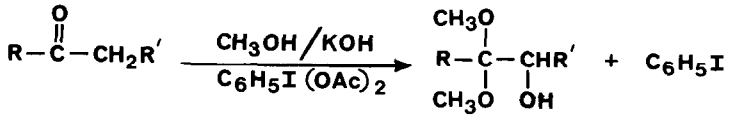
Tetrahedron Letters,Vol.25,No.7,pp 691-694,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

α-Hydroxylation of Ketones Using o-Iodosylbenzoic Acid

Robert M. Moriarty and Kwang-Chung Hou
Department of Chemistry
University of Illinois at Chicago
Chicago, Illinois 60680

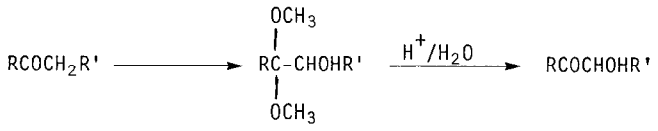
Summary - o-Iodosylbenzoic acid (KOH/CH_3OH) converts various ketones to α-hydroxydimethylacetals in high yield with the advantageous feature of solubility of the reduction product o-iodobenzoic acid under the basic reaction conditions thus allowing isolation of the oxidation product by simple CH_2Cl_2 extraction.

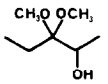
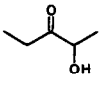
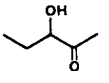
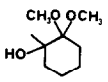
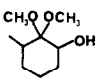
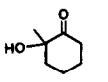
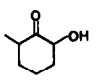
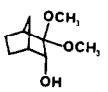
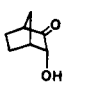
In past work we have demonstrated the synthetic usefulness of iodosylbenzene and diacetoxyphenyliodine(III) in methanolic KOH for the α-hydroxylation of ketones,[1-3] esters and carboxylic acids.[4] In the case of ketones the primary product is the α-hydroxydimethylacetal and iodobenzene (Eqn 1).



(Eqn 1)

Chromatography on neutral alumina allowed separation of iodobenzene from the oxidation product. We report now that the method is significantly improved by use of o-iodosylbenzoic acid[5] which analogously yields base soluble o-iodobenzoic acid under the reaction conditions allowing isolation of the α-hydroxydimethylacetal by direct extraction. Table 1 presents a comparison of the original and present methods for representative ketones. In a typical experiment 0.15 mole KOH is dissolved in 80 ml of CH_3OH with ice-cooling and 0.05 mole of the ketone dissolved in 20 ml CH_3OH is added dropwise with stirring. Then solid o-iodosylbenzoic acid (0.055 mole) is added portionwise over a 30 minute period. The reaction mixture is stirred at room temperature overnight. The α-hydroxydimethylacetal is isolated by removing most of the CH_3OH in vacuo, adding H_2O and extraction with CH_2Cl_2. The product is purified by distillation and yields range from 47-80%. Acid hydrolysis of the α-hydroxydimethylacetal using 5% H_2SO_4 in $CHCl_3$ proceeded in 33-85% yield although higher yields of the α-hydroxyketone were obtained by omitting isolation of the acetal and direct hydrolysis of the reaction product. Problems associated with acid hydrolysis of α-hydroxydimethylacetals (specifically $-C(OCH_3)_2CHOH$ - --------> - $CHOCH_3-CO-$) have been discussed.[4]



	α-hydroxydimethylacetal			α-hydroxyketone
	diacetoxyphenyliodine (% yield)[a]	o-iodosylbenzoic acid (% yield)[a]		(% yield)[a]
1) acetophenone	1[7](81)	(84)		2[8](80)
2) 1-phenyl-1-propanone	3[9](71)	(70)		4[10](83)
3) 3-pentanone	5[11](65)	(62)		6[12](81)
				
	6a		5.8:1	6b
4) cyclopentanone	7[6](78)	(83)		8[13](81)
5) cyclohexanone	9[6](75)	(74)		10[13](80)→dimer on standing
6) cycloheptanone	11[14](68)	(71)		12[13](65)
7) cyclododecanone	13[15](56)	(61)		14[13](72)
8) 2-methylcyclohexanone	15[16](62)	(67)		16[17](80)
	 15a	6:1  15b		 16a	6:1  16b
9) 2-norbornanone	17[18](47)			18[19](33)
				
10) benzalacetone	19[20][d]	(67)[b]		20[21](77)

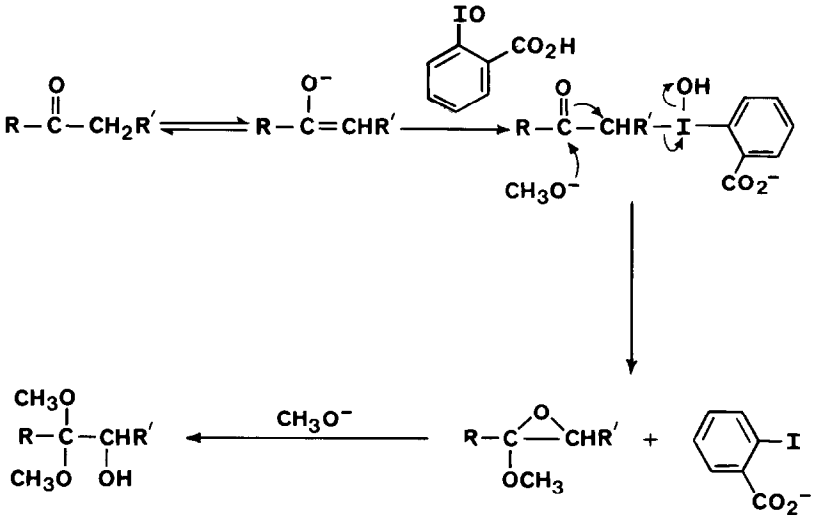
[a]Yields refer to pure product isolated by distillation.

[b]Products polymerize readily.

[c]Ratio determined by gc/ms.

[d]Acetal could not be separated by chromatography.

The pathway by which these reactions occur involves attack of the enolate anion at the I=O bond of o-iodosylbenzoic acid followed by reductive elimination of o-iodobenzoic acid upon addition of CH_3O^- to the carbonyl group. Ring-opening of the thus formed epoxide yields the hydroxydimethylacetal:



o-Iodosylbenzoic acid has been used for cleavage of tryptophanyl bonds in proteins.[22,23] Recently Barton et al., pointed out the advantages of using o-iodylbenzoic acid in a catalytic reaction for the oxidation of various functional groups.[24] The present work further extends the synthetic utility of hypervalent iodine oxidants.[25]

Acknowledgements

We thank the donors of the Petroleum Research Fund, administered by the ACS for support of the research under grant PRF 14773-AC1

References

1. R. M. Moriarty, H. Hu and S. C. Gupta, Tetrahedron Letters, 22, 1283 (1981).
2. R. M. Moriarty, L. S. John and P. C. Du, J. Chem. Soc. Chem. Commun., 641 (1981).
3. R. M. Moriarty, S. C. Gupta, H. Hu, D. R. Berenschot and K. B. White, J. Am. Chem. Soc., 103, 686 (1981).
4. R. M. Moriarty and H. Hu, Tetrahedron Letters, 22, 2747 (1981).
5. O-Iodosylbenzoic acid can be prepared either by treatment of o-iodobenzoic acid with fuming nitric acid (P. Askenasy and V. Meyer, Ber. Dtsch. Chem. Ges., 26, 1354 (1893) or by treatment with 40% peracetic acid. o-Iodosylbenzoic acid is also available from Sigma Chemical Co. and Pierce Chemical Co.,
6. X. Creary and A. J. Rollin, J. Org. Chem, 42, 4231 (1977).

7. 1, b.p. 99-101°C (0.5 mm); IR (neat) 3470 cm^{-1} (OH); ^{1}HNMR (60 MHz, $CDCl_3$) δ 7.27-7.67 (m, 5H) 3.73 (s, 2H) 3.23 (s, 6H) 1.83 (bs, 1H, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$) δ 139.3, 128.4, 127.4, 102.4, 65.3, 49.1; mass spectrum (70 eV) M/e 151 (M^+ - OCH_3 100%), 105 (29.7%), 91 (31.7%), 77 (7.0%); Anal. Cacld. for $C_{10}H_{14}O_3$: C, 65.93; H, 7.69. Found: C, 66.47; H, 8.22.
8. 2, mp 86-87°C, see the Sadtler standard spectra. ^{1}H NMR 17161 M, grating IR 24179 K.
9. 3, C. L. Stevens, W. Malik and R. Pratt, J. Am. Chem. Soc., 72, 4758 (1950).
10. 4, T. I. Temnikova and E. N. Kropacheva, J. Gen. Chem. USSR., 19, 1917 (1949).
11. 5, bp 50-51°C (1.25 mm), IR (neat) 3500 cm^{-1} (OH); ^{1}H NMR (60 MHz, $CDCl_3$) δ 3.95 (q, 1H, J=7 Hz), 3.30 (s, 3H), 3.27 (s, 3H), 2.77 (bs, 1H, exchangeable with D_2O), 1.68 (q, 2H, J=7Hz), 1.18 (d, 3H, J=7Hz), 0.92 (t, 3H, J=7Hz); ^{13}C NMR ($CDCl_3$) δ 102.7, 69.4, 49.6, 48.8, 24.8, 16.7, 8.4; mass spectrum (15 ev) M/e 148 (M^+, 0.04%), 119 (M^+-C_2H_5, 4.71%) 117 (M^+-OCH_3, 21.48%), 103 (M^+-$CHOHCH_3$, 100%); Anal. Calcd. for $C_7H_{16}O_3$: C, 56.76; H, 10.81. Found: C, 56.03; H, 10.61.
12. 6a, 6b, M. Pechal, Z. Cvengrosova, S. Holotik, L. Malik and M. Hrusovsky, J. of Chromatography, 206, 541 (1981).
13. 8, E. Friedrich and W. Lutz, Chem. Ber., 113, 1245 (1980).
14. 11, bp 94~95°C (3 mm); IR (neat) 3480-3500 cm^{-1} (OH); ^{1}H NMR (60 MHz, $CDCl_3$) δ 3.80 (m, 1H), 3.20 (s, 6H) 2.63 (bs, 1H, exchangeable with D_2O), 1.36-1.96 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 103.6, 72.2, 49.0, 48.5 30.9, 29.7, 27.0, 20.8, 20.3; mass spectrum (15 eV), M/e 174 (M^+, 2.4%) 143 (M^+-OCH_3, 9.1%), 101 (CH_2=CH-C(OCH_3)$^+$, 100%).
15. 13, mp 117-119°C; IR (KBr) 3480-3510 cm^{-1} (OH); ^{1}H NMR (60 MHz, $CDCl_3$) δ 3.83 - 4.10 (m, 1H), 3.40 (s, 3H) 3.30 (s, 3H), 2.80 (bs, 1H, exchangeable with D_2O), 1.13-2.0 (m, 20H); mass spectrum (70 eV) M/e 244 (M^+, 33%) 213 (M^+-OCH_3, 8.3%), 101 (CH_2=CH-C(OCH_3)$^+$, 100%); Anal. Calcd for $C_{14}H_{28}O_3$: C, 68.85; H, 11.48. Found: C, 69.19; H, 11.38.
16. 15a, 15b, identified by mass spectrum (70 eV)
15a M/e 174 (M^+, 0.9%), 143 (M^+,-OCH_3, 20.1%), 101 (CH_2=CH-C(OCH_3)$^+$, 100%).
15b M/e 174 (M^+, 25.8%), 143 (M^+-OCH_3, 11.0%), 117 (CH_2-C(OH)C(OCH_3)$^+$, 15.8%), 115 (CH_2=C(CH_3)C(OCH_3)$^+$, 100%).
17. 16a, 16b, M-P. Strobel and L. M. D. Paquer., Tetra. Lett., 21, 523 (1980).
18. X. Creary and A. J. Rollin, J. Org. Chem., 42, 4226 (1977).
19. P. Yates and R. J. Crawford, J. Amer. Chem. Soc., 88, 1561 (1966). also see reference 18.
20. 19, IR (CCl_4) 3440-3480 cm^{-1} (OH); ^{1}H NMR (60 MHz, $CDCl_3$), δ 7.07-7.50 (m, 5H), 6.78 (d, 1H, J=16 Hz), 5.99 (d, 1H, J=16 Hz), 3.57 (s, 2H), 3.20 (s, 6H), 2.41 (bs, 1H, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$) δ 136.0, 134.3, 128.5, 127.9, 127.0, 126.7, 100.6, 63.9, 48.9; mass spectrum (70 eV) M/e 177 (M^+-OCH_3, 28%), 147 (100%), 115 (90%) 103 (81%) 77 (76%).
21. 20, mp 69-70.5°C; IR (KBr) 3375-3445 cm^{-1} (OH), 1660 (conj. c=o) 1625 (conj. c=c); ^{1}H NMR (60 MHz, $CDCl_3$) δ 7.70 (d, 1H, J=16 Hz), 7.70-7.27 (m, 5H), 6.75 (d, 1H, J=16 Hz), 4.53 (s, 2H), 3.37 (bs, 1H, exchangeable with D_2O); ^{13}C NMR ($CDCl_3$) δ 198.1, 144.0, 133.8, 131.0, 129.0, 128.4, 121.3, 66.9; mass spectrum (70 eV) M/e 162 (M^+, 7.5%), 131 (M^+-CH_2OH, 100%), 103 (131-CO 70.7%), 77 (51.7%), Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.07; H, 6.17, Found: C, 74.02; H, 6.48.
22. W. C. Mahoney and M. A. Hermodson, Biochemistry, 18, 3810 (1979).
23. W. C. Mahoney, P. K. Smith, and M. A. Hermodson, Biochemistry, 20, 443 (1981), for comments on the mechanism of this reaction see A. Fontana, D. Dalzoppo, C. Grandi and M. Zambonin, Biochemistry, 20, 6997 (1981).
24. D. H. R. Barton, J. W. Morzycki, W. B. Motherwell, J. Chem. Soc. Chem. Commun., 1044 (1981)., D. H. R. Barton, C. R. A. Godfrey, J. W. Morzycki, W. B. Motherwell and A. Stobic, Tetrahedron Letters, 23, 957 (1982).
25. P. Müller and J. Godoy, Tetrahedron Letters, 22, 2361 (1981).

(Received in USA 19 October 1983)