Mild Carbon–Carbon Bond Cleavage of Carbonyl Compounds using Pentafluoroiodobenzene Bis(trifluoroacetate)

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Acetophenones, α-hydroxyacetophenones, deoxybenzoin, benzoin, and benzil are cleaved oxidatively with pentafluoroiodobenzene bis-(trifluoroacetate) in wet benzene at room temperature to give the corresponding benzoic acids; cyclohexanone and dimedone are cleaved to give the diacids adipic acid and 3,3-dimethylglutaric acid, respectively.

There has been a renewed interest in organohypervalent iodine reagents as oxidants in organic synthesis recently.[1] One of the earliest studies of the oxidative capabilities of iodobenzene diacetate was carried out by Criegee and Beuker who compared this reagent with $Pb(OAc)_4$.[2] They recognized an important fact, namely, in contrast with other oxidants in organic chemistry, the reactivity of $ArI(OAc)_2$ could be regulated by varying the substituents on the aryl group.† The pentafluorophenyl group as in pentafluoroiodobenzene bis-(trifluoroacetate) exerts a strong accelerating effect upon the oxidizing capability of this hypervalent iodine oxidant and we report now a novel application, namely, high yield carbon–carbon bond cleavage in carbonyl compounds. This process is formally related to the earlier work[2] because cleavage occurs ultimately at a vicinal diol stage.

Treatment of acetophenones (**1a—d**) with pentafluoroiodobenzene bis(trifluoroacetate)[3] in wet benzene afforded the corresponding benzoic acids (**2**)‡ (entries 1—4, Table 1) in the isolated yields indicated. The balance of material was the starting acetophenone which could be recycled for optimization of the total yield. That these cleavage reactions proceed

$$\underset{(1)}{ArCOR} \qquad \underset{(2)}{ArCO_2H} \qquad \underset{(3),\,(4)}{ArC(OSiMe_3)=CH_2}$$

via the α-hydroxyketone was demonstrated by separate oxidation of α-hydroxy-*p*-nitroacetophenone (**1e**) with $C_6F_5I(OCOCF_3)_3$ to yield *p*-nitrobenzoic acid (entry 7, Table 1). The cleavage reaction proceeds similarly with trimethylsilyl enol ethers of acetophenone, (**3**) and (**4**) and $C_6F_5I(OCOCF_3)_2$ (entries 5 and 6, Table 1). In contrast, the reaction does not proceed with either acetophenone or acetophenone trimethylsilyl enol ether and iodobenzene diacetate in wet benzene under standard conditions.

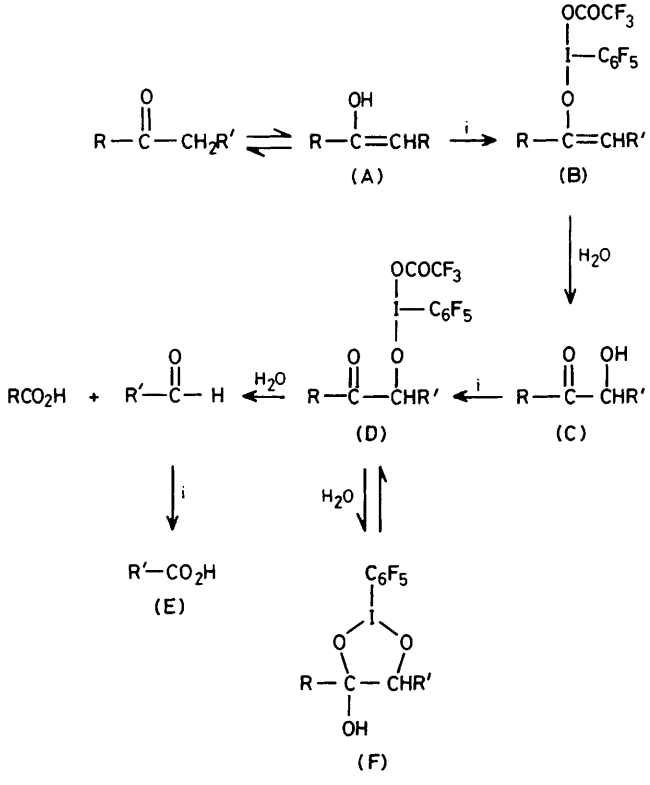
† Criegee and Beuker (ref. 2) observed large differences in the oxidizing capabilities of $p\text{-}NO_2C_6H_4I(OAc)_2$ relative to $p\text{-}MeC_6H_4I(OAc)_2$ depending upon the specific reaction. In glycol cleavage electron-withdrawing groups on the ring facilitate the reaction which could be due to rate-limiting ligand exchange. In direct oxidation of double bonds, electron-donating groups are rate-accelerating possibly owing to the intermediacy of the electrophile $ArI^{+}OAc$.

‡ In a typical experiment, substrate (0.01 mol) was dissolved in benzene (25 ml) and water (2—5 drops) was added. Pentafluoroiodobenzene bis(trifluoroacetate) (0.01—0.03 mol) was added with stirring to the above reaction mixture and stirring was continued overnight at room temperature. The reaction mixture was extracted with aqueous sodium bicarbonate solution, neutralized with dilute hydrochloric acid and again extracted with diethyl ether. Concentration of the diethyl ether layer *in vacuo* afforded the crude products. Pure products were obtained by crystallization.

Table 1. Results of the oxidative cleavage of carbonyl compounds.

	Substrate							
Entry	Compound no.	Ar	R	Reagent[a]	Products (2)	% Yield[b]	M.p. (lit. m.p.)[c]/°C	
1	(1a)	Ph	Me	i (2 equiv.)	$PhCO_2H$	51	123—124	(122—123)
2	(1b)	*p*-ClC_6H_4	Me	i (2 equiv.)	*p*-$ClC_6H_4CO_2H$	54	239—240	(239—241)
3	(1c)	*p*-FC_6H_4	Me	i (2 equiv.)	*p*-$FC_6H_4CO_2H$	56	181—182	(182—184)
4	(1d)	*p*-$NO_2C_6H_4$	Me	i (2 equiv.)	*p*-$NO_2C_6H_4CO_2H$	56	239—240	(239—241)
5	(3)	*p*-ClC_6H_4	—	i (2 equiv.)	*p*-$ClC_6H_4CO_2H$	61	239—240	(239—241)
6	(4)	*p*-$NO_2C_6H_4$	—	i (2 equiv.)	*p*-$NO_2C_6H_4CO_2H$	65	239—241	(239—241)
7	(1e)	*p*-$NO_2C_6H_4$	CH_2OH	i (2 equiv.)	*p*-$NO_2C_6H_4CO_2H$	90	239—240	(239—241)
8	(1f)	Ph	CH_2Ph	i (3 equiv.)	$PhCO_2H$	91	123—124	(122—123)
9	(1g)	Ph	CH(OH)Ph	i (2 equiv.)	$PhCO_2H$	94	122—124	(122—123)
10	(1h)	Ph	H	i (1 equiv.)	$PhCO_2H$	95	120—122	(122—123)
11	(1i)	Ph	COPh	i (3 equiv.)	$PhCO_2H$	96	123—124	(122—123)
12	(1j)	$-[CH_2]_5-$		i (3 equiv.)	$HO_2C[CH_2]_4CO_2H$	42	149—151	(152—154)
13	(1k)	$-CH_2C(Me)_2CH_2COCH_2-$		i (3 equiv.)	$HO_2CCH_2C(Me)_2$-CH_2CO_2H	50	102—103	(100—102)

[a] i, $C_6F_5I(OCOCF_3)_2$–C_6H_6–H_2O. [b] Isolated yield by direct crystallization. ^1H N.m.r. analysis of balance of product indicated unchanged starting material in all cases. [c] Lit. values are m.p.s of the commercially available compounds from Aldrich.



Scheme 1. i, $C_6F_5I(OCOCF_3)_2$.

The conversion of deoxybenzoin (**1f**) into benzoic acid was like-wise observed (entry 8, Table 1). In this reaction, we may consider first the α-hydroxylation of (**1f**) to give benzoin (**1g**), and then cleavage of (**1g**) to give benzaldehyde (**1h**) which finally is oxidized to give benzoic acid. In order to confirm the course of this reaction, (**1g**) and (**1h**) were treated separately under the same conditions with 2 and 1 mole of $C_6F_5I(OCOF_3)_2$, respectively (entries 9 and 10, Table 1). The final product obtained in each case was benzoic acid. When this reaction was applied to benzil (**1i**) with 3 moles of $C_6F_5I(OCOCF)_2$, benzoic acid was obtained (entry 11, Table 1).

Finally, this reaction was extended to cyclohexanone (**1j**) and dimedone (**1k**). Cyclohexanone (**1j**) on treatment with 3 moles of $C_6F_5I(OCOCF_3)$ in wet benzene afforded adipic acid (entry 12, Table 1). Similarly dimedone (**1k**) gives 3,3-dimethylglutaric acid (entry 13, Table 1).

Scheme 1 presents a possible mechanistic pathway for the above reactions. The mechanism includes ligand exchange between $C_6F_5I(OCOCF_3)_2$ and the enol of trimethylsilyl enol, (A) → (B). This intermediate is represented as a T-shape molecule at iodine with the most electronegative substituents diaxial. Addition of H_2O with reductive elimination of C_6F_5I yields the α-hydroxyketone, (B) → (C), which undergoes ligand exchange with a second molecule of $C_6F_5I(OCOCF_3)_2$. Addition of H_2O leads to either C–C cleavage, (C) → (D) → (E), or formation of an α-diketone as in the case of benzil (**1i**). The intramolecular counterpart of this mechanism may be applied to the cyclic ketones cyclohexanone and dimedone. Oxidation of –CHO to $-CO_2H$ is the final step. It is entirely possible that cyclic structures may intervene, (D) → (F), as has been proposed in periodic acid oxidation of vicinal diols.[4] Our results do not require their intermediacy.

In summary this work represents a valuable degradative reaction for ketones, aldehydes, α-diketones,[5] β-diketones,[5] and precursors which may be transformed under the reaction conditions to these types of molecules.[6]

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