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OXYGENATION OF TOLUENE WITH BENZOYL PEROXIDE-CUPRIC CHLORIDE IN ACETONITRILE

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Since the discovery that benzoyl peroxide is capable of phenylating aromatic substrates (free radical process), this reagent has been used extensively as a source of phenyl radicals(1,2). Benzoyloxylation was recognized as a competing reaction of varying importance depending on the activity of the aromatic substrate. For example, oxygenation took place to an appreciable extent with reactive aromatics(1), such as polynuclears(3) and aromatic ethers(4), whereas this constituted a negligible pathway in the case of less active types(1,2,5). We wish at this time to report some preliminary results concerning the more effective use of benzoyl peroxide as an oxygenating agent with an aromatic nucleus of diminished activity.

Tolyl benzoates (o:m:p = 56:18:26) were formed in 38% yield in a system consisting of benzoyl peroxide, cupric chloride, and toluene in acetonitrile solvent. The reaction was carried out for 19-26 hr. at 60° with a toluene:peroxide:catalyst ratio of 16-17:1:0.3-0.5 in the presence of a small amount (0.02 molar ratio) of cuprous chloride. In addition to the benzoate product, benzoic acid and carbon dioxide were generated together with materials arising from the intermediacy of phenyl radicals: benzene, chlorobenzene, small amounts of phenyltoluenes, benzyl chloride and an unidentified substance. The overall material balance based on the phenyl group was 96%, while

99% of the CO_2 residues was accounted for. A control experiment involving thermal homolysis of the peroxide under similar conditions resulted in minor decomposition (16%) of the peroxide with only trace quantities of ester being formed. Furthermore, the following observations apply: (a) the yield and isomer distribution of the benzoate esters remained essentially constant with variance in the catalyst:peroxide ratio over the range, 0.3-1, with less of this route being followed at lower ratios; (b) copper halides produced an acceleration in reaction rate; (c) substitution of cuprous chloride for cupric chloride also resulted in oxygenation, but to a lesser extent (15%).

The indicated scheme is consistent with these observations.

$$Cu^{I} + (C_6H_5CO_2)_2 \longrightarrow Cu^{II}O_2CC_6H_5 + C_6H_5CO_2\cdot \qquad (1)$$

$$C_6H_5CO_2\cdot + ArH + Cu^{II}O_2CC_6H_5 \longrightarrow ArO_2CC_6H_5 + C_6H_5CO_2H + Cu^{I} \qquad (2)$$

Induced decomposition of benzoyl peroxide by cuprous salts is known to occur(6,7). The second step is believed to entail oxidation of the oxy radical to an oxonium ion species which then effects electrophilic substitution. This can be represented in a grossly oversimplified form by eq. 3.

$$C_6H_5CO_2\cdot + Cu^{II} \longrightarrow C_6H_5CO_2^{+} + Cu^{I} \qquad (3)$$

The orientation of the tolyl benzoates is characteristic of electrophilic substitution by a species of appreciable activity. However, caution must be applied in interpretation of the isomer distribution, since oxy radicals are known to be quite electrophilic(8). Cuprous ion regenerated in eq. 2 can function as the chain carrier.

An alternative pathway, consisting of reversible attack on the aromatic by a benzoyloxy radical with subsequent oxidation of the resulting complex by cupric ion (eq. 4) should also be considered.

$$C_6H_5CO_2\cdot + ArH \rightleftharpoons C_6H_5CO_2ArH\cdot \xrightarrow{Cu^{II}} C_6H_5CO_2Ar + H^+ + Cu^I \quad (4)$$

Homolytic substitution by hydroxyl radicals is now known to involve initial addition to the nucleus rather than abstraction of hydrogen(9,10). On the basis of a deuterium isotope effect in cyclization of the 2-phenylbenzoyloxy radical to benzcoumarin, Denney and Klemchuk(11) postulated a reversible addition of the oxy radical to the aromatic ring. Oxidation of intermediate cyclohexadienyl radicals as shown in eq. 4 has ample literature analogy(9,12). It should be emphasized that at this stage the theoretical interpretations are to be regarded as tentative.

Previous investigators have studied related systems containing benzoyl peroxide and copper salts. Thus, this combination was found to react with olefins leading to formation of alkenyl benzoates(6,7). The process presumably can be described as an addition of benzoyloxy radical to the double bond followed by oxidation of the ensuant carbon radical(6). Although these reactions were carried out in some instances in aromatic solvents, the presence of reactive olefinic substrates and use of cuprous salts in low concentration apparently precluded the occurrence of aromatic benzoyloxylation.

Preliminary investigations(13) point to an element of specificity regarding the peroxide, catalyst, and other variables in the oxygenation reaction. In this regard related studies involving aromatic oxygenation with dialkyl peroxydicarbonates in acetonitrile in the presence of cupric halides or ferric chloride have been carried out(13). Diisopropyl peroxydicarbonate-cupric chloride provided tolyl isopropyl carbonates in 92% yield from toluene. The lower yield of aryl ester from benzoyl peroxide is perhaps a reflection of the greater instability of the benzoyloxy radical compared to the analogous isopropoxycarboxy species.

Further studies concerning the scope and mechanistic elucidation of this intriguing reaction are underway.

References

1. G. H. Williams, "Homolytic Aromatic Substitution," Pergamon Press, New York, N. Y., 1960.
2. G. B. Gill and G. H. Williams, *J. Chem. Soc.*, 7127 (1965) and references cited therein.
3. M. Mingin and K. H. Pausacker, *Aus. J. Chem.*, **18**, 831 (1965).
4. B. M. Lynch and R. B. Moore, *Can. J. Chem.*, **40**, 1461 (1962).
5. M. Mingin and K. H. Pausacker, *Aus. J. Chem.*, **18**, 821 (1965).
6. J. K. Kochi, *J. Am. Chem. Soc.*, **84**, 1572 (1962).
7. M. Kharasch and A. Fono, *J. Org. Chem.*, **24**, 606 (1959).
8. A. J. Davidson and R. O. C. Norman, *J. Chem. Soc.*, 5404 (1964).
9. J. R. Lindsay Smith and R. O. C. Norman, *J. Chem. Soc.*, 2897 (1963).
10. R. W. Matthews and D. F. Sangster, *J. Phys. Chem.*, **69**, 1938 (1965).
11. D. B. Denney and P. P. Klemchuk, *J. Am. Chem. Soc.*, **80**, 3289 (1958).
12. E. L. Eliel, J. G. Saha, and S. Meyerson, *J. Org. Chem.*, **30**, 2451 (1965); M. Eberhardt and E. L. Eliel, *ibid.*, **27**, 2289 (1962); S. C. Dickerman and G. B. Vermont, *J. Am. Chem. Soc.*, **84**, 4150 (1962); J. K. Kochi and R. D. Gilliom, *ibid.*, **86**, 5251 (1964).
13. P. Kovacic and M. E. Kurz, unpublished work.