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Hypervalent Iodine Oxidation of α,β -Unsaturated Carbonyl Compounds

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Oxidation of non-enolizable α,β -unsaturated carbonyl compounds and enolizable β -monosubstituted α,β -unsaturated carbonyl compounds with phenyl iodine(III) diacetate (PIDA) in methanolic potassium hydroxide gave α -hydroxydimethylacetal β -methoxy products, and oxidation of enolizable β,β -disubstituted α,β -unsaturated carbonyl compounds under the same conditions gave α' -hydroxy products.

Keywords—phenyl iodine(III) diacetate; oxidation of α,β -unsaturated carbonyl compound; α -hydroxydimethylacetal β -methoxy product; α' -hydroxy- α,β -unsaturated ketone; methanolic potassium hydroxide solution

In spite of considerable interest in the hypervalent iodine oxidation of ketones leading to α -hydroxydimethylacetals (**1**),¹⁾ only a few reports on the oxidation of α,β -unsaturated ketones have appeared. The reaction of $\text{PhI}(\text{OAc})_2$ [phenyl iodine(III) diacetate, PIDA] in methanolic potassium hydroxide with non-enolizable α,β -unsaturated ketones which cannot form anions by α -hydrogen abstraction, such as chromones, flavone, and chalcone, was shown to give α -hydroxydimethylacetal β -methoxy products.²⁾ Further, an enolizable α,β -unsaturated ketone, 3,5,5-trimethyl-2-cyclohexenone (isophorone), was shown to give the α -hydroxy product, 2-hydroxy-3,5,5-trimethyl-2-cyclohexenone.³⁾ As a part of our study of the chemistry of hypervalent iodine reagents,⁴⁾ we have examined the reaction of PIDA with various types of α,β -unsaturated carbonyl systems, some of which possess α' and γ CH_2 -units. It was found that both non-enolizable α,β -unsaturated carbonyl compounds (**2a**, **b**) and enolizable β -monosubstituted α,β -unsaturated carbonyl compounds (**2c**–**f**) react with PIDA in KOH – MeOH to give α -hydroxydimethylacetal β -methoxy products (**3a**, **b** and **3c**–**f**), and enolizable β,β -disubstituted α,β -unsaturated carbonyl compounds (**7a**–**c**) react with PIDA/ KOH – MeOH to give α' -hydroxy products (**8a**–**c**, **9a**, **b** and **10**).

Results and Discussion

To establish the generality of the oxidation of non-enolizable α,β -unsaturated carbonyl compounds with PIDA/ KOH – MeOH , which was shown to give α -hydroxydimethylacetal β -methoxy products,²⁾ we first examined the reaction of acyclic systems (**2a**, **b**) with PIDA/ KOH – MeOH . The oxidation of *trans*-cinnamaldehyde (**2a**) takes place at the α -position at room temperature for 30 min to give the α -hydroxydimethylacetal β -methoxy product (**3a**) in 62% yield. The oxidation of **2b** with PIDA was accomplished under similar conditions to give a 78% yield of a 1:2 mixture of α -hydroxydimethylacetal β -methoxy product (**3b**) and its deacetalization product (**3b'**), from which only the latter compound was isolated in a pure state because of the ready deacetalization of **3b** (Chart 1).

Chart 1

The present oxidation of **2a** gave a mixture of diastereomers with no stereoselectivity. Thus, stereoisomers [*threo*-**3a** (**3a-syn**) and *erythro*-**3a** (**3a-anti**)] were separated by column chromatography on silica gel in a ratio of 53:47. A tentative assignment of the stereostructures was made on the basis of nuclear magnetic resonance (NMR) studies of the derivatives (**4**–**6**) from each stereoisomer, since Heathcock and co-workers have pointed out⁵⁾ that the C-3 proton in the *anti*-aldol adducts generally resonates at higher field than the corresponding proton in the *syn*-diastereomers, and the vicinal coupling constant ($J_{2,3}$) in the *anti*-isomers has a larger value than that of the *syn*-isomers. Data for all these derivatives (**4**, **5**) are in good accord with the expected values. The stereochemistry of **3a** was finally confirmed by direct comparison of the methylated **3a-syn** (**6-syn**) with an authentic specimen prepared from *trans*-cinnamaldehyde dimethylacetal⁶⁾ by stereospecific *cis*-hydroxylation with osmium tetroxide followed by dimethylation of the resultant *vic*-glycol, as shown in Chart 2.

Chart 2

Next, we examined the oxidation of enolizable β -monosubstituted α,β -unsaturated carbonyl compounds (**2c–f**) with PIDA/KOH–MeOH. The oxidation takes place at the α -position under similar conditions to give the corresponding α -hydroxydimethylacetal β -methoxy products (**3c–f**) in moderate yields. The *cis*-relationship of the C(2)-hydroxy and C(3)-methoxy groups of **3c–e** was deduced from a comparison of the coupling constants with those of related compounds.^{2a)} The formation of **3c–e** from **2c–e** is best explained by the same mechanistic pathway as proposed for the reaction of non-enolizable α,β -unsaturated carbonyl compounds with PIDA/KOH–MeOH by Moriarty *et al.*,²⁾ as shown in Chart 3.

Chart 3

On the other hand, the oxidation of β,β -disubstituted α,β -unsaturated ketones **7a–c** with PIDA takes place at the α' -position to give α' -hydroxy products (**8a–c**) together with α' -hydroxy- γ -methoxy products (**9a, b** and **10**) (Chart 4).⁷⁾ The structures of **8a, b** were confirmed by direct comparison of their *O*-acetates (**11a, b**) with authentic specimens prepared by an alternative method⁸⁾ and those of other novel compounds (**3a–f, 4–6, 8c, 9a, b** and **10**) were fully supported by satisfactory spectral data⁹⁾ (given in the experimental section). Although the mechanism of formation of these α' -hydroxy products (**8–10**) is not rigorously defined, it is suggested that Michael addition of the methoxy anion to the enones is restricted by steric hindrance, and α' - and γ -enolizations occur to give the products.

Chart 4

The reaction conditions, products, and yields are summarized in Table I.

Experimental

All melting and boiling points are uncorrected. Infrared (IR) absorption spectra were recorded on a JASCO

TABLE I. Oxidation of α,β -Unsaturated Carbonyl Compounds with PIDA/KOH-MeOH

Run	α,β -Unsaturated carbonyl compounds	Reaction conditions	Products (Yields)
1	2a	2 eq PIDA r.t. 30 min	3a (62%) ^{a)}
2	2b	1.1 eq PIDA r.t. 20 min	3b + 3b' 3b/3b' = 1/2 (76%), ^{b)} 2/1 (69%) ^{c)}
3	2c	1.1 eq PIDA 0 °C, 40 min	3c (55%)
4	2d	1.1 eq PIDA 0 °C, 1 h	3d (52%)
5	2e	1.1 eq PIDA r.t. 30 min	3e (23%)
6	2f	2 eq PIDA r.t. 40 min	3f (67%) ^{d)}
7	7a	3 eq PIDA r.t. 1 h	8a (32%) + 9a (15%)
8	7b	3 eq PIDA r.t. 30 min	8b (15%) + 9b (8%)
9	7c	2 eq PIDA r.t. 30 min	8c (58%) + 10 (15%) ^{e)}

a) A diastereo-mixture of **3a-syn** and **3a-anti** (**3a-syn**:**3a-anti**=53:47) was obtained. b) The reaction mixture was worked-up by the general procedure. c) The reaction mixture was concentrated and subjected directly to column chromatography without washing with saturated aqueous NaCl. d) A 15:5:5:3 diastereo-mixture was obtained. e) A 3:2 diastereo-mixture was obtained.

HPIR-102 spectrometer, and ¹H-NMR spectra (10% solution in CDCl₃) on a Hitachi R-22 (90 MHz) spectrometer (with tetramethylsilane as an internal standard). Low- and high-resolution mass spectra (MS) were obtained with a JEOL JMS D-300 instrument, with a direct inlet system at 70 eV. Column chromatography was carried out on Merck Silica gel 60.

General Procedure for the Oxidation of α,β -Unsaturated Carbonyl Compounds (2a–f and 7a–c) with PIDA/KOH-MeOH—A solution of α,β -unsaturated carbonyl compound (2 mmol) in anhydrous MeOH (3 ml) and a solution of KOH (12–18 mmol) in anhydrous MeOH (5 ml) were added dropwise to a stirred solution of PIDA (4 mmol) in anhydrous MeOH (12 ml) at room temperature under nitrogen. The reaction mixture was stirred for 30 min under the same conditions, concentrated under reduced pressure, and partitioned between water (20 ml) and

methylene chloride (20 ml). The aqueous layer was extracted with methylene chloride (10 ml $\times$ 2). The combined extract was washed with saturated aqueous NaCl, dried over MgSO_4 , and concentrated under reduced pressure to give the crude oxidized product, which contains iodobenzene. A pure sample was isolated by column chromatography on silica gel with *n*-hexane-ethyl acetate (2:1—10:1).

2-Hydroxy-3-methoxy-3-phenylpropanal Dimethylacetal (3a), 2-Acetoxy-3-methoxy-3-phenylpropanal Dimethylacetal (4) and 2-Acetoxy-3-methoxy-3-phenylpropanal-1',3'-dioxolane (5)—Compound **3a** (280 mg) was obtained from **2a** (264 mg, 2 mmol), PIDA (1.288 g, 4 mmol) and KOH (672 mg, 12 mmol) as a diastereo-mixture of **3a-anti** and **3a-syn** in a ratio of 53:47. The mixture was chromatographed on silica gel to give pure **3a-anti** (148.5 mg) and **3a-syn** (131.6 mg). **3a-anti**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3500, 1595, 1450. $^1\text{H-NMR}$ δ : 2.32 (brs, 1H, OH, disappeared on addition of D_2O), 3.22 (s, 3H, OMe), 3.34 (s, 3H, OMe), 3.42 (s, 3H, OMe), 3.9—4.1 (m, 1H, $\text{C}_2\text{-H}$), 4.13 (d, 1H, $J=4.5$ Hz, $\text{C}_1\text{-H}$), 4.25 (d, 1H, $J=5$ Hz, $\text{C}_3\text{-H}$), 7.30 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4\text{-H}_2\text{O}$: 208.1097. Found: 208.1081. **3a-syn**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3500, 1600, 1450. $^1\text{H-NMR}$ δ : 2.75 (brs, 1H, OH, disappeared on addition of D_2O), 3.26 (s, 3H, OMe), 3.38 (s, 6H, $\text{OMe} \times 2$), 3.6—3.8 (m, 1H, $\text{C}_2\text{-H}$), 4.24 (d, 1H, $J=5$ Hz, $\text{C}_1\text{-H}$), 4.31 (d, 1H, $J=4.5$ Hz, $\text{C}_3\text{-H}$), 7.31 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4\text{-H}_2\text{O}$: 208.1099. Found: 208.1102. The acetates (**4-anti** and **4-syn**) were obtained from **3a-anti** and **3a-syn** by treatment with Ac_2O -pyridine. **4-anti**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1745. $^1\text{H-NMR}$ δ : 1.94 (s, 3H, OCOMe), 3.25 (s, 3H, OMe), 3.37 (s, 3H, OMe), 3.41 (s, 3H, OMe), 4.29 (d, 1H, $J=5$ Hz, $\text{C}_1\text{-H}$), 4.38 (d, 1H, $J=6.3$ Hz, $\text{C}_3\text{-H}$), 5.33 (dd, 1H, $J=5$ and 6.3 Hz, $\text{C}_2\text{-H}$), 7.32 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_5\text{-CH}_3\text{CO}_2\text{H}$: 208.1097. Found: 208.1081. **4-syn**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740. $^1\text{H-NMR}$ δ : 1.96 (s, 3H, OCOMe), 3.26 (s, 3H, OMe), 3.30 (s, 3H, OMe), 3.42 (s, 3H, OMe), 4.43 (d, 1H, $J=7.5$ Hz, $\text{C}_1\text{-H}$), 4.49 (d, 1H, $J=4$ Hz, $\text{C}_3\text{-H}$), 5.12 (dd, 1H, $J=4$ and 7.5 Hz, $\text{C}_2\text{-H}$), 7.28 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_5\text{-CH}_3\text{CO}_2\text{H}$: 208.1100. Found: 208.1122. The 1,3-dioxolanes (**5-anti** and **5-syn**) were obtained from **3a-anti** and **3a-syn**, respectively, by treatment with ethylene glycol in the presence of a catalytic amount of *p*-TsOH in methylene chloride at room temperature overnight, followed by acetylation with Ac_2O -pyridine. **5-anti**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740. $^1\text{H-NMR}$ δ : 1.84 (s, 3H, OCOMe), 3.22 (s, 3H, OMe), 3.8—4.0 (m, 4H, $\text{CH}_2 \times 2$), 4.37 (d, 1H, $J=7$ Hz, $\text{C}_3\text{-H}$), 5.1—5.3 (m, 2H, $\text{C}_1\text{-H}$ and $\text{C}_2\text{-H}$), 7.28 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_5\text{-CH}_3\text{CO}_2\text{H}$: 206.0943. Found: 206.0946. **5-syn**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740. $^1\text{H-NMR}$ δ : 2.01 (s, 3H, OCOMe), 3.24 (s, 3H, OMe), 3.8—4.1 (m, 4H, $\text{CH}_2 \times 2$), 4.45 (d, 1H, $J=4$ Hz, $\text{C}_3\text{-H}$), 4.9—5.1 (m, 2H, $\text{C}_1\text{-H}$ and $\text{C}_2\text{-H}$), 7.27 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_5\text{-CH}_3\text{CO}_2\text{H}$: 206.0944. Found: 206.0945.

threo-2,3-Dimethoxy-3-phenylpropanal Dimethylacetal (6-syn)—i) From *threo*-2-Hydroxy-3-methoxy-3-phenylpropanal Dimethylacetal (**3a-syn**): The acetal (**3a-syn**) was methylated by the Hakomori method.¹⁰⁾ Anhydrous dimethyl sulfoxide (2 ml) was added dropwise to oil-free NaH (100 mg) with stirring under nitrogen at 60—70 °C until hydrogen was no longer evolved (about 1 h). Then **3a-syn** (118 mg, 0.5 mmol) in dimethyl sulfoxide (2 ml) was added dropwise to a stirred solution of sodium methylsulfinylmethide at room temperature under nitrogen. The mixture was stirred for 1 h under the same conditions and methyl iodide (0.5 ml) was added. After being stirred for 30 min, the reaction mixture was poured into ice-water (20 ml) and extracted with methylene chloride. The extract was washed with aqueous 10% $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaCl, dried over MgSO_4 , and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel to give a 98% yield (122 mg) of **6-syn** as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1600, 1450, 1355, 1185, 1100. $^1\text{H-NMR}$ δ : 3.17 (s, 3H, OMe), 3.24 (s, 3H, OMe), 3.44 (s, 3H, OMe), 3.46 (s, 3H, OMe), 3.0—3.2 (m, 1H, $\text{C}_2\text{-H}$), 4.33 (d, 1H, $J=4.8$ Hz, $\text{C}_1\text{-H}$), 4.38 (d, 1H, $J=1.8$ Hz, $\text{C}_3\text{-H}$), 7.29 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_4\text{-CH}_3\text{OH}$: 208.1100. Found: 208.1123.

ii) From *trans*-Cinnamaldehyde Dimethylacetal: *trans*-Cinnamaldehyde dimethylacetal, obtained by the reaction of *trans*-cinnamaldehyde with $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ and trimethyl orthoformate,⁶⁾ was converted into **6-syn** by osmium tetroxide-catalyzed *cis*-hydroxylation¹¹⁾ followed by dimethylation of the resultant *vic*-glycol by the Hakomori method.¹⁰⁾ Then 2 mol-equivalents of $\text{Me}_3\text{N} \rightarrow \text{O} \cdot 2\text{H}_2\text{O}$ (222 mg) and 0.4 M osmium tetroxide in *tert*-butanol (25 ml) were added to a stirred solution of *trans*-cinnamaldehyde dimethylacetal (178 mg, 1 mmol) in $\text{THF}/\text{H}_2\text{O}$ (9:1, 5 ml) cooled to 0 °C. The mixture was allowed to warm to room temperature, stirred for 5 h, quenched by addition of solid NaHSO_3 with vigorous stirring for 30 min, and concentrated under reduced pressure. Methylene chloride was added to the residue, and the mixture was filtered through a short celite column. The filtrate was concentrated under reduced pressure to give a residue, which was purified by column chromatography on silica gel to give *threo*-2,3-dihydroxy-3-phenylpropanal dimethylacetal in 71% yield (150 mg). Recrystallization from *n*-hexane gave a pure sample as colorless crystals, mp 79—81 °C. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3500, 1450, 1205. $^1\text{H-NMR}$ δ : 2.5—2.7 (brs, 1H, OH, disappeared on addition of D_2O), 2.9—3.1 (brs, 1H, OH, disappeared on addition of D_2O), 3.44 (s, 6H, $\text{OMe} \times 2$), 3.6—3.8 (m, 1H, $\text{C}_2\text{-H}$), 4.32 (d, 1H, $J=4.8$ Hz, $\text{C}_1\text{-H}$), 4.8—4.9 (m, 1H, $\text{C}_3\text{-H}$), 7.31 (brs, 5H, ArH). Anal. Calcd for $\text{C}_{11}\text{H}_{16}\text{O}_4$: C, 62.25; H, 7.60. Found: C, 62.10; H, 7.63. The *threo*-glycol (53 mg, 0.25 mmol) was dimethylated by the method described for i) to give an 85% yield (51 mg) of **6-syn** as a colorless oil. This was identical with the sample obtained above.

2-Hydroxy-3-methoxy-1-phenyl-1-propanone Dimethylacetal (3b) and 2-Hydroxy-3-methoxy-1-phenyl-1-propanone (3b')—A solution of **2a** (132 mg, 1 mmol) in anhydrous MeOH (1 ml) and a solution of KOH (185 mg, 3.3 mmol) in anhydrous MeOH (1.5 ml) were added dropwise to a solution of PIDA (354 mg, 1.1 mmol) in anhydrous MeOH (2.5 ml) at room temperature under nitrogen. The reaction mixture was worked up according to the general

procedure to give a residue, which was subjected to column chromatography on silica gel with methylene chloride to give a 78% yield (153 mg) of an inseparable mixture of **3b** and **3b'** in a ratio of 1:2 (calculated from the relative intensities of the methoxy signals in the $^1\text{H-NMR}$ spectra). When the reaction mixture was concentrated under reduced pressure without treatment with water, only crude **3b** was obtained. The crude **3b** was subjected to column chromatography on silica gel with *n*-hexane:ethyl acetate = 5:1 to give a 2:1 ratio of **3b** and **3b'** in 69% yield. Crude **3b**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3550, 1595, 1450, 1225, 1115. $^1\text{H-NMR}$ δ : 3.29 (s, 3H, OMe), 3.31 (s, 3H, OMe), 3.42 (s, 3H, OMe), 3.5—3.7 (m, 1H, $\text{C}_3\text{-H}$), 3.7—3.85 (m, 1H, $\text{C}_3\text{-H}$), 3.85—4.05 (br s, 1H, OH, disappeared on addition of D_2O), 4.28 (dd, 1H, $J=8.5$ and 2 Hz, $\text{C}_2\text{-H}$), 7.3—7.6 (m, 5H, ArH). Exact mass Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4\text{-CH}_3\text{O}$: 195.1020. Found: 195.1010. The 1:2 mixture of **3b** and **3b'** was converted into **3b'** in a quantitative yield by stirring in methylene chloride for 1 week or by passage through a long silica gel column in methylene chloride:*n*-hexane = 2:1. **3b'**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3550—3450, 1685, 1600, 1450, 1265, 1130. $^1\text{H-NMR}$ δ : 3.36 (s, 3H, OMe), 3.78 (dd, 2H, $J=4$ and 3 Hz, CH_2OMe), 3.9—4.1 (br s, 1H, OH, disappeared on addition of D_2O), 5.1—5.4 (m, 1H, CHOH), 7.5—7.8 (m, 3H, ArH), 8.0—8.15 (m, 2H, ArH). Exact mass Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_3$: 180.0784. Found: 180.0761.

2-Hydroxy-3-methoxycyclopentanone Dimethylacetal (3c)—This (98 mg) was obtained from **2c** (84 mg, 1 mmol), PIDA (354 mg, 1.1 mmol) and KOH (185 mg, 3.3 mmol). Distillation under reduced pressure gave pure **3c** as a colorless oil, bp 135—145 $^\circ\text{C}/10$ mmHg (bath temp.). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3500, 1460, 1090, 910. $^1\text{H-NMR}$ δ : 1.7—2.1 (m, 4H, $\text{CH}_2 \times 2$), 2.6—2.8 (br s, 1H, OH, disappeared on addition of D_2O), 3.30 (s, 3H, OMe), 3.38 (s, 3H, OMe), 3.44 (s, 3H, OMe), 3.8—4.1 (m, 2H, $\text{C}_2\text{-H}$ and $\text{C}_3\text{-H}$). MS m/z : 176 (M^+). Anal. Calcd for $\text{C}_8\text{H}_{16}\text{O}_4$: C, 54.53; H, 9.15. Found: C, 54.68; H, 9.34. The acetate (**3c**·acetate) was obtained from **3c** by treatment with Ac_2O -pyridine. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1735. $^1\text{H-NMR}$ δ : 1.8—2.1 (m, 4H, $\text{CH}_2 \times 2$), 2.18 (s, 3H, OCOMe), 3.24 (s, 3H, OMe), 3.26 (s, 3H, OMe), 3.36 (s, 3H, OMe), 3.8—4.1 (m, 1H, $\text{C}_3\text{-H}$), 5.31 (d, 1H, $J=4$ Hz, $\text{C}_2\text{-H}$).

2-Hydroxy-3-methoxycyclohexanone Dimethylacetal (3d)—This (303 mg) was obtained from **2d** (297 mg, 3.1 mmol), PIDA (1.09 g, 3.4 mmol) and KOH (571 mg, 10 mmol). Distillation under reduced pressure gave pure **3d** as a colorless oil, bp 140—150 $^\circ\text{C}/15$ mmHg (bath temp.). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3500, 1460, 1140, 1085. $^1\text{H-NMR}$ δ : 1.3—1.7 (m, 6H, $\text{CH}_2 \times 3$), 2.16 (br s, 1H, OH, disappeared on addition of D_2O), 3.14 (s, 3H, OMe), 3.24 (s, 3H, OMe), 3.35 (s, 3H, OMe), 3.3—3.4 (m, 1H, $-\text{CHOMe}$), 4.02 (d, 1H, $J=3$ Hz, $-\text{CHOH}$). MS m/z : 190 (M^+). Anal. Calcd for $\text{C}_9\text{H}_{18}\text{O}_4$: C, 56.82; H, 9.54. Found: C, 56.80; H, 9.69. The acetate (**3d**·acetate) was obtained from **3d** by treatment with Ac_2O -pyridine. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1725. $^1\text{H-NMR}$ δ : 1.2—1.8 (m, 6H, $\text{CH}_2 \times 3$), 2.10 (s, 3H, OCOMe), 3.16 (s, 6H, OMe $\times 2$), 3.33 (s, 3H, OMe), 3.3—3.4 (m, 1H, $-\text{CHOMe}$), 5.43 (d, 1H, $J=3$ Hz, $-\text{CHOAc}$). Exact mass Calcd for $\text{C}_{11}\text{H}_{20}\text{O}_5$: 232.1308. Found: 232.1280.

2-Hydroxy-3-methoxy-5,5-dimethyl-2-cyclohexanone Dimethylacetal (3e)—This (76.5 mg) was obtained from **2e** (191 mg, 1.5 mmol), PIDA (731 mg, 1.7 mmol) and KOH (285 mg, 5.1 mmol) as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3550, 1460, 1145, 1085. $^1\text{H-NMR}$ δ : 0.95 (s, 3H, Me), 1.01 (s, 3H, Me), 1.4—1.8 (m, 4H, $\text{CH}_2 \times 2$), 2.22 (br s, 1H, OH, disappeared on addition of D_2O), 3.16 (s, 3H, OMe), 3.25 (s, 3H, OMe), 3.38 (s, 3H, OMe), 3.4—3.7 (m, 1H, $-\text{CHOMe}$), 4.00 (d, 1H, $J=3$ Hz, $-\text{CHOH}$). The acetate (**3e**·acetate) was obtained from **3e** by treatment with Ac_2O -pyridine. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1725. $^1\text{H-NMR}$ δ : 0.96 (s, 3H, Me), 1.03 (s, 3H, Me), 1.4—1.7 (m, 4H, $\text{CH}_2 \times 2$), 2.08 (s, 3H, OCOMe), 3.11 (s, 3H, OMe), 3.15 (s, 3H, OMe), 3.33 (s, 3H, OMe), 3.4—3.7 (m, 1H, $-\text{CHOMe}$), 5.38 (br s, 1H, $-\text{CHOAc}$). Exact mass Calcd for $\text{C}_{13}\text{H}_{24}\text{O}_5$: 260.1621. Found: 260.1615.

4,5-O-Isopropylidene-2,4,5-trihydroxy-3-methoxypentanal Dimethylacetal (3f)—This (84 mg) was obtained from **2f** (78 mg, 0.5 mmol), PIDA (322 mg, 1.0 mmol) and KOH (168 mg, 3.0 mmol) as a mixture of four inseparable diastereomers (checked by $^1\text{H-NMR}$). A small amount of one major diastereomer was isolated in a pure state by chromatography on a long column of silica gel with *n*-hexane:ethyl acetate = 3:1, colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3400, 1450, 1380, 1375, 1235. $^1\text{H-NMR}$ δ : 1.34 (s, 3H, Me), 1.43 (s, 3H, Me), 2.35—2.45 (m, 1H, OH), 3.43 (s, 3H, OMe), 3.48 (s, 6H, OMe $\times 2$), 3.7—4.4 (m, 5H, $\text{C}_2\text{-H}$, $\text{C}_3\text{-H}$, $\text{C}_4\text{-H}$, $\text{C}_5\text{-2H}$), 4.47 (d, 1H, $J=6$ Hz, $\text{C}_1\text{-H}$). Exact mass Calcd for $\text{C}_{11}\text{H}_{22}\text{O}_6\text{-CH}_3$: 235.1179. Found: 235.1169. The acetate (**3f**·acetate) was obtained from **3f** by treatment with Ac_2O -pyridine. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1450, 1370. $^1\text{H-NMR}$ δ : 1.34 (s, 3H, Me), 1.40 (s, 3H, Me), 2.09 (s, 3H, OCOMe), 3.33 (s, 3H, OMe), 3.37 (s, 3H, OMe), 3.42 (s, 3H, OMe), 3.4—3.6 (m, 1H, $\text{C}_5\text{-H}$), 3.7—4.4 (m, 3H, $\text{C}_3\text{-H}$, $\text{C}_4\text{-H}$, $\text{C}_5\text{-H}$), 4.57 (d, 1H, $J=7$ Hz, $\text{C}_1\text{-H}$), 5.26 (dd, 1H, $J=3$ and 7 Hz, $\text{C}_2\text{-H}$). Exact mass Calcd for $\text{C}_{13}\text{H}_{24}\text{O}_7\text{-CH}_3$: 277.1284. Found: 277.1281.

6-Hydroxy-3-methyl-2-cyclohexenone (8a), 6-Hydroxy-3-methoxymethyl-2-cyclohexenone (9a) and 6-Acetoxy-3-methyl-2-cyclohexenone (11a)—Compounds **8a** (73 mg) and **9a** (45 mg) were obtained from **7a** (223 mg, 2.0 mmol), PIDA (1.921 g, 6.0 mmol) and KOH (1.00 g, 18 mmol), **8a**: colorless oil, IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3400, 1670. $^1\text{H-NMR}$ δ : 1.99 (s, 3H, Me), 2.2—2.6 (m, 5H, $\text{CH}_2 \times 2$ and OH), 4.11 (dd, 1H, $J=6$ and 12 Hz, $-\text{CHOH}$), 5.94 (m, 1H, $-\text{CH=}$). The acetate (**11a**) was obtained from **8a** by treatment with Ac_2O -pyridine. Recrystallization from pet. ether gave pure **11a** as colorless crystals, mp 67.5—68.5 $^\circ\text{C}$ (lit.^{8a)} 60—62 $^\circ\text{C}$). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1690, 1240. $^1\text{H-NMR}$ δ : 1.98 (s, 3H, Me), 2.2—2.6 (m, 4H, $\text{CH}_2 \times 2$), 2.18 (s, 3H, OCOMe), 5.18 (dd, 1H, $J=6$ and 12 Hz, $-\text{CHOAc}$), 5.90 (m, 1H, CH=). MS m/z : 168 (M^+). **9a**: Colorless oil, IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3550—3450, 1680. $^1\text{H-NMR}$ δ : 2.3—2.6 (m, 4H, $\text{CH}_2 \times 2$), 3.38 (s, 3H, OMe), 3.73 (br s, 1H, OH, disappeared on addition of D_2O), 4.01 (br s, 2H, CH_2OMe), 4.16 (dd, 1H, $J=5$ and 13 Hz, $-\text{CHOH}$), 6.13 (m, 1H, $-\text{CH=}$). The acetate (**9a**·acetate) was obtained from **9a** by

treatment with Ac_2O -pyridine as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1690, 1230. $^1\text{H-NMR}$ δ : 2.16 (s, 3H, OCOMe), 2.2—2.6 (m, 4H, $\text{CH}_2 \times 2$), 3.36 (s, 3H, OMe), 4.00 (brs, 2H, CH_2OMe), 5.31 (dd, 1H, $J=6$ and 13 Hz, $-\text{CHOAc}$), 6.10 (m, 1H, $-\text{CH}=\text{}$). Exact mass Calcd for $\text{C}_{10}\text{H}_{14}\text{O}_4$: 198.0889. Found: 198.0871.

6-Hydroxy-3,5,5-trimethyl-2-cyclohexenone (8b), 6-Hydroxy-3-methoxymethyl-5,5-dimethyl-2-cyclohexenone (9b) and 6-Acetoxy-3,5,5-trimethyl-2-cyclohexenone (11b)—Compounds **8b** (46 mg) and **9b** (32 mg) were obtained from **7b** (283 mg, 2.1 mmol), PIDA (1.980 g, 6.2 mmol) and KOH (1.03 g, 18 mmol). **8b**: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3400, 1670. $^1\text{H-NMR}$ δ : 0.82 (s, 3H, Me), 1.19 (s, 3H, Me), 1.95 (s, 3H, Me), 2.2—2.4 (m, 2H, CH_2), 3.67 (brs, 1H, OH, disappeared on addition of D_2O), 3.93 (brs, 1H, $-\text{CHOH}$), 5.9—6.0 (m, 1H, $-\text{CH}=\text{}$). The acetate (**11b**) was obtained from **8b** by treatment with Ac_2O -pyridine. Recrystallization from pet. ether gave pure **11b** as colorless crystals, mp 77—78 °C (lit.^{8b} 77—77.5 °C, lit.^{8c} 76—78 °C). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1680, 1635, 1235. $^1\text{H-NMR}$ δ : 0.98 (s, 3H, Me), 1.09 (s, 3H, Me), 1.96 (s, 3H, Me), 2.20 (s, 3H, OCOMe), 2.2—2.7 (m, 2H, CH_2), 5.19 (s, 1H, $-\text{CHOAc}$), 5.8—5.9 (m, 1H, $-\text{CH}=\text{}$). MS m/z : 196 (M^+). **9b**: Pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3600—3400, 1680. $^1\text{H-NMR}$ δ : 0.82 (s, 3H, Me), 1.21 (s, 3H, Me), 2.2—2.4 (m, 2H, CH_2), 3.37 (s, 3H, OMe), 3.67 (brs, 1H, OH, disappeared on addition of D_2O), 3.98 (m, 3H, $-\text{CH}_2\text{OMe}$ and $-\text{CHOH}$), 6.1—6.2 (m, 1H, $-\text{CH}=\text{}$). The acetate (**9b**-acetate) was obtained from **9b** by treatment with Ac_2O -pyridine as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1690, 1640, 1230. $^1\text{H-NMR}$ δ : 0.98 (s, 3H, Me), 1.11 (s, 3H, Me), 2.21 (s, 3H, OCOMe), 2.3—2.5 (m, 2H, CH_2), 3.39 (s, 3H, OMe), 4.20 (s, 2H, CH_2OMe), 5.23 (s, 1H, $-\text{CHOAc}$), 6.1—6.2 (m, 1H, $-\text{CH}=\text{}$). Exact mass Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4$: 226.1205. Found: 226.1205.

6-Hydroxy-3-phenyl-2-cyclohexenone (8c) and 6-Hydroxy-4-methoxy-3-phenyl-2-cyclohexenone (10)—Compound **8c** (110 mg) and a 3:2 diastereo-mixture of **10** (32 mg) were obtained from **7c** (172 mg, 1 mmol), PIDA (644 mg, 2 mmol) and KOH (336 mg, 6 mmol). Recrystallization of **8c** from benzene-*n*-hexane gave the pure sample as colorless crystals, mp 71—74 °C (lit.¹²) no physical or spectral data). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3550—3450, 1670, 1605, 1105, 910. $^1\text{H-NMR}$ δ : 1.9—2.3 (m, 1H, $\text{C}_5\text{-H}$), 2.5—2.8 (m, 1H, $\text{C}_5\text{-H}$), 2.9—3.1 (m, 2H, $\text{C}_4\text{-H}$), 3.8—4.0 (brs, 1H, OH, disappeared on addition of D_2O), 4.32 (dd, 1H, $J=6$ and 14 Hz, $\text{C}_6\text{-H}$), 6.57 (s, 1H, $\text{C}_2\text{-H}$), 7.4—7.7 (m, 5H, ArH). Exact mass Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_2$: 188.0835. Found: 188.0823. A 3:2 diastereo-mixture of **10**: IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3550—3450, 1680, 1605, 1425, 1265, 1080. $^1\text{H-NMR}$ δ : 1.5—1.8 (brs, 1H, OH), 1.9—2.3 (m, 1H, $\text{C}_5\text{-H}$), 2.8—3.2 (m, 1H, $\text{C}_5\text{-H}$), 3.37 (s, 9/5H, OMe $\times$ 3/5), 3.59 (s, 6/5H, OMe $\times$ 2/5), 4.2—5.0 (m, 2H, $\text{C}_4\text{-H}$ and $\text{C}_6\text{-H}$), 6.42 (d, 3/5H, $-\text{CH}=\text{}$ $\times$ 3/5), 6.52 (s, 2/5H, $-\text{CH}=\text{}$ $\times$ 2/5), 7.3—7.8 (m, 5H, ArH). Exact mass Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$: 218.0941. Found: 218.0913. The acetate (**10**-acetate) was obtained from **10** by treatment with Ac_2O -pyridine. Careful separation of the 3:2 diastereo-mixture of **10**-acetate by column chromatography on silica gel with *n*-hexane: ethyl acetate = 5:1 gave two isomers (**10**-acetate-A and **10**-acetate-B) in a 3:2 ratio. **10**-acetate-A: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1690, 1600, 1425, 1375, 1230. $^1\text{H-NMR}$ δ : 2.25 (s, 3H, OCOMe), 2.3—2.55 (m, 1H, $\text{C}_5\text{-H}$), 2.8—3.1 (m, 1H, $\text{C}_5\text{-H}$), 3.38 (s, 3H, OMe), 4.8—5.1 (m, 1H, $\text{C}_4\text{-H}$), 5.53 (dd, 1H, $J=14$ and 5 Hz, $\text{C}_6\text{-H}$), 6.38 (d, 1H, $J=2$ Hz, $\text{C}_2\text{-H}$), 7.52 (s, 5H, ArH). Exact mass Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4$: 260.1049. Found: 260.1071. **10**-acetate-B: Colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1685, 1610, 1420, 1375, 1230. $^1\text{H-NMR}$ δ : 2.25 (s, 3H, OCOMe), 2.7—2.9 (m, 1H, $\text{C}_5\text{-H}$), 3.2—3.5 (m, 1H, $\text{C}_5\text{-H}$), 3.59 (s, 3H, OMe), 4.5—4.7 (m, 1H, $\text{C}_4\text{-H}$), 5.88 (dd, 1H, $J=13$ and 5 Hz, $\text{C}_6\text{-H}$), 6.49 (s, 1H, $\text{C}_2\text{-H}$), 7.4—7.8 (m, 5H, ArH). Exact mass Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4$: 260.1048. Found: 260.1063.

References and Notes

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