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ISOPROPYL- AND BUTYLTRICHLOROMETHYL CARBINOLS

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Introduction

The alcohols containing the trichloromethyl group have attracted attention due both to their medicinal use and certain limitations in the methods available for their preparation.

Two members have been used medicinally. Trichloro-*tert.*-butyl alcohol, under the trade name of chloretone, is used as a local anesthetic, antiseptic and antispasmodic. Trichloro-*iso*propyl alcohol, known more commonly as isoprol, is an hypnotic.[1] It has also furnished the basis for the first of a series of studies[2] of the effect on physiological action of replacing the methyl with the trichloromethyl group in alcohols. On comparison with *iso*propyl alcohol it was found to have both a stronger antiseptic action and toxicity.

The methods used for preparation have been either the condensation of aldehydes or ketones with chloroform in the presence of potassium hydroxide[3] or the condensation of chloral with the proper alkyl magnesium halide under the procedure of the Grignard reaction.[4] The former method has shown decided limitations as to the aldehydes[3e] and ketones[4] which may be used.

The object of the present study was to make the list of trichloromethyl alcohols more complete by adding the *iso*propyl and butyl members.

The fact that both *iso*propyl and butyl alcohols are now prepared on an industrial scale adds a further incentive to the preparation and study of compounds containing these groups.

Experimental Part

Preparation of the Alcohols.—The procedure followed was in general that of the Grignard reaction. The organomagnesium halides were prepared by treating 12g. portions of magnesium turnings with 68 g. of *iso*propyl bromide and 70 g. of butyl bromide, respectively; 74 g. of freshly distilled chloral in an equal volume of dry ether was slowly added to ethereal solutions of the organomagnesium halides. The first two thirds of the

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[1] Impens, *Therap. Monatsh.*, **17**, 533 (1903).

[2] Howard and Simpert, *J. Am. Pharm. Assoc.*, **14**, 487 (1925).

[3] (a) Jocicz, *Chem. Centr.*, **68** [I], 1013 (1897). (b) Willgerodt, *Ber.*, **14**, 2451 (1881); **15**, 2305 (1882); **16**, 1585 (1883). (c) Guèdras, *Compt. rend.*, **133**, 1011 (1901). (d) Ekeley and Klemme, THIS JOURNAL, **46**, 1252 (1924). (e) Howard, *ibid.*, **47**, 455 (1925).

[4] Henry, *Compt. rend.*, **138**, 205 (1904). Howard, THIS JOURNAL, **48**, 774 (1926).

chloral reacted very readily, but it was necessary to warm the reaction mixture gently during the addition of the last third and then reflux for an hour and a half to complete the reaction. The resulting product was then decomposed with 2 *N* hydrochloric acid and the ether washed in turn with water, sodium bicarbonate solution, sodium bisulfite solution and water. It was dehydrated over anhydrous sodium sulfate, the ether removed by distillation and the alcohol distilled in a vacuum. The product always darkened perceptibly by the time the distillation was completed. It was then subjected to steam distillation which readily removed it from the dark portions, giving a product which remained a light yellow for several weeks.

Preparation of the Esters.—The acetates, propionates and butyrates were prepared by heating the alcohols with an excess of the corresponding anhydrides for two hours at 130–135°.

The benzoates were prepared by treatment with benzoyl chloride according to the usual procedure of the Schotten-Baumann reaction.

The results are given in Table I.

TABLE I

RESULTS

	Substance	B. p., °C.	Press., mm.
1.	Trichloromethyl-*iso*propyl carbinol	105	674
2	Trichloromethylbutyl carbinol	108	673

	Yield, g.	Anal. for Cl Calcd., %	Anal. for Cl Found, %	D_{20}^{20}	B. p. of acetate, °C.	Press., mm.
1.	30–32	55.55	55.59	1.402	156–157	685
2.	35–37	51.78	51.82	1.327	157–158	684

	Propionate		Butyrate		Benzoate	
	B. p., °C.	Press., mm.	B. p., °C.	Press., mm.	B. p., °C.	Press., mm.
1.	163–164	685	176–177	685	180–181	685
2.	166–167	684	177–178	684	182–183	684

Both of these alcohols would be classified as "very sparingly soluble" in water. However, the *iso*propyl is slightly more soluble than the butyl compound. Both are readily soluble in ether, ethyl alcohol, benzene, carbon tetrachloride, chloroform, carbon disulfide, methyl alcohol and acetone.

Summary

*iso*Propyl- and butyltrichloromethyl carbinols as well as their acetic, propionic, butyric and benzoic esters have been prepared and studied.

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