[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

Reactions of Per Acids. I. The Reaction of Perbenzoic Acid with Some Simple Ketones

BY S. L. FRIESS[1]

It has been shown by previous investigators that per acids are capable of converting acetyl substituents on the steroid nucleus into acetate groups, in moderately good yields. For example, Marker[2a] and co-workers demonstrated that a mixture of acetic, sulfuric and persulfuric acids could convert allopregnanol-3(β)-one-20 into a mixture of epimeric carbinols, presumably by way of the monoacetates. These carbinols were subsequently oxidized to androstanedione-3,17. Further work by Marker[2b] showed that allopregnanone-20 would be converted by persulfuric acid into a mixture of the compound possessing a 17-acetate grouping, and allopregnanol-21-one-20, corresponding to oxidation at carbon 21.

Subsequent work by Reichstein[3] using perbenzoic acid as the oxidizing agent indicated that the acetate of allopregnanol-3-one-20 could be converted into the corresponding diacetate, which in turn was characterized by saponification to the crystalline androstanediol-3(β),17(α).

Most recently, Sarett[4] has shown that in certain instances relatively high yields may be obtained on oxidation of 17-acetyl steroids to the corresponding 17-acetates, using perbenzoic acid in chloroform solution. A specific example of the reactions cited in this work is the perbenzoic acid oxidation of pregnane-3(α)-ol-11,20-dione acetate in 85% yield, corrected for recovery of starting material, to the compound etiocholane-3(α), 17(α)-diol-11-one diacetate.

In an effort to determine the general utility of this novel reaction, it was considered expedient to test it on somewhat less complicated systems than those found among the steroids. For this purpose, each member of the varied set of simple methyl ketones shown in formulas I-V was subjected to the action of perbenzoic acid in moist chloroform solution, at 23–26°, for a fixed reaction time of ten days.

$R—COCH_3$		$R—O—COCH_3$	
I.	R = cyclohexyl	VI.	R = cyclohexyl
II.	R = phenyl	VII.	R = phenyl
III.	R = cyclopropyl	VIII.	R = β-naphthyl
IV.	R = β-naphthyl		
V.	R = mesityl		

It was found that the reaction of perbenzoic acid with a methyl ketone proceeds quite smoothly for the compounds cyclohexyl methyl ketone, acetophenone and β-acetonaphthone, resulting in the corresponding acetates VI, VII and VIII, respectively, in yields of 67, 63 and 67% based on ketone. This demonstrates quite clearly that the reaction is not confined to these alicyclic systems dealt with in the steroids, but is equally applicable to aromatic systems in the benzene and naphthalene series.

When cyclopropyl methyl ketone (III) was subjected to the action of perbenzoic acid in moist chloroform, however, the expected oxidation did not occur, and indeed only 10% of the theoretically required amount of perbenzoic acid was consumed during the standard reaction period. Furthermore, it would seem that the recovery of 36% of the starting material, unchanged, indicates that the lack of reaction is not to be attributed solely to the possible destruction of the ketone in solution before reaction with perbenzoic acid can occur, but rather to the non-reactivity of the ketone itself.

Having extended the reaction to aromatic systems, it was also considered desirable to ascertain whether the effective action of perbenzoic acid is restricted solely to methyl ketones. To investigate this point, propiophenone was subjected to the action of the per acid under the standard reaction conditions adopted in this work. It was found again that the reaction occurred easily, with the production of the single compound phenyl propionate in 73% yield as based on ketone.

Finally, to determine the possible effect of bulky ortho substituents on the course of the reaction, acetomesitylene (V) was sent through the customary oxidation procedure. It was found that 107% of the required amount of perbenzoic acid was consumed, but the complex reaction product has not been completely analyzed. Further work on this reaction is in progress.

Also in progress and contemplated are further studies on the generality of the reaction, and stereochemical and rate studies on the mechanism of the oxidation. Postulation of a reaction mechanism will await completion of this work.

Experimental

General Procedure.—To 0.10 mole of the pure ketone was added about 315 ml. of a standardized, moist chloroform solution containing approximately 0.12 mole of perbenzoic acid. The resulting cloudy solution was swirled at intervals, and allowed to stand in the dark at 23–26° for ten days. An aliquot was then titrated for residual oxidizing agent in the customary way.[5] A titration was also made on a portion of the stock perbenzoic acid solution which had been subjected to these conditions, to

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(2) (a) Marker, Rohrmann, Wittle, Crooks and Jones, THIS JOURNAL, **62**, 650 (1940); (b) R. E. Marker, *ibid.*, **62**, 2543 (1940).

(3) Burckhardt and Reichstein, *Helv. Chim. Acta*, **25**, 1434 (1942).

(4) L. H. Sarett, THIS JOURNAL, **69**, 2899 (1947).

(5) G. Braun, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 434.

TABLE I

REACTIONS WITH PERBENZOIC ACID

Ketone RCOR' R	R'	Moles of per acid consumed[a] by 0.10 mole of ketone	Product ROCOR' B. p., °C.	Mm.	$n^{25}D$	Yield,[b] %	M. p. α-naphthylurethan
Cyclohexyl	CH_3	0.100	74.5–76.5	23	1.4401	67	127–128
Phenyl	CH_3	.065	93–93.5	22	1.5200	63	133
Cyclopropyl	CH_3	.010					
β-Naphthyl	CH_3	.095	M. p. 67–68			67	123[c]
Mesityl	CH_3	.107	111–120	12[d]			
Phenyl	C_2H_5	.073	98–99	18	1.5003	73	132–133

[a] Corrected for approximate degree of spontaneous decomposition of per acid. [b] Based on ketone and corrected for recovered ketone. [c] M. p. of the β-naphthol itself; not converted to urethan. [d] No mesitol could be detected upon attempted saponification with base.

determine the extent of spontaneous decomposition of the per acid during this time interval.

The chloroform solution was then shaken with dilute sodium carbonate solution to remove the benzoic and residual perbenzoic acids, and this treatment followed by a water wash. The chloroform was then distilled off, and the residual product separated into ketonic and non-ketonic fractions by the use, where possible, of Girard Reagent T. The ketonic fraction, when liquid, was converted to its semicarbazone for purification and identification, while the non-ketonic ester fraction was generally distilled directly under reduced pressure.

A portion of each ester fraction was saponified with base, and the resulting alcohol or phenol converted into its α-naphthylurethan for final identification purposes. In all cases, only a single α-naphthylurethan was obtained from each ester product.

The data obtained from the reactions studied are shown in Table I.

Summary

The reaction of perbenzoic acid in moist chloroform solution with cyclohexyl methyl ketone, acetophenone and β-acetonaphthone for ten day periods at room temperature furnishes cyclohexyl acetate, phenyl acetate and β-naphthyl acetate, respectively, in yields approximating 65%.

The reaction of perbenzoic acid with cyclopropylmethyl ketone under these conditions does not occur.

Propiophenone reacts smoothly under these conditions to furnish the single product phenyl propionate in 73% yield.

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Reaction of Hydroxyaldehydes with Ethyl Orthoformate. I. Hydroxypivaldehyde

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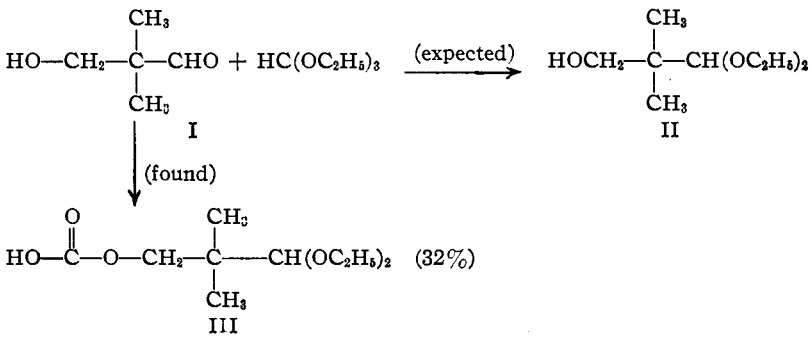
During another investigation the preparation of hydroxypivaldehyde diethyl acetal (II) was attempted by allowing hydroxypivaldehyde (I) to react with ethyl orthoformate.[2] Instead of the expected hydroxy acetal (II), the only product



which could be isolated from the reaction mixture was 3,3-diethoxy-2,2-dimethylpropyl formate (III).

The structure of III was established by saponification of the ester with potassium hydroxide in dry ethanol. Potassium formate was isolated and a new compound was formed which had the correct molar refractivity and analysis for the hydroxy acetal (II). In addition, the structure for the formate ester (III) is supported by an infrared analysis (which showed the presence of an ester group but no hydroxyl group), by the correct molecular refractivity and by a molecular weight determination.

The formation of the ester (III) during the reaction was surprising. An examination of the literature has revealed that apparently the simultaneous formation of acetal and ester is novel in type. One explanation might be that an ester interchange occurred between the hydroxy acetal and ethyl formate or ethyl orthoformate. Experiment, however, has ruled out either of these possi-

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(2) Claisen, *Ber.*, **29**, 1007 (1896).