Oxidative Assistance in the Conversion of α-Iodoketones to α-Ketols

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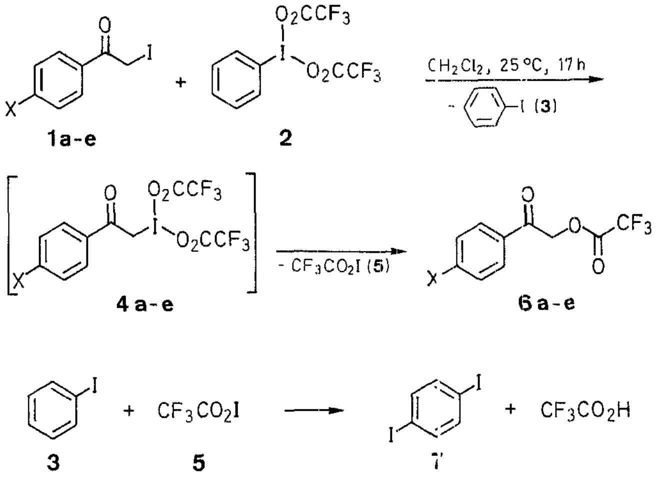
Treatment with bis(trifluoroacetoxy)iodobenzene (**2**) followed by hydrolysis converted five phenacyl iodides **1a–e** to phenacyl alcohols **8a–d**, **9** but failed to convert *exo*-3-iodonorbornan-2-one (**10**) and 2-iodocyclohexanone (**11**) to α-ketols. Iodinations by proposed intermediate trifluoroacetoxy iodide (**5**) were assumed to explain the formation of *p*-diiodobenzene (**7**) and 2-hydroxy-1-(3′-iodo-4′-methoxyphenyl) ethanone (**9**).

Oxidatively assisted nucleophilic substitution of alkyl iodides offered a new technique for the replacement of iodine with acetate, or other halo, or hydroxy groups.[1] An unsuccessful attempt to obtain an α-hydroxyester from a 2-iodo-3-phenylpropanoate by treatment with *m*-chloroperbenzoic acid in a mixture of *tert*-butyl alcohol and water revealed resistance by an α-iodocarbonyl derivative to an oxidatively assisted conversion.[2] We have now investigated five phenacyl iodides **1a–e** (2-iodo-1-phenylethanones), *exo*-3-iodonorbornan-2-one (**10**), and 2-iodocyclohexanone (**11**) in reactions with bis(trifluoroacetoxy)iodobenzene (**2**) under mild neutral conditions.

On treatment with bis(trifluoroacetoxy)iodobenzene (**2**), phenacyl iodide (**1a**) was initially converted to phenacyl trifluoroacetate (**6a**) detected by NMR in a mixture with iodobenzene, 1,4-diiodobenzene (**7**), and phenacyl alcohol (**8a**). Chromatographic separation of the mixture from a column of silica gel by a mixture of methanol and dichloromethane completed the conversion of the ester **6a** to the alcohol **8a**, and permitted the isolation of the diiodide **7**.[3] In conformity with similar reactions from other alkyl iodides,[1,3] it is proposed that the overall exchange of an iodo with a trifluoroacetoxy group occurred via a ligand transfer from bis(trifluoroacetoxy)iodobenzene (**2**) to give iodobenzene and α-[bis(trifluoroacetoxy)iodo]acetophenone (**4a**),[1,3–6] and that dissociation of the latter gave phenacyl trifluoroacetate (**6a**) and trifluoroacetoxy iodide (**5**). The latter compound, a positive iodine reagent, was not detected, but was assumed to bring about the conversion of iodobenzene (released from its ditrifluoroacetate derivative) to 1,4-diiodobenzene (**7**). The *p*-nitro, *p*-chloro, *p*-methyl, and *p*-methoxy derivatives **1b–e** of phenacyl iodide gave similar reactions (Table).

The competitive coformation of *p*-diiodobenzene (**7**) was nearly eliminated in the conversion of *p*-methoxyphenacyl iodide (**1e**) to 2-hydroxy-1-(3′-iodo-4′-methoxyphenyl)ethanone (**9**). Presumably trifluoroacetoxy iodide (**5**) or an equivalent intermediate iodinated one or more of the *p*-methoxyphenyl derivatives



1, 4, 6, 8	X	1, 4, 6, 8	X
a	H	**d**	CH_3
b	Cl	**e**	OCH_3
c	NO_2		

Table. Phenacyl Alcohols **8a–d** and **9** Prepared[a–c]

Product[d]	Reaction Time	Yield[e] (%)	mp (°C) (solvent)	Molecular Formula[f] or Lit. mp (°C)	^{1}H-NMR (solvent/TMS) δ, *J*(Hz)	^{13}C-NMR (solvent/TMS) δ
8a	17 h	74 (57, 60)	83–85 (*n*-hexane)	86–87[4–6]	$CDCl_3$: 3.5 (s, 1H); 4.8 (s, 2H); 7.4–7.7 (m, 3H); 7.8–8.1 (m, 2H)	$CDCl_3$: 65.4, 127.7, 128.9, 133.4, 134.2, 198.4
8b	17 h	88 (63)	124–126 (EtOH)	121–122[4–6]	DMSO-d_6: 4.8 (d, 2H, *J* = 6)[g]; 5.1 (t, 1H, *J* = 6)[h]; 7.6 (d, 2H, *J* = 8); 8.0 (d, 2H, *J* = 8)	DMSO-d_6: 65.7, 129.6, 130.0, 133.5, 139.2, 199.0
8c	17 h	61 (48)	138–140[15] (EtOH)	$C_8H_7NO_4$ (181.1)	DMSO-d_6: 4.8 (d, 2H, *J* = 5)[g]; 5.3 (t, 1H, *J* = 5)[h]; 8.1–8.5 (m, 4H)	DMSO-d_6: 65.8, 123.8, 129.1, 139.4, 144.9, 198.6
8d	17 h	58 (45)	85–87 (*n*-hexane)	86.5–88[16]	$CDCl_3$: 2.4 (s, 3H); 3.6 (s, 1H); 4.8 (s, 2H); 7.3 (d, 2H, *J* = 8); 7.8 (d, 2H, *J* = 8)	$CDCl_3$: 21.7, 65.2, 127.6, 129.4, 130.8, 145.2, 197.8
9	10 d	34	132–133 (CH_2Cl_2/*n*-hexane)	$C_9H_9IO_3$ (292.1)	$CDCl_3$: 3.5 (t, 1H, *J* = 4)[h]; 3.8 (s, 3H); 4.8 (d, 2H, *J* = 4)[g]; 6.8 (d, 1H, *J* = 9); 7.9 (dd, 1H, *J* = 9, 2); 8.3 (d, 1H, *J* = 2)	$CDCl_3$: 56.7, 65.0, 86.2, 110.3, 127.9, 129.9, 139.3, 162.5, 195.7

[a] Instruments include Varian EM-360 (60 MHz) and JEOL FX-90 (90 MHz) NMR spectrometers a Pye Unicam (Sargent-Welch) 3-200 IR spectrometer, a Hitachi Perkin-Elmer RMU-6E mass spectrometer, and a Hewlett Packard 5985 GC-MS.

[b] IR (KBr) $\nu = 1675–1680\ cm^{-1}$ for products **8a–d**, $1660\ cm^{-1}$ for product **9**. MS (70 eV) gave *m/z* (%) for M^+ (6-32) and $M^+ - CH_2OH$ (100) for all the phenacyl alcohols.

[c] *p*-Diiodobenzene, mp 126–128 °C (Lit.[7] mp 126–128 °C) is obtained in yields of 51, 68, 36, 40%, and trace amounts with products **8a–d** and **9**, respectively.

[d] Each alcohol **8a–d** and *p*-diiodobenzene (**7**) is obtained pure by flash chromatography (silica gel, Merck grade 60, CH_2Cl_2/CH_3OH, 50 : 1).

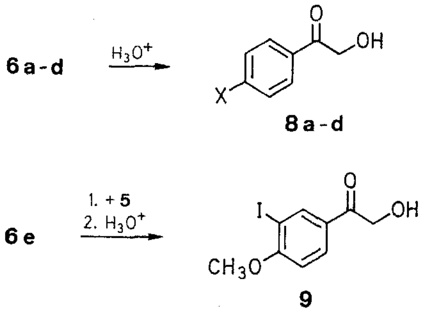
[e] Yields in parentheses were previously reported for conversions of the corresponding acetophenones or their enol silyl ether derivatives to the phenacyl alcohols by treatment with iodosylbenzene or *o*-iodosylbenzoic acid. Refs. 4–6.

[f] Satisfactory microanalyses obtained: C ±0.11, H ±0.10, N ±0.10, I ±0.26.

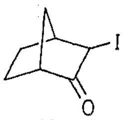
[g] Treatment with D_2O gave a singlet.

[h] Treatment with D_2O caused the signal to disappear.

available either as starting material (**1e**) and/or derived intermediates. Previously iodination of aromatic compounds treated with bis(trifluoroacetoxy)iodobenzene (**2**) was also attributed to the intermediacy of trifluoroacetoxy iodide (**5**).[7]



Attempts to obtain aliphatic α-ketols from α-iodoketones in oxidatively assisted reactions were unsuccessful. Similar treatment of *exo*-3-iodonorbornan-2-one (**10**)[8] with the bis(trifluoroacetoxy)iodobenzene (**2**) gave the diiodide 7 (30%), but the formation of 3-hydroxynorbornan-2-one was not detected. An intractable mixture was obtained from 2-iodocyclohexanone (**11**)[9] when treated with **2**.



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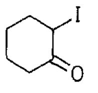

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$CF_3SO_3SiMe_3$ (99%) and *N*-iodosuccinimide (95%) were purchased from the Aldrich Chemical Co.; reagent grade I_2 (resublimed) was obtained from the EM Science Chemical Company, and $AgNO_3$ was obtained from the Sargent-Welch Scientific Co. Bis(trifluoroacetoxy)iodobenzene **2** was prepared from iodobenzene diacetate and trifluoroacetic anhydride.[10] *exo*-3-Iodonorbornan-2-one (**10**),[8] and 2-iodocyclohexanone (**11**) were prepared by reported methods. The iodide **11** was stirred in the refrigerator, but decomposed on storage at 25 °C.

Phenacyl iodide (**1a**), mp 35–36 °C, was prepared (91%) from the enol silyl ether of acetophenone[11] and *N*-iodosuccinimide.[9] The phenacyl iodides **1b–e** were prepared by $I_2/AgNO_3$ method.[12] **1b**; mp 71–73 °C; **1c**; mp 59–61 °C. A typical procedure for the preparation of **1d** is given below.

p-Methylphenacyl Iodide (1d); Typical Procedure:

I_2 (4.3 g, 17 mmol) is added to a mixture of *p*-methylacetophenone (2.3 g, 17 mmol) and $AgNO_3$ (2.9 g, 17 mmol) in CH_3OH (50 mL). After heating with stirring at 60 °C for 1 h, the precipitated AgI is removed, the liquid phase is concentrated, and combined with ether (100 mL). The organic phase is washed with 5% aq. $Na_2S_2O_3$ solution (5%, 75 mL), sat. aq. $NaHCO_3$ solution (100 mL), and water (100 mL). The ether phase is dried (Na_2SO_4) and concentrated to leave a brown oil. Flash chromatography (silica gel Merck grade 60, CH_2Cl_2/*n*-hexane, 3:1) gives *p*-methylphenacyl iodide (**1d**) as a colorless solid; yield: 2.7 g (62%); mp 42–44 °C after recrystallization from a mixture of ether/petroleum ether (bp 40–60 °C) (Lit.[13] mp 44 °C).

In a similar but slower reaction *p*-nitroacetophenone gives *p*-nitrophenacyl iodide (**1c**) as a pale yellow solid; yield: 38%; mp 94–96 °C (Lit.[14] mp 97–98 °C).

Phenacyl Alcohol (8a); Typical Procedure:

To a solution of phenacyl iodide (**1a**) (0.3 g, 1.2 mmol) in dry CH_2Cl_2 (5 mL) PhI $(O_2CCF_3)_2$ (**2**;[1] 0.6 g, 1.4 mmol) is added and the resulting mixture is stirred at room temperature for 17 h. The mixture is diluted with ether (15 mL) and washed successively with aq. $NaHSO_3$ solution (10%, 2×10 mL), sat. aq. $NaHCO_3$ solution (10 mL), and brine (10 mL). The ether extract is dried (Na_2SO_4) and the solvent is removed under reduced pressure. The ^{1}H-NMR of the crude product shows a mixture of phenacyl trifluoroacetate (**6**), iodobenzene, 1,4-diiodobenzene (**7**), and some phenacyl alcohol (**8a**). Iodobenzene is removed by evaporation at 25 °C/1.3 mbar. Flash column chromatography (silica gel, Merck grade 60, CH_2Cl_2/CH_3OH, 50:1) of the residue gives 1,4-diiodobenzene (**7**); yield: 0.20 g (51%); mp 126–128 °C (Lit.[7] mp 127–128 °C), and phenacyl alcohol (**8a**); yield: 0.12 g (74%); mp 83–85 °C (Lit.[6] mp 86–87 °C) (Table).

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