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PREPARATION OF ^{18}O-LABELLED m-CHLOROPERBENZOIC ACID

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Summary

A method for the preparation of ^{18}O-labelled m-chloroperbenzoic acid (MCPBA) from $H_2{}^{18}O_2$ is described.

Key words: Oxygen-^{18}O, hydrogen peroxide, m-chloroperbenzoic acid.

Introduction. m-Chloroperbenzoic acid (MCPBA) is widely used as an oxidizing agent, mostly in oxygen insertion and epoxidation reactions.[1] Isotopically labelled MCPBA may be used as a donor of ^{17}O and ^{18}O oxygen. Perbenzoic acids are prepared by reaction of the corresponding benzoyl chloride with hydrogen peroxide:

$$\text{R-C(O)Cl} + H_2O_2 \rightarrow \text{R-C(O)OOH} + \text{HCl}$$

We examined different procedures available in the literature[2-4] and we have found that one[4] of them can be applied to the synthesis of MCPBA with satisfactory yield on small scale. Hydrogen peroxide-^{18}O was synthesised according to a published procedure[5] with some modifications.

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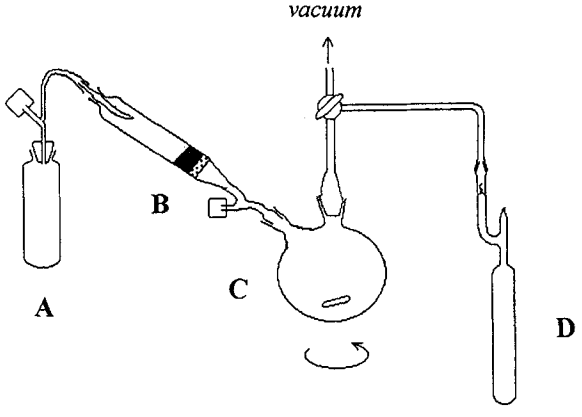
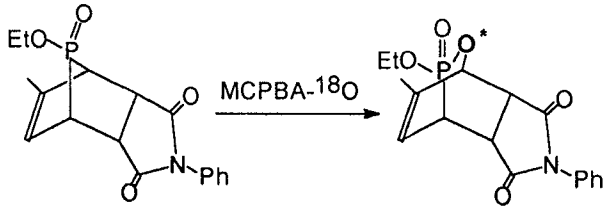
Experimental. $^{18}O_2$ (10 mmol) was prepared[6] by the electrolysis of alkaline ^{18}O-water (30% enrichment, EG&G Mound Applied Technologies, Miamisburg, Ohio) and collected in a glass bottle with a side arm and breakable glass seal. A solution of 2-ethylanthraquinone (Aldrich) (4.2 g, 17.7 mmol) in a mixture (90 mL) of 1-decanol (Aldrich) and toluene (7:2, v/v) was hydrogenated overnight (at least 12 hours) in the presence of a catalytic amount of 5% palladium on alumina (Aldrich), in a hydrogenation apparatus (Parr Corp., Moline, Ill) under a hydrogen pressure of 3 atmospheres.



When the hydrogenation was complete, the flask (**A**) with 2-ethylhydroquinol solution (fluorescent dark green-brown) was purged with argon and closed with a stopper equipped with a high-vacuum one-way valve. Then the flask was attached to an oxidation flask (**C**) (two-neck, 500 mL) via a fritted (with additional Celite layer) dropping funel (**B**). The oxidation flask and ^{18}O-oxygen container (**D**) were attached through a three-way stopcock to a vacuum line. The system was evacuated (0.01 mm Hg) and 2-ethylhydroquinol solution was filtered into the oxidation flask (fluorescent, bright yellow-green after filtration), then the seal on the $^{18}O_2$ vessel was broken and the oxidation was carried out with vigorous stirring. The oxidation proceeded via a dark-brown intermediate and oxidation was complete in approximately four hours (the reaction mixture returned to a bright yellow colour of 2-ethylanthraquinone). The solution was then transfered to a separatory funnel and extracted four times with 2 mL of chilled (4°C) water. The solution (5.8 g containing 5.7 mmol of $H_2{}^{18}O_2$, from iodometric titration, 57% in respect to $^{18}O_2$) was used in the next step of the synthesis. Further extraction of hydrogen peroxide led to an overall yield of hydrogen peroxide

higher then 90%, but the solution was too dilute for the synthesis of MCPBA. The solution (1.5 mL) of sodium hydroxide (0.216 g, 5.4 mmol), 15 mg of $MgSO_4$, chilled (~0°C) solution of $H_2{}^{18}O_2$ and dioxane (5 mL) was added to a plastic vial (20 mL) equipped with a magnetic stirrer. The reaction mixture was placed in an ice-bath and stirred vigorously. Then 3-chlorobenzoyl chloride (Lancaster, 0.41 g, 2.3 mmol) was injected with a syringe under the surface of the solution and stirring was continued for 30 min. The reaction mixture was transferred to the separatory funnel, 10 mL of sulphuric acid (20%) was added and the MCPBA was extracted with four volumes (5 mL) of chilled dichloromethane. The extract was dried over magnesium sulphate, filtered and evaporated under reduced pressure (5 mm Hg) and dried under vacuum. The white solid of MCPBA (0.28 g) was dissolved in dry chloroform (3 mL) and used as required. We have always prepared peroxyacid -^{18}O directly before use, dry MCPBA was, however, reported[4] as being relatively stable. The yield of MCPBA (from iodometric titration) was 1.2 mmol (52% with respect to benzoyl chloride and 12% based on the available oxygen).

We applied MCPBA-^{18}O for the insertion of oxygen-^{18}O into the P-C bond of the 7-phosphanorbornene system:[7]



1 **2**

The 7-PNB derivative **1** (0.165 g, 0.5 mmol) was added to MCPBA-^{18}O and the chloroform solution was stirred overnight. Then KF (0.2 g) was added and the suspension was stirred for 3 hr to complex unreacted MCPBA and 3-chlorobenzoic acid. The solid was filtered off and product **2** was isolated by column chromatography on Florisil with dichloromethane-methanol (3%) as an eluent and recrystallized from chloroform-hexane, yield 0.18 mmol (36 %), (30.8 % ^{18}O from FAB mass spectrometry).

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