# 2-Dimethylaminopropyl Esters of Some Substituted Acetic Acids

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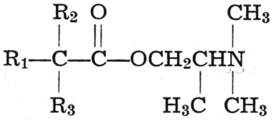
2-dimethylaminopropyl esters of folowing acids were prepared: benzoic, phenylacetic, diphenylacetic, β, β-diphenylpropionic, α-phenylbutyric, acetylmandelic and benzilic.

In search of compounds which may have desirable spasmolytic activity, we have prepared some esters of 2-dimethylaminopropan-1-ol. These esters were prepared by allowing the acid chloride of the requisite acid to react with the 2-dimethylaminopropan-1-ol, except in the case of benzilic acid, when the sodium salt was allowed to react with 2-dimethylaminopropyl chloride. The esters were isolated as their hydrochlorides and converted to the free bases. In the case of benzoic and α-phenylbutyric acid, when the hydrochlorides of the esters were very hygroscopic, neutral oxalates were prepared instead.

The derivatives prepared are listed below:



$$R_1\text{—}\underset{R_3}{\overset{R_2}{C}}\text{—}\overset{O}{\overset{\|}{C}}\text{—}OCH_2\underset{H_3C}{CH}\underset{CH_3}{\overset{CH_3}{N}}$$

I $R_1 = C_6H_5$; $R_2,R_3 = H$

II $R_1,H_2 = C_6H_5$; $R_3 = H$

III $R_1 = (C_6H_5)_2CH$; $R_2,R_3 = H$

IV $R_1 = C_6H_5$; $R_2 = C_2H_5$; $R_3 = H$

V $R_1 = C_6H_5$; $R_2 = OCOCH_3$; $R_3 = H$

VI $R_1,R_2 = C_6H_5$; $R_3 = OH$

The corresponding benzoic acid derivatives were also prepared.

Pharmacological investigation of these compounds is in progress and the results will be published later.

## EXPERIMENTAL*

### *General procedure*

The hydrochlorides were prepared by a general procedure similar to the procedure reported by Koloff et al.[1] for the preparation of pyrrolidylalkyl esters.

To a solution of the apropriate acid chloride (0.25 mole) in benzene (40 ml.) 2-dimethylaminopropan-1-ol (0.28 mole) in benzene (40 ml.) was added gradually on order to control the exothermic reaction. After refluxing for 15 minutes the mixture was allowed to stand overnight. By adding light petroleum ether or ether hte hydrochlorides were precipitated as a crystalline solid, which was filtered off and washed with petroleum ether or ether.

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* The melting points were determined with a Kofler micro melting point apparatus unless otherwise indicated.

The free bases were prepared by dissolving the appropriate hydrochloride in water, washing the aqueous solution with ether and adding cold 50% aqueous sodium hydroxide solution. The oily amino ester was taken up in ether, washed thoroughly with water, and dried over anhydrous sodium sulfate. After removing the solvent, the product was distilled under reduced pressure. The free bases were colorless oils.

### *2-Dimethylaminopropyl benzoate*

Prepared from benzoyl chloride and 2-dimethylaminopropan-1-ol as described in the general procedure, b. p. 60°/0.1 mm.

*Anal.* 3.995 mg. subst.: 0.24 ml $N_2$ (22°, 748 mm.)
$C_{12}H_{17}NO_2$ (207.25) calc'd: N 6.76%
found: N 6.70%

The corresponding neutral oxalate was prepared by adding an absolute ethanolic solution (10 ml.) of oxalic acid (0.0025 mole) to the free base (0.005 mole). After standing overnight the solvent was evaporated under reduced pressure and the residue crystallized from methanol, m. p. 169—171° (uncorr.)

*Anal.* 3.465 mg. subst.: 0.16 ml $N_2$ (18°, 751 mm.)
$C_{26}H_{36}N_2O_8$ (504.53) calc'd: N 5.55%
found: N 5.24%

### *2-Dimethylaminopropyl phenylacetate* [I], *hydrochloride*

Prepared from phenylacetyl chloride and 2-dimethylaminopropan-1-ol as described in the general procedure. Yield, 51.2%. Hygroscopic crystalline solid (absolute ethanol), m. p. 178—179°.

*Anal.* 9.265 mg subst.: 20.448 mg $CO_2$, 6.465 mg $H_2O$
4.658 mg. subst. : 0.22 ml $N_2$ (19°, 759 mm)
$C_{13}H_{20}ClNO_2$ (257.73) calc'd: C 60.58; H 7.82; N 5.44%
found: C 60.23; H 7.81; N 5.41%

The corresponding free base was prepared from the hydrochloride as described in the general procedure, b. p. 84°/0.2 mm.

*Anal.* 3.766 mg. subst.: 0.23 ml $N_2$ (19°, 747 mm.)
$C_{13}H_{19}NO_2$ (221.27) calc'd: N 6.33%
found: N 6.87%

### *2-Dimethylaminopropyl diphenylacetate* [II], *hydrochloride*

Prepared from diphenylacetyl chloride and 2-dimethylaminopropan-1-ol as described in the general procedure. Yield, 38.8%. White hygroscopic crystalline prisms (absolute ethanol), m. p. 179—183°.

*Anal.* 11.180 mg. subst.: 28.09 mg $CO_2$, 7.30 mg $H_2O$
5.261 mg. subst.: 0.21 ml $N_2$ (20°, 758 mm)
$C_{19}H_{24}ClNO_2$ (333.65) calc'd: C 68.36; H 7.24; N 4.20%
found: C 68.56; H 7.31; N 4.54%

The corresponding free base was prepared from the hydrochloride as described in the general procedure, b. p. 145°/0.05 mm.

*Anal.* $C_{19}H_{23}NO_2$ (297.36) calc'd: N 4.71%
found: N 4.62% (Kjeldahl)

### *2-Dimethylaminopropyl ββ-diphenylpropionate* [III], *hydrochloride*

Prepared from ββ-diphenylpropionyl chloride and 2-dimethylaminopropan-1-ol as described in the general procedure. Yield, 96,8%. White crystalline powder (absolute ethanol), m .p. 160—166°.

*Anal.* 4.135 mg. subst.: 0.11 ml $N_2$ (22°, 756 mm.)
$C_{20}H_{26}ClNO_2$ (347.85) calc'd: N 4.03%
found: N 3.96%

The corresponding free base was prepared from the hydrochloride as described in the general procedure, b. p. 112°/0.1 mm.

*Anal.* $C_{20}H_{25}NO_2$ (311.38) calc'd: N 4.50%
found: N 4.55% (Kjeldahl)

### *2-Dimethylaminopropyl α-phenylbutyrate* [IV]

Prepared from α-phenylbutyryl chloride and 2-dimethylaminopropan-1-ol as described in the general procedure, b. p. 78°/0.1 mm.

*Anal.* 7.533 mg. subst.: 0.36 ml. $N_2$ (24°, 748 mm.)
$C_{15}H_{23}NO_2$ (249.32) calc'd: N 5.62%
found: N 5.30%

The corresponding neutral oxalate was prepared as reported earlier for the corresponding benzoate. Crystalline solid (ethyl acetate), m. p. 125—127°.

*Anal.* 2.712 mg. subst.: 0.115 ml. $N_2$ (19°, 754 mm.)
$C_{32}H_{48}N_2O_8$ (588.67) calc'd: N 4.76%
found: N 4.82%

### *2-Dimethylaminopropyl 0-acetylmandelate* [V], *hydrochloride*

Prepared from acetylmandelyl chloride and 2-dimethylaminopropan-1-ol as described in the general procedure. Yield, 90.7%. White crystalline prisms (benzene/light petroleum ether), m. p. 140—147°.

*Anal.* 5.825 mg. subst.: 0.22 ml. $N_2$ (21°, 754 mm.)
$C_{15}H_{22}ClNO_4$ (315.77) calc'd: N 4.44%
found: N 4.26%

The corresponding free base was prepared from the hydrochloride as described in the general procedure, b. p. 105°/0.05 mm.

*Anal.* $C_{15}H_{21}NO_4$ (279.30) calc'd: N 5.02%
found: N 5.01% (Kjeldahl)

### *2-Dimethylaminopropyl benzilate* [VI], *hydrochloride*

The hydrochloride was prepared by a procedure as reported by Moffet et al. for the preparation of diethylaminoethyl esters[2], i. e. a solution of benzilic acid (34.2 g., 0.15 mole) in isopropanol (85 ml.) was neutralized with a 25% methanolic sodium methoxide solution. After the addition of 2-dimethylaminopropyl chloride (18.2 g., 0.15 mole) the mixture was refluxed for three hours. From the cooled mixture the precipitated sodium chloride was removed by filtration (7.6 g., 87.3%) and the filtrate evaporated to dryness under reduced pressure. The residual pale yellow oil was dissolved in absolute ethanol and neutralized with a saturated absolute ethanolic solution of hydrogen chloride. On addition of light petroleum ether the hydrochloride was precipitated as a crystalline solid. Yield, 62.3%. Recrystallized from absolute ethanol the product melted at 165—166.5°.

*Anal.* 9.106 mg. subst.: 21.76 mg. $CO_2$, 5.63 mg. $H_2O$
3.665 mg. subst: 0.135 ml. $N_2$ (21°, 750 mm.)
$C_{19}H_{24}ClNO_3$ (349.82) calc'd: C 65.23; H 6.91; N 4.01%
found: C 65.23; H 6.93; N 4.12%

The free base was prepared from the hydrochloride as described in the general procedure, b. p. 125°/0.05 mm.

*Anal.* $C_{19}H_{23}NO_3$ (313.36) calc'd: N 4.47%
found: N 4.52% (Kjeldahl)

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## REFERENCES

1. H. G. Koloff, J. H. Hunter, E. H. Woodruff and R. B. Moffett, *J. Am. Chem. Soc.* **70** (1948) 3863.
2. R. B. Moffett, C. A. Hart and W. M. Hohen, *J. Am. Chem. Soc.* **69** (1947) 1849.

## IZVOD

### 2-dimetilaminopropilni esteri nekih supstituiranih octenih kiselina

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Pri traženju spojeva s mogućim spasmolitskim svojstvima pripremljeno je nekoliko estera 2-dimetilaminopropan-1-ola. Esteri su pripremljeni djelovanjem odnosnoga kiselinskog klorida na 2-dimetilaminopropan-1-ol, samo što je kod benzilne kiseline ester pripremljen djelovanjem 2-dimetilaminopropil klorida na njezinu natrijsku sol.

Rezultati farmakoloških ispitivanja bit će objavljeni kasnije.

Mikroanalize su izvršili dr. L. Filipović (u Kemijskom institutu Prirodoslovno-matematičkog fakulteta u Zagrebu) te ing. N. Manger i ing. F. Abaffy (u našem mikroanalitičkom laboratoriju). Tališta je odredio ing. N. Manger prema mikroskopskoj metodi po Kofleru.

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