[CONTRIBUTION FROM THE UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY]

Derivatives of Some 2,2,2-Trialkylethanols[1,2]

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In the study of a series of 2,2,2-trialkylethanols dealing with their synthesis and pharmacological properties it was found that while certain of the alcohols had been prepared previously very few derivatives of them had been made which would be useful for their characterization. For this purpose the phenylurethans, α-naphthylurethans, acid phthalates and acid tetrachlorophthalates of four 2,2,2-trialkylethanols, namely, 2,2-dimethylpropanol-1 (I), 2,2-dimethylbutanol-1 (II), 2-ethyl-2-methylbutanol-1 (III), and 2,2-diethylbutanol-1 (IV), have been prepared and analyzed.

These alcohols were obtained by the use of the Grignard reaction according to the procedure of Conant, Webb and Mendum[5] and their boiling points and refractive indices agree with the values previously reported. The phenyl urethans prepared were found to agree in properties and composition with compounds reported in the literature.

Experimental

Naphthylurethans.—Molecular quantities of the alcohol and α-naphthyl isocyanate were mixed together and placed in a steam-bath for about thirty minutes and the solid product formed on cooling was purified by recrystallizing it twice from ligroin. Quantitative yields of the crude product were obtained while the yield of purified product was 80–85%.

TABLE I

α-NAPHTHYLURETHANS PREPARED

Alcohol	M. p. of derivative, °C.	Kjeldahl N analyses, % Calcd.	Found	
I	99–100	5.45	5.40	5.28
II	80–81	5.16	5.06	5.26
III	Liquid	...	...	...
IV	135–136	4.63	4.57	4.53

Acid Phthalates.—Two-tenths of a mole of the alcohol was heated with 0.3 mole of phthalic anhydride on an oil-bath at 130–140° for four to five hours. The resulting product was cooled in ice and stirred until crystallization took place, then dissolved in ether and filtered to separate the unreacted phthalic anhydride. The ether solution was extracted with cold 5% sodium hydroxide solution and the alkaline aqueous portion was made distinctly acid with 6 *N* hydrochloric acid. The oily layer which separated crystallized on cooling and stirring. After drying the product in a vacuum desiccator, it was recrystallized twice from petroleum benzine. Yields were 85–90% of purified product. Analysis was carried out by saponifying weighed samples of the esters in an excess of standard alcoholic potassium hydroxide solution and titrating the excess alkali with acid.

TABLE II

ACID PHTHALATES PREPARED

Alcohol	M. p. of derivative, °C.	Analyses, % acid phthalate	
I	70–71	100.97	100.90
II	68–69	100.53	100.42
III	44.5–45.5	99.53	99.60
IV	84–85	98.59	98.39

Acid Tetrachlorophthalates.—One-tenth mole of tetrachlorophthalic acid was refluxed with a slight excess of the alcohol in 100 cc. of benzene for four to five hours using an apparatus equipped with a trap to separate the water formed in the reaction. The solution resulting was evaporated to a volume of about 40 cc. and allowed to crystallize and the product which separated was purified by recrystallizing it twice from benzene. Yields of 60–70% were obtained but could be increased to 90% by further treatment of the first mother liquor. Analyses were made for chlorine content by the Parr bomb–sodium peroxide method.

TABLE III

ACID TETRACHLOROPHTHALATES PREPARED

Alcohol	M. p. of derivative, °C.	Chlorine analyses, % Calcd.	Found	
I	140–141	37.93	37.72	37.72
II	149.5–150.5	36.54	36.82	36.69
III	144–145	35.28	35.53	35.42
IV	138–139	34.10	34.24	34.44

Summary

The phenylurethans, α-naphthylurethans, acid phthalates and acid tetrachlorophthalates of four closely related 2,2,2-trialkylethanols have been prepared and analyzed. Twelve of these compounds have not been reported previously in the literature.

A pharmacological study of these trialkylethanols using guinea pigs, rats and mice as the test animals has shown that although the compounds do possess some narcotic action, it is decidely weaker than that of 2,2,2-tribromoethanol to which they were compared. Details of this investigation will be reported elsewhere.

BALTIMORE, MD. RECEIVED JUNE 18, 1937

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[1] Presented before the Division of Medicinal Chemistry, American Chemical Society, Chapel Hill, N. C., April, 1937.

[2] Abstracted in part from a thesis by Robb V. Rice, presented to the graduate faculty of the University of Maryland in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1937.

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[5] Conant, Webb and Mendum, THIS JOURNAL, **51**, 1246–54 (1929).