SPASMOLYTIC ESTERS OF *N*-SUBSTITUTED α-AMINOPHENYLACETIC ACIDS

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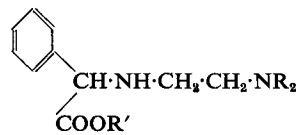
A series of alkyl and cycloalkyl esters of α-(2-pyrrolidin-1′-ylethylamino-), α-(2-piperidinoethylamino)- and α-(2-diethylaminoethylamino)-phenylacetic acid has been synthesised and examined for spasmolytic activity. The isopentyl- and cyclohexyl esters of α-(2-pyrrolidin-1′-ylethylamino)phenylacetic acid are new compounds possessing spasmolytic properties greater than papaverine and, in addition, 1 per cent and 4 per cent respectively of the antimuscarine activity of atropine as measured on the guinea pig ileum.

A CURRENT hypothesis[1] of antimuscarinic action is that acetylcholine-sensitive receptor-surfaces of parasympathetically innervated organs can be effectively blocked only by a compound which has two foci for attachment to the surface. One of these is a quaternary or tertiary nitrogen atom, and the other, which must be between 5 and 10 Å distant from the nitrogen atom, may be one of a number of, as yet, ill-defined groups to which is attached one or more groups large enough to form a protective shield over the receptors and prevent access to them of the natural neurohormone. By considering the structure of the widely used antispasmodics it appears that the unshared electrons of a polarised carbonyl or ethylene group, or the lone pair on a hydroxyl oxygen or second nitrogen atom, may constitute the second focus for attachment to the receptor surface[2].



I

In compounds based on I the pKa of the terminal tertiary nitrogen atom is above 7 and, accordingly, at physiological pH values the compounds is partially protonised and possesses in part a terminal cationic group which is known to increase antimuscarinic activity. The protecting or umbrella groups in these compounds comprise the phenyl group and the large alkoxycarbonyl-CO·OR′ group.

The present communication relates to compounds based on I, in which the esterifying group is ethyl, isopentyl, phenyl, cyclohexyl or 3,5,5-trimethylcyclohexyl, and the terminal tertiary nitrogen group-NR_2 is diethylamino, piperidino or pyrrolidin-l-yl. In one series the non-terminal secondary amino group has been converted into a tertiary group.

The compounds were prepared by the Hell-Volhard-Zelinsky bromination of phenylacetic acid and reaction of the resulting α-bromophenylacetyl bromide with the appropriate alkanol. Condensation of the α-bromo

esters with the required 2-dialkylaminoethylamine gave the amino esters of type I: these were distilled and converted into a salt. Isopentyl α-(2-diethylaminoethylamino)phenylacetate (compound 3) has been prepared previously by a similar route[3,4] and also by the diethylaminoethylation of isopentyl α-aminophenylacetate[5].

Spasmolytic Activities

The spasmolytic activities of the amino esters against acetylcholine, histamine, 5-hydroxytryptamine, nicotine and barium-ion spasm of isolated guinea pig ileum were determined by the Magnus method and are recorded in Table I. The spasmogen dilution (pD) given at the head

TABLE I

SPASMOLYTIC ACTIVITIES OF COMPOUNDS OF GENERAL FORMULA
$Ph{\cdot}CH(COOR'){\cdot}NR''{\cdot}CH_2{\cdot}CH_2{\cdot}R$
AGAINST ACETYLCHOLINE, HISTAMINE, 5-HYDROXYTRYPTAMINE, NICOTINE AND BARIUM ION ON THE ISOLATED GUINEA PIG ILEUM

Cpd. No.	R″	R′	R	Acetylcholine pD* 7·08†	Histamine pD 7·08†	Nicotine pD 5·34†	5-HT pD 5·78†	Barium chloride pD 3·7†
1	H	isopentyl	piperidino	6·24	5·36	6·2	6·08	5·14
2	H	,,	pyrrolidin-l-yl	6·75	5·70	6·56	6·05	5·04
3	H	,,	diethylamino	6·71	5·49	6·7	6·2	5·28
4	Me	,,	diethylamino	5·87	5·42	5·86	5·33	5·28
5	H	cyclohexyl	piperidino	6·69	5·38	6·69	6·06	5·34
6	H	,,	pyrrolidin-l-yl	7·43	5·57	6·76	6·26	5·38
7	H	,,	diethylamino	7·38	5·26	6·65	5·87	5·30
8	Me	,,	diethylamino	6·23	5·42	5·87	5·51	5·22
9	H	3,5,5-trimethylcyclohexyl	piperidino	6·08	5·95	5·79	5·43	5·26
10	H	,,	pyrrolidin-l-yl	6·48	6·79	5·87	5·26	5·40
11	H	,,	diethylamino	5·99	5·37	5·87	5·38	5·36
12	Me	,,	diethylamino	5·60	5·62	5·70	5·54	5·49
13	H	ethyl	piperidino	5·36	5·15	5·43	5·08	4·78
14	H	,,	pyrrolidin-l-yl	5·45	5·67	5·08	4·81	4·75
15	H	,,	diethylamino	5·48	5·19	5·39	5·15	5·13
16	Me	,,	diethylamino	5·46	4·94	5·46	5·10	4·98
17	H	phenyl	diethylamino	4·94	4·86	4·85	4·59	4·56
		atropine		8·85	5·53	7·77	7·17	Nil
		papaverine		5·04	5·40	5·40	5·10	4·90

* Dilutions given on the pD scale. pDx means 1 part of compound in 10^x parts of solution.
† Dilutions effecting 40 per cent reduction of the normal length of ileum strip.

of each column produced about a 40 per cent reduction of the normal length of the ileum strip. The activities of the spasmolytic agents are recorded as the dilution which gave a 50 per cent reduction of the spasm; the figures are the means from 6 ileum strips. Dilutions are given on the pD scale; pDx means 1 part of spasmolyte in 10^x parts of solution.

The following structure-activity observations may be made from the results in Table I. For a given group $-NR_2$ (i) the activity against acetylcholine, nicotine and 5-hydroxytryptamine spasm decreases along the series of ester groupings (–CO·OR′), cyclohexyl, isopentyl, trimethylcylcohexyl, ethyl, phenyl; (ii) the activity against histamine spasm is substantially the same for the cyclohexyl, isopentyl, trimethylcyclohexyl

and ethyl esters and lower for the phenyl esters; (iii) the activity against barium ion spasm is about the same for the cyclohexyl, isopentyl, trimethylcyclohexyl esters and is lower for the ethyl and phenyl esters. For a given ester grouping –CO·OR′ (i) the activity against acetylcholine and histamine spasm is higher for the pyrrolidin-l-yl than for the piperidino and diethylamino compounds; (ii) the activity against nicotine, 5-hydroxytryptamine and barium ion spasm does not vary with a discernible pattern in the series pyrrolidin-l-yl, piperidino and diethylamino. Conversion of the central secondary amino to a tertiary group lowers activity.

Toxicity of Isopentyl α-(2-pyrrolidin-1′-ylethylamino)phenylacetate Di-(hydrogen maleate)

The toxicity of this compound was determined in groups of four mice using closely spaced dosages. The LD50 values were: 1,100 to 1,200 mg./kg. (oral); 250 mg./kg. (intraperitoneal); 70 mg./kg. (intravenous). A dose of 50 mg./kg. i.p. to guinea pigs made the animals flaccid and tranquil: this effect disappeared in 1 to 2 hours. In the rabbit 10 mg./kg. i.v. was just tolerated; at 15 mg./kg. the animals died quickly; at 25 mg./kg. the animals died instantly, apparently by auricular-ventricular block.

For purposes of comparison the LD50 of papaverine hydrochloride in mice was found to be 300 mg./kg. (oral); 120 mg./kg. (intraperitoneal) and 33 mg./kg. (intravenous). Rabbits tolerated 10 mg./kg. i.v. of papaverine hydrochloride; at 20 mg./kg. there were violent tetanic spasms frequently followed by death. The LD50 for atropine sulphate in mice was 400 mg./kg. (oral); 250 mg./kg. (intraperitoneal) and 90 mg./kg. (intravenous).

Mydriatic Activity of Isopentyl α-(2-pyrrolidin-l′-ylethylamino)phenylacetate Di(hydrogen maleate)

Six adult rabbits were used for comparing the mydriatic activity of this compound and atropine sulphate. Two drops (0·2 ml.) of a 1·0 per cent aqueous solution of the ester were instilled into the left eye of three rabbits and the same volume of a 0·1 per cent solution of atropine sulphate into the left eye of the other three rabbits; the right eye of each rabbit was used as control. The pupillary diameters of the test and control eyes were measured at suitable time intervals and the average mydriasis expressed as the per cent increase or decrease of the test pupil diameter relative to the control pupil. The ester effected a 25 per cent mydriasis which lasted for 5 hours; in 6 hours the eye was normal. Atropine sulphate effected 42 per cent mydriasis which persisted for 50 hours; the eye was not normal until after 60 hours.

Nine adult rabbits were used for comparing the activities of the ester and atropine sulphate in the eserinized eye. In all animals the left eye was treated, the right eye being used as a control. Three rabbits received 0·2 ml. of 0·5 per cent solution of eserine; three rabbits received 0·2 ml. of a 0·5 per cent solution of eserine followed immediately by 0·2 ml. of a

1 per cent aqueous solution of the ester; the other three rabbits received 0·2 ml. of 0·5 per cent eserine followed by 0·2 ml. of a 0·1 per cent solution of atropine sulphate. The average results are shown in Table II: the mydriasis is expressed as the per cent increase or decrease in average test

TABLE II

MYDRIATIC EFFECT OF ISOPENTYL α-(2-PYRROLIDIN-1'-YLETHYLAMINO)PHENYLACETATE DI(HYDROGEN MALEATE) AND ATROPINE SULPHATE IN ESERINISED RABBIT EYE

Time in hours	Per cent mydriasis		
	Eserine	Eserine + ester (1·0 per cent)	Eserine + atropine sulphate (0·1 per cent)
0	0	0	0
1/4	−29	+22	+58
½	−50	+22	+86
1	−50	+24	+86
2	−50	+22	+86
4	−21	+20	+57
6	−20	+15	+56
8	−14	+14	+50
24	0	0	+36

pupil diameter relative to the average control pupil diameter. It is evident that the mydriatic activity of the ester is less than that of atropine sulphate, but has the advantage that the mydriasis is of shorter duration.

The isopentyl and cyclohexyl esters of α-(2-pyrrolidin-1'-ylethylamino) phenylacetic acid (Compounds 2 and 6 of Table I) are new compounds possessing spasmolytic properties greater than papaverine; in addition they have 1 and 4 per cent respectively of the antimuscarine activity of atropine as tested on the guinea pig ileum.

CHEMICAL

Isopentyl α-bromophenylacetate. Phenylacetic acid (68 g.; 0·5 mol) and red phosphorus (5 g.; 0·166 atom; washed with water and dried at 90°) were placed in a flask and heated on the water bath to 80 to 85° (int.) until the phenylacetic acid was molten. Dry bromine (160 g.; 53 ml.; 2 atom) was added dropwise during 1 hour, the flask being occasionally swirled and the escaping HBr led away. After the addition, the flask was heated on the water bath for a further 3½ hours, then cooled in an ice bath and dry isopentyl alcohol (88 g.; 109 ml.; 1·0 mol) added in a slow stream over 10 minutes with swirling. When the vigorous evolution of HBr had ceased, the mixture was heated on the water bath for a further 20 minutes, cooled and poured into stirred benzene (400 ml.) and water (400 ml.). The mixture was stirred vigorously and solid potassium bicarbonate added until there was no more effervescence and the pH value was 8. The benzene layer was separated and the aqueous layer washed with benzene (100 ml.). The combined benzene solutions were washed with water (50 ml.), dried over sodium sulphate, filtered and the benzene and excess isopentyl alcohol removed by distillation from the water bath at 16 to 20 mm. The residual oil was distilled, a small fraction b.p. 170 to 184°/18 mm. being rejected; the main fraction (125 g.) b.p. 184 to 187°/18 mm.

was collected. This was redistilled, the fraction b.p. 125 to 138°/1 mm. being rejected; pure isopentyl α-bromophenylacetate b.p. 138 to 144°/1 mm. (150 to 154°/3 mm.) came over as a pale yellow oil (120 g.; 85 per cent).

Ordinary isopentyl alcohol contains 80 per cent of isopentyl alcohol $Me_2CH{\cdot}CH_2{\cdot}CH_2OH$ and 20 per cent of 2-methylbutanol, the latter boils 2·5° lower than the former and is more soluble in water. The Isopentyl alcohol used in this preparation was commercial material which had been washed with a large volume of 2 N sodium hydroxide and then with a large volume of 2 N sulphuric acid. The alcohol was then distilled in steam, the distillate dried and redistilled through an efficient column rejecting about one quarter as forerun. The alcohol used had b.p. 129·5 to 130·5°; it probably still contained a few per cent of the isomer.

The following esters of α-bromophenylacetic acid were prepared in the same manner; the yields are in parentheses. Ethyl: b.p. 120 to 122°/10 mm. (86 per cent). Found: Br, 33·1. Calc. for $C_{10}H_{11}O_2$ Br: Br, 33·0 per cent. *Cyclohexyl*: b.p. 194 to 196°/10 mm. (82 per cent). Found: Br, 27·2. $C_{14}H_{17}O_2Br$ requires Br, 26·9 per cent. 3,5,5-*Trimethylcyclohexyl*: b.p. 176 to 182°/1·5 mm. (80 per cent); m.p. 72 to 74°. Found: C, 60·8; H, 6·8; Br, 24·2. $C_{17}H_{23}O_2Br$ requires C, 60·2; H, 6·8; Br, 23·6 per cent. 3,5,5-*Trimethylhexyl*: b.p. 198 to 200°/11 mm. (91 per cent). Found: Br, 24·5. $C_{17}H_{25}O_2Br$ requires Br, 23·5 per cent. *Phenyl*: b.p. 194 to 196°/1·5 mm.; m.p. 46 to 48° (53 per cent). Found: C, 57·2; H, 3·5; Br, 27·9. $C_{14}H_{11}O_2Br$ requires C, 57·8; H, 3·8; Br, 27·5 per cent).

2-*Pyrrolidin*-1′-*ylethylamine*. Pyrrolidine (177·5 g.; 205 ml.; 2·5 mol) was placed in a 3-necked flask and stirred at −1° (int.) in an ice-salt bath. Solid 2-bromoethylamine hydrobromide[6] (102·5 g.; 0·5 mol) was added in 6 portions at intervals of 10 minutes; the maximum internal temperature following each addition was +15° and a further portion was not added until the temperature had again dropped to −1°. After the whole addition, the mixture was stirred at 15° for 30 minutes and then distilled from a graphite bath to recover some of the excess pyrrolidine, the distillation being stopped when the *internal* temperature of the liquid reached 160°. (The pyrrolidine recovered at this stage was 78 g.; b.p. 85 to 88°.) The residual pale yellow liquid was cooled to 5° and a solution of sodium hydroxide (50 g.; 1·25 mol) in water (50 ml.) added. The mixture was chilled, the supernatant oil poured off, and the sludge of sodium bromide and caustic soda washed with ether (3 × 100 ml.). The combined oil and ether washings were dried three times over sodium hydroxide pellets; after each drying the residual sludge of caustic pellets was washed with 3 × 100 ml. of dry ether. The dry ethereal solution (vol. 1,200 ml.) was distilled through a 30 cm. column of Fenske glass spirals; ether, containing a little pyrrolidine, came over at 34 to 36° and then pyrrolidine (54 g.) at 87 to 88°/747 mm. (The total recovery of pyrrolidine was 132 g., 93 per cent of the excess used in the reaction.) The residual oil was distilled through a 10 cm. Fenske glass spiral column and gave 46·2 g. (81 per cent) of 2-pyrrolidin-1′-ylethylamine, b.p. 166 to

167°/747 mm. 2-Piperidinoethylamine was obtained in the same manner in 80 per cent yield.

(2-*Diethylaminoethyl*)*methylamine*. The following is more convenient than the literature[7] method. 2-Diethylaminoethyl chloride hydrochloride (129 g.; 0·75 mol) was added during 5 minutes to a stirred mixture of 25 per cent aqueous methylamine (120 ml.; 3 mol) and 10 N potassium hydroxide (150 ml.; 1·5 mol) at 0 to 5°. The mixture was stirred at this temperature for 1¼ hours and then heated to 60°; an exothermic reaction resulted, the temperature rising to 70°. The mixture was kept at 70° for a further 2½ hours; cooled and set aside overnight. Flake sodium hydroxide (about 250 g.) was added until the solution was almost saturated. Ether (200 ml.) was added to dissolve the supernatant oil and the whole filtered to remove inorganic solid, the latter being washed into the filtrate with a mixture of 10 N sodium hydroxide and ether. The ether layer was separated and the aqueous layer extracted with ether (6 × 100 ml.). The combined ethereal extracts were *thoroughly* dried over potassium hydroxide and the filtered solution distilled, the fraction b.p. 130 to 170° being collected. Refractionation of the latter gave the product b.p. 152 to 156° as a pungent colourless oil (54 g.; 55 per cent).

Isopentyl α-(*2-pyrrolidin-1'-ylethylamino*)*phenylacetate*. 2-Pyrrolidin-1'-ylethylamine (23 g.; 0·2 mol) was added to isopentyl α-bromophenylacetate (57 g.; 45·2 ml.; 0·2 mol) during 5 minutes, the temperature not being allowed to rise above 40°. The residue of base was washed in with benzene (10 ml.) and the mixture heated on the water bath for 4 hours. The resulting brown oil was dissolved in water (200 ml.), the solution stirred, cooled to 0°, and 10 N sodium hydroxide (20 ml.; 0·2 mol) added dropwise, keeping the temperature at 0°. Sodium bicarbonate (8 g.) was added and the solution extracted with ether (3 × 100 ml.). The combined ether extracts were washed with water (50 ml.), dried over sodium sulphate, the ether removed and the residual oil distilled. A small forerun was rejected, the main fraction b.p. 180 to 188°/1·0 to 0·5 mm. being collected (52 g.; 82 per cent); redistillation gave the *product* as a colourless oil (46 g.; 73 per cent), b.p. 184 to 188°/1·0 to 0·5 mm.

The foregoing ester (40 g.) was dissolved in hot ethanol (40 ml.) and to this solution was added a solution of maleic acid (30·6 g.; 1·05 mol) in hot ethanol (70 ml.). The resulting clear solution was allowed to stand overnight and then dry ether (150 ml.) added; the *di*(*hydrogen maleate*) separated as colourless lustrous flakes (60·6 g.; 88 per cent) m.p. 122 to 123°. Found: *M*, 550; N, 5·0. $C_{27}H_{38}O_{10}N_2$ requires *M*, 550; N, 5·1 per cent. The following esters were prepared in similar manner: the yields obtained being in parentheses. *Isopentyl* α-(2-piperidinoethylamino)phenylacetate (80 per cent); pale yellow oil b.p. 198 to 202°/2 mm. Found: *M*, 340. $C_{20}H_{32}O_2N_2$ requires *M*, 332; the *di*(*hydrogen oxalate*) separated from ethanol as colourless micro needles m.p. 154 to 156° (decomp.). Found: *M*, 512. $C_{24}H_{36}O_{10}N_2$ requires *M*, 512.

Cyclohexyl α-(2-diethylaminoethylamino)phenylacetate (67 per cent); colourless oil b.p. 200 to 204°/1 mm. Found: *M*, 334. $C_{20}H_{32}O_2N_2$

requires *M*, 332; the *di(hydrogen oxalate)* separated from ethanol as needles m.p. 154 to 156° (decomp.). Found: N, 5·5. $C_{24}H_{36}O_{10}N_2$ requires N, 5·5 per cent.

Cyclohexyl α-(2-*piperidinoethylamino)phenylacetate* (73 per cent); colourless oil b.p. 214 to 216°/2 mm. (Found: *M*, 346. $C_{21}H_{32}O_2N_2$ requires *M*, 344.) The *dihydrochloride* separated as hygroscopic colourless microneedles, m.p. 88 to 90° (decomp.). Found: *M*, 424. $C_{21}H_{34}O_2N_2Cl_2$ requires *M*, 417.

Cyclohexyl α-(2-*pyrrolidin*-1′-*ylethylamino)phenylacetate* (60 per cent); pale yellow oil b.p. 208 to 212°/2 mm. (Found: *M*, 324. $C_{20}H_{30}O_2N_2$ requires *M*, 330.) The *di(hydrogen oxalate)* separated from ethanol as colourless plates m.p. 172 to 174°(decomp.). Found: *M*, 514. $C_{24}H_{34}O_{10}N_2$ requires *M*, 510.

Isopentyl α-(2-diethylaminoethylamino)phenylacetate 64 per cent; pale yellow oil b.p. 174 to 178°/1·5 mm. Found: *M*, 327. calc. for $C_{19}H_{32}O_2N_2$, *M*, 320. The dihydrochloride had m.p. 172°. (Lit. m.p. 173°.)

3,5,5-*Trimethylcyclohexyl* α-(2-*piperidinoethylamino)phenylacetate* (60 per cent); pale yellow oil b.p. 218 to 222°/2 mm. (Found: *M*, 386. $C_{24}H_{38}O_2N_2$ requires *M*, 386.) The *di(hydrogen oxalate)* separated as soapy microplates from ethanol-ether m.p. 110° (decomp.). Found: *M*, 568; N, 4·6. $C_{28}H_{42}O_{10}N_2$ requires *M*, 566; N, 4·9 per cent.

3,5,5-*Trimethylcyclohexyl* α-(2-*pyrrolidin*-1′-*ylethylamino)phenylacetate* (69 per cent), b.p. 206 to 210°/2 mm. Found: *M*, 372. $C_{23}H_{36}O_2N_2$ requires *M*, 372; *di(hydrogen oxalate)* m.p. 139 to 140°. Found: *M*, 546. $C_{27}H_{40}O_{10}N_2$ requires *M*, 552.

3,5,5-*Trimethylcyclohexyl* α-(2-*diethylaminoethylamino)phenylacetate* (60 per cent); b.p. 200 to 202°/1·5 mm. Found: *M*, 384. $C_{23}H_{38}O_2N_2$ requires *M*, 374; *di(hydrogen oxalate)* m.p. 102 to 104°. Found: *M*, 540; N, 5·2. $C_{27}H_{42}O_{10}N_2$ requires *M*, 554; N, 5·1 per cent. Ethyl α-(2-diethylaminoethylamino)phenylacetate; colourless oil (52 per cent) b.p. 156 to 158°/1·5 mm. Found: *M*, 278. $C_{16}H_{26}O_2N_2$ requires *M*, 278; *di(hydrogen oxalate)* colourless needles from ethanol, m.p. 174° (decomp.). Found: *M*, 454; N, 6·4. $C_{20}H_{30}O_{10}N_2$ requires *M*, 458; N, 6·1 per cent.

Ethyl α-(2-*pyrrolidin*-1′-*ylethylamino)phenylacetate*: pale yellow oil (80 per cent) b.p. 163 to 166°/1·5 mm. Found: *M*, 272. $C_{16}H_{24}O_2N_2$ requires *M*, 278; *di(hydrogen oxalate)* (from ethanol) m.p. 158 to 160° (decomp.). Found: *M*, 452. $C_{20}H_{28}O_{10}N_2$ requires *M*, 456.

Ethyl α-(2-*piperidinoethylamino)phenylacetate*: pale yellow oil (76 per cent) b.p. 172 to 176°/2 mm. Found: *M*, 292. $C_{17}H_{26}O_2N_2$ requires *M* 290; *di(hydrogen oxalate)* m.p. 160 to 162°. Found: *M*,472; N, 6·1. $C_{21}H_{30}O_{10}N_2$ requires *M*, 470; N, 6·0 per cent.

Phenyl α-(2-*diethylaminoethylamino)phenylacetate*: yellow oil (20 per cent) b.p. 222 to 224°/1·5 mm. Found: *M*, 338. $C_{20}H_{26}O_2N_2$ requires *M*, 326.

The following esters of α-(2-diethylaminoethylmethylamino)phenyl acetic acid were obtained by condensation of the appropriate α-bromo ester with (2-diethylaminoethyl)methylamine:—*isopentyl*—: colourless oil

(74 per cent) b.p. 174 to 176°/1 mm. Found: *M*, 332. $C_{20}H_{34}O_2N_2$ requires *M*, 334. *Cyclohexyl*—: colourless oil (77 per cent) b.p. 194°/1·5 mm. Found: *M*, 344. $C_{21}H_{34}O_2N_2$ requires *M*, 346. 3,5,5-*Trimethylcyclohexyl*—: pale yellow oil (82 per cent) b.p. 196 to 198°/2 mm. Found: *M*, 384. $C_{24}H_{40}O_2N_2$ requires *M*, 388. *Ethyl*—: yellow oil (45 per cent) b.p. 148 to 152°/1 mm. Found: *M*, 290. $C_{17}H_{28}O_2N_2$ requires *M*, 292.

α-(2-*Diethylaminoethylamino*)*phenylacetamide*, b.p. 200 to 206°/1 mm. crystallised from ethanol as pale yellow needles m.p. 56 to 60°. Found: *M*, 245. $C_{14}H_{23}ON_3$ requires *M*, 249.

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