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PREPARATIVE SCALE OXYGENATIONS OF ORGANIC MOLECULES IN THE SOLID PHASE USING MICROWAVE DISCHARGE-GENERATED SINGLET OXYGEN

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Preparative scale singlet oxygen oxygenations are by necessity always carried out in solution. Since we wished, in another connection, to study the preparative scale reactions of certain substrates with singlet oxygen in the absence of solvent, we have recently been concerned with developing such a method and would like to report our preliminary results with known acceptors at this time.

The experimental setup is that of Ogryzlo (1) and is shown in Figure 1. The oxygenations were carried out by adsorbing the substrate to be oxygenated (3-4% by weight) on either microcrystalline cellulose (Whatman Standard Grade) or silica gel (Davison Chemical, Grade 923, 100-200 mesh), placing this sample in the reactor vessel, evacuating the system to approximately 5 mm Hg and maintaining this pressure by regulating the oxygen flow with the needle valve. The flow rate was approximately 0.2 mmoles per second. The microwave discharge (2) was then initiated with a Tesla coil with stopcock A open and stopcock B closed and the cavity adjusted to its maximum coupling as indicated by the brightness of the blue glow of the discharge. A small amount of mercury was next distilled into the system by gentle heating of the mercury reservoir whereupon a film of mercuric oxide was rapidly formed in the tubing for a distance of 5-10 cm below the microwave cavity. This technique, which was repeated from time to time throughout the oxygenation, served to remove oxygen atoms from the gas flow (3). Finally, the flow was admitted to the reactor vessel by opening stopcock B and closing stopcock A and the oxygenation continued for the requisite time (1-5 hrs). The singlet oxygen concentration in an apparatus similar to this has been estimated to be approximately 6.5% of the ground state oxygen concentration in the flow system (4).

RESULTS

The substrates studied and the yields of oxygenated products are summarized in Table I. All oxygenations were carried out in the dark. Control experiments showed that the substrates did not react under these conditions in the absence of the electric discharge. The yields are based, in each case, on unrecovered starting material. All products were identified by comparison with authentic samples or by comparison with published spectral and physical data. In some cases, comparisons were made after sodium borohydride reduction of the initially formed hydroperoxide. (See Table.)

DISCUSSION

The results in Table I indicate that the solid phase method is a useful alternative to solution methods of oxygenation. Particularly attractive are, (1) the mildness of the method, and (2) the ease of product workup.

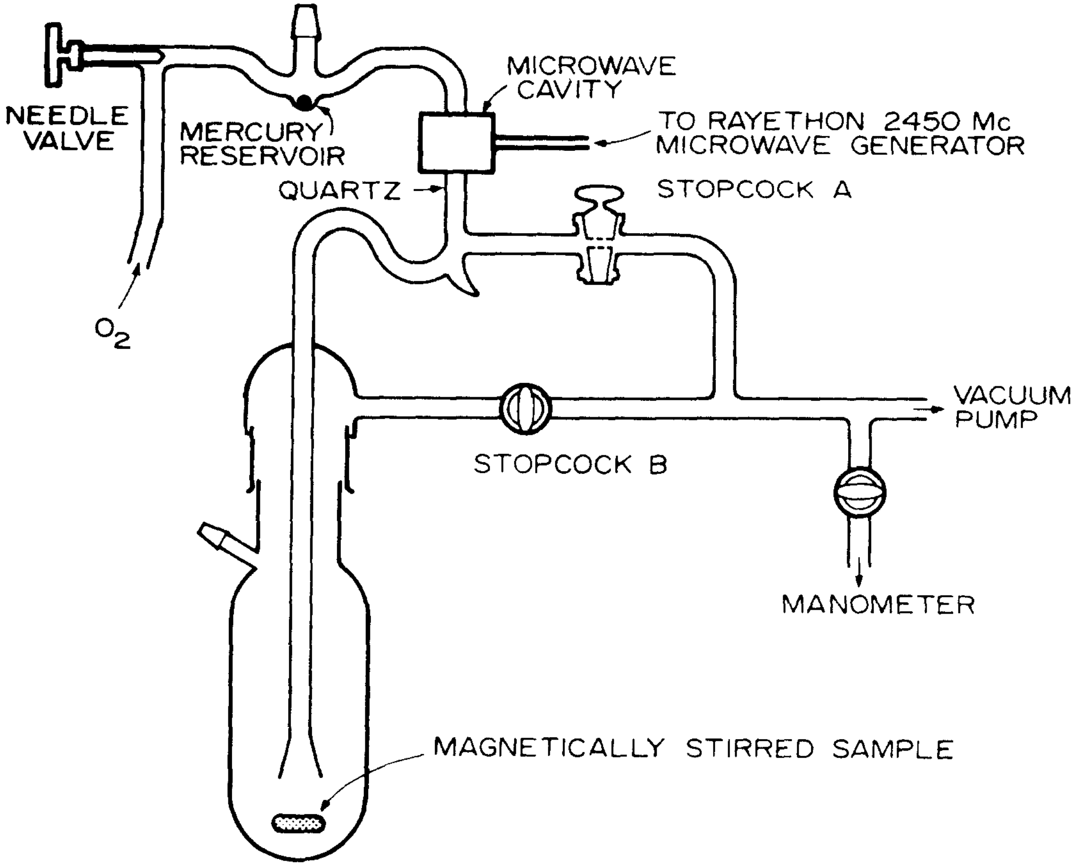


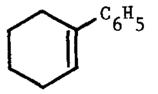
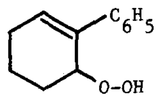
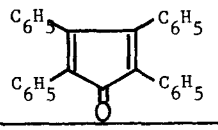
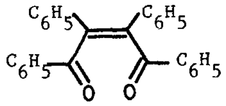
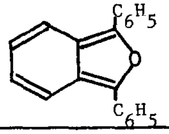
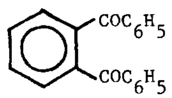
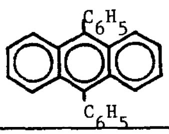
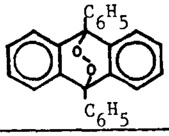
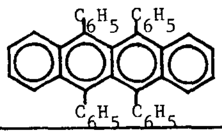
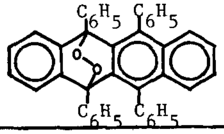
FIG.1.- OXYGENATION APPARATUS

For example, problems of sensitizer bleaching and reactant or product photolysis associated with some photooxygenations are eliminated. The need for strongly basic solutions as in the NaOCl-H_2O_2 (10) and Br_2-alkaline H_2O_2 (11) methods is eliminated. Extreme temperatures are not required with the present system as in the 9,10-diphenylanthracene peroxide decomposition method (80°)(12) and the triphenylphosphite-ozone complex decomposition method (-78°)(13); the reaction may be run at any desired temperature (room temperature in our work).

The workup involved in the solid phase method consists of elution of the product(s) from the support, concentration, and direct recrystallization, or if more than one product is present, chromatography. Aqueous workup (NaOCl-H_2O_2 method) and removal of sensitizers (photooxidation) or side products (9,10-diphenylanthracene peroxide and triphenylphosphite-ozone complex methods) are unnecessary.

Finally, and perhaps most importantly, problems of substrate solubility are eliminated in the present method since any organic molecule may adsorbed on the surface of microcrystalline cellulose or silica gel.

Table I - Oxygenation Results

Substrate	Product	Yield	Reference
		33%^{a,c}	(5)
		76%^{a} 86%^{b}	(6)
		91%^{a}	(7)
		79%^{a} 60%^{b}	(8)
		73%^{a}	(9)

(a) microcrystalline cellulose adsorbent (b) silica gel adsorbent
(c) isolated as the alcohol

On the other hand, the solid phase method requires reduced pressure which necessitates the use of acceptors which are relatively non-volatile. In addition, a more complex apparatus is necessary in the present case, although once it is assembled, the oxygenations are routine (14).

The apparatus of Figure 1 may also be used to bring about the oxygenations of organic molecules in solution, a finding which supports the observations of Corey and Taylor (15). The oxygenations were carried out at -78° in toluene solution and gave the following results: tetracyclone to *cis*-dibenzoylstilbene (76%), 1,3-diphenylisobenzofuran to *o*-dibenzoylbenzene (82%), 9,10-diphenylanthracene to 9,10-diphenylanthracene peroxide (64%), and tetramethylethylene to 2,3-dimethyl-3-hydroperoxy-1-butene, isolated as the alcohol, (14%) (16). The solid phase method is to be preferred over the solution method since the latter was complicated by appreciable solvent evaporation at the pressures employed. The conditions for the solid phase oxygenations have not been optimized. Quenching studies (17) have shown that microcrystalline cellulose should be a better support than silica gel since the latter quenches $^1\Delta_g$ oxygen much more efficiently than the former. Despite this, no real differences could be detected between the two supports on the basis of overall yield or length of oxygenation. Studies are in progress to determine the effect that changing other variables has on the efficiency of oxygenation.

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