

THE CHEMISTRY OF PERMALEIC ACID

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Abstract The preparation and reactivity of permaleic acid have been investigated, and its utility as an oxidizing agent has been demonstrated.

ALTHOUGH many organic peracids are well known and have been well characterized,¹ no report of the preparation or utility of permaleic acid has appeared in the literature. We have found that solutions of permaleic acid (I), prepared from maleic anhydride and hydrogen peroxide in an inert solvent,



provide a very convenient and occasionally superior means for the oxidation of

- (1) ketones to esters (the Baeyer-Villiger reaction)
- (2) negatively substituted and simple anilines to the corresponding aromatic nitro compounds.
- (3) certain olefins to epoxides.

Previously it has been possible to effect most of these oxidations using either peracetic, perbenzoic, or perphthalic acid or the more recently developed trifluoroperacetic acid.² However, all of the older methods suffer from disadvantages: trifluoroperacetic acid must often be used in a solvent system which is strongly buffered by inorganic salts while the other peracids are quite slow in some oxidations. The rate of permaleic acid oxidations is nearly as great as that of trifluoroperacetic acid, and permaleic acid may be used in a non-buffered system. A permaleic acid solution in methylene chloride is reasonably stable, decomposing to the extent of 5 per cent in 6 hours at ambient temperatures.

The experimental results have been summarized in Tables 1-3 along with the physical constants of the products obtained. In all cases, the constants obtained were identical to those found in the literature. The reactions were carried out by simply adding a solution of the reactant to a solution of permaleic acid in methylene chloride held at the appropriate temperature. As the reaction proceeds, maleic acid precipitates from the solution and may be removed by filtration when the oxidation is complete. The products were then isolated by conventional means.

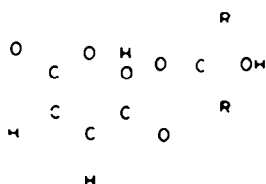
While permaleic acid is not quite as potent a peracid as trifluoroperacetic acid, it is a much stronger oxidant than other laboratory peracids. It also has the advantage of being easily prepared and used without any intermediate transfers, and of having a reduction product which is insoluble in the media used. The solution of permaleic acid contains only 20 mole per cent maleic acid as compared to the 60-70 mole per cent of free acids in the solutions of normal peracids prepared from anhydrides and hydrogen peroxide. No external buffering system was found necessary for the oxidations

¹ D. Swern, *Org. React.* Vol. VII, 435 (1953).

² W. D. Emons and G. B. Lucas, *J. Amer. Chem. Soc.* 77, 2287 (1955).

described here. The peracid was prepared and used in solution; when the concentration of permaleic acid exceeded 10–15 per cent a second heavier layer appeared. This new layer contained a larger amount of peracid than solvent, as shown by iodimetric titration, but formation of this layer did not interfere with oxidation reactions if efficient stirring was maintained.

The greater activity of permaleic acid as compared to peracetic, performic, or the aromatic peracids is attributed to the lower basicity and higher stability of the mono-anion of maleic acid compared to the other acid anions. The combination of low basicity and high stability allows the electron-deficient oxygen in the transition state to be transferred to the substrate at a lower net energy cost. In the Baeyer-Villiger oxidation an additional effect may be partially responsible for the increased activity of permaleic acid since it was previously shown that the rate-determining step of this oxidation is the acid-catalyzed decomposition of the peracid-ketone complex.³ An examination of the molecular model shows that in the transition state the acidic hydrogen on the carboxyl group of permaleic acid is in close proximity to the oxygen of the peracid group on which is developing a negative charge.



This autocatalysis will result in a transition state with a more favorable entropy of activation for the permaleic acid oxidation as compared to other peracids.

Ketone oxidation. The Baeyer-Villiger reaction (Table I) has been reviewed⁴ and

TABLE I. OXIDATION OF KETONES TO ESTERS

Substrate	Time of reaction (hr)	Product	b.p.	Yield (%)
Methyl isobutyl ketone ^a	3	Isobutyl acetate	115–116°	72
Diisobutyl ketone	3	Isobutyl isovalerate	52–54° (10 mm)	83
Octanone-2	3	Hexyl acetate	56–58° (10 mm)	71
Cyclooctanone ^b	3	ω -Hydroxyoctanoic acid lactone	73–74° (9 mm)	67 ^c
Estrone acetate ^c	12	Estronolactone acetate	m.p. 141–144°	40
Benzophenone	2	Phenyl benzoate	m.p. 69–70°	70
Acetophenone	2	Phenyl acetate	89–90° (17 mm)	70
Desoxybenzoil ^d	2	Benzyl benzoate		75
		Phenyl phenylacetate		

^a Unless otherwise noted, reactions were run in methylene chloride solution at reflux, with a 70 per cent excess of peracid to ketone.

^b An inseparable mixture of 2:1 lactone: starting ketone was formed in nearly quantitative amount. Yield based on I.R. analysis [cf. R. Huisgen and H. Ott, *Angew. Chem.* 70, 312 (1958)].

^c See experimental section for details.

^d A mixture, 75 per cent of the theoretical amount, was isolated consisting of 86 per cent benzyl benzoate and 14 per cent of phenyl phenylacetate by infrared analysis.

³ M. F. Hawthorne and W. D. Emons, *J. Amer. Chem. Soc.* 80, 6398 (1958).

⁴ C. H. Hassall, *Org. React.* Vol. IX, 73 (1957).

has been shown to proceed well on simple aliphatic ketones with only one oxidant, trifluoroperacetic acid, where buffering of the solution was needed to prevent transesterification of the product by the free trifluoroacetic acid. We have found that permaleic acid oxidized all classes of ketones smoothly and easily to the corresponding esters, with no noticeable transesterification of products. A greater tendency toward selective migration is noted using permaleic acid in contrast to trifluoroperacetic acid. When desoxybenzoin was subjected to the action of permaleic acid, both possible products, benzyl benzoate and phenyl phenylacetate were found, but in a 7 : 1 ratio as compared to a nearly 1 : 1 ratio when trifluoroperacetic acid was used as oxidant.⁵ The greater selectivity when permaleic acid is used may be attributed to the lower reactivity of maleic acid as a leaving group when compared to trifluoroacetic acid.

TABLE 2. OXIDATION OF AROMATIC AMINES

Substrate	Product	m p	Yield (%)
<i>p</i> -Nitroaniline*	<i>p</i> -Dinitrobenzene	171-173	87
2,4,6-Tribromoaniline	2,4,6-Tribromonitrobenzene	122-124	90
2-Naphthylamine	2-Nitronaphthalene	77-79	40

* Reactions run in CH_2Cl_2 at reflux with a 5 : 1 molar ratio of peracid to aniline.

The lower reactivity necessitates that the migrating group supply more driving force in the rearrangement, permitting a greater selection of the group which migrates.

Oxidation of aromatic amines. The oxidation of aromatic amines to nitro compounds using peroxyacids has been previously described.^{6,7} Because of the experimentally simple techniques, permaleic acid may serve to supplement and extend this reaction (Table 2). The oxidation of 2-naphthylamine to 2-nitronaphthalene using peracids has not been reported; when trifluoroperacetic acid was used as oxidant, overoxidation occurred with formation of phenolic products. If permaleic acid is used a 40 per cent yield of 2-nitronaphthalene is obtained. Unsubstituted and negatively substituted anilines quickly and easily yielded the corresponding nitrocompounds in high yield, while anilines with strongly electron donating groups were themselves overoxidized to phenolic products by permaleic acid.

Epoxidation. The olefinic link in the permaleic acid molecule is not subject to attack by the reagent itself. Internal olefins such as 9-nonadecene or 1-methylcyclohexene reacted extremely rapidly with permaleic acid at 0° but no oxirane could be isolated. Instead only products which can be derived from an acid-catalyzed attack on the intermediate epoxide such as ketones or diol monomaleates were isolated. No search for buffering conditions to prevent this facile ring-opening was made. If the double bond is deactivated by being in a terminal position or by conjugation epoxidation was possible with no buffer system (Table 3). Thus at 0° octene-1 yielded octene-1 oxide in 80 per cent yield, while at 25° only a 40 per cent yield was obtained along with a large amount of diol monoester. Methyl α -methyl glycidate could be prepared in 74 per cent yield by epoxidation of methyl methacrylate. It should be noted that the oxidation of deactivated olefins with peracetic acid prepared by air oxidation of

⁵ M. F. Hawthorne, W. D. Emmons and K. S. McCallum, *J. Amer. Chem. Soc.* **80**, 6393 (1958).

⁶ J. D'Ans and A. Kneip, *Ber. Disch. Chem. Ges.* **48**, 1144 (1915); F. P. Greenspan *Industr. Engng. Chem.* **39**, 847 (1947); F. Bamberger and F. Tschirmer, *Ber. Disch. Chem. Ges.* **32**, 1675 (1899); W. D. Langley, *Org. Synth.* **22**, 44 (1942).

⁷ W. D. Emmons, *J. Amer. Chem. Soc.* **79**, 5528 (1957); **76**, 3470 (1954).

TABLE 3. EPOXIDATION OF OLEFINS

Substrate	Product	b.p.	Yield (%)
Octene-1 ^a	Octene-1 oxide	51-54° (10 mm)	80
Methyl methacrylate ^c	Methyl α -methylglycidate	50° (16 mm)	74
Ethyl acrylate ^c	Ethyl glycidate	60-62 (17 mm)	33
Diallyl sulfoxide ^d	Diallyl sulfone	88-90° (0.4 mm)	87

^a All reactions run in methylene chloride with 50 per cent excess peracid

^b Run at 0

^c Run at reflux

^d Attack of peracid occurred on the S-O rather than the olefinic link

acetaldehyde has recently been described.⁸ While this is an excellent procedure the preparation of this acetic acid-free peracetic acid requires special facilities not normally available.⁹

EXPERIMENTAL

All reactions were carried out in essentially similar fashion and typical examples are given. The usual safety precautions regarding use of highly concentrated hydrogen peroxide¹⁰ should be rigorously observed. Methylene chloride was obtained from Merck and Co.; 90 per cent hydrogen peroxide was purchased from the Buffalo Electrochemical Co.

The preparation of isobutyl acetate from methyl isobutyl ketone To an ice-cold stirred solution of 11.6 g (0.34 mole) of 90 per cent hydrogen peroxide and 150 ml of methylene chloride was added in one batch 39.2 g (0.4 mole) of freshly crushed maleic anhydride. When the major portion of the maleic anhydride had reacted, the solution was heated to reflux and 20 g (0.2 mole) of methyl isobutyl ketone was added in an equal volume of methylene chloride. When the theoretical amount of peracid had disappeared, as determined by iodimetric titration of aliquots the solution was cooled, and the maleic acid removed by filtration. The filtrate was washed twice with 100 cc of 10% sodium carbonate solution, once with 100 cc of 10% sodium bisulfite solution, and once with 100 cc of a saturated sodium chloride solution, and dried over magnesium sulfate. Distillation through a short Vigreux column yielded after removal of solvent, 16.7 g (72%) of isobutyl acetate, b.p. 115-116°, n_D^{20} 1.3908.

2,4,6-Tribromonitrobenzene To a refluxing peracid solution prepared from 3.4 g (0.1 mole) of 90 per cent hydrogen peroxide, 12.3 g (0.125 mole) of maleic anhydride and 70 ml of methylene chloride was added a solution of 6.6 g (0.02 mole) of 2,4,6-tribromoaniline and the solution was heated at reflux for 1 hr. After a workup identical to that described above, the solvent was removed to yield 6.5 g (90%) of 2,4,6-tribromonitrobenzene, m.p. 122-124°.

Octene-1 oxide To a peracid solution at 0° prepared from 10.2 g (0.3 mole) of 90% hydrogen peroxide, 37.3 g (0.38 mole) of maleic anhydride and 150 ml of methylene chloride, was added a mixture of 22.4 g (0.2 mole) of octene-1 in an equal volume of methylene chloride. The theoretical amount of peracid had disappeared after 1.8 hr.; and the mixture was worked up as usual to give 20.4 g (80%) of octene-1 oxide, b.p. 51-54° (10 mm) n_D^{20} 1.4150.

Extronolactone acetate To a refluxing peracid solution, prepared from 1.36 g (40 mm) of 90% hydrogen peroxide, 4.9 g (50 mm) of maleic anhydride, and 10 ml of methylene chloride was added 3.12 g (10 mm) of estrone acetate in 5 ml of methylene chloride, and the solution refluxed overnight. The precipitated maleic acid was removed by filtration, and the filtrate washed with 10 cc each of 10% sodium hydroxide, 10% sodium carbonate, 10% sodium bisulfite, and saturated sodium chloride solution. After drying over magnesium sulfate, the solvent was removed and the reddish solid was chromatographed on 35 g of cationic alumina, grade 1 (Woelm). Elution with 150 ml of benzene yielded 1 g of recovered starting material, m.p. 118-120°; further elution with 600 ml of ether gave 900 mg (40%) of estronolactone acetate, m.p. 142-144° (lit.¹¹ 145°). Passage of 500 ml of methanol through the column removed 1.0 g of amorphous red material, whose infrared spectrum showed bands attributable to a quinoid-type structure, possibly arising from attack of the peracid on the A ring.

⁸ D. I. MacPeck, P. S. Starcher and B. Phillips, *J. Amer. Chem. Soc.* **81**, 680 (1959).

⁹ B. Phillips, F. C. Frostick, Jr. and P. S. Starcher, *J. Amer. Chem. Soc.* **79**, 5982 (1957).

¹⁰ F. P. Greenspan, *Industr. Engng. Chem.* **39**, 847 (1947).

¹¹ R. P. Jacobsen, *J. Biol. Chem.* **171**, 61 (1947).