# Notes

## Substituted 2-Oxazolidinethiones

HERMAN J. EICHEL, RONALD J. MEYER, and PAUL F. BUZZI

*Research Laboratories, Hoechst Pharmaceutical Company, Division of American Hoechst Corporation, Cincinnati, Ohio*

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In a program designed for the preparation of potential antithyroid compounds, a series of substituted 2-oxazolidinethiones were synthesized and tested for activity in rats.[1] A list of new compounds prepared is given in Table I. While none of the compounds in Table I showed marked antithyroid activity as compared to *dl*-goitrin (*dl*-5-vinyl-2-oxazolidinethione),[2] compounds IV, IVa, and XI were minimally active in suppressing $I^{131}$ uptake. Compounds I, Ia, V, and VIII caused increased thyroid weight but were ineffective in iodine suppression. One compound, 3-(2-dodecanol)-5-decyl-2-oxazolidinethione (VII), caused a significant increase in $I^{131}$ uptake and decrease in thyroid weight. 5-Decyl-2-oxazolidinethione (X) resulted in a decreased thyroid weight only. The reaction of hydroxyoxazolidinethiones with isocyanates, sulfonyl chlorides, or aroyl chlorides was found to take place at the hydroxyl group and not at the ring nitrogen or sulfur. Infrared spectra of these compounds (KBr pellet) displayed the characteristic thioureide band (>NC=S) at 1560–1475 $cm^{-1}$ [3,4] and also the position of the carbonyl band was in agreement with the carbamoyloxy (carbanilinooxy) or benzoxy configuration and the hydroxyl band was no longer evident. The fact that the thioureide band was not destroyed during reactions of the hydroxy- or aminooxazolidinethiones with isocyanates or aroyl or sulfonyl chlorides is further evidence for the predominance of the thione configuration for the oxazolidinethione structure.

### Experimental Section[5]

**4-Methyl-4-phenylcarbamoyloxymethyl-2-oxazolidinethione (I).**—The starting 4-methyl-4-hydroxymethyl-2-oxazolidinethione was prepared according to Skulski, *et al.*[6] Phenyl isocyanate (11.9 g, 0.1 mole) in 50 ml of dioxane was added over 1–2 hr to a refluxing solution of 4-methyl-4-hydroxymethyl-2-oxazolidinethione (14.7 g, 0.1 mole) and refluxing continued for 2 hr. The solution was rotary vacuum evaporated to dryness and crystallized from aqueous methanol. Compounds Ia–f were prepared similarly.

**5-Benzamidomethyl-2-oxazolidinethione (II). 3-Benzoyl-5-benzamidomethyl-2-oxazolidinethione (III).**—Into a cold dioxane slurry of 5-aminomethyl-2-oxazolidinethione (13.2 g, 0.1 mole) and triethylamine (10.1 g, 0.1 mole) was added benzoyl chloride (14.1 g, 0.1 mole) with rapid stirring. The solution was stirred at room temperature for 5 hr, became bright yellow, and was warmed to 80° for 1 hr. The solution was filtered after cooling, removing the triethylamine hydrochloride formed and approximately 5.3 g of starting oxazolidinethione, and vacuum evaporated to a yellow waxy material. This residue was dissolved in acetone and precipitated by addition of water. The yellow waxy material was triturated with hot benzene, yielding a benzene-soluble fraction. Crystals obtained from this fraction were recrystallized from benzene: mp 178–179°, uv $\lambda_{max}$ 241 mμ (EtOH), yield 34% (IV). The benzene-insoluble residue was crystallized from water: mp 152–153°, uv $\lambda_{max}$ 247 mμ (EtOH), yield 15% (III).

**4-Methyl-4-benzoxymethyl-2-oxazolidinethione (IV).**—A solution of 0.1 mole of benzoyl chloride in 100 ml of dioxane was added slowly over 2 hr at room temperature to a stirred solution of 4-methyl-4-hydroxymethyl-2-oxazolidinethione (14.7 g, 0.1 mole) in 200 ml of dioxane containing 0.1 mole of pyridine. An additional 0.1 mole of pyridine was added and the temperature was raised to 60° for 4 hr. The solution was vacuum evaporated, slurried in 3% NaCl, extracted with ethyl acetate, dried over Drierite, and the solvent was removed under reduced pressure. The residue was crystallized from absolute ethanol. Similarly, IVa–g were prepared.

**4-Methyl-4-(*p*-tolylsulfonyloxymethyl)-2-oxazolidinethione (V).**—A solution of *p*-toluenesulfonyl chloride (38.2 g, 0.2 mole) in 100 ml of pyridine was added slowly over 2 hr to a stirred solution of 4-methyl-4-hydroxymethyl-2-oxazolidinethione (29.5 g, 0.2 mole) in 150 ml of pyridine at 50°. After complete addition, the reaction was allowed to proceed for an additional 2 hr. The contents was vacuum evaporated to a dark, semicrystalline oil which was slurried in 200 ml of 10% NaCl solution and repeatedly extracted with ethyl acetate (total 600 ml) and, finally, with 150 ml of $CHCl_3$. The combined extracts were dried over Drierite and vacuum evaporated to a crude residue which was repeatedly crystallized from absolute ethanol.

**4-Methyl-4-benzenesulfonyloxymethyl-2-oxazolidinethione (Va).**—A solution of benzenesulfonyl chloride (35.4 g, 0.2 mole) in 50 ml of pyridine was added dropwise over 3 hr and at room temperature to a pyridine solution of 29.4 g (0.2 mole) of the hydroxyoxazolidinethione. The pyridine was removed under reduced pressure and the resulting oil was slurried in 250 ml of 10% NaCl solution, extracted with ethyl acetate, decolorized, dried over Drierite, and vacuum evaporated. The methanol-soluble residue was repeatedly crystallized from methanol.

**5-Aminomethyl-2-oxazolidinethione (VI).**—To 1,3-diamino-2-hydroxypropane (50 g, 0.55 mole) dissolved in 400 ml of 95% ethanol was added dropwise over 90 min at 10°, $CS_2$ (38.1 g, 0.5 mole) in 200 ml of 95% methanol. A gummy, cream-colored precipitate began forming after one-half of the $CS_2$ was added. At the end of the addition, the reaction flask was allowed to reach room temperature and stirred for an additional hour. The solution was then heated to reflux for 8 hr to remove $H_2S$, whereupon a white precipitate formed. The reaction flask was cooled, and the contents was washed with ethanol and dried *in vacuo* yielding off-white crystals which were recrystallized from water.

**Di(2-dodecanol)amine.** To a cold saturated solution of $NH_3$ in 500 ml of methanol was added 92 g (0.5 mole) of 1,2-epoxydodecane. The resulting solution was allowed to stand 3 days during which time a white fluffy precipitate formed. The precipitate was removed by filtration and the solution was evaporated to one-third its volume and additional precipitate was removed. The di(2-dodecanol)amine thus formed was treated with $CS_2$ without further purification, mp 105–110° (see below).

**3-(2-Dodecanol)-5-decyl-2-oxazolidinethione (VII).**—A solution of di(2-dodecanol)amine (28.15 g, 0.14 mole) and 19.6 ml of triethylamine in 150 ml of dioxane was chilled in an ice bath and treated with $CS_2$ (11.4 g, 0.15 mole). The solution was allowed to warm to room temperature, chilled, and treated dropwise with ethyl chloroformate (18.5 g, 0.17 mole). The triethylamine hydrochloride which formed was removed and 50 ml of $CCl_4$ and 19.6 ml of triethylamine were added. The solution was stirred

(1) C. Fabiau, R. J. Ryan, and H. J. Eichel, *Endocrinology*, in press.
(2) M. G. Ettlinger, *J. Am. Chem. Soc.*, **72**, 4792 (1950).
(3) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Methuen and Co., Ltd., London, 1958, p 357.
(4) M. G. Ettlinger, *J. Am. Chem. Soc.*, **72**, 4699 (1950).
(5) Infrared spectra were determined on a Perkin-Elmer Model 137B using KBr pellets. Ultraviolet spectra were determined using a Bausch and Lomb Model 505. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Elemental analysis were performed by Micro-Tech Laboratories, Skokie, Ill.
(6) M. Skulski, D. L. Garmaise, and A. F. McKay, *Can. J. Chem.*, **34**, 815 (1956).

TABLE I

| Compound | Mp, °C | Yield, % | Formula | Calcd, % C | H | N | Cl | S | Found, % C | H | N | Cl | S |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4-Methyl-4-X-phenylcarbamoyloxymethyl-2-oxazolidinethione | | | | | | | | | | | | | |
| X = H (I) | 183–185[a] | 77 | $C_{12}H_{14}N_2O_3S$ | 54.12 | 5.30 | 10.52 | | | 54.46 | 5.24 | 10.42 | | |
| X = *o*-Cl (Ia) | 162.5–163.5[a] | 75 | $C_{12}H_{13}ClN_2O_3S$ | 47.92 | 4.36 | 9.32 | 11.79 | | 48.18 | 4.36 | 9.79 | 11.57 | |
| X = *p*-Cl (Ib) | 160–161.5[a] | 59 | $C_{12}H_{13}ClN_2O_3S$ | 47.92 | 4.36 | 9.32 | 11.79 | | 48.31 | 4.73 | 9.42 | 11.23 | |
| X = *o*-$NO_2$ (Ic) | 172–173[b] | 58 | $C_{12}H_{13}N_3O_5S$ | 46.30 | 4.21 | 13.50 | | | 46.35 | 4.27 | 12.98 | | |
| X = *o*-F (Id) | 182–184[b] | 45 | $C_{12}H_{13}FN_2O_3S$ | 50.69 | 4.61 | 9.85 | | | 50.99 | 4.80 | 9.91 | | |
| X = *p*-$CH_2F$ (Ie) | 152–162[c] | 42 | $C_{12}H_{13}FN_2O_3S$ | 50.69 | 4.61 | 9.85 | | | 51.00 | 4.72 | 9.83 | | |
| X = $CF_3$ (If) | 168–170[d] | 30 | $C_{13}H_{13}F_3N_2O_3S$ | 46.70 | 3.92 | 8.38 | | | 47.15 | 4.23 | 8.22 | | |
| II | 152–153[e] | 15 | $C_{11}H_{12}N_2O_2S$ | 55.91 | 5.12 | 11.86 | | 13.57 | 55.93 | 5.10 | 12.04 | | 13.78 |
| III | 178–179[f] | 34 | $C_{18}H_{16}N_2O_3S$ | 63.51 | 4.74 | 8.23 | | 9.42 | 63.60 | 4.87 | 8.31 | | 9.64 |
| 4-Methyl-4-X-benzoxymethyl-2-oxazolidinethione | | | | | | | | | | | | | |
| X = H (IV) | 153–155[g] | 68 | $C_{12}H_{13}NO_3S$ | 57.35 | 5.21 | 5.57 | | | 57.69 | 5.18 | 5.83 | | |
| X = 3,5-$(NO_2)_2$ (IVa) | 160–161[g] | 35 | $C_{12}H_{11}N_3O_7S$ | 42.23 | 3.25 | 12.31 | | | 42.24 | 3.21 | 12.62 | | |
| X = *o*-Cl (IVb) | 139.5–141.5[g] | 58 | $C_{12}H_{12}ClNO_3S$ | 50.44 | 4.23 | | 12.41 | | 50.66 | 4.30 | | 12.10 | |
| X = *p*-Cl (IVc) | 180.5–181.5[g] | 47 | $C_{12}H_{12}ClNO_3S$ | 50.44 | 4.23 | | 12.41 | | 50.69 | 4.33 | | 11.97 | |
| X = *o*-F (IVd) | 144–146[g] | 67.5 | $C_{12}H_{12}FNO_3S$ | 53.52 | 4.49 | 5.20 | | | 53.62 | 4.68 | 5.07 | | |
| X = *m*-F (IVe) | 134–136[g] | 62 | $C_{12}H_{12}FNO_3S$ | 53.52 | 4.49 | 5.20 | | | 53.63 | 4.65 | 5.14 | | |
| X = *p*-F (IVf) | 141–143[g] | 66 | $C_{12}H_{12}FNO_3S$ | 53.52 | 4.49 | 5.20 | | | 53.75 | 4.53 | 5.35 | | |
| X = *m*-$CF_3$ (IVg) | 107–109[h] | 35 | $C_{13}H_{12}F_3NO_3S$ | 48.90 | 3.79 | 4.39 | | | 49.29 | 4.00 | 4.46 | | |
| V | 140–141[g] | 20 | $C_{12}H_{15}NO_4S_2$ | 47.82 | 5.02 | 4.65 | | 21.28 | 48.35 | 5.21 | 4.78 | | 21.41 |
| Va | 130–132[c] | 7 | $C_{11}H_{13}NO_4S_2$ | 45.98 | 4.56 | 4.88 | | | 46.13 | 4.56 | 4.88 | | |
| VI | 238–240[e] | 75 | $C_4H_8N_2OS$ | 36.34 | 6.10 | 21.19 | | 24.25 | 36.78 | 6.26 | 20.01 | | 24.62 |
| VII | 89–91[i] | 30 | $C_{38}H_{49}NO_2S$ | 70.28 | 11.60 | 3.49 | | 7.37 | 70.20 | 11.55 | 3.27 | | 7.50 |
| VIII | 60–61[j] | 11 | $C_9H_{15}NOS$ | 58.34 | 8.16 | 7.56 | | 17.31 | 58.56 | 8.28 | 7.86 | | 17.41 |
| IX | 95–97[g] | 60 | $C_{12}H_{15}NO_2S$ | 60.72 | 6.37 | 5.90 | | 13.51 | 61.04 | 6.49 | 6.03 | | 13.54 |
| X | 92–92.5[k] | 67 | $C_{13}H_{23}NOS$ | 64.15 | 10.35 | 5.75 | | 13.17 | 64.24 | 10.15 | 5.94 | | 13.14 |
| XI | 139.5–140.5[l] | 22.6 | $C_5H_9NOS$ | 45.77 | 6.91 | 10.68 | | 24.44 | 45.98 | 6.98 | 10.90 | | 24.34 |
| XII | 45–48[h] | 66 | $C_6H_9NOS$ | 50.34 | 6.34 | | | 22.36 | 50.24 | 6.38 | | | 22.55 |

[a] Aqueous methanol. [b] Methanol–dioxane. [c] Methanol. [d] Isopropyl ether–acetone. [e] Water. [f] Benzene. [g] Absolute ethanol. [h] Diethyl ether. [i] Aqueous ethanol. [j] Petroleum ether (bp 90–120°)–*sec*-butyl alcohol. [k] Ether–petroleum ether. [l] Ethyl acetate.

for 2 hr at room temperature and evaporated to dryness under vacuum at 40°. The residue was crystallized from 80% aqueous ethanol.

**3-Ethylhexahydro-2-benzoxazolidinethione (VIII).**—To 45.1 g (1.0 mole) of ethylamine in 250 ml of cold ethanol was added 49 g (0.5 mole) of 1,2-epoxycyclohexane. The solution was stirred for 6 hr and then allowed to stand 2 days. The solvent and excess ethylamine were removed by vacuum evaporation at 40° leaving a light brown oil. The oil was dissolved in 200 ml of dioxane to which was added 69 ml of triethylamine. The solution was cooled in an ice bath to 0–10° and $CS_2$ (38.1 g, 0.5 mole) was added dropwise. The reaction was allowed to come to room temperature and stirred for 1 hr. After the dropwise addition of ethyl chloroformate (54.3 g, 0.5 mole) and removal of triethylamine hydrochloride, 69 ml of triethylamine, and 50 ml of $CCl_4$ were added. The solution was warmed to 50° for 15 min, solvents were removed under vacuum at 40°, and the residual oil solidified and was crystallized from petroleum ether (bp 90–120°) and *sec*-butyl alcohol yielding off-white crystals.

**3-Ethyl-5-phenoxymethyl-2-oxazolidinethione (IX).**—To a solution of ethylamine (45.1 g, 1.0 mole) in ethanol (250 ml) at 10° was added 1,2-epoxy-3-phenoxypropane (30 g, 0.2 mole). The excess amine was removed by boiling after 4 days of standing at room temperature and the solvent was removed by vacuum evaporation at 40° leaving a white solid. The solid was dissolved in cold dioxane and treated with $CS_2$ (15.2 g, 0.2 mole) and ethyl chloroformate as in the procedure for IX. Colorless crystals were obtained from absolute ethanol.

**5-Decyl-2-oxazolidinethione (X).**—The 1-amino-2-hydroxydodecane was prepared according to the method of Petrow and Stephenson.[7] A mixture of 1,2-epoxydodecane (92.2 g, 0.5 mole) and succinimide (50 g, 0.5 mole) and 10 drops of pyridine in 500 ml of absolute ethanol was refluxed for 24 hr. The resulting solution was evaporated under reduced pressure to an amber oil which solidified on standing. The solid was slurried in petroleum ether, filtered, and dried yielding 92 g of the crude succinimide adduct. A portion was recrystallized from petroleum ether, mp 70–73°. This material (90 g) was hydrolyzed by refluxing in 500 ml of concentrated HCl for 8 hr. The solution was cooled, diluted with 500 ml of water, and neutralized with 50% NaOH. The resulting precipitate was filtered off and crystallized from absolute ethanol, mp 156–157°, yield 22 g.

The amino alcohol (22 g, 0.11 mole) was dissolved in 250 ml of acetone containing 16 ml of triethylamine. $CS_2$ (11.4 g, 0.15 mole) was added slowly and the reaction was stirred at room temperature for 2 hr and refluxed for 6 hr. The solution was vacuum evaporated to a solid and crystallized from an ether–petroleum ether mixture yielding 16 g of white crystals.

**4-Methyl-tetrahydro-1,3-oxazine-2-thione (XI).**—3-Aminobutanol (21.2 g, 0.238 mole) was dissolved in 100 ml of dioxane containing 33 ml of triethylamine. $CS_2$ (18.2 g, 0.238 mole) was added to the stirred solution. After 2 hr the solution was cooled and ethyl chloroformate (25.8 g, 0.238 mole) was added dropwise. The triethylamine hydrochloride formed was filtered off and 50 ml of $CHCl_3$ and 33 ml of triethylamine were added and the solution was stirred at room temperature and mildly heated to remove COS. It was then vacuum evaporated to a thick oil and slurried in acetone, and the solid was filtered off. Crystallization was affected from ethyl acetate yielding 7 g of product.

**5-Methyl-5-vinyl-2-oxazolidinethione (XII).**—The preparation of isoprene oxide was according to Reist, *et al.*,[8] and the conversion to the amino alcohol followed Ettlinger[2] and Al'bitskaya and Petrov.[9] Isoprene oxide (25 g, 0.3 mole) was added slowly over 1–2 hr to 1 l. of cold (5°) concentrated $NH_4OH$. After complete addition, the reaction was stirred for an additional 2 hr at 5°, refrigerated for 12 hr, and allowed to stand at room temperature for 24 hr. The solution was then boiled to one-half volume and further concentrated to an oil in a vacuum evaporator. The oil was distilled (pyrogallol was added to retard polymerization) and 11.5 ml of the amino alcohol was collected at 67–73° (13 mm). The conversion to the oxazolidinethione followed the method of Ettlinger.[2] The 1-amino-2-hydroxy-2-methyl-3-butene (11.5 ml, 0.114 mole) was dissolved in 100 ml of water containing 8 g of KOH. To the rapidly stirring solution was added dropwise over 60 min $CS_2$ (9.2 g, 0.12 mole) in 80 ml of dioxane. Consecutively, 8 g of KOH in 100 ml of water and 40 g of lead nitrate in 200 ml of water were added. The solution

(7) V. Petrow and O. Stephenson, *J. Pharm. Pharmacol.*, **5**, 359 (1953).

(8) E. J. Reist, I. G. Junga, and B. R. Baker, *J. Org. Chem.*, **25**, 1673 (1960).

(9) V. M. Al'bitskaya and A. A. Petrov, *Zh. Obshch. Khim.*, **28**, 901 (1958); *Chem. Abstr.*, **52**, 17098*f* (1958).

was warmed to 60° for 30 min, filtered, and vacuum evaporated to an oil. The oil was slurried in 150 ml of saturated salt solution, extracted with ethyl acetate, dried with Drierite, and vacuum evaporated to an oil (10.7 g) which was slow to crystallize. The solid material was recrystallized from ether: uv $\lambda_{max}$ 240 mμ (ethanol).

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## Agents Acting on the Central Nervous System. X. 1-Substituted 3-Phenyl-2,3,4,5-tetrahydro-1H-1-benzazepines

J. M. KHANNA AND NITYA ANAND

*Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow, India*

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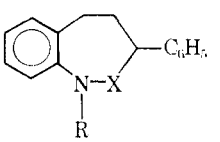
In view of the clinically useful CNS activity of dibenzazepines,[1] the synthesis of 1-substituted 3-phenyl-1,3,4,5-tetrahydro-2H-1-benzazepin-2-ones (I) and 1-substituted 3-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepines (II) has been carried out. 2-Phenyl-1-tetralone[2] on treatment with $HN_3$ gave 3-phenyl-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (Ia). The structure of Ia was confirmed by hydrolysis to 2-phenyl-4-(2-aminophenyl)butyric acid, followed by deamination, when α,γ-diphenylbutyric acid was obtained. 3-Phenyl-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (Ia) on reduction with $LiAlH_4$ gave 3-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepine (IIa). Ia and IIa on treatment with NaH and the appropriately substituted halides gave Ib, Ic, IIb and IIc, respectively. IIa on treatment with NaCNO and $CH_3COOH$ gave the corresponding carbamoyl derivative (IId), while condensation with $ClCH_2COCl$ gave the chloroacetyl compound (IIe) which on condensing with 4-(β-hydroxyethyl)piperazine followed by $LiAlH_4$ reduction gave IIg.



I, X = CO
II, X = $CH_2$

a, R = H
b, R = $(CH_3)_2N(C_2H_5)_2$
c, R = $(CH_3)_2N(C_4H_9)_2$
d, R = $CONH_2$
e, R = $COCH_2Cl$
f, R = $COCH_2N$⟨⟩$N(CH_2)_2OH$
g, R = $(CH_2)_2N$⟨⟩$N(CH_2)_2OH$

**Biological Activity.**—The methods used for screening have been described earlier. Except for 1-(γ-diethylaminopropyl)-3-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepine and 1-β-[4-(β-hydroxyethyl)piperazinyl]ethyl-3-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepine, none of the compounds showed any significant effect on the central nervous or cardiovascular systems nor did any of the compounds show any diuretic or hypoglycemic activity. 1-(γ-Diethylaminopropyl)-3-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepine (IIc) at 16 mg/kg ip ($LD_{50}$ (mice) 82 mg/kg ip) counteracted amphetamine toxicity, while 1-β-[4-(β-hydroxyethyl)piperazinyl]-ethyl-3-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepine at 17 mg/kg ip ($LD_{50}$ (mice) 86 mg/kg ip) gave protection against maximal electroshock seizures and antagonized the action of 5-hydroxytryptamine on isolated guinea pig ileum up to a concentration of $10^{-6}$ g/ml.

### Experimental Section[3]

**3-Phenyl-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (Ia).**—Concentrated $H_2SO_4$ (3 ml) was added dropwise to a stirred mixture of 2-phenyl-1-tetralone (2.22 g, 0.01 mole), AcOH (12 ml), and $NaN_3$ (1.30 g, 0.02 mole) at 50–60°, and stirring was continued for 2 hr after the completion of the addition. The reaction mixture was then poured onto crushed ice (200 g), the product which separated was filtered, washed with ice-cold aqueous ethanol (50%), and crystallized from benzene–petroleum ether (bp 40–60°); mp 192–194°, yield 1.42 g (60%).

*Anal.* Calcd for $C_{16}H_{15}NO$: C, 81.01; H, 6.32; N, 5.90. Found: C, 81.08; H, 6.42; N, 5.48.

**γ-(o-Aminophenyl)-α-phenylbutyric Acid Hydrochloride.**—A mixture of Ia (2.37 g, 0.01 mole) and 6 *N* HCl (100 ml) was refluxed for 4 hr, cooled, and filtered. The filtrate on concentration gave a colorless crystalline product which was recrystallized from ethanol–ether; mp 209°, yield 2.56 g (95%).

*Anal.* Calcd for $C_{16}H_{17}NO_2 \cdot HCl$: C, 65.86; H, 6.17; N, 4.80. Found: C, 65.49; H, 6.49; N, 5.20.

**α,γ-Diphenylbutyric Acid.**—A solution of γ-(o-aminophenyl)-α-phenylbutyric acid hydrochloride (2.91 g, 0.01 mole) in 6 *N* HCl (15 ml) was treated below 20° with $NaNO_2$ (1.38 g, 0.02 mole). $CuSO_4$ (0.04 g) and ethanol (25 ml) were added to the diazonium salt solution and the mixture was heated at 60–70° for 30 min, then cooled, and extracted with ethyl acetate. The extract was dried ($Na_2SO_4$) and the solvent was removed. The residue was crystallized from benzene–petroleum ether; mp and mmp (with authentic sample of α,γ-diphenylbutyric acid) 70° (lit.[4] mp 72°).

**3-Phenyl-2,3,4,5-tetrahydro-1H-1-benzazepine (IIa).**—A solution of Ia (2.37 g, 0.01 mole) in dry tetrahydrofuran (THF) (75 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (0.95 g, 0.025 mole) in dry THF (25 ml). The mixture was stirred and refluxed for 12 hr and cooled and the excess $LiAlH_4$ was decomposed by addition of ethyl acetate followed by water. The reaction mixture was extracted with ethyl acetate, the extract was dried ($Na_2SO_4$), the solvent was removed, and the residue was crystallized from benzene–petroleum ether; mp 124°, yield 1.88 g (75%).

*Anal.* Calcd for $C_{16}H_{17}N$: C, 86.09; H, 7.62; N, 6.27. Found: C, 86.37; H, 8.04; N, 6.59.

**Hydrochloride,** from ethanol–ether, colorless needles, mp 217–218°.

*Anal.* Calcd for $C_{16}H_{17}N \cdot HCl$: C, 73.98; H, 6.93; N, 5.39. Found: C, 74.14; H, 7.04; N, 5.35.

**1-(β-Diethylaminoethyl)-3-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepine (IIb).**—A mixture of IIa (2.23 g, 0.01 mole) and NaH (1 g, 50%) in dry dioxane (15 ml) was refluxed for 1 hr and cooled. To this a solution of β-diethylaminoethyl chloride (1.35 g, 0.01 mole) in dry toluene (5 ml) was added and the mixture was refluxed for 1 hr, cooled, and filtered. The filtrate was evaporated to dryness under reduced pressure, the residue was extracted with ether, the ether solution in turn was extracted with 1 *N* $H_2SO_4$, the acidic layer was made alkaline, the liberated base was taken up in ether, the ether solution was dried ($Na_2SO_4$), and the solvent was removed. The residue was chromatographed

(1) R. Kuhn, *Schweiz. Med. Wochschr.*, **87**, 1135 (1957).
(2) M. S. Newman, *J. Am. Chem. Soc.*, **60**, 2949 (1938).
(3) Melting points were recorded in a bath.