crystals came out at once; the mixture was left at 0° overnight, filtered, and the crystals washed with water and dried in the desiccator over calcium chloride and potassium hydroxide. On recrystallization from methanol at 0°, long slender needles were slowly deposited; yield, 24 mg. melting at 152°.

Anal. Calcd. for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.13; H, 7.51.

Solubility of Isoestriol-A.—No direct solubility measurements were made; however, in attempting to prepare a solution for polarimetry it was found impossible to dissolve 23.66 mg. of the triol in 3.00 ml. of 95% ethanol at room temperature. The solubility of theelol in 95% ethanol has been found to be 1.20 g. (10°) and 1.65 g. (30°) in 100 g. of solvent.[17] It was further observed that isoestriol-A dissolves in 0.5 *N* sodium hydroxide much more readily than does theelol.

Ultraviolet Absorption Spectrum.—Ultraviolet absorption spectra of isoestriol-A and of theelol were obtained by use of the Hilger medium spectrograph. The two curves were identical, each with the other, and with that of theelol previously published by Callow.[18] This finding was anticipated, since isomers of this nature are not expected to show differences in ultraviolet absorption spectra.

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Summary

1. 16-Oximinoestrone has been prepared from estrone benzoate.

2. Using 16-oximinoestrone as an intermediate, an estriol isomeric with theelol has been synthesized. Like theelol, the new estriol is a Δ1,3,5-estratrientriol-3,16,17.

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[17] Doisy, Huffman, Thayer and Doisy, *J. Biol. Chem.*, **138**, 283 (1941).

[18] Callow, *Biochem. J.*, **30**, 906 (1936).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF DUKE UNIVERSITY]

The Use of Certain Phenyl Esters in the Reformatsky Reaction[1]

BY MELVIN S. BLOOM AND CHARLES R. HAUSER

The Reformatsky reaction using ethyl esters instead of aldehydes or ketones as the carbonyl component has not generally been very satisfactory.[2] Since phenyl esters have a more reactive carbonyl group than the corresponding ethyl esters (judging from their relative rates of alkaline hydrolysis)[3] it seemed possible that phenyl esters might serve satisfactorily as the carbonyl component in the Reformatsky reaction. This has been realized in certain cases but not in others.

It has been found that, although ethyl benzoate fails, phenyl benzoate undergoes satisfactorily the Reformatsky reaction with ethyl α-bromoisobutyrate to form ethyl benzoyldimethylacetate.

$$C_6H_5CO_2C_6H_5 + BrC(CH_3)_2CO_2C_2H_5 \xrightarrow{Zn} C_6H_5COC(CH_3)_2CO_2C_2H_5 + C_6H_5OZnBr$$

The yield (52%) of the β-keto ester obtained by this method is essentially the same as that obtained by the benzoylation of ethyl isobutyrate in the presence of the triphenylmethide ion.[4]

Phenyl esters are satisfactory as the carbonyl component in the Reformatsky reaction apparently only when neither the phenyl ester nor the bromoester has α-hydrogens. With 4-phenylphenyl acetate and ethyl α-bromoisobutyrate, ethyl α,α-dimethylacetoacetate was obtained in only low yield (11%), while with phenyl benzoate and ethyl α-bromoacetate or with 4-phenylphenyl propionate and ethyl α-bromoacetate, only very low yields of the respective β-keto esters appeared to be formed. Since most of the zinc was used up in these experiments, the low yields in these cases appears to be due to the predominance of side or subsequent reactions, which, among others, may involve the self-condensation of the phenyl ester (when it has an α-hydrogen) and the enolization of the β-keto ester formed from bromoesters having α-hydrogens. Both of these reactions could probably be effected by the organozinc halide which is presumably the intermediate in the Reformatsky reaction.[2]

Experimental

Ethyl Benzoyldimethylacetate.—In a 500-cc. three-necked flask fitted with a mechanical stirrer, a separatory funnel, and a reflux condenser protected with a calcium chloride tube was placed 16.4 g. (0.25 mole) of zinc foil which had been sandpapered and cut into small strips. A mixture of 48.8 g. (0.25 mole) of ethyl α-bromoisobutyrate (b. p. 49–51° (10 mm.)), 49.6 g. (0.25 mole) of phenyl benzoate (m. p. 68–68.5°), 100 cc. of dry benzene, and 150 cc. of dry toluene was placed in the separatory funnel. About 50 cc. of this solution was added to the zinc and the flask was heated to 150° in an oil-bath until the reaction started. The mixture was then stirred and the rest of the solution introduced at such a rate that gentle refluxing occurred, about thirty minutes being required. Refluxing and stirring were continued for an additional three hours. The flask was cooled in an ice-bath and its contents poured into ice-cold 10% sulfuric acid with vigorous stirring. The acid layer was separated and the benzene–toluene layer was washed with water. The combined wash water and

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[1] Paper XXI on "Condensations"; paper XX, THIS JOURNAL, **65**, 2051 (1943).

[2] See especially Shriner, "Organic Reactions," Roger Adams, Editor-in-Chief, John Wiley and Sons, New York, N. Y., 1942, Chapter I.

[3] See Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 211.

[4] Hauser and Renfrow, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, New York, N. Y., 1943, p. 268.

the acid layer was extracted with ether, and the combined ether and benzene–toluene solution was dried over anhydrous sodium sulfate followed by Drierite. The solution was distilled up to 140° and the residue was fractionated at 9 mm., collecting fractions at 72–130° and at 130–145°. To the residue was added the fraction boiling at 72–130° (9 mm.), and the mixture distilled, the material boiling at 129–149° (9 mm.) being collected and combined with the fraction boiling at 130–145 (9 mm.). Redistillation yielded 28.5 g. (52%) of ethyl benzoyldimethylacetate boiling at 132–135° (9 mm.). Some phenyl benzoate was recovered in the residues.

With hydroxylamine hydrochloride, the β-keto ester gave 3-phenyl-4-dimethylisoxazolone-5 (m. p. 69–70°)[5] in 90% yield. On ketonic hydrolysis by the acetic-sulfuric acid method,[6] the β-keto ester gave a 77% yield of phenyl isopropyl ketone (102–103° (15 mm.)); m. p. of 2,4-dinitrophenylhydrazone, 162–163°.[7]

In the Reformatsky reaction described above, in which approximately 80% of the zinc was used up, the zinc tended to become coated with a precipitate in the course of the reaction, and the yield was satisfactory only when the reaction mixture was stirred vigorously using zinc foil. With 20–30 mesh zinc 30% of the zinc was used up, giving an 18% yield of the β-keto ester. When magnesium turnings were used instead of zinc only an 18% yield of the β-keto ester was obtained even though practically all of the magnesium was used up.

In an experiment in which ethyl benzoate was used instead of phenyl benzoate, less than 10% of the zinc reacted, and the reaction was not further studied.

Other Reactions.—The following reactions were carried out essentially as described for the preparation of ethyl benzoyldimethylacetate.

Ethyl α-bromoisobutyrate with 4-phenylphenyl acetate[8] (m. p. 87–88°) gave an 11% yield of ethyl α,α-dimethylacetoacetate, b. p. 75–76° (14 mm.). When phenyl acetate was used instead of 4-phenylphenyl acetate, the β-keto ester could not be freed from the unreacted phenyl acetate. Ketonic cleavage by the acetic-sulfuric acid method,[6] gave a small amount of methyl isopropyl ketone, b. p. 93–95°; m. p. of 2,4-dinitrophenylhydrazone of the ketone, 118°.[9]

Ethyl bromoacetate with phenyl benzoate yielded a small fraction boiling at 141–143° (6 mm.) which apparently contained, in addition to phenyl benzoate, at least a trace of ethyl benzoylacetate since it gave the red enol test and the green copper salt.[10]

Ethyl bromoacetate with 4-phenylphenyl propionate[11] (m. p. 92.0–92.5°) yielded a small fraction of product boiling over a large range, giving the red enol test and the copper salt,[12] (m. p. 143–144°) of ethyl propionylacetate.

Summary

1. Phenyl benzoate has been found to undergo the Reformatsky reaction with ethyl α-bromoisobutyrate to form ethyl benzoyldimethylacetate in good yield.

2. Phenyl esters appear to be satisfactory as the carbonyl component for the Reformatsky reaction only when neither the phenyl ester nor the bromoester has α-hydrogens.

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[5] Renfrow and Hauser, THIS JOURNAL, **60**, 464 (1938).

[6] Hudson and Hauser, *ibid.*, **63**, 3163 (1941).

[7] Huntress and Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, New York, N. Y., 1941, p. 391.

[8] This ester was prepared in 74% yield from 4-phenylphenol and acetic anhydride essentially as described for the corresponding propionate, see ref. 11.

[9] Huntress and Mulliken, *op. cit.*, p. 375.

[10] Huntress and Mulliken, *ibid.*, p. 268.

[11] Abramovitch and Hauser, THIS JOURNAL, **64**, 2272 (1942).

[12] Beilstein, "Handbuch der organischen Chemie," Julius Springer, Berlin, 1921, Vol. III, p. 671.

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NOTES

2,3,4-Triacetyl-α-methylglucopyranoside-6-nitrate and 3,4,6-Triacetyl-β-methylglucopyranoside-2-nitrate

BY E. K. GLADDING[1] AND C. B. PURVES

Although these two compounds were synthesized, apparently for the first time, by conventional methods as an incident in a larger research, it seems advisable to make a brief, separate record of their preparation and their properties.

The nitration of 2,3,4-triacetyl-6-trityl-α-methylglucoside[2] produced a crystalline residue consisting of triphenylmethyl carbinol and the desired 6-nitrate in equimolecular amount.[3] A fractional crystallization, carried out exactly as specified below, resulted in a 79% yield of pure 2,3,4-triacetyl-α-methylglucoside-6-nitrate, which occurred as well formed prisms having m. p. 112–113° (cor.). No wandering of acetyl groups occurred during the nitration because the same nitrate was obtained by heating 2,3,4-triacetyl-6-iodo-6-desoxy-α-methylglucopyranoside[4] with excess silver nitrate in acetonitrile. Conversely, the 6-iodo compound was produced in 91% yield by heating the nitrate with excess sodium iodide dissolved in acetonylacetone.[5] The specific rotation of the nitrate in 1.11% chloroform solution was $[\alpha]^{20}\text{D}$ 132°, and this value, in conjunction with that of $-14.3°$ found for triacetyl-β-methylglucopyranoside-6-nitrate,[6] leads to a molecular rotation difference of 53,400. The fact that this difference is very close to that of 53,900, accepted for tetraacetyl α- and β-methylglucoside[7] supports the conclusion that the two isomeric nitrates differ only in the configuration of the glycosidic carbon atom.

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[2] Haworth, Owen and Smith, *J. Chem. Soc.*, 88 (1941).

[3] *Cf.* Oldham and Bell, THIS JOURNAL, **60**, 323 (1938).

[4] Compton, *ibid.*, **60**, 395 (1938).

[5] Murray and Purves, *ibid.*, **62**, 3194 (1940).

[6] Oldham, *J. Chem. Soc.*, 2840 (1925).

[7] Hudson and Dale, THIS JOURNAL, **40**, 997 (1918).