivative (Ve; R′ = Me) was inactive at 75 mg./kg. The *o*-methyl derivatives (Va and g; R′ = Me) were both inactive at 100 mg./kg. in the tail-pinch test. The activities of related diphenylpropylamine analgesics (*e.g.*, methadone) are also reduced when aromatic substituents are present.[8] An additional methylene group between C-2 and the 2-phenyl group of the ester (VII)



(VII)



(VIII)



(IX)

R = $CHMe{\cdot}CH_2{\cdot}NMe_2$.

produced little change in potency [compound (VIII) was as active as pethidine in the hot-plate test], the isomer (IX; methylene between C-1 and the 1-phenyl group) being inactive at 100 mg./kg. in the tail-pinch test. These results may be related to the dependence of analgesic activity upon molecular rigidity, the ester (IX) being a much less crowded (and more mobile) molecule, than either compound (VII) or compound (VIII).

[6] A. F. Casy, A. H. Beckett, and N. A. Armstrong, *Tetrahedron*, 1961, **16**, 85.
[7] A. F. Casy and N. A. Armstrong, *J. Medicin. Chem.*, 1965, **8**, 57.
[8] O. J. Braenden, N. B. Eddy, and H. Halbach, *Bull. Hlth. Org.*, 1955, **13**, 937.

Experimental

Equivalent weights of bases and salts were determined by titration with 0·02N-perchloric acid in glacial acetic acid using Oracet Blue B as indicator. Salts were crystallised from ethanol–ether unless otherwise stated. Infrared spectra were recorded on a Unicam S.P. 200 spectrophotometer and were consistent with assigned structures.

Ethyl 2-furyl, 2-pyridyl, and 2-thienyl ketones were prepared by methods reported by Heid and Levine,[9] Nakashima,[10] and Blicke and Burckhalter,[11] respectively.

Amino-ketones (II).—β-*Dimethylamino-α-methyl*-p-*methoxypropiophenone hydrochloride*, m. p. 149—150° (Found: C, 61·1; H, 7·8. $C_{13}H_{20}ClNO_2$ requires C, 60·5; H, 7·75%) was prepared by the method of Mannich and Lammering.[12] The amino-ketone (II; Ar = 2-furyl), characterised as a *methiodide*, m. p. 170—171° (Found: C, 40·85; H, 5·8%; Equiv., 322. $C_{11}H_{18}INO_2$ requires: C, 40·9; H, 5·6%; Equiv., 323) (it gave a hydrochloride, m. p. 161—162°), the amino-ketone (II; Ar = 2-thienyl) hydrochloride, m. p. 157—159° (lit.,[11] 154—156°) and β-*dimethylamino*-p-*bromopropiophenone hydrochloride* m. p. 200·5—201·5° (Found: C, 45·5; H, 5·4%; Equiv., 293. $C_{11}H_{15}BrClNO$ requires C, 45·05; H, 5·1%; Equiv., 293) were similarly prepared.

3-*Dimethylamino*-2-*methylpropanoic Acid*.—Methyl 3-dimethylamino-2-methylpropanoate [13] (100 g.) was heated under reflux with water (300 ml.) for 18 hr. The solvents were evaporated and the residue, after vacuum desiccation, crystallised from ether–methanol to give the amino-acid (III), m. p. 120—122° (Found: Equiv., 134. Calc. for $C_6H_{13}NO_2$: Equiv., 131). It gave a *picrate*, m. p. 149—150° (from methanol) (Found: C, 40·1; H, 4·6, N, 15·6; Equiv., 355. $C_{12}H_{16}N_4O_9$ requires C, 40·0; H, 4·4; N, 15·6%; Equiv., 360).

β-*Dimethylamino-α-methyl*-o-*methylpropiophenone*.—*o*-Tolyl-lithium in ether (150 ml.), prepared from *o*-bromotoluene (34·5 g.) and lithium (3·0 g.) was added to a stirred suspension of the amino-acid (III) (13·1 g.) in ether (150 ml.) and the mixture, after being heated under reflux for 4 hr., poured on to crushed ice and excess of ammonium chloride. The organic phase was separated, dried (Na_2SO_4), and evaporated; the residual oil was distilled to give the amino-ketone (II; Ar = *o*-C_6H_4Me), b. p. 131—133°/0·1 mm. It gave a hydrochloride, m. p. 136° (lit.,[4] m. p. 134—135°). The *p*-methyl analogue (II; Ar = *p*-C_6H_4Me), similarly prepared, gave a *hydrochloride*, m. p. 152—153° (Found: C, 63·9; H, 8·1. $C_{13}H_{20}ClNO$ requires C, 64·6; H, 8·3%).

α- *and* β-4-*Dimethylamino*-3-*methyl*-2-*phenyl*-1-o-*tolylbutan*-2-*ol* (IVa).—β-Dimethylamino-α-methylpropiophenone (10·1 g., 0·05 mole) in ether (50 ml.) was added to a Grignard reagent in ether (350 ml.), prepared from *o*-methylbenzyl chloride (18·5 g., 0·13 mole) and magnesium (3·15 g., 0·13 g.-atom). The mixture, after being heated under reflux for 3 hr., was poured on to ice and excess of ammonium chloride, the organic phase separated, dried (Na_2SO_4), and evaporated. The residue was converted to the hydrochloride salts and recrystallised from ethyl acetate–methanol to give the α-*isomer* (IVa) *hydrochloride* (7 g.), m. p. 254—256° (Found: C, 71·5; H, 8·3%; Equiv., 332. $C_{20}H_{28}ClNO$ requires C, 71·9; H, 8·4%; Equiv., 333) and the corresponding β-*isomer hydrochloride* (2·3 g.), m. p. 187—189° (Found: C, 72·3; H, 8·5%; Equiv., 334).

Similarly prepared were the *hydrochlorides* of the 1-p-*tolylbutanol* (IVb), m. p. 229—230° (Found: C, 72·3; H, 8·3; N, 4·4. $C_{20}H_{28}ClNO$ requires: C, 71·9; H, 8·4; N, 4·2%), the 1-m-*fluorophenylbutanol* (IVc), m. p. 231—233° (Found: C, 67·5; H, 7·4%; Equiv., 337. $C_{19}H_{25}ClFNO$ requires C, 67·25; H, 7·4%; Equiv., 338), the 1-p-*fluorophenylbutanol* (IVd), m. p. 204—206° (Found: C, 67·5; H, 7·5%; Equiv., 338) and the 1-p-*methoxyphenylbutanol* (IVe), m. p. 218—219° (Found: C, 68·1; H, 8·1; N, 4·0%; Equiv., 341. $C_{20}H_{28}ClNO_2$ requires C, 68·7; H, 8·0; N, 4·0%; Equiv., 350). *p*-Methoxybenzylmagnesium chloride used in the last synthesis, was prepared by the method of Van Campen, Meisner, and Parmerter.[14] The 2-o-*tolybutanol* (IVg) *hydrochloride*, m. p. 249—250° (Found: C, 71·6; H, 8·5%; Equiv., 334. $C_{20}H_{28}ClNO$ requires C, 71·4; H, 8·4%; Equiv., 333) and the 2-p-*tolybutanol* (IVh) *hydrochloride*, m. p. 240—242° (Found: C, 71·8; H, 8·3%; Equiv., 330) were obtained by

[9] J. V. Heid and R. Levine, *J. Org. Chem.*, 1948, **13**, 409.
[10] T. Nakashima, *J. Pharm. Soc. Japan*, 1957, **77**, 1298.
[11] F. F. Blicke and J. H. Burckhalter, *J. Amer. Chem. Soc.*, 1942, **64**, 451.
[12] C. Mannich and D. Lammering, *Ber.*, 1922, **55**, 3510.
[13] T. D. Perrine, *J. Org. Chem.*, 1953, **18**, 898.
[14] M. G. Van Campen, D. F. Meisner, and S. M. Parmerter, *J. Amer. Chem. Soc.*, 1948, **70**, 2296.

treating the corresponding amino-ketone (II) with benzylmagnesium chloride. The similarly prepared 2-(2-thienyl)butanol (IVi) hydrochloride, m. p. 180—181° (Found: N, 4·3; S, 9·6%; Equiv., 328. Calc. for $C_{17}H_{24}ClNOS$: N, 4·3; S, 9·85%; Equiv., 325) was obtained in 66% yield (lit.,[2] m. p. 180—184°, yield 57%). Use of the free amino-ketone (II; Ar = 2-thienyl) reduced the yield of hydrochloride to 29%. The 2-(2-*furyl*)*butanol* (IVj) *hydrochloride* had m. p. 145—147° (Found: C, 65·0; H, 7·7%; Equiv., 306. $C_{17}H_{24}ClNO_2$ requires: C, 65·8; H, 7·7%; Equiv., 309).

4-*Dimethylamino*-3-*methyl*-2-*phenyl*-1-(2-*pyridyl*)*butan*-2-*ol* (IVf).—A suspension of the amino-ketone (II; Ar = Ph) hydrochloride (10 g.) in ether (150 ml.) was added slowly to 2-picolyl-lithium [prepared from lithium (2·76 g.), bromobenzene (31·7 g.), and 2-picoline (18·4 g.) in ether (300 ml.)]. The mixture, after being stirred for 18 hr. at room temperature, was poured on to ice and excess of acetic acid, the aqueous phase separated, made basic with aqueous ammonia, and extracted with ether. After being dried (Na_2SO_4), the ether was evaporated and the residue (10·9 g.) chromatographed on alumina (Spence, grade H). Elution with benzene–ether (4 : 1) and evaporation of solvent gave an oil (7·5 g.) which, on distillation, gave the 1-(2-pyridyl)butanol (IVf) (6·5 g.) b. p. 143—145°/0·4 mm. (Found: C, 76·2; H, 8·4%; Equiv., 292. Calc. for $C_{18}H_{24}N_2O$: C, 76·1; H, 8·45%; Equiv., 284) (lit.,[15] b. p. 150—160°/0·6 mm.). It gave a *monopicrate*, m. p. 126—127° from ethyl acetate (Found: C, 56·5; H, 5·4%; Equiv., 516. $C_{24}H_{27}N_5O_8$ requires C, 56·0; H, 5·2%; Equiv., 513). The 1-(2-pyridyl)-2-(2-thienyl)butanol (IVk), purified by chromatography on alumina (benzene as eluant), gave a *dipicrate*, m. p. 191—193° (from ethyl acetate) (Found: C, 44·9; H, 3·5; N, 15·2%; Equiv., 740. $C_{28}H_{28}N_8O_{15}S$ requires C, 44·9; H, 3·7; N, 15·0%; Equiv., 748).

Esterification of the Amino-butanols (IV).—A mixture of the 1-*o*-tolylbutanol (IVa) hydrochloride (10 g.), acetic anhydride (10 ml.), and pyridine (50 ml.) was heated on a steam-bath for 3 hr. Solvents were evaporated under reduced pressure and the residue was treated with excess of ethanolic hydrogen chloride and crystallised from ethyl acetate–methanol to give the 1-o-*tolylbutyl ester* (Va; R′ = Me) *hydrochloride*, m. p. 184—185° (Found: C, 70·6; H, 8·1; N, 3·5%; Equiv., 380. $C_{22}H_{30}ClNO_2$ requires C, 70·2; H, 8·0; N, 3·7%; Equiv., 376). The *hydrochlorides* of the 1-p-*fluorophenylbutyl ester* (Vd; R′ = Me), m. p. 185—186° (Found: C, 65·6; H, 7·1; N, 3·8%; Equiv., 385. $C_{21}H_{27}ClFNO_2$ requires C, 66·3; H, 7·1; N, 3·7%; Equiv., 380) and the 2-o-*tolylbutyl ester* (Vg), m. p. 179—181° (Found: C, 69·6; H, 8·1; N, 4·0%; Equiv., 375) were similarly prepared. Acetyl chloride (5·0 g.) in chloroform (25 ml.) was added dropwise to a solution of the 2-*p*-methoxyphenylbutanol (IVe) hydrochloride (5 g.) in chloroform (100 ml.) containing anhydrous sodium carbonate in suspension. The mixture, after being stirred for 3 hr. at room temperature, was extracted with dilute aqueous ammonia, the organic phase separated, dried (Na_2SO_4), and evaporated. The residue on treatment with ethanolic hydrogen chloride, gave the 2-p-*methoxyphenylbutyl ester* (Ve; R′ = Me) *hydrochloride*, m. p. 204—205° (from acetone–methanol) (Found: C, 67·5; H, 7·5; N, 3·4%; Equiv., 395. $C_{22}H_{30}ClNO_3$ requires C, 67·35; H, 7·65; N, 3·6%; Equiv., 392). The amino-ketone (II; Ar = Ph) (10 g.) in ether (50 ml.) was added to a Grignard reagent prepared from *p*-methylbenzyl chloride (18·5 g.) and magnesium (3·15 g.) in ether (250 ml.). The mixture, after being heated under reflux for 2 hr., was cooled and treated with acetic anhydride (13·4 g.) in ether (150 ml.) and the product heated under reflux for a further 3 hr. Basic material (isolated as described above after decomposition with acetic acid) gave, on treatment with ethanolic hydrogen chloride, the 2-p-*tolylbutyl ester* (Vb; R′ = Me) *hydrochloride* (7·5 g.), m. p. 177·5—179·5° (from ethyl acetate–methanol) (Found: C, 70·5; H, 8·1; N, 3·5%; Equiv., 375. $C_{22}H_{30}ClNO_2$ requires C, 70·2; H, 8·0; N, 3·7%; Equiv., 376). Also prepared in this manner were 2-*acetoxy*-2-p-*bromophenyl*-4-*dimethylamino*-1-*phenylbutane hydrochloride*, m. p. 254° (from chloroform–methanol) (Found: C, 56·4; H, 5·7; N, 3·2%; Equiv., 427. $C_{20}H_{25}BrClNO_2$ requires C, 56·2; H, 5·85; N, 3·3%; Equiv., 426) and 3-*acetoxy*-5-*dimethylamino*-1,3-*diphenyl*-4-*methylpentane* (IX) *hydrochloride*, m. p. 166—167° (Found: C, 69·7; H, 8·1%; Equiv., 380. $C_{22}H_{30}ClNO_2$ requires C, 70·2; H, 8·0%; Equiv., 376). 2-Acetoxy-2-benzyl-4-dimethylamino-3-methyl-1-phenylbutane (VIII) was prepared by treating methyl 3-dimethylamino-2-methylpropanoate[13] with benzyl magnesium chloride and decomposing the product with acetyl chloride. It gave a *hydrochloride*, m. p. 214—215° from ethanol–ethyl acetate (Found: C, 69·7; H, 8·0; N, 3·4%; Equiv., 376). The 1-(2-*pyridyl*)*butyl ester* (Vf; R′ = Me), b. p. 167—170°/0·5 mm.

[15] G. DeStevens, A. Halamandaris, P. Strachan, E. Donoghue, L. Dorfman, and C. F. Huebner, *J. Medicin. Chem.*, 1963, **6**, 357.

(Found: C, 73·15; H, 7·8%; Equiv., 338. $C_{20}H_{26}N_2O_2$ requires C, 73·6; H, 8·0; Equiv., 326) was similarly prepared by treating the lithium salt of the aminobutanol (IVf) (obtained from the butanol and phenyl-lithium) with acetyl chloride. The related ester (Vf; R′ = Et) was isolated as a *dipicrate*, m. p. 166·5—168·5° (from ethyl acetate) (Found: C, 49·3; H, 4·55; N, 14·25%; Equiv., 795. $C_{33}H_{34}N_8O_{16}$ requires C, 49·6; H, 4·3; N, 14·0%; Equiv., 798).

The lithium salt of the thienyl alcohol (IVi), prepared as above, after treatment with propionyl chloride gave a basic oil which was neutralised with ethanolic hydrogen chloride and fractionally crystallised. The first fraction was the thienyl alcohol (IVi) hydrochloride and the second *4-dimethylamino-3-methyl-1-phenyl-2-(2′-thienyl)but-1-ene hydrochloride*, m. p. 160—161° (from ethyl acetate–methanol) (Found: C, 66·2; H, 7·5; N, 4·4%; Equiv., 310. $C_{17}H_{22}ClNS$ requires C, 66·2; H, 7·15; N, 4·55%; Equiv., 307). Its n.m.r. spectrum had the following characteristics: τ 2·5—3·07 (complex band, 8 aryl protons); τ 3·23 (singlet, one vinylic proton); τ 7·13 (singlet, 6 protons of NMe_2 group); τ 8·47 (doublet, J = 6·5 c./sec. 3 protons of 3-Me group). A mixture of the 2-(2-furyl)butanol (IVj) (2·5 g.), propionyl chloride (2·5 g.), and anhydrous potassium carbonate (2·5 g.) in dry chloroform (100 ml.) was allowed to stand at room temperature for 18 hr., filtered, and the filtrate evaporated under reduced pressure. The residue, with methyl iodide, gave *4-dimethylamino-2-(2-furyl)-3-methyl-1-phenylbutene methiodide*, m. p. 149—150° from ethyl acetate-methanol (Found: C, 54·1; H, 5·85; N, 3·7%; Equiv., 390. $C_{18}H_{24}INO$ requires C, 54·4; H, 6·0; N, 3·5%; Equiv., 397).

Hydrolysis and Attempted Methanolysis of α-2-Acetoxy-4-dimethylamino-3-methyl-1,2-diphenylbutane.—A solution of the amino-ester (V; Ar = Ar′ = Ph, R′ = Me) hydrochloride (10 g.), in water (200 ml.) containing one drop of concentrated hydrochloric acid, was heated under reflux for 18 hr. and concentrated under reduced pressure. The basic product, isolated as usual and treated with excess of hydrochloric acid, gave, on fractional crystallisation, hydrochloride salts of starting material (1·25 g.), m. p. 171—173° α- (1·05 g.), m. p. 235—236°, and β-4-dimethylamino-3-methyl-1,2-diphenylbutan-2-ol (0·75 g.), m. p. 199—201°. The melting points of all salts were undepressed when mixed with authentic samples (Pohland and Sullivan [3]). When 2·5% hydrochloric acid (200 ml.) was used as solvent, hydrochlorides of the α- (3·4 g.), m. p. 231—232° and β-amino-alcohol (IV; Ar = Ar′ = Ph) (3·0 g.), m. p. 197—199°, were recovered from the ester (1·5 g.). When methanol containing one drop of acetyl chloride was used, starting material (67%) was the only product isolated. A mixture of the same amino-ester (V; Ar = Ar′ = Ph, R′ = Me) hydrochloride (7·5 g.), methanol (200 ml.), and concentrated sulphuric acid (20 ml.) was heated under reflux for 6 hr., cooled, and made alkaline with strong aqueous ammonia. The ammonium sulphate which separated was removed by filtration, the filtrate evaporated, and the residue dissolved in water. The base, isolated as usual and treated with hydrogen chloride, was crystallised from ethyl acetate–methanol to give 4-dimethylamino-3-methyl-1,2-diphenylbut-1-ene hydrochloride (0·75 g.), m. p. 184—186°, undepressed when mixed with an authentic sample [16] and starting material (1·25 g.).

The n.m.r. spectrum was recorded on a 60 Mc./sec. Varian A-60 instrument (in $CDCl_3$ with tetramethylsilane as internal standard).

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London S.W.3. [*Received, November 11th*, 1964.]

[16] L. J. Myers, 1963, Ph.D. Thesis, University of London.