On the Mechanism of Peracid Oxidation of α-Diketones to Acid Anhydrides: An ^{17}O and ^{18}O Isotope Study

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Peracid oxidation of ^{17}O or ^{18}O isotopically labelled benzil gave rise to benzoic acid anhydride in which both the bridging oxygen and the carbonyl oxygen were enriched as judged by ^{17}O and ^{13}C n.m.r. spectroscopy and mass spectrometry; these observations are inconsistent with a simple Baeyer–Villiger-type oxidation mechanism.

It is known that α-diketones, such as benzil, are oxidised by peracids or hydrogen peroxide to the corresponding acid anhydrides or their cleavage products in good yield depending on the conditions of the reaction.[1—4] This reaction is related to the Baeyer–Villiger reaction in which formally an acyl group migrates and as such it is perhaps surprising that there is no formation of an α-ketoester that would arise from competing alkyl or aryl migration. Several studies on the mechanism of this reaction have reached conflicting conclusions.[2,3] We report here a definitive study in which the origin of the inserted oxygen in the acid anhydride on peracid oxidation is directly and unambiguously identified by ^{17}O n.m.r. spectroscopy amongst other techniques.

[^{17}O] and [^{18}O]Benzil were readily prepared by acid catalysed exchange of benzil with the appropriately labelled water in dry dioxane. Rapid, smooth oxidation to benzoic anhydride occurred with *m*-chloroperbenzoic acid (*m*CPBA) in dichloromethane over anhydrous sodium hydrogen carbonate. The product from the oxidation of [^{17}O]benzil was isolated and the ^{17}O n.m.r. spectrum was recorded (Bruker AM-500, $CHCl_3$, 307 K). Two resonances at 235 p.p.m. (linewidth at half height 750 Hz) and 382 p.p.m. (linewidth at half height 1000 Hz) (reference D_2O) were detected corresponding to enrichment of the bridging oxygen and the carbonyl oxygen respectively as determined from the natural abundance ^{17}O n.m.r. spectrum of authentic benzoic anhydride, and comparison with literature values.[5] ^{13}C N.m.r.

Table 1. Mass spectral data and predicted ^{18}O content.

		Predicted/%		
m/z	Observed/%	Epoxide mechanism	Baeyer–Villiger mechanism	Intra-molecular exchange
150 PhC(^{16}O)OEt	57 ± 2	56	12	34
152 PhC(^{18}O)OEt	43 ± 2	44	88	66

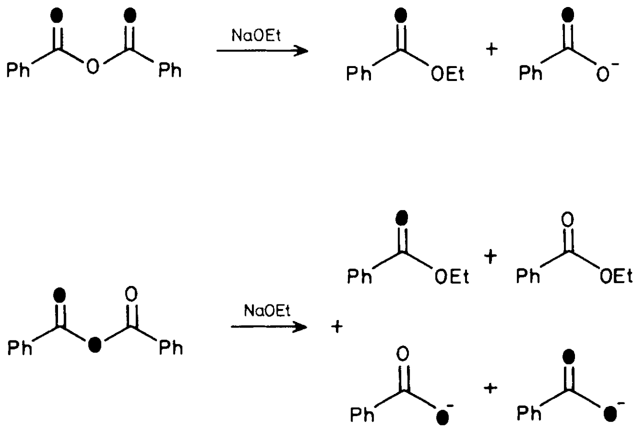
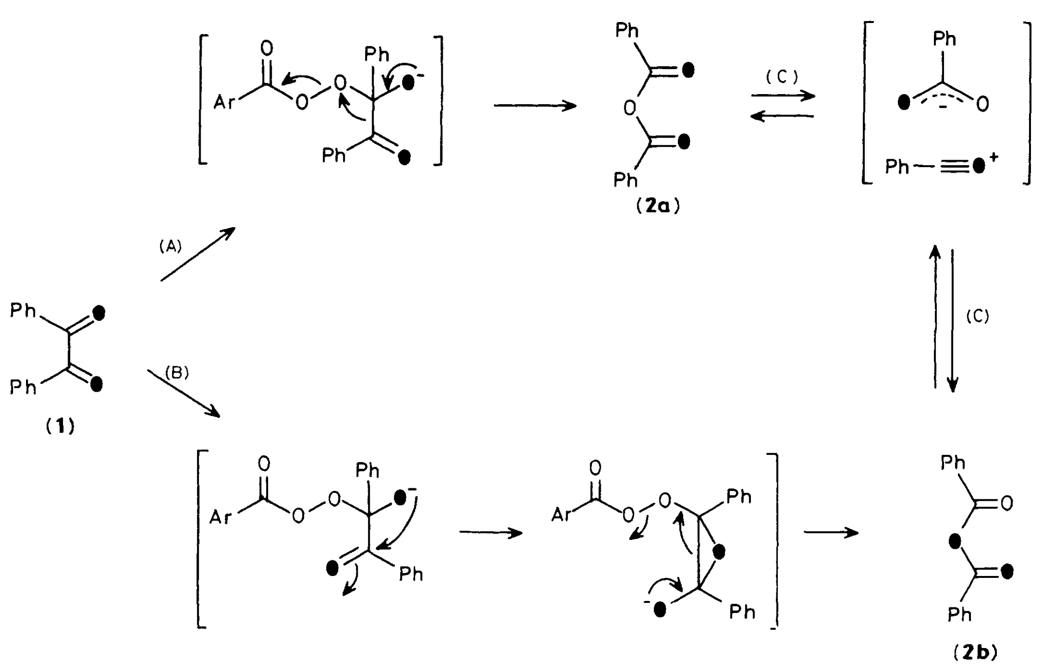


Figure 1. ● = isotopic labelling.



Scheme 1

spectroscopy (Bruker AM-500, $CDCl_3$) of the anhydride derived from *m*CPBA oxidation of [^{18}O]benzil revealed a major resonance at 157 p.p.m. corresponding to the carbonyl carbon and in addition two smaller upfield shifted resonances ($\Delta\delta$ 0.008 and $\Delta\delta$ 0.037 p.p.m.) corresponding to an isotopic shift from an isotope in a single or in a double bond,[6] *i.e.* the bridging and non-bridging positions.

Finally, cleavage of the ^{18}O-labelled anhydride with sodium ethoxide gave ethyl benzoate and sodium benzoate. The isotopic content in the isolated ethyl benzoate was determined by mass spectrometry and depends upon the initial ^{18}O distribution in the anhydride as shown, Figure 1. Results consistent with ^{18}O in the bridging position were obtained.

The mechanistic alternatives are outlined in Scheme 1. The simple Baeyer–Villiger mechanism with acyl group migration, pathway (A), would lead to isotope only in the carbonyl groups of the anhydride (**2a**). The 'epoxide' mechanism, pathway (B), would give rise to isotope in the bridge and one of the carbonyl groups (**2b**). A mixture of these two labelling patterns would arise if the oxidation occurred *via* either pathway followed by a subsequent intramolecular exchange pathway such as (C) and if occurring this would effectively prevent any deductions concerning the initial oxidation mechanism. Finally, intermolecular exchange would give rise to total scrambling of the isotope and would be evident from the triply labelled benzoic anhydride that would arise.

The unambiguous demonstration by ^{17}O n.m.r. spectroscopy that one of the carbonyl oxygens of benzil ends up in the bridging position in the anhydride effectively excludes the simple Baeyer–Villiger oxidation mechanism. However, a Baeyer–Villiger oxidation mechanism coupled with some inter- or intra-molecular exchange would allow isotope to scramble into the bridge. An initial control experiment in which labelled benzoic acid ($PhC^{18}O_2H$; 0.5 mole equiv.) was stirred with unlabelled benzoic anhydride (0.4 M) under the conditions used for the benzil oxidation, had shown that intermolecular exchange occurs over extended reaction times. Small amounts of labelled anhydride could be detected by mass spectrometry after *ca.* 3 h and almost complete scrambling had occurred after 24 h. Oxidation of unlabelled benzil with *m*CPBA in the presence of added [^{18}O]benzoic acid (0.5 mole equiv.), after 20 min gave benzoic anhydride with no incorporation of isotope as judged from the mass spectrum. These oxidation conditions were used in the mechanistic studies, such that adventitious benzoate *i.e.* intermolecular exchange, could not lead to scrambling of the isotope in the oxidation reactions. This was further confirmed by the complete absence of triply labelled benzoic anhydride (no $M + 6$ peak in the mass spectrum) on oxidation of [^{18}O]benzil.

Based on the known isotopic content of the [^{18}O]benzil determined from the mass spectrum, the predicted content of the ethyl benzoate obtained following *m*CPBA oxidation and cleavage with sodium ethoxide can be calculated on the basis of the various mechanisms shown in Scheme 1 and Table 1. Clearly there is a close correspondence between the observed isotopic labelling and that predicted on the basis of the 'epoxide' mechanism. The Baeyer–Villiger type mechanism followed by intramolecular exchange can thus be excluded. The data are clearly in support of an 'epoxide' mechanism for the peracid oxidation of α-diketones,[1] in contrast to the simple Baeyer–Villiger type pathway when hydrogen peroxide is used in place of the peracid.[2]

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References

1 H. Kwart and N. J. Wegemer, *J. Am. Chem. Soc.*, 1961, **83**, 2746.
2 Y. Sawaki and C. S. Foote, *J. Am. Chem. Soc.*, 1979, **101**, 6292.
3 J. E. Leffler, *J. Org. Chem.*, 1951, **16**, 1785.
4 C. H. Hassall, *Org. React.*, 1957, **9**, 73.
5 C. P. Cheng, S. C. Lin and G.-S. Shaw, *J. Magn. Reson.*, 1986, **69**, 58.
6 J. M. Risley and R. L. Van Etten, *J. Am. Chem. Soc.*, 1980, **102**, 4609 and 6699.