

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Performic Acid Hydroxylation of α,β -Unsaturated Acids and Esters¹BY JAMES ENGLISH, JR., AND J. DELAFIELD GREGORY²

Recent reports^{3,4} have shown that performic acid is a convenient and efficient hydroxylating agent for olefins with isolated double bonds. The reagent was prepared *in situ* by the action of 30% hydrogen peroxide on commercial 98–100% formic acid, and the hydroxylation carried out on the unsaturated material at 40°. The heat of the reaction was more than enough to maintain this temperature for part of the reaction time. Greenspan,⁵ using a sulfuric acid catalyst, showed that 90% hydrogen peroxide under similar conditions gave a six to seven times higher concentration of peracid than did 30% hydrogen peroxide. These studies and others,^{6,7} on the rate of formation and decay of performic acid have all been made at room temperature or below.

This paper reports data on the stability at 60 and 80° of performic acid prepared with 90% hydrogen peroxide, and on the applicability of this reagent to some α,β -unsaturated acids and esters. Most other reagents for the addition of hydroxyl groups are relatively unreactive toward a double bond α,β to a carboxyl group. Those specialized methods which have found use are generally applicable only to water soluble compounds. Perbenzoic acid and chlorates catalyzed

by osmic acid have both been used⁸ successfully with a few water-insoluble α,β unsaturated acids, but the reactions required weeks for completion. It was felt that if performic acid should prove sufficiently stable at elevated temperatures a more rapid and convenient method for the hydroxylation of relatively inert α,β double bonds might be developed.

In following the rate of decay of the peracid, the titration method of d'Ans and Frey⁷ was used. In Fig. 1, the molar concentrations of peracid in the reaction mixtures are plotted against time. The maximum conversion of formic to performic acid is about 60% (curve 2), reached in one-half hour with sulfuric acid catalysis, which agrees well with Greenspan's results.⁵ In the runs at elevated temperature, the heating was not begun until the mixture had stood for 25° for twenty minutes, when the concentration of peracid had approached its maximum.

At 80° (curve 4) the decomposition of the performic acid with liberation of carbon dioxide was relatively rapid. By adding further portions of hydrogen peroxide during the reaction at this temperature, it was possible to restore only a small fraction of the original peracid concentration, even though excess formic acid was present in the solution. In some cases, this decomposition at 80° was used to advantage for destroying excess peracid after reaction with an unsaturated compound before removing the formic acid by distillation. In none of these experiments was any attempt made to isolate the monoformate of the glycol, which might have been expected.³ Instead, the products were saponified after being freed of most of the formic acid.

In subsequent hydroxylations, performic acid solutions similar to those studied above were used, the formation of peracid being allowed to proceed for twenty minutes at room temperature before addition of the olefin. According to other peracid hydroxylations in which known diastereoisomers of the glycols have been obtained, the reaction should proceed by way of an intermediate epoxide. Cleavage of these epoxides in acid solution is accompanied by an inversion of one of the carbon atoms producing a *threo*- or a *trans*- configuration. For confirmation of this mechanism in the case of performic acid, cyclohexene was oxidized, giving the expected *trans*-1,2-cyclohexanediol in 70% yield.

A comparison of hydroxylation reagents formed from 30 and from 90% hydrogen peroxide was made on 2-nonenic acid, showing a yield of 25% of dihydroxypelargonic acid in the former case, and of 51% in the latter. Methyl 2-nonenate

(8) Braun, *THIS JOURNAL*, **51**, 228 (1929); **52**, 3188 (1930).

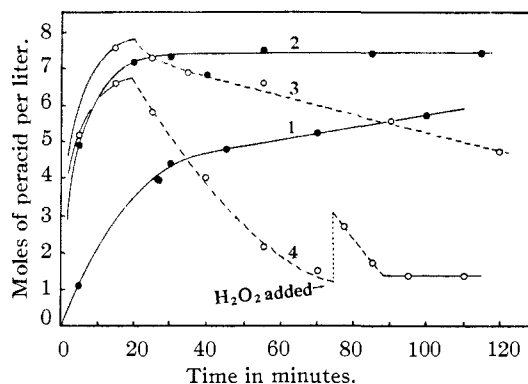


Fig. 1.—The stability of performic acid solutions: curve 1 (by Charles A. Russell), no catalyst, 25°. All others sulfuric acid catalyzed: curve 2, 25°; curve 3, 25° for twenty minutes, then 60° (dashed); curve 4, 25° for twenty minutes, then 80° (dashed).

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(3) Swern, Billen, Findley and Scanlan, *THIS JOURNAL*, **67**, 1786 (1945).

(4) Swern, Billen, and Scanlan, *ibid.*, **68**, 1504 (1946).

(5) Greenspan, *ibid.*, **68**, 907 (1946).

(6) Toennies and Homiller, *ibid.*, **64**, 3054 (1942).

(7) d'Ans and Frey, *Z. anorg. Chem.*, **84**, 145 (1913).

gave virtually the same yield as the free acid with 90% hydrogen peroxide; it was observed that about half of the hydroxylated product from this reaction appeared as ester, and half as free acid. Similar results were obtained with the homolog, 2-undecenoic acid, which yielded 46% of dihydroxyundecanoic acid.

Among other α,β -unsaturated acids investigated, cinnamic acid gave a small yield (10%) of a product which unexpectedly proved to be that isomer of phenylglyceric acid which is known to result from the *cis* hydroxylation of cinnamic acid with permanganates. It is felt that this might be the result of an inversion similar to that observed by Böeseken,⁹ or of the selective destruction of the expected isomer (or a precursor) by the peracid. Dimethyl traumate¹⁰ gave a 6.5% yield of 1,2-dihydroxydecane-1,10-dicarboxylic acid. Maleic acid could not be hydroxylated under the conditions used, being recovered unchanged.

It should be emphasized that the exothermic reaction in the case of 90% hydrogen peroxide may become violent, especially in the presence of a reactive olefin. An attempt to hydroxylate mesityl oxide resulted in the explosive ejection of the entire flask contents when the peracid was added to the olefin too rapidly. When this olefin, diluted with two volumes of formic acid, was treated slowly with a dilute performic acid solution (10%), the temperature was easily controlled, but the only product was a high-boiling black oil. Similar violent reactions have been observed in this laboratory with olefins of a substituted styrene type.

Experimental¹¹

The Stability of Performic Acid Solutions.—For curves 1, 2 and 3 a mixture was made of 11.5 g. (0.25 mole) of 98–100% formic acid, 14.2 g. (0.38 mole) of 90% hydrogen peroxide,¹² and in 2 and 3, 0.25 g. of concentrated sulfuric acid was added. For curve 4, the mixture contained 23.0 g. of formic acid (0.5 mole), 9.5 g. (0.25 mole) of hydrogen peroxide, and 0.25 g. of sulfuric acid. To this solution there was added, after seventy-five minutes, a further 7.3 g. of hydrogen peroxide (0.5 molar proportion adjusted for new volume after withdrawal of six aliquots).

After being stirred at 25° for twenty minutes, number 3 was heated to 60°, and number 4 to 80°. These temperatures were maintained with continuous stirring within a few degrees by occasional dipping in a cold water-bath.

For titration, a 1-cc. aliquot was quickly diluted to 100 cc. with ice water, and 20 cc. of this solution titrated according to d'Ans and Frey.⁷

1,2-Cyclohexanediol.—To a mixture of 105 g. of 98–100% formic acid and 13 g. of 30% hydrogen peroxide (Superoxol) was added 8.0 g. of cyclohexene. The immiscible layers were shaken briefly together; spontaneous heating began, and the suspension became homogeneous at 65–70°, where it was held for two hours in a water-bath. Most of the formic acid was removed by distillation and the residue heated on steam for forty-five minutes

with 50 cc. of 20% sodium hydroxide. On cooling, the yellow solution was neutralized to litmus with hydrochloric acid and evaporated to dryness under vacuum on the steam-bath.

The resulting solid was distilled, using a simple distilling apparatus. Most of the fraction, b. p. 128–132° (15 mm.), weighing 10.25 g., solidified immediately. Recrystallization from acetone gave 7.9 g. (70%) of white prisms; m. p. 102–103°. One more crystallization raised the m. p. to 103.5–104°. 1,2-Cyclohexanediol has been described,¹³ *trans* m. p. 103.6–104.4°, *cis* m. p. 98.4–99.2°.

2-Nonenoic Acid and Amide.—Heptaldehyde was condensed with malonic acid according to the method of Harding and Weizmann,¹⁴ and the undistilled product stirred at 80° with 1.5 volumes of 85% sulfuric acid¹⁵ in order to lactonize any 3-nonenic acid. The α,β -unsaturated acid was separated by means of sodium bicarbonate; b. p. 116–121° (1 mm.), yield 41%.

A sample of this acid was converted to the chloride with thionyl chloride, and reacted with aqueous ammonia. The amide was recrystallized from benzene, white leaflets, m. p. 130–131°.¹⁶

2-Undecenoic Acid and Amide.—Nonanal was condensed with malonic acid and the product isolated exactly as in the above preparation. 2-Undecenoic acid,¹⁷ b. p. 121–126° (0.5 mm.), crystallizes in ice water; yield 33%.

Anal. Calcd. for C₁₁H₂₀O₂: C, 71.69; H, 10.94. Found: C, 71.94; H, 10.98.

A sample of this acid converted to the amide crystallized in large needles from benzene, m. p. 115–116°. van Caillie¹⁸ gives the m. p. as 114–115°.

Anal. Calcd. for C₁₁H₂₁ON: N, 7.64. Found: N, 7.40.

Performic Acid Reagent.—The performic acid solution used in most of these hydroxylations was a mixture of 34.5 g. of 98–100% formic acid, 9.5 g. (0.33 mole) of 90% hydrogen peroxide, and 0.25 g. of sulfuric acid, which was kept at room temperature for twenty minutes before use.

Hydroxylation of 2-Nonenoic Acid (90% Hydrogen Peroxide).—Twenty grams of 2-nonenic acid was added to a performic acid solution of double the above quantities and stirred well to emulsify. Heating to 55–60° started the spontaneous reaction, and the solution became homogeneous. This temperature was held for two hours with continued stirring, then allowed to rise to 95° until the spontaneous reaction was over (twenty-five minutes) and the excess peracid largely destroyed. Most of the formic acid was removed by vacuum distillation, and the residue saponified on the steam-bath with 175 cc. of 10% sodium hydroxide for one half hour. After acidification with hydrochloric acid, the oily product was extracted with ether and the extract dried over sodium sulfate. The ether was removed, leaving a colorless oil which set to a waxy solid on cooling. This was suspended in benzene and filtered, giving white slippery platelets. The filtrate, on concentration and addition of ligroin, gave two further crops, the total yield of dihydroxypelargonic acid being 12.4 g. (51%), which on crystallization from ethyl acetate or water formed large thin plates, m. p. 118–118.5°. A mixed m. p. with the dihydroxyacid (m. p. 123–124°) from permanganate oxidation of 2-nonenic acid¹⁹ was depressed to 101–103°.

(13) Verkade, Coops, Maan and Verkade-Sandbergen, *Ann.*, **467**, 217 (1928).

(14) Harding and Weizmann, *J. Chem. Soc.*, **97**, 301 (1910).

(15) "Organic Reactions," Vol. I, John Wiley and Sons, New York, N. Y., 1942, p. 226.

(16) Scanlan and Swern, *THIS JOURNAL*, **62**, 2311 (1940).

(17) Tulus, *Rev. faculte sci. univ. Istanbul*, **9A**, 105 (1944); *C. A.*, **40**, 3722 (1946).

(18) van Caillie, *Bull. soc. chim. Belg.*, **44**, 438 (1935), *Chem. Zentr.*, **107**, I, 4423 (1936).

(19) Krohs, *Ber. pharm. Ges.*, **32**, 366 (1922), *Chem. Zentr.*, **94**, I, 819 (1923).

(9) Böeseken, *Rec. trav. chim.*, **41**, 204 (1922).

(10) English, Bonner and Haagen-Smit, *Proc. Nat. Acad. Sci.*, **25**, 323 (1939). We are indebted to Dr. R. T. Major of Merck & Company, Inc., for the synthetic sample of traumatic acid from which this ester was made.

(11) All m. p. and b. p. are corrected.

(12) The 90% hydrogen peroxide was kindly furnished by the Buffalo Electro-Chemical Company, Inc.

Anal. Calcd. for $C_9H_{18}O_4$: C, 56.84; H, 9.54. Found: C, 57.05; H, 9.45.

Hydroxylation of 2-Undecenoic Acid.—Ten grams of 2-undecenoic acid was stirred into the performic acid reagent described above. The temperature was raised to 60° and held there with rapid stirring for forty-five minutes, then raised to 70° (the solution became homogeneous), for forty-five minutes more. The remainder of the procedure was as described for 2-nonenic acid. The somewhat gummy white product was recrystallized from ethyl acetate giving 5.5 g. of small plates (46%). Repeated recrystallization from ethyl acetate gave dihydroxyundecanoic acid, m. p. 111–112°.

Anal. Calcd. for $C_{11}H_{22}O_4$: C, 60.53; H, 10.16. Found: C, 60.06; H, 10.16.

Hydroxylation of Methyl 2-Nonenoate.—After the addition of 11.0 g. of methyl 2-nonenate (b. p. 111–120° (19 mm.)), prepared through the acid chloride) to a performic acid solution prepared as above, the mixture was stirred and held at 50–55° for two and one-half hours. It became homogeneous after one hour. One-half hour at 85° then served to destroy most of the excessive peracid. Evaporation under vacuum of most of the formic acid left 13.2 g. of colorless oil, which was diluted with 100 cc. of ether and well washed with sodium bicarbonate solution. The ether was removed, leaving 7.3 g. of oil, which was saponified on the steam-bath with 50 cc. of 10% sodium hydroxide. A yield of 3.5 g. (28%) of dihydroxy acid isolated as above was obtained from this fraction.

The bicarbonate extract was acidified, and yielded 2.7 g. (22%) of dihydroxy acid isolated as above. (In spite of the fact that saponification was omitted, this product was free glycol, not a formate.) The total yield of dihydroxypelargonic acid was 50%.

Hydroxylation of 2-Nonenoic Acid (30% Hydrogen Peroxide).—A mixture of 53 g. of 98–100% formic acid, 6.5 g. of 30% hydrogen peroxide (Superoxol), and 7.8 g. of 2-nonenic acid was heated and stirred at 60–63° in a water-bath for three and one-quarter hours. Most of the formic acid was removed by vacuum distillation on the steam-bath, and the residue saponified as above. The dihydroxypelargonic acid, isolated in two crops, weighed 2.4 g. (25%).

Hydroxylation of Dimethyl Traumatate.—Dimethyl traumatate (9.8 g.) was treated with a solution containing 15 g. of formic acid, 7.0 g. of 90% hydrogen peroxide, and 0.1 g. of sulfuric acid which had stood twenty minutes at room temperature. The mixture was stirred at 50° for forty-five minutes, then another portion of performic acid solution, identical with the first, was added and this temperature maintained for one and three-quarters hours more. Most of the formic acid was then removed by distillation under vacuum.

The residue (11.9 g.) was diluted to 150 cc. with ether and washed with sodium bicarbonate solution. After drying over sodium sulfate, the ether was removed and the residue fractionated in a very small distilling flask. When the vapor temperature reached 156° (0.5 mm.), the distillation was stopped (dimethyl traumatate b. p.

136–146° (0.5 mm.) in the same apparatus). The higher boiling residue, 4.3 g. of brown oil, was saponified for one hour on the steam-bath with 30 cc. of 10% sodium hydroxide. A small amount of undissolved material was extracted with ether and the solution acidified with sulfuric acid.

A precipitate of 2.2 g. of whitish powder was removed by filtration. Two crystallizations from absolute ethanol gave a white powder, m. p. 163–165.5°, near that of traumatic acid.¹⁰ The filtrate was thoroughly extracted with ether, the extract dried, and the ether removed. There remained 0.65 g. of white solid (6.5%). This 1,2-dihydroxydecane-1,10-dicarboxylic acid, after several recrystallizations from ethyl acetate, was a microcrystalline white powder, m. p. 118–119° preceded by slight sintering.

Anal. Calcd. for $C_{12}H_{22}O_6$: neut. equiv., 131; C, 54.94; H, 8.46. Found: neut. equiv., 132; C, 54.96; H, 8.63.

Hydroxylation of Cinnamic Acid.—Ten grams of cinnamic acid was suspended in a solution containing 46 g. of formic acid, 12.6 g. of 90% hydrogen peroxide, and 0.4 g. of sulfuric acid, which had stood twenty minutes at room temperature. The mixture was stirred at 50° for one and one-half hours; the solid dissolved after about fifteen minutes. After cooling and the addition of 10 cc. of water, sulfur dioxide was bubbled through until no further heat of reaction could be detected and starch-iodide paper was no longer colored.

The volatile materials were removed by distillation under vacuum, leaving a partially solid, dark residue. This was dissolved in 150 cc. of 15% sodium hydroxide and ether extracted. After acidification of the aqueous solution with hydrochloric acid, a preliminary extraction with 50 cc. of ether was made. This extract was discarded and the aqueous layer continuously extracted with ether for seven hours. The extract was dried over sodium sulfate and the ether removed, leaving 5.8 g. of gummy brown solid. This was dissolved in water, treated with Norite, filtered and evaporated to dryness, yielding 1.2 g. (10%) of tan crystals. Recrystallization from acetone gave white prisms, m. p. 142–143°. Calcd. for phenylglyceric acid: neut. equiv., 182. Found: neut. equiv., 182. A mixed melting point with a sample prepared by permanganate oxidation of ethyl cinnamate was not depressed.

Summary

A study has been made of the stability at 60 and 80° of solutions of performic acid prepared by the reaction of formic acid with 90% hydrogen peroxide.

This reagent has been applied to the hydroxylation of α,β unsaturated acids and esters. In this case of 2-nonenic and 2-undecenoic acids, the yields of dihydroxy acids are 46–51%.

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