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Communication

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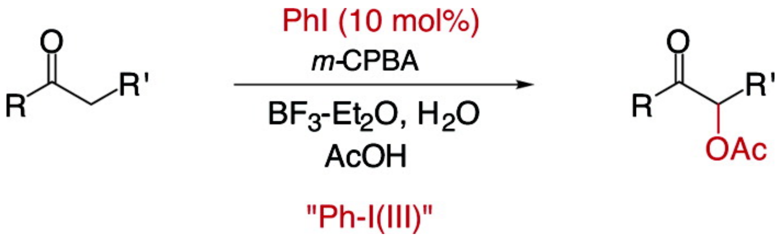

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COMMUNICATIONS

Iodobenzene-Catalyzed α-Acetoxylation of Ketones. In Situ Generation of Hypervalent (Diacyloxyiodo)benzenes Using *m*-Chloroperbenzoic Acid

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Hypervalent aryl-λ^3-iodanes (ArILL′) with two heteroatom ligands on iodine(III) undergo oxidation of a broad range of diverse functional groups.[1] In the oxidation, these heteroatom ligands serve as leaving groups in both the ligand exchange step on iodine(III) and the reductive elimination process of λ^3-iodanyl groups.[1c] Introduction of oxygen functionalities to α-carbons of carbonyl compounds by aryl-λ^3-iodanes has been extensively investigated by the Moriarty and Koser groups and has broad synthetic utility.[2,3] Facile reduction of iodine(III) to univalent iodide in the reductive elimination step constitutes a driving force for the oxidation. Stoichiometric amounts of λ^3-iodanes are required in the oxidation, and hence, the reaction produces equimolecular amounts of aryl iodides as a waste. It occurred to us that if an aryl iodide is reoxidized to a hypervalent aryl-λ^3-iodane under these conditions, the oxidation needs only a catalytic amount of the expensive aryl-λ^3-iodane or aryl iodide (Scheme 1). Such a catalytic cycle has never been realized except for electrochemical oxidations.[4] We report herein for the first time a catalytic α-oxidation of ketones in which diacyloxy(phenyl)-λ^3-iodanes act as real oxidants of ketones and *m*-chloroperbenzoic acid (*m*-CPBA) serves as a terminal oxidant.

Alkyl iodides are smoothly oxidized by *m*-CPBA at room temperature, yielding alcohols and/or their derivatives or olefins, depending upon the conditions and the substrate structures, in which initial formation of labile alkyl-λ^3-iodanes is involved.[5] *m*-CPBA (4 equiv) also oxidizes iodobenzene in methanol and affords a λ^5-iodane, iodoxybenzene,[5d] suggesting the possible use of *m*-CPBA as a terminal oxidant in the catalytic α-oxidation of carbonyl compounds.

Exposure of acetophenone to dried *m*-CPBA[6] (1.4 equiv) in acetic acid in the presence of a catalytic amount (10 mol %) of iodobenzene, $BF_3{\cdot}Et_2O$ (3 equiv), and water (5 equiv) at room temperature under argon afforded α-acetoxyacetophenone in 84% yield (Table 1, entry 4). It is noted that addition of water is crucial to the success of α-acetoxylation of acetophenone (entries 1−8); in the absence of water, the α-oxidation was almost inhibited with 95% of the recovered ketone. Larger amounts (7−10 equiv) of added water also led to a decreased yield (ca. 50%) of the product. Use of (diacetoxyiodo)benzene (10 mol %), instead of iodobenzene, in the presence of water (5 equiv) resulted in a high yield of the α-oxidation (entry 9).

Use of 5 mol % of iodobenzene gave a slightly decreased yield (75%) of the α-acetoxy ketone. Iodobenzene is indispensable for this catalytic oxidation: thus, no formation of α-acetoxyacetophenone was observed when the reaction was carried out in the absence of iodobenzene (entry 13). In this reaction, however, Baeyer−Villiger oxidation took place, yielding phenyl acetate in 38% yield.[7]

$BF_3{\cdot}Et_2O$ is also essential for this direct α-oxidation of acetophenone. Although the oxidation of iodobenzene to (diacyloxyiodo)benzenes with *m*-CPBA rapidly proceeds in acetic acid at room temperature without using the Lewis acid (Figure S1), α-acetoxylation of acetophenone did not take place at all in the absence of $BF_3{\cdot}Et_2O$ (Table S1, entry 1). Addition of $BF_3{\cdot}Et_2O$ seems to be essential to induce the enolization of acetophenone, and only the resulting enol will react with (diacyloxyiodo)benzenes generated in situ;[3] in fact, no enolization was observed in the absence of $BF_3{\cdot}Et_2O$ (Scheme S1 and Figure S2). Use of other acids such as $Yb(OTf)_3$, CF_3SO_3H, and $HBF_4{\cdot}Me_2O$ afforded a moderate yield (ca. 40%) of α-acetoxyacetophenone (Table S1).

Scheme 1

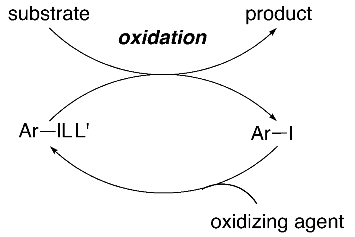

Table 1. Effects of Water and Iodobenzene on α-Acetoxylation of Acetophenone[a]

entry	amt of PhI (equiv)	amt of H_2O (equiv)	yield (%)[b]	entry	amt of PhI (equiv)	amt of H_2O (equiv)	yield (%)[b]
1	0.1	0	5	8	0.1	10	49
2	0.1	3	35	9	0.1[c]	5	86
3	0.1	4	61	10	1	5	83
4	0.1	5	84	11	0.2	5	83
5	0.1	6	73	12	0.05	5	75
6	0.1	7	55	13		5	0[d]
7	0.1	8	55				

[a] Reaction conditions: acetophenone (0.25 M) in acetic acid, *m*-CPBA (1.4 equiv), and $BF_3{\cdot}Et_2O$ (3 equiv) at 25−30 °C for 24 h under argon. [b] GC yields. [c] Instead of PhI, (diacetoxyiodo)benzene was used. [d] Phenyl acetate (38%) was obtained.

Both *p*-methyl- and *p*-chloroiodobenzene also serve as efficient catalysts for this direct oxidation, and use of 10 mol % of these iodoarenes afforded α-acetoxyacetophenone in more than 80% yields under similar conditions (Table S2). Introduction of powerful electron-withdrawing (*p*-NO_2) and electron-donating substituents (*p*-MeO), however, decreased the catalytic efficiency of iodoarenes.

A variety of dialkyl and alkyl aryl ketones are smoothly oxidized at the α-positions under our catalytic conditions and afford α-acetoxy ketones in good yields (Table 2). Substituted acetophenones with halogens (F, Cl, Br, and I) at the para position gave comparable results, indicating the high selectivity for oxidation of iodobenzene by *m*-CPBA over *p*-iodoacetophenone (entries 4−7). This oxidation can be extended to α-acetoxylation of *β*-keto ester (entry 11).

In the case of unsymmetrical ketones, oxidation of a methylene group of linear alkyl chains is favored over that of a methyl group (entry 12).[2d,8] Entries 13 and 14 indicate that the reactivity of

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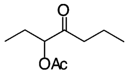
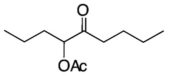
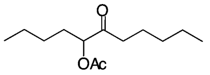
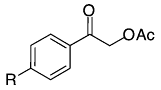
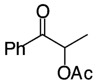
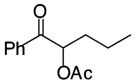
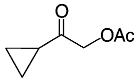
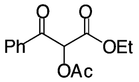
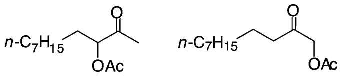
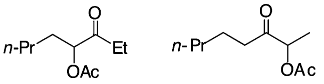
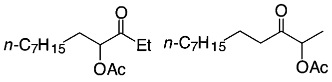
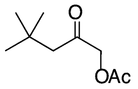
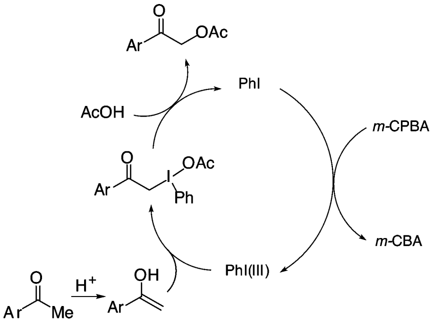
Table 2. Catalytic α-Acetoxylation of Ketones with *m*-CPBA[a]

entry	product	yield (%)[b]
1		46 (79)
2		50 (73)
3		58 (65)
		
4	R = F	55 (76)
5	Cl	59 (72)
6	Br	52 (76)[c]
7	I	50 (67)[d]
8		58 (84)[e]
9		53 (78)[e]
10		43 (71)[d]
11		49[d]
12	 (62 : 38)	46 (64)
13	 (41 : 59)	46 (63)
14	 (36 : 64)	59
15		63[d]

[a] Reaction conditions: ketone (0.25 M) in acetic acid, *m*-CPBA (2 equiv), PhI (0.1 equiv), H_2O (5 equiv), and $BF_3\cdot Et_2O$ (3 equiv) at 25−30 °C for 20−48 h under argon. [b] Isolated yields. Parentheses are GC yields. [c] H_2O (3 equiv). [d] PhI (0.3 equiv). [e] *m*-CPBA (1.4 equiv) and PhI (0.3 equiv).

Scheme 2



α-methylene groups toward acetoxylation decreases in the order ethyl > pentyl > nonyl. This tendency is in good agreement with the preferred direction for the reported acid-catalyzed enolization of unsymmetrical ketones.[9] Steric effects appear to be significant in the oxidation of 4,4-dimethyl-2-pentanone, in which the methylene group that is flanked by a *tert*-butyl group is less reactive than the methyl group (entry 15).[10]

A catalytic cycle for this oxidation is shown in Scheme 2. $BF_3\cdot Et_2O$ accelerates oxidation of iodobenzene to (diacyloxyiodo)benzenes by *m*-CPBA, being completed within 10 min under our conditions. Because of the facile ligand exchange on iodine(III),[1c] $PhI(OAc)_2$ is produced as a major λ^3-iodane in the reaction, along with the formation of small amounts of $PhI(OCOAr)_2$ and PhI(OAc)OCOAr (Ar = *m*-ClC_6H_4).[11] Ligand exchange of a (diacyloxyiodo)benzene with an enol derived from a ketone through the formation of tetracoordinated iodate[1c] produces an α-λ^3-iodanyl ketone, which on S_N2 displacement by acetic acid affords an α-acetoxy ketone with liberation of PhI.[12] The effect of added water in this catalytic oxidation is interesting; however, we found that the presence of water slows down the rate of enolization of acetophenone (Figure S2) as well as slightly decreases the rate of oxidation of iodobenzene by *m*-CPBA to λ^3-iodanes (Figure S3).

In summary, we have developed an efficient method for catalytic α-oxidation of ketones. The method involves in situ generation of hypervalent phenyl-λ^3-iodanes by the oxidation of a catalytic amount of iodobenzene with *m*-CPBA.

Supporting Information Available: Text giving experimental details, Scheme S1, Figures S1−S4, and Tables S1 and S2. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) A mixture of equal amounts of $PhI(OAc)_2$ and $PhI(OCOAr)_2$ (Ar = *m*-ClC_6H_4) in $CDCl_3$ at 22 °C reaches equilibrium within 1 h via ligand exchange, yielding a statistical 1:2:1 mixture of $PhI(OAc)_2$, PhI(OAc)OCOAr, and $PhI(OCOAr)_2$ (Figure S4).
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