[Contribution from the Shell Development Co.]

Hydrogen Peroxide–Boron Trifluoride Etherate, a New Oxidizing Agent

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A new oxidizing agent, prepared from 90% hydrogen peroxide and boron trifluoride etherate, has been found to oxidize simple aliphatic ketones to esters in good yields. The nuclear oxidation of *m*-xylene and toluene was also effected with this reagent.

The Baeyer-Villiger oxidation of ketones to esters has been accomplished with a variety of organic peroxy acids in those cases where the ketone is alicyclic, aralkyl, or aromatic, It has been reported that simple ketones of the type RCH_2COCH_2R' [1] do not readily undergo oxidation to the corresponding esters with conventional reagents such as perbenzoic, peroxyacetic, and Caro's acids. Recently, however, trifluoroperoxyacetic acid[2] has been shown to be an effective reagent for this reaction.

Boron trifluoride has long been known to form coordination compounds with a diversity of inorganic and organic substances containing elements (*e.g.*, oxygen, nitrogen, sulfur) with a free pair of electrons. It occurred to us that boron trifluoride should coordinate with hydrogen peroxide to form a complex which might exhibit oxidizing properties similar to those of trifluoroperoxyacetic acid.

A solution of 90% hydrogen peroxide in boron trifluoride etherate rapidly converted simple aliphatic ketones to esters in good yields at room temperatures. Small amounts of the alcohols formed by hydrolysis of the esters were also isolated. The results of a series of experiments in which several ketones were treated with an equimolar quantity of hydrogen peroxide in the presence of boron trifluoride etherate are summarized in Table I.

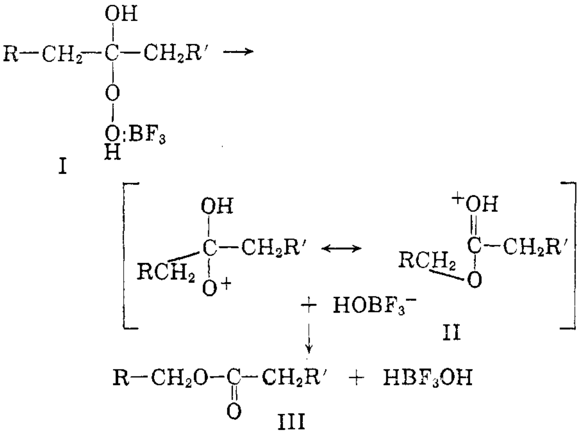
TABLE I

Oxidation of Ketones to Esters with Hydrogen Peroxide–Boron Trifluoride

Ketone	Conversion, %	Yield of Esters, %	Yield of Alcohol, %
2-Octanone	73	62	12
Methyl isobutyl ketone	77	58	14
Diethyl ketone	75	60	—
2-Heptanone	74	60	13

In general, a mixture of ester, alcohol, and unchanged ketone was isolated by distillation, and the relative amount of each was determined by chemical analysis. In those cases where 2-octanone and 2-heptanone were the starting ketones, esters were freed from ketones by treatment with Girard's reagent P and then separated from alcoholic impurities by fractional distillation. The purified esters thus obtained from 2-heptanone and 2-octanone contained at least 98% *n*-amyl acetate and 98% *n*-hexyl acetate, respectively, as determined by infrared spectroscopy.[3]

It is probable that the mechanism of this oxidation with hydrogen peroxide–boron trifluoride is similar to that postulated for other examples of the Baeyer-Villiger reaction,[4,5] where the oxidant is an organic peroxy acid. The reaction may proceed by way of the boron trifluoride complex of the hydrogen peroxide–ketone adduct (I). This by loss of $[HOBF_3^-]$ and the concerted migration of an alkyl group yields the ester (III).



The excellence of trifluoroperoxyacetic acid in accomplishing this reaction has been attributed[2] to a facile heterolysis of the oxygen-oxygen bond in the ketone-peroxy acid adduct. The highly electronegative trifluoroacetyl substituent (see IV) was considered responsible for this effect. Undoubtedly, the same rationale can be used to explain the efficiency of hydrogen peroxide–boron trifluoride in effecting this reaction.

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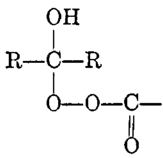
[1] C. H. Hassall, *Org. Reactions*, IX, 76 (1957).

[2] W. O. Emmons and G. B. Lucas, *J. Am. Chem. Soc.*, **77**, 2287 (1955).

[3] Infrared analysis did not exclude the possibility of the presence of 2% or less methyl hexanoate in the amyl acetate or 2% or less methyl heptanoate in the *n*-hexyl acetate.

[4] M. F. Hawthorne, W. D. Emmons, and K. S. McCallum, *J. Am. Chem. Soc.*, **80**, 6393 (1958).

[5] M. F. Hawthorne, and W. D. Emmons, *J. Am. Chem. Soc.*, **80**, 6398 (1958).



$\mathrm{R{-}C(OH)(R){-}O{-}O{-}C({=}O){-}CF_3}$

IV

A boron trifluoride substituent on the peroxy oxygen should greatly aid heterolysis.

It has been established[5] that the migratory ability of alkyl groups in the Baeyer-Villiger reaction decreases in the order tertiary >secondary >primary > methyl. This effect has been discussed in terms of the ability of the migrating group to accommodate positive charge in the transition state. According to this interpretation, then, the migrating group should principally be that one which is most stabilized by inductive or hyperconjugative electron release. This was observed to be true for the two cases examined most thoroughly here. Thus, *n*-hexyl acetate (*n*-hexyl migration) and *n*-amyl acetate (*n*-amyl migration) were the only esters which were isolated from the oxidation of 2-octanone and 2-heptanone, respectively.

Several aromatic hydrocarbons were successfully oxidized to phenols and quinones in low yields when treated with hydrogen peroxide-boron trifluoride etherate. With *m*-xylene the reaction products, 2,4-dimethylphenol, 2,6-dimethylphenol, 2,6-dimethylhydroquinone and 2,6-dimethyl-3-hydroxybenzoquinone,[6] were essentially the same as those obtained by us on reaction with trifluoroperoxyacetic acid. Toluene gave principally a polymeric material which contained both phenolic and carboxylic acidity. Small amounts of cresol were also obtained from the reaction with toluene. Musgrave[6] and co-workers have reported that they were unable to isolate any cresol from the complex mixture of products obtained from the reaction of toluene with trifluoroperoxyacetic acid.

EXPERIMENTAL

Preparation of hydrogen peroxide–boron trifluoride etherate reagent. Ninety per cent hydrogen peroxide[7] (7.9 g., 0.21 mole) was added dropwise to a vigorously stirred quantity of freshly distilled boron trifluoride etherate (37–57 g., 0.26–0.40 mole). Very little heat was developed during the addition. The resulting homogeneous solution could be stored for several days at 5° without appreciable decomposition and failed to detonate in ten experiments in a dropweight test[8] apparatus.

Methods of analysis. The mixtures were analyzed for ester content by saponification according to Bryant and Smith.[9] The amount of carbonyl present was determined with hydroxylamine hydrochloride.[10] Hydroxyl was determined with lithium aluminum hydride according to the method of Stenmark and Weiss.[11]

Oxidation of 2-octanone. A solution of 90% hydrogen peroxide (7.9 g., 0.21 mole) in boron trifluoride etherate (57 g., 0.4 mole) was added dropwise behind a safety shield over a 2-hr. period to a stirred mixture of 2-octanone (25.8 g., 0.2 mole) and 20 ml. of ether. The reaction was very exothermic during the first part of the addition and it was necessary to cool the reaction flask in an ice water bath to maintain the temperature at 15–25°. Stirring was continued at 25–30° for 1 hr. at which time 95% of the peroxide had been consumed. The mixture was diluted with ether and extracted with 500 ml. of 10% sodium bicarbonate solution. The bicarbonate extract was washed four times with ether and the washings added to the organic solution. The latter was dried and most of the solvent was removed by distillation at atmospheric pressure. Distillation of the residual liquid through a semimicro Vigreux column yielded 22.0 g., b.p. 81–86° (42 mm.) and 3.0–3.5 g. of higher boiling residue. Analysis of the distillate was in agreement for a mixture containing 60% by weight of hexyl acetate, 32% of 2-octanone, and 8% of hexanol.

Anal. Calcd. for 60% $C_8H_{16}O_2$, 32% $C_8H_{16}O$, and 8% $C_6H_{14}O$: sapon. equiv., 86; carbonyl value, 0.25 eq./100 g.; hydroxyl value, 0.082 eq./100 g. Found: sapon. equiv., 85: carbonyl value, 0.25 eq./100 g.; hydroxyl value, 0.083 eq./100 g.

The product (20.0 g.) was refluxed for 12 hr. in a solution containing Girard's Reagent P (37.4 g.), acetic acid (20 ml.), and methanol (180 ml). The mixture was cooled, transferred to 600 ml. of ice water, partially neutralized with a solution of sodium bicarbonate (25 g.) in 200 ml. of water, and extracted with five 200-ml. portions of methylene chloride. The organic solution was washed with 300 ml. of 10% sodium bicarbonate, dried, and most of the solvent removed by distillation at atmospheric pressure. The residue was distilled through a semimicro Vigreux column to give product, 13.5 g. (79–84° at 40 mm.). Fractional distillation of this material through a Piros-Glover micro spinning band column at 100 mm. pressure gave the following: fraction 1: 94–98°, 2.0 g.; fraction 2: 102–107°, 2.5 g.; and fraction 3: 107–107.5°, 8.5 g.

Fraction 1 contained principally *n*-hexyl alcohol and was converted to a 3,5-dinitrobenzoate ester. On recrystallization from ethanol the derivative was obtained as white crystals, m.p. 58–59° (lit.[12] m.p. 58°). Analysis of fraction 3 gave a saponification equivalent that was 99% of the theoretical value. The infrared spectrum of fraction 3 in carbon tetrachloride solution was identical with that of an authentic sample of *n*-hexyl acetate, n_{D}^{25} 1.4066 (the refractive index of distilled Matheson, Coleman and Bell *n*-hexyl acetate was n_{D}^{25} 1.4067).

Anal. Calcd. for $C_8H_{16}O_2$: sapon. equiv., 144.2. Found: sapon. equiv., 142.5.

Oxidation of 2-heptanone. The reaction was carried out and processed in the same manner as that described for 2-octanone. The purified ester, isolated by fractional distillation of the product, had an infrared spectrum identical with that of an authentic sample of *n*-amyl acetate, n_{D}^{20} 1.4028 (reported[13] n_{D}^{20} 1.4031).

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(6) R. D. Chambers, P. Goggin, and W. K. R. Musgrave, *J. Chem. Soc.*, 1804 (1959) failed to isolate 2,6-dimethyl-3-hydroxybenzoquinone in their studies of the reaction of *m*-xylene with trifluoroperoxyacetic acid.

(7) See E. S. Shanley and F. P. Greenspan, *Ind. Eng. Chem.*, **39**, 1536 (1947) for a discussion of the potential hazards involved in the use of high strength hydrogen peroxide.

(8) The test apparatus and method are described in Tech. Bull. 59–44, *Concentrated Hydrogen Peroxide*, p. 15, Shell Chemical Co., New York, 1959.

(9) W. M. D. Bryant and D. M. Smith, *J. Am. Chem. Soc.*, **58**, 1014 (1936).

(10) J. Mitchell, Jr., D. M. Smith, and W. M. D. Bryant, *J. Am. Chem. Soc.*, **63**, 573 (1941).

(11) G. A. Stenmark and F. T. Weiss, *Anal. Chem.*, **28**, 1784 (1956).

(12) R. L. Shriner and R. C. Fuson, *Systematic Identification of Organic Compounds*, Wiley, N. Y., 1948, p. 226.

(13) T. Hannotte, *Bull. Soc. Chim. Belg.*, **35**, 104 (1926).

Anal. Calcd. for $C_7H_{14}O_2$: sapon. equiv., 130.2. Found: sapon. equiv., 129.

Oxidation of m-xylene with hydrogen peroxide in presence of trifluoroacetic acid. The procedure described below was designed to maximize the yield of 2,6-dimethyl-3-hydroxybenzoquinone.[14]

Ninety per cent hydrogen peroxide (31.0 g., 0.8 mole) was added in five portions 4 hr. apart to a stirred solution containing *m*-xylene (21.5 g., 0.2 mole) and trifluoroacetic acid (7.5 g., 0.065 mole) in 100 ml. of methylene chloride. The temperature of the mixture gradually rose to 35° after each addition and maintained itself there for about 1 hr. Stirring was continued at 25–30° for 20 hr., the color of the reaction becoming dark orange. The mixture was diluted with methylene chloride and washed twice with water to remove most of the trifluoroacetic acid. The methylene chloride solution was then extracted four times with 10% sodium bicarbonate. The combined alkaline extracts were washed twice with methylene chloride and the washings added to the original organic solution.

The sodium bicarbonate extracts (deep wine color) were acidified with 20% sulfuric acid and extracted thrice with methylene chloride. Drying and removal of the solvent on the Rinco evaporator left 4.0 g. of orange crystalline residue. Sublimation at 80–100° and 0.5 mm. yielded 3.0 g. (15% yield) of orange crystals, m.p. 98–100°. On recrystallization from *n*-hexane there was obtained 2,6-dimethyl-3-hydroxybenzoquinone, m.p. 102–103° (lit.[15] m.p. 103°). The infrared spectrum in chloroform solution exhibited absorption peaks at 2.95 μ, 6.09 μ, and 6.17 μ.

Anal. Calcd. for $C_8H_8O_3$: C, 63.2; H, 5.30; neut. equiv., 152. Found: C, 63.6; H, 5.45; neut. equiv., 151.

The original methylene chloride solution after bicarbonate extraction was dried and most of the solvent removed by distillation at atmospheric pressure. The residual red liquid was distilled through a semimicro Vigreux column to give *m*-xylene, 7.0 g. (53–55° at 50 mm.) and 4.0 g. (60–80° at 3 mm.). The latter gave 2,6-dimethylbenzoquinone as yellow needles, m.p. 70–71°, after recrystallization from *n*-hexane.

Oxidation of m-xylene. A solution of 90% hydrogen peroxide (7.9 g., 10.21 mole) in boron trifluoride etherate (37 g., 0.26 mole) was added dropwise behind a safety shield over a 2-hr. period to a vigorously stirred solution of *m*-xylene (21.5 g., 0.2 mole) in 100 ml. of methylene chloride. The temperature was maintained at 10–15° by means of an ice water bath. Stirring was continued at 15–25° for 2–3 hr. and then the brownish red reaction mixture was extracted with 200 ml. of water. The aqueous extract was washed twice with methylene chloride and the washings were added to the organic solution.

The methylene chloride solution was extracted twice with a 10% solution of sodium bicarbonate. After washing twice with fresh methylene chloride the bicarbonate solution was acidified with 20% sulfuric acid and extracted twice with methylene chloride. Drying and removal of the solvent on the Rinco evaporator gave an orange oil (0.5 g.). 2,6-Dimethyl-3-hydroxybenzoquinone, m.p. 101–102°, was isolated from this oil by sublimation and recrystallization of the sublimate from *n*-hexane. The hydroxyquinone had an identical mixed melting point with a sample prepared from *m*-xylene and trifluoroperoxyacetic acid.

The methylene chloride solution after bicarbonate extraction was dried and most of the solvent removed by distillation at atmospheric pressure. The red liquid remaining was distilled through a semimicro Vigreux column to give *m*-xylene, 12 g., (52–53° at 40 mm.) and fraction 2, 1.5 g., (65–70° at 4 mm). Fraction 2 had an elemental analysis and phenolic acidity that was in accord for a material containing 97% xylenol.

Anal. Calcd. for $C_8H_{10}O$: C, 78.7; H, 8.25; phenolic acidity, 0.82 eq./100 g. Found: C, 79.0; H, 8.32; phenolic acidity, 0.79 eq./100 g.

Fraction 2 was separated by gas-liquid chromatography at 180° on a column packed with DC-710 and at a helium flow rate of 60 ml./min. into two main components (95%) and two minor ones (5%). Comparison of the chromatogram with those of mixtures of authentic specimens indicated that the major components were 2,4-dimethylphenol (60–65%) and 2,6-dimethylphenol (30–35%).

The residue from the distillation was sublimed at 130–160° and 1 mm. to give fraction 3, 0.2 g. (m.p. 140–145°). Fraction 3 had an identical mixed melting point (149–150°) with an authentic sample of 2,6-dimethylhydroquinone after recrystallization from chloroform.

Oxidation of toluene. The reaction was conducted and processed in the same manner as that described for *m*-xylene with the exceptions that boron trifluoride etherate (20 g., 0.14 mole) was substituted for the methylene chloride diluent and ether was the solvent employed for the extractions.

Upon acidification, the sodium bicarbonate extract yielded 2.0–3.0 g. of a brownish polymeric material which contained phenolic as well as carboxylic acidity.

The ether solution after bicarbonate extraction was dried and most of the solvent removed by distillation at atmospheric pressure. Distillation of the residual liquid through a semimicro Vigreux column yielded toluene, 10.5 g. (50–51° at 100 mm.) and a phenolic fraction, 0.8 g. (50–55° at 5 mm.). The elemental analysis and phenolic acidity of the second fraction was in accord for a material containing 93% cresol.

Anal. Calcd. for C_7H_8O: C, 77.8; H, 7.45; phenolic acidity, 0.92 eq./100 g. Found: C, 77.8; H, 7.83; phenolic acidity, 0.86 eq./100 g.

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(14) The reaction of *m*-xylene with an equimolar amount of preformed trifluoroperoxyacetic acid afforded only a 4% yield of 2,6-dimethyl-3-hydroxybenzoquinone.

(15) E. Dane and J. Schmitt, *Ann.*, **536**, 196–203 (1938).