[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Derivatives of Tertiary Alcohols. Acid Phthalic Esters

BY W. A. FESSLER[1] AND R. L. SHRINER

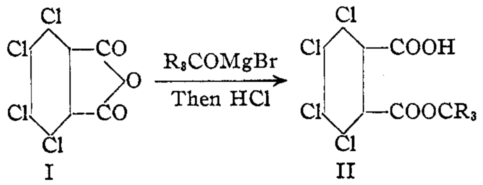
Many reagents are available for the preparation of derivatives of primary and secondary alcohols, but very few of these are applicable to tertiary alcohols. A few urethans and 3,5-dinitrobenzoates of *t*-butyl and *t*-amyl alcohols are reported.[2] The difficulties in obtaining derivatives of tertiary alcohols are due not only to the slowness with which they react, but also to the ease with which replacement of the hydroxyl or elimination of water takes place.

The preparation of solid esters of tertiary alcohols by using the tertiary alkoxymagnesium halide as one reactant seemed to offer a procedure which would avoid the dehydration reaction, since mild conditions could be used. The reaction of alkoxymagnesium halides with acid chlorides was first observed by Grignard[3] as a secondary reaction taking place when ethyl oxalyl chloride was treated with methylmagnesium iodide. Houben[4] later used the reaction with acid chlorides and anhydrides as a general method of esterification for primary and secondary alcohols. Recently Yabroff and Porter[5] prepared *t*-butyl phenylacetate by the action of *t*-butoxymagnesium bromide on phenylacetyl chloride.

In the present work, a study was made of the reaction between *t*-alkoxymagnesium halides and phthalic anhydride and three readily available substituted phthalic anhydrides. In order to determine the best conditions for the reaction and the most suitable anhydride, a series of preliminary experiments were carried out, using *t*-butoxymagnesium bromide prepared from *t*-butyl alcohol and ethylmagnesium bromide. Some of the runs are summarized in Table I.

The addition of dioxane increased the yield of the ester since it is a better solvent for the anhydrides than ether alone. Higher yields of the *t*-butyl ester were obtained at 50–55° than at lower or higher temperatures. The phthalic acid ester melts rather low and the esters of higher alcohols crystallized with difficulty. 3-Nitrophthalic anhydride gave crystalline esters, but the use of this anhydride may give rise to isomeric esters. It was found that ethoxymagnesium bromide reacted with 3-nitrophthalic anhydride to produce the 2-ethyl-3-nitro acid phthalate which melted at 156–158°, and was identical with that previously prepared by direct esterification.[6] It may, therefore, be assumed tentatively that the *t*-butoxymagnesium bromide produces the 2-*t*-butyl-3-nitro acid phthalate. No isomeric ester could be isolated, but it may have been lost during purification.

On the basis of the preliminary experiments, tetrachlorophthalic anhydride (I) seemed to be the most suitable since no isomeric esters are possible and the products crystallized more readily. Accordingly, it was used to prepare the tetrachlorophthalic acid esters (II) of the tertiary alcohols listed in Table II. This table also shows the best time and temperature for the reaction and indicates the best procedure for isolation.



Examination of the data in Table II shows that the tetrachlorophthalic acid esters of tertiary alcohols are satisfactory solid derivatives which may be characterized by their decomposition points and neutral equivalents. Although the yields are not high, the reaction can be used satisfactorily when sufficient amounts of material are available.

The experimental conditions and method of isolation must be varied according to the molecular weight of the tertiary alcohol. For alcohols of low molecular weight a short reaction period at 50° is preferable, whereas the higher alcohols require a long time at a low temperature. The tetrachlorophthalic acid esters of alcohols below tri-*n*-propylcarbinol were soluble in aqueous alkalies, whereas the higher esters were insoluble. The neutral equivalents of these higher esters hence must be determined by titration in acetone solution.

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[1] Chemical Foundation Fellow in Organic Chemistry.

[2] Knoevenagel, *Ann.*, **297**, 148 (1897); Neuberg and Kansky, *Biochem. Z.*, **20**, 448 (1909); Reichstein, *Helv. Chim. Acta*, **9**, 799 (1926); Hoeke, Thesis, Leyden, 1934.

[3] Grignard, *Compt. rend.*, **136**, 1200 (1903).

[4] Houben, *Ber.*, **39**, 1736 (1906).

[5] Yabroff and Porter, THIS JOURNAL, **54**, 2453 (1932).

[6] Nicolet and Sacks, *ibid.*, **47**, 2348 (1925).

TABLE I

REACTION OF *t*-BUTOXYMAGNESIUM BROMIDE AND VARIOUS PHTHALIC ANHYDRIDES

Anhydride	Reaction solvent	Reaction Temp., °C.	Reaction Time, hr.	Dec. point	Yield of ester, %	Neut. equiv. Calcd.	Neut. equiv. Found
Phthalic	Ether	36	1	85.0–86.0 (melts)	17.5	222	220
Phthalic	Ether–dioxane	50–55	1	85.5–86.5 (melts)	42.8	222	221
3-Nitrophthalic	Ether–dioxane	50–55	1	145 dec.	54.3	267	267
Tetrabromophthalic	Ether	50–55	1	147 dec.	4.1	538	531
Tetrachlorophthalic	Ether–dioxane	50–55	1	142 dec.	54.2	360	360
Tetrachlorophthalic	Ether–dioxane	0	20	142 dec.	15.4	360	358

TABLE II

REACTION OF VARIOUS *t*-ALKOXYMAGNESIUM BROMIDES WITH TETRACHLOROPHTHALIC ANHYDRIDE

Alcohol	Reaction Temp., °C.	Reaction Time, hrs.	Yield, %	Dec. point, °C.	Neut. equiv. Calcd.	Neut. equiv. Found	Procedure[7]
t-Butyl	50–55	1	54.2	142	360	360	A
t-Amyl	50–55	1	38.4	126	374	372	A
Triethylcarbinol	25	2	66.0	145	402	398	A
Tri-*n*-propylcarbinol	0	10	54.3	138	444	443	B
Tri-*n*-butylcarbinol	0	10	36.2	112	486	482	B
Tri-*n*-amylcarbinol	0	20	47.0	102	528	529	B

The reaction with aryl carbinols was also studied. Diphenylcarbinol can be converted into the acid phthalate in 74% yields by use of the alkoxymagnesium bromide, whereas the direct reaction of diphenylcarbinol with phthalic anhydride gave only 18% yields of the ester.

All attempts to prepare acid phthalates of triphenylcarbinol (by varying the experimental conditions) have failed up to the present time.

Experimental

Tertiary Alkoxymagnesium Bromides.—A solution of 0.1 mole of the tertiary alcohol in 50 cc. of anhydrous ether was added dropwise to a vigorously stirred solution of 0.1 mole of ethylmagnesium bromide in 150 cc. of absolute ether in a flask equipped with a reflux condenser.

In the case of *t*-butyl alcohol a white precipitate appeared. With the higher alcohols no precipitate formed. The resulting solution or suspension was used in the following procedure.

In one run with *t*-butyl alcohol the precipitate was filtered, dried *in vacuo* and analyzed. The analysis showed that the precipitate was *t*-butoxymagnesium bromide containing some ether.

Anal. Calcd. for $C_4H_9OMgBr \cdot 0.5(C_2H_5)_2O$: Mg, 11.35; Br, 37.30. Found: Mg, 10.47, 10.57; Br, 35.81, 35.19. Atomic ratio: Mg:Br::1.00:1.02.

Phthalic Acid Esters.—To a vigorously stirred solution of 0.1 mole of the tertiary alkoxymagnesium bromide in 175 cc. of ether was slowly added 175 cc. of anhydrous dioxane (175 cc. of anhydrous ether was substituted on two occasions as noted in Table I). One-tenth mole of phthalic or the substituted phthalic anhydride was then introduced and the reaction flask surrounded by a bath to maintain a constant temperature. After the reaction mixture had been stirred at the temperature and for the time indicated in the tables, the contents of the flask was poured on 500 g. of ice and acidified with 125 cc. of 2 *N* hydrochloric acid. The unreacted anhydride was then filtered, after which the ether layer of the filtrate was separated and the water layer extracted once with a 75-cc. portion of ether. The combined ether layers were then washed with two 50-cc. portions of ice-cold water. Isolation of the acid ester was accomplished by one of two methods, depending upon whether or not it was soluble in a 5% solution of sodium hydroxide. It was found that the tetrachlorophthalic acid esters of the aliphatic alcohols above triethylcarbinol were insoluble in this solution.

Procedure A.—The ether layer was extracted with ice-cold, 5% sodium hydroxide, using a 100-cc. portion followed by a 25-cc. portion. The combined sodium hydroxide layers containing the sodium salt of the acid ester were acidified by slowly stirring in 6 *N* hydrochloric acid until addition of the acid caused no further precipitation. Acid esters separated by procedure A were, in each case, purified by recrystallization from a mixture of ether and low-boiling petroleum ether.

Procedure B.—The ether was evaporated from the ethereal solution of the acid ester by heating on a steam cone. The resultant mass was then placed in a vacuum desiccator over concentrated sulfuric acid for three days. At the end of this time most of the unreacted alcohol had been removed. Purification was completed by dissolving in acetone and precipitating by the addition of water. This was repeated three times, and the product washed with two 50-cc. portions of low-boiling petroleum ether chilled in solid carbon dioxide and acetone.

In each instance, a white amorphous precipitate was formed when dioxane was added to the solution of tertiary alkoxymagnesium bromide in the preparation of the acid ester. In one run with triethylcarbinol this precipitate was separated and found to contain a large and somewhat variable amount of $MgBr_2$ obtained by the effect of dioxane on the probable equilibrium in solution, $2ROMgBr \rightleftarrows (RO)_2Mg + MgBr_2$.

The properties and neutral equivalents of the esters are recorded in Table II and the analyses in Table III.

Diphenylcarbinyl Acid Phthalate.—Treatment of diphenylcarbinol with ethylmagnesium bromide and subsequent reaction with phthalic anhydride produced this

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(7) See Experimental Part.

TABLE III

Compounds	Molecular formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
t-Butyl acid phthalate	$C_{12}H_{14}O_4$	64.83	6.35	64.60	6.30
t-Butyl acid 3-nitrophthalate	$C_{12}H_{13}O_6N$	53.91	4.90	53.88	4.88
t-Amyl acid 3-nitrophthalate	$C_{13}H_{15}O_6N$	55.49	5.38	55.22	5.06
t-Butyl acid tetrachlorophthalate	$C_{12}H_{10}O_4Cl_4$	39.98	2.80	39.65	3.05
t-Amyl acid tetrachlorophthalate	$C_{13}H_{12}O_4Cl_4$	41.69	3.23	41.58	3.12
Triethylcarbinyl acid tetrachlorophthalate	$C_{15}H_{16}O_4Cl_4$	44.75	4.01	44.47	3.95
Tri-*n*-propylcarbinyl acid tetrachlorophthalate	$C_{18}H_{22}O_4Cl_4$	48.62	4.99	48.49	5.03
Tri-*n*-butylcarbinyl acid tetrachlorophthalate	$C_{21}H_{28}O_4Cl_4$	51.82	5.67	51.64	5.60
Tri-*n*-amylcarbinyl acid tetrachlorophthalate	$C_{24}H_{34}O_4Cl_4$	54.54	6.49	54.41	6.85

ester in 74% yield. The reaction mixture was kept at 0° for twenty hours, and the acid ester separated by procedure A. The product melted at 164–165° and possessed a neutral equivalent of 333. Calcd. for $C_{21}H_{16}O_4$, 332.

By heating equimolar amounts of diphenylcarbinol with phthalic anhydride at 110° for fifteen hours, a yield of 18% of the diphenylcarbinyl acid phthalate resulted.

Summary

The reaction between *t*-alkoxymagnesium bromides and tetrachlorophthalic anhydride produces the *t*-alkyl acid tetrachlorophthalates in 36–66% yields. These solid esters may be characterized by their neutral equivalents and decomposition points.

The acid phthalate of diphenylcarbinol may be prepared in 74% yield by the reaction between phthalic anhydride and the alkoxymagnesium bromide.

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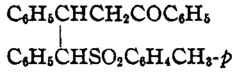
The Michael Condensation. IV. The Active Methylene Group in Sulfones

BY RALPH CONNOR, C. L. FLEMING, JR., AND TEMPLE CLAYTON

Sulfones having the structure RCH_2SO_2R' (in which R is either aryl or another sulfone grouping) are of interest because the methylene group is attached to two activating groups, yet enolization is not possible unless sulfur expands its valence shell. Previous investigators[1] have shown that methylene disulfones form sodio derivatives and may be alkylated by methods similar to those used for the alkylation of 1,3-diketones and that benzyl phenyl sulfone forms a sodio derivative (but may not be alkylated). These are apparently the only characteristic reactions of the active methylene group which have previously been shown to apply to sulfones of this type.[2] This paper demonstrates the ability of benzyl *p*-tolyl sulfone to undergo the Michael condensation.

The product (I) obtained from the condensation of benzyl *p*-tolyl sulfone with benzalacetophenone



$$\begin{array}{l} C_6H_5CHCH_2COC_6H_5 \\ \quad | \\ C_6H_5CHSO_2C_6H_4CH_3\text{-}p \end{array} \qquad (I)$$

was present in two stereoisomeric forms, m. p. 139–141° and 197–197.5°. The total yield of the pure products was 26%; this does not represent the actual extent of the reaction, however, because of the losses encountered in the difficult separation of the isomers from each other and from unreacted benzyl *p*-tolyl sulfone.

The addition of benzyl *p*-tolyl sulfone to benzalacetophenone is similar to the behavior of the ketonic analog of the former[4] (desoxybenzoin). The analogy between the reactions of ketones and sulfones in the Michael condensation may be carried still further. Both dibenzoylmethane[5] and bis-(phenylsulfonyl)-methane do not condense with benzalacetophenone and both benzyl *p*-tolyl sulfone and desoxybenzoin fail to react with methyl cinnamate. However, the failure of

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[1] Shriner, Struck and Jorison, THIS JOURNAL, **52**, 2060 (1930).

[2] Aside from active methylene compounds, three other points of similarity may be noted[3] in the behavior of sulfones and their ketonic analogs: (1) the addition reactions of α,β-unsaturated sulfones, (2) the condensation of benzaldehyde with methyl *p*-tolyl sulfone and (3) the reaction of the Grignard reagent with sulfones to give magnesium derivatives similar to those obtained with certain ketones.

[3] Kohler and Potter, THIS JOURNAL, **57**, 1316 (1935).

[4] Knoevenagel and Schmidt, *Ann.*, **281**, 53 (1894).

[5] Connor and Andrews, THIS JOURNAL, **56**, 2713 (1934).