*Ethyl* n-*valeryl*-n-*valerate*. The same procedure as above was used, except that 400 ml of xylene was used instead of the toluene and 130 g (1 mole) of dry ethyl *n*-valerate instead of the ethyl *n*-butyrate. Yield 80 g (75 %) of pure ethyl *n*-valeryl-*n*-valerate boiling at 124–126°/10 mm.

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2. Briese, R. R., and Mc Elvain, S. M. *J. Am. Chem. Soc.* **55** (1933) 1697.
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## Quaternary Derivatives of 2-Benzylphenoxyethylamines

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In the search for new adrenergic blocking agents related to the basic ethers of phenol [1] several quaternary ammonium compounds derived from *o*- and *p*-benzylphenol were prepared. The physical and chemical data for four such compounds are presented below (see table).

Because of the incidental relation to 2-benzylphenoxydimethylaminoethane HCl which was found by Cheney *et al.*[2] to be a potent histamine antagonist it was of interest to investigate the above mentioned quaternary compounds in this respect.

The pharmacological results, the details of which will be dealt with by others elsewhere, indicate that all these compounds are considerably less active than the hydrobromide of 2-benzylphenoxydimethylaminoethane which is as active as the corresponding hydrochloride described by Cheney *et al.*[2], and approximately twice as active as Benadryl.

The quaternaries are somewhat less active than Benadryl.

The ammonium compounds were prepared by refluxing for three hours two moles of the appropriate tertiary amine with one mole of crude 2-benzylphenoxyethylhalide and removing excess volatile amine *in vacuo*, or, more conveniently, by refluxing the free tertiary benzylphenoxyethylamine prepared according to ref. 2 with an excess of the appropriate halide in ethanol. The yields were from 85 to 90 % of the theoretical.

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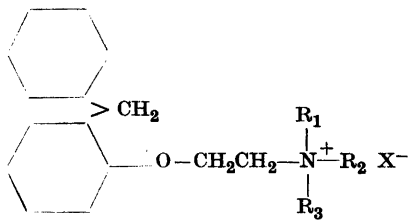
*Table 1. 2-Benzylphenoxyethylammonium halides.*




| | m. p. °C | % X calc. | % X found | cryst. from | solubility in water |
|---|---|---|---|---|---|
| $R_1=CH_3$, $R_2=CH_3$, $R_3=CH_3$, X=I | 159 | 32.17 | 32.04 | abs. ethanol | sl. soluble |
| $R_1=C_2H_5$, $R_2=C_2H_5$, $R_3=C_2H_5$, X=Br | 151 | 20.38 | 20.26 | abs. ethanol-ether (1 : 1) | » |
| $R_1=CH_3$, $R_2=CH_3$, $R_3=C_2H_5$, X=Br | 110 | 21.94 | 21.46 | » » | very » |
| $R_1=CH_3$, $R_2CH_3$, $R_3=CH_2COOC_2H_5$, X=Cl | 154 | 9.40 | 9.72 | ethylacetate: alcohol (1 : 1) | » » |