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Manganese(III) acetate based tandem oxidation of various α and β-alkoxy α,β-unsaturated ketones

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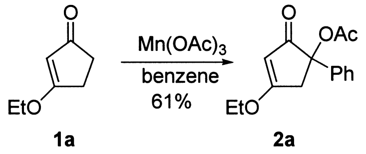
Abstract—We described the unusual results of manganese(III) acetate based tandem oxidation of various α and β-alkoxy α,β-unsaturated ketones to afford the corresponding α′-acetoxy-α′-phenyl substituted oxidation products in good yields. The tandem oxidation to monoacetoxylation ratio can be tuned by the amount of manganese(III) acetate. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

In the last decade, Manganese(III)-based oxidative free-radical reactions have been developed into a versatile protocol for the formation of highly functionalised products from simple precursors.[1–10] In 1976, Williams and Hunter reported that $Mn(OAc)_3 \cdot 2H_2O$ oxidation of enones in AcOH at reflux affords α′-acetoxy enones in low yields.[11] In connection with our synthetic studies with manganese(III) acetate,[12] we found that trapping the α′-keto radicals obtained from β-alkoxy α,β-unsaturated ketones by benzene used as a solvent is much faster than acetoxylation, affording good yields of tandem oxidation products.[12d] These interesting results prompted us towards the development of a new method in the field of the regioselective tandem oxidation of α-alkoxy and β-alkoxy α,β-unsaturated ketones. Here, we report our results obtained from the $Mn(OAc)_3$ oxidation of various α-alkoxy and β-alkoxy α,β-unsaturated ketones and an optimization of the reaction conditions.

2. Results and discussion

As a starting point, various β-alkoxy α,β-unsaturated ketones **1** were prepared from the corresponding 1,3-diketones using slightly modified literature procedures[13,14] and were then allowed to react with $Mn(OAc)_3$. We have found that Mn(III)-based oxidation of β-alkoxy α,β-unsaturated ketones is infact a versatile synthetic procedure with broad applicability.[15] For instance, reaction of **1a** with 3 equiv. of $Mn(OAc)_3$ in benzene as the solvent for 8 h at reflux afforded 61% of tandem oxidation product **2a**.



Scheme 1.

Characterization of the product revealed the introduction of a phenyl group together with an acetoxy moiety on the α′ position (Scheme 1). The full results are summarized in Table 1.

The reaction presumably proceeds via the formation of the Mn(III) enolate **3**, which loses Mn(II) upon one-electron oxidation to give α′-keto radical **4**[6,10d,16,17] (Scheme 2). Addition of this radical to benzene yields another radical, **5**. One-electron oxidation of the resultant radical **5** gives α′-phenyl β-alkoxy α,β-unsaturated ketones **6**. The introduction of aryl groups to ketones was reported to be confined to acetone, by Vinogradov et al.,[18] since α′-keto radicals generated by higher ketones would result in secondary radicals which would dimerize, or tertiary radicals that are prone to further oxidation. In contrast to this conclusion, in this study, no dimerization was observed. Oxidation of intermediate **6** by another equivalent of $Mn(OAc)_3$ provides α′-acetoxy α′-phenyl β-alkoxy α,β-unsaturated ketones **2**. Similarly, cyclopentenones **1b** and **1c** (entries 2 and 3) give 73 and 68% of tandem oxidation products **2b** and **2c**, respectively, together with a small amount of recovered starting material and some unidentified polymeric products.

With cyclohexenone derivatives **1d–h**, acetoxylation at the α′-position competes effectively with the tandem oxidation. For instance, reaction of 3-ethoxy-2-cyclohexenone **1d** with 3 equiv. of $Mn(OAc)_3$ in benzene for 8 h at reflux gives **2d** in 56% yield, **7d** in 35% yield and monophenylated product

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Keywords: enones; manganese and compounds; oxidation.

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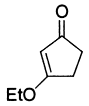
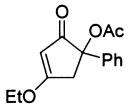
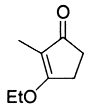
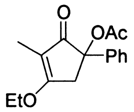
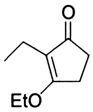
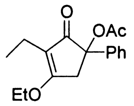
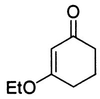
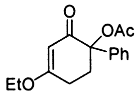
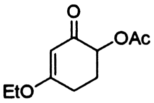
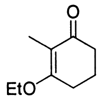
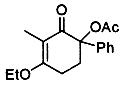
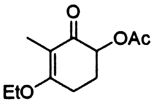
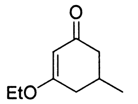
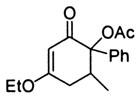
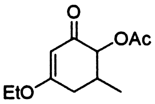
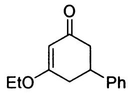
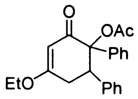
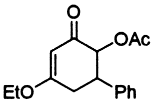
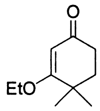
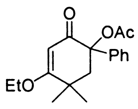
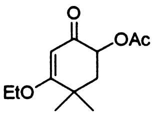
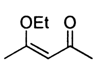
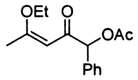
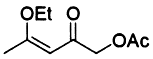
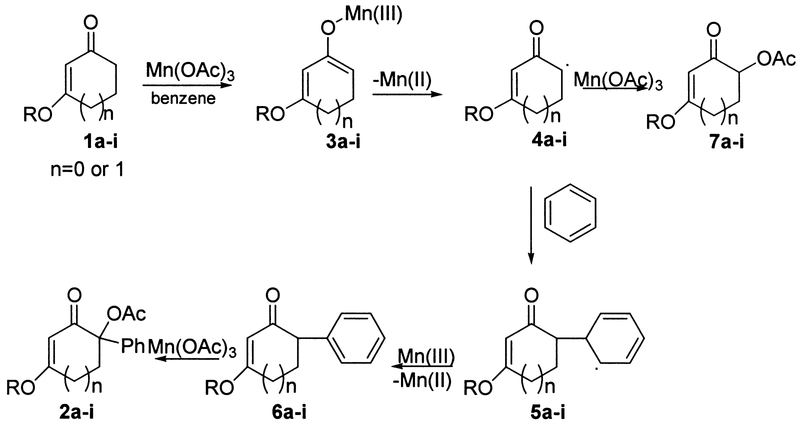
Table 1. Tandem oxidation of β-alkoxy α,β-unsaturated ketones with $Mn(OAc)_3$ in benzene

Entry	Reactant	Product	**2**	Yield (%)	Product	**7**	Yield (%)	Time (h)
1			a	61		–		8
2			b	73		–		8
3			c	68		–		8
4			d	56		d	35	12
5			e	59		e	28	12
6[a]			f	62		f	26	11
7[b]			g	65		g	25	10
8			h	60		h	31	12
9[c]			i	58		i	35	12

[a] The reaction was carried out with racemic mixture of **1f**. **2f** was isolated as 6:4 diastereomeric mixture, while **7f** was isolated as 8:2 *E*/*Z* mixture and **6f** as only *E* isomer by using ^1H NMR data.

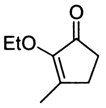
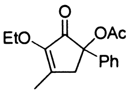
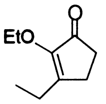
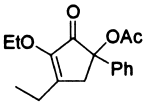
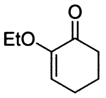
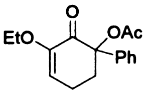
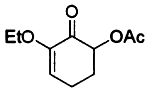
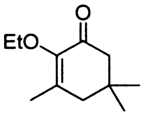
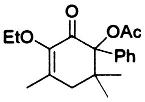
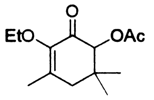
[b] **2g** was isolated as 7:3 diastereomeric mixture. Only isolable product **7g** has *E* configuration which was determined from ^1H NMR.

[c] **2i** was isolated as 7:3 diastereomeric mixture.



Scheme 2.

Table 2. Tandem oxidation of α-alkoxy α,β-unsaturated ketones with $Mn(OAc)_3$ in benzene

Entry	Reactant	Product	9	Yield (%)	Product	10	Yield (%)	Time (h)
1			a	72	–			8
2			b	75	–			8
3			c	63		c	28	12
4			d	59		d	32	10

6d in 5% yield. The isolation of monophenylated product was also achieved in entry 6 as **6f** with 6% yield. As a model study, monoacetoxylation product **7d** was subjected to $Mn(OAc)_3$ oxidation in a similar manner in entry 4 (3 equiv. $Mn(OAc)_3$ in benzene). As expected from the proposed reaction mechanism, no product formation was observed. When 4 equiv. of $Mn(OAc)_3$ was used (entry 4), we observed drastic increase in the chemical yield of monoacetoxylated product **7d** (53%) and a decrease in the tandem oxidation product **2d** (31%). Similar results were obtained for entries 5–8. Hence, we decided that the critical amount of oxidant for six-membered enones was 3 equiv.

Notably *Z*-3-ethoxy-2-pentenone (entry 9) behaves very similarly, giving **2i** in 58% yield as a 7:3 diastereomeric mixture. 35% of monoacetoxylated product **7i** was also isolated.

In the next step of this study, 3-ethoxy-2-cyclopentenone (entry 1) was chosen as a model compound. The $Mn(OAc)_3$ oxidation was performed in various solvents. With nitrobenzene and pyridine, no product formation was observed. With anisole, aniline and furan, only uncharacterized oxidation products were obtained. Bromobenzene and chlorobenzene each yielded 5-acetoxy-3-ethoxy-5-phenyl-2-cyclopentenone in 38 and 12% yields, respectively.

Other substrates various α-alkoxy α,β-unsaturated ketones **8** were next prepared from the corresponding 1,2-diketones using slightly modified literature procedures.[15] On reaction of **8a** with 3 equiv. of $Mn(OAc)_3$ in benzene at reflux for 8 h, **9a** was produced in 72% yield. Further examples of the reaction are summarized in Table 2. We suggest that reactions follow a similar route to that obtained in Scheme 2.

In conclusion, we have discovered an interesting and potentially useful $Mn(OAc)_3$ based tandem oxidation reaction. The applicability of a one-pot double oxidation method is attractive for further use in synthesis.

3. Experimental

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker Spectrospin Avance DPX 400 spectrometers. Chemical shifts are given in ppm from tetramethylsilane. Coupling constants (J) were recorded in Hertz. IR spectra were obtained from a Perkin–Elmer Model 1600 series FT–IR spectrometer and are reported in cm^{-1}. Mass spectra were recorded on a Varian MAT 212. Thin layer chromatography (TLC) was performed on Merck plastic-backed silica gel plates. Compounds were visualised under a UV lamp. Column chromatography was performed using silica gel (Flash Silica 60, 32–63 μm). 1,2- and 1,3-Diketones were purchased from Aldrich. α-Ethoxy and β-ethoxy α,β-unsaturated compounds were synthesized according to literature procedure.[13,14]

3.1. General procedure for the $Mn(OAc)_3$ oxidation of β-alkoxy α,β-unsaturated ketones

A mixture of $Mn(OAc)_3$ (2.41 g, 9.0 mmol) in benzene (or corresponding solvent) (100 mL) was refluxed for 45 min. under a Dean–Stark trap, then cooled to room temperature. β-Alkoxy α,β-unsaturated ketone (3.0 mmol) was gradually added and the mixture was allowed to reflux until the dark brown colour disappeared (TLC monitoring). The reaction mixture was diluted with ethyl acetate (100 mL) and the organic phase was washed with 1N HCl (100 mL), saturated $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$ and evaporated in vacuo. The crude product was separated by flash column chromatography using ethyl acetate/hexane as eluent to afford the product.

3.1.1. 5-Acetoxy-3-ethoxy-5-phenyl-2-cyclopentenone 2a. (0.48 g, 61%) as a white solid, mp 94–96°C; R_f (EtOAc/hexane 1:3) 0.35; ν_{max} (neat) 1740, 1715 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.18–7.34 (5H, m, Ph), 5.25 (1H, s, $CH{=}$), 4.02–4.13 (2H, m, $MeCH_2O$), 3.30 (1H, d, J=18 Hz, $CH_aH_bCOAcPh$), 3.13 (1H, d, J=18 Hz, CH_aH_b-COAcPh), 2.10 (3H, s, $MeCO_2$), 1.36 (3H, t, J=7 Hz, $MeCH_2O$); δ_C (100.6 MHz, $CDCl_3$) 199.4, 185.8, 170.1, 138.6, 129.0, 128.5, 125.1, 102.5, 84.1, 68.2, 43.0, 21.7, 14.5; *m/z* (EI) 260 (9), 218 (32), 217 (28), 200 (25), 105 (100), 77 (22%). HRMS (EI): M^+, found 260.1049. $C_{15}H_{16}O_4$ requires 260.1048.

3.1.2. 5-Acetoxy-3-ethoxy-2-methyl-5-phenyl-2-cyclopentenone 2b. (0.60 g, 73%) as a colourless oil; R_f (EtOAc/hexane 1:2) 0.33; ν_{max} (neat) 1743, 1714 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.13–7.40 (5H, m, Ph), 4.29 (2H, q, *J*=7 Hz, MeC*H*$_2$O), 3.66 (1H, d, *J*=17 Hz, C*H*$_a$H$_b$-COAcPh), 3.33 (1H, d, *J*=17 Hz, CH$_a$*H*$_b$COAcPh), 2.19 (3H, s, *Me*CO$_2$), 1.71 (3H, s, *Me*C=), 1.45 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, $CDCl_3$) 204.9, 183.3, 170.3, 140.2, 139.1, 129.0, 127.9, 127.3, 124.9, 114.3, 84.0, 50.9, 35.5, 21.8, 15.7, 6.8; *m/z* (EI) 276 (18), 275 (83), 247 (13), 231 (11), 218 (22), 217 (100), 215 (29%). HRMS (EI): M^+, found 274.1198. $C_{16}H_{18}O_4$ requires 274.1206.

3.1.3. 5-Acetoxy-3-ethoxy-2-ethyl-5-phenyl-2-cyclopentenone 2c. (0.59 g, 68%) as a colourless oil; R_f (EtOAc/hexane 1:2) 0.35; ν_{max} (neat) 1746, 1715 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.15–7.33 (5H, m, Ph), 4.24 (2H, q, *J*=7 Hz, MeC*H*$_2$O), 3.64 (2H, d, *J*=17 Hz, C*H*$_2$COAcPh), 2.22 (2H, q, *J*=7 Hz, MeC*H*$_2$C=), 2.18 (3H, s, *Me*CO$_2$), 1.43 (3H, t, *J*=7 Hz, *Me*CH$_2$O), 1.04 (3H, t, *J*=7 Hz, *Me*CH$_2$C=); δ_C (100.6 MHz, $CDCl_3$) 201.1, 176.9, 170.6, 139.1, 128.3, 125.7, 124.9, 121.8, 120.5, 119.9, 84.0, 68.4, 42.2, 21.7, 15.4, 15.2, 13.1; *m/z* (EI) 290 (15), 289 (83), 261 (18), 232 (16), 231 (100), 229 (17%). HRMS (EI): M^+, found 288.1371. $C_{17}H_{20}O_4$ requires 288.1362.

3.1.4. 6-Acetoxy-3-ethoxy-6-phenyl-2-cyclohexenone 2d. (0.46 g, 56%) as a colourless oil; R_f (EtOAc/hexane 1:8) 0.81; ν_{max} (neat) 3066, 1758, 1675 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.19–7.38 (5H, m, Ph), 5.56 (1H, s, C*H*=), 3.83–3.95 (2H, m, MeC*H*$_2$O), 2.10–2.30 (4H, m, C*H*$_2$C*H*$_2$-COAcPh), 2.05 (3H, s, *Me*CO$_2$), 1.29 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, $CDCl_3$) 199.3, 176.6, 169.9, 137.6, 128.6, 128.5, 128.3, 126.8, 126.7, 103.2, 96.1, 64.9, 29.4, 28.2, 21.8, 14.1; HRMS (EI): M^+, found 274.1211. $C_{16}H_{18}O_4$ requires 274.1206.

3.1.5. 6-Acetoxy-3-ethoxy-2-cyclohexenone 7d. (0.21 g, 35%) as a colourless oil; R_f (EtOAc/hexane 1:8) 0.66; ν_{max} (neat) 1736, 1665 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 5.37 (1H, s, C*H*=), 5.29 (1H, dd, *J*=5, 13 Hz, C*H*OAc), 3.92 (2H, q, *J*=7 Hz, MeC*H*$_2$O), 2.63–2.67 (1H, m, C*H*$_a$CH$_b$C=), 2.52–2.54 (1H, m, CH$_a$C*H*$_b$C=), 2.20–2.24 (1H, m, C*H*$_a$CH$_b$COAc), 2.19 (3H, s, *Me*OAc), 2.07–2.16 (1H, m, CH$_a$C*H*$_b$COAc), 1.37 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, $CDCl_3$) 193.4, 177.1, 170.5, 101.5, 72.8, 65.2, 28.3 27.1, 21.2, 14.4; *m/z* (EI) 217 (19), 200 (14), 199 (100%); HRMS (EI): M^+, found 198.0883. $C_{10}H_{14}O_4$ requires 198.0892.

3.1.6. 3-Ethoxy-6-phenyl-2-cyclohexenone 6d. (0.03 g, 5%) as a colourless oil; R_f (EtOAc/hexane 1:8) 0.72; ν_{max} (neat) 3150, 1691, 1641 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.10–7.28 (5H, m, Ph), 5.44 (1H, s, C*H*=), 3.88 (2H, q, *J*=7 Hz, MeC*H*$_2$O), 3.44–3.49 (1H, dd, *J*=5, 10 Hz, C*H*Ph), 2.40–2.51 (2H, m, =CC*H*$_2$), 2.12–2.17 (2H, m, CH$_2$C*H*$_2$CHPh), 1.32 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, $CDCl_3$) 199.6, 177.7, 140.3, 128.9, 128.7, 127.6, 127.2, 126.6, 103.6, 64.8, 52.3, 29.8, 28.6, 14.5; HRMS (EI): M^+, found 216.1147. $C_{14}H_{16}O_2$ requires 216.1151.

3.1.7. 6-Acetoxy-3-ethoxy-2-methyl-6-phenyl-2-cyclohexenone 2e. (0.51 g, 59%) as a colourless oil; R_f (EtOAc/hexane 1:2) 0.66; ν_{max} (neat) 3020, 2975, 1725, 1695 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.14–7.33 (5H, m, Ph), 4.01 (2H, q, *J*=7 Hz, MeC*H*$_2$O), 2.16–2.61 (4H, m, C*H*$_2$C*H*$_2$), 2.14 (3H, s, *Me*OAc), 1.78 (3H, s, *Me*C=), 1.37 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, $CDCl_3$) 195.0, 177.2, 170.5, 137.2, 129.3, 128.5, 127.9, 127.1, 126.9, 121.1, 87.4, 65.5, 59.2, 47.3, 22.1, 20.8, 14.5; HRMS (EI): M^+, found 288.1359. $C_{17}H_{20}O_4$ requires 288.1362.

3.1.8. 6-Acetoxy-3-ethoxy-2-methyl-2-cyclohexenone 7e. (0.18 g, 28%) as a colourless oil; R_f (EtOAc/hexane 1:2) 0.51; ν_{max} (neat) 1733, 1658 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 5.90–5.91 (1H, m, C*H*OAc), 4.04 (2H, q, *J*=7 Hz, MeC*H*$_2$O), 2.54–2.63 (1H, m, =CC*H*$_a$H$_b$CH$_2$), 2.34–2.39 (1H, m, =CH$_a$*H*$_b$CH$_2$), 2.15–2.17 (2H, m, CH$_2$C*H*$_2$-COAc), 2.14 (3H, s, *Me*CO$_2$), 1.76 (3H, s, *Me*C=), 1.33 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, $CDCl_3$) 198.7, 170.6, 164.8, 120.1, 70.1, 64.7, 32.1, 27.0, 21.2, 15.9, 15.7; *m/z* (EI) 213 (100), 153 (11%). HRMS (EI): M^+, found 212.1052. $C_{11}H_{16}O_4$ requires 212.1049.

3.1.9. 6-Acetoxy-3-ethoxy-5-methyl-6-phenyl-2-cyclohexenone 2f. (0.54 g, 62%) as a colourless oil; R_f (EtOAc/hexane 1:4) 0.24; ν_{max} (neat) 3016, 2976, 1728, 1685 cm^{-1}; δ_H (400 MHz, $CDCl_3$) (6:4 diastereomeric mixture) 7.01–7.30 (2×5H, m, Ph), 5.43 (1H, s, C*H*=), 5.36 (1H, s, C*H*=), 3.82–3.96 (2×2H, m, MeC*H*$_2$O), 2.43–2.48 (2×1H, m, C*H*Me), 2.23–2.36 (2×2H, m, C*H*$_2$CHMe), 2.11 (3H, s, *Me*CO$_2$), 2.10 (3H, s, *Me*CO$_2$), 1.36 (3H, t, *J*=7 Hz, *Me*CH$_2$O), 1.35 (3H, t, *J*=7 Hz, *Me*CH$_2$O), 0.91 (3H, d, *J*=6 Hz, *Me*CH), 0.84 (3H, d, *J*=6 Hz, *Me*CH); δ_C (100.6 MHz, $CDCl_3$) 195.3, 193.5, 178.2, 177.4, 170.2, 166.5, 140.1, 138.9, 129.5, 128.8, 128.5, 128.3, 127.2, 103.2, 101.3, 64.7, 63.5, 61.4, 60.8, 38.1, 37.5, 35.7, 34.8, 31.3, 30.8, 21.1, 20.6, 14.7, 14.6; HRMS (EI): M^+, found 288.1356. $C_{17}H_{20}O_4$ requires 288.1362.

3.1.10. 6-Acetoxy-3-ethoxy-5-methyl-2-cyclohexenone 7f. (0.17 g, 26%) as a colourless oil; R_f (EtOAc/hexane 1:4) 0.21; ν_{max} (neat) 1739, 1646 cm^{-1}; δ_H (400 MHz, $CDCl_3$) (8:2 *E*/*Z* mixture) 5.46 (1H, d, *J*=5 Hz, C*H*=), 5.40 (1H, s, C*H*=), 5.38 (1H, s, C*H*OAc), 5.09 (1H, d, *J*=12 Hz, C*H*OAc), 3.89–4.02 (2×2H, m, MeC*H*$_2$O), 2.83–2.89 (2×1H, m, C*H*Me), 2.45–2.61 (2×1H, m, =CC*H*$_a$H$_b$), 2.34–2.43 (2×1H, m, =CCH$_a$C*H*$_b$), 2.24 (3H, s, *Me*CO$_2$), 2.23 (3H, s, MeCO$_2$), 1.39–1.43 (2×3H, m, *Me*CH$_2$O), 1.12 (3H, d, *J*=7 Hz, *Me*CH), 1.09 (3H, d, *J*=7 Hz, *Me*CH); δ_C (100.6 MHz, $CDCl_3$) 193.2, 192.7, 176.1, 174.9, 170.9, 170.5, 102.7, 101.4, 101.0, 78.3, 75.8, 65.2, 64.6, 45.5, 37.6, 36.9, 35.7, 33.8, 31.9, 21.2, 21.1, 18.1, 14.4, 13.7; HRMS (EI): M^+, found 212.1042. $C_{11}H_{16}O_4$ requires 212.1049.

3.1.11. 3-Ethoxy-5-methyl-6-phenyl-2-cyclohexenone 6f. (0.04 g, 6%) as a colourless oil; R_f (EtOAc/hexane 1:4) 0.26; ν_{max} (neat) 3210, 1693, 1643 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.03–7.28 (5H, m, Ph), 5.45 (1H, s, C*H*=), 3.80–3.92 (2H, m, MeC*H*$_2$O), 3.06 (1H, d, *J*=11 Hz, C*H*Ph), 2.44–2.49 (1H, dd, *J*=4, 16 Hz, C*H*$_a$H$_b$CHMe), 2.32–2.41

(2H, m, CH$_a$*H$_b$*C*H*Me), 1.33 (3H, t, *J*=7 Hz, *Me*CH$_2$O), 0.84 (3H, d, *J*=6 Hz, *Me*CH); δ_C (100.6 MHz, CDCl$_3$) 198.7, 176.7, 139.7, 128.6, 128.3, 127.9, 127.4, 126.3, 101.3, 65.4, 53.2, 30.2, 21.3, 15.2, 14.3; HRMS (EI): M$^+$, found 230.1302. $C_{15}H_{18}O_2$ requires 230.1307.

3.1.12. 6-Acetoxy-3-ethoxy-5,6-diphenyl-2-cyclohexenone 2g. (0.68 g, 65%) as a colourless oil; R_f (EtOAc/hexane 1:3) 0.42; ν_{max} (neat) 3010, 2973, 1738, 1674 cm^{-1}; δ_H (400 MHz, CDCl$_3$) (7:3 diastereomeric mixture) 6.93–7.16 (10H, m, Ph), 5.71 (1H, s, C*H*=), 5.60 (1H, s, C*H*=), 3.75–3.83 (2×3H, m, MeC*H$_2$*O), 2.33–2.40 (2×2H, m, C*H$_2$*CHPh), 1.91 (3H, s, *Me*CO$_2$), 1.89 (3H, s, *Me*CO$_2$), 1.13 (3H, t, *J*=7 Hz, *Me*CH$_2$O), 1.09 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, CDCl$_3$) 196.7, 194.2, 176.1, 175.7, 172.3, 171.6, 140.4, 139.8, 129.1, 127.9, 127.7, 126.5, 109.8, 102.0, 101.3, 65.3, 64.8, 42.4, 41.2, 36.2, 35.4, 20.1, 19.8, 14.3, 14.1; HRMS (EI): M$^+$, found 350.1531. $C_{22}H_{22}O_4$ requires 350.1518.

3.1.13. 6-Acetoxy-3-ethoxy-5-phenyl-2-cyclohexenone 7g. (0.21 g, 25%) as a colourless oil; R_f (EtOAc/hexane 1:3) 0.37; ν_{max} (neat) 3015, 2875, 1734 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.24–7.36 (5H, m, Ph), 5.63 (1H, d, *J*=13 Hz, C*H*OAc), 5.46 (1H, s, C*H*=), 3.96 (2H, q, *J*=7 Hz, MeC*H$_2$*O), 3.50 (1H, dt, *J*=5, 13 Hz, C*H*Ph), 2.87 (1H, dd, *J*=6, 18 Hz, C*H$_a$*H$_b$CHPh), 2.70 (1H, dd, *J*=5, 18 Hz, CH$_a$*H$_b$*CHPh), 1.95 (3H, s, *Me*CO$_2$), 1.33 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, CDCl$_3$) 192.8, 175.8, 170.6, 139.6, 129.1, 128.8, 128.5, 127.9, 127.7, 101.4, 76.0, 65.5, 45.0, 37.3, 20.9, 14.4; *m/z* (EI) 274 (100), 215 (22%); HRMS (EI): M$^+$, found 274.1193. $C_{16}H_{18}O_4$ requires 274.1206.

3.1.14. 6-Acetoxy-3-ethoxy-4,4-dimethyl-6-phenyl-2-cyclohexenone 2h. (0.54 g, 60%) as a colourless oil; R_f (EtOAc/hexane 1:5) 0.68; ν_{max} (neat) 3012, 2970, 1742, 1682 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.09–7.28 (5H, m, Ph), 5.50 (1H, s, C*H*=), 3.82–4.05 (2H, m, MeC*H$_2$*O), 2.17 (1H, d, *J*=13 Hz, C*H$_a$*H$_b$COAcPh), 2.10 (3H, s, *Me*CO$_2$), 1.87 (1H, d, *J*=13 Hz, CH$_a$*H$_b$*COAcPh), 1.32 (3H, t, *J*=7 Hz, *Me*CH$_2$O), 1.29 (3H, s, *Me*MeC), 1.14 (3H, s, Me*Me*C); δ_C (100.6 MHz, CDCl$_3$) 192.8, 175.7, 170.6, 139.6, 129.1, 128.5, 127.9, 127.7, 126.8, 101.4, 96.5, 76.0, 65.5, 45.0, 37.3, 27.7, 20.9, 14.5; HRMS (EI): M$^+$, found 302.1511. $C_{18}H_{22}O_4$ requires 302.1518.

3.1.15. 6-Acetoxy-3-ethoxy-4,4-dimethyl-2-cyclohexenone 7h. (0.21 g, 31%) as a colourless oil; R_f (EtOAc/hexane 1:5) 0.60; ν_{max} (neat) 1745, 1660 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 5.30 (1H, dd, *J*=7, 12 Hz, C*H*OAc), 5.09 (1H, s, C*H*=), 3.74 (2H, q, *J*=7 Hz, MeC*H$_2$*O), 2.01 (3H, s, *Me*CO$_2$), 1.84–1.90 (2H, m, C*H$_2$*CHOAc), 1.21 (3H, t, *J*=7 Hz, *Me*CH$_2$O), 1.19 (3H, s, *Me*MeC), 1.06 (3H, s, Me*Me*C); δ_C (100.6 MHz, CDCl$_3$) 193.7, 182.2, 170.7, 99.8, 70.9, 65.2, 41.7, 37.7, 27.7, 25.8, 21.3, 14.3; *m/z* (EI) 227 (100), 215 (7%); HRMS (EI): M$^+$, found 226.1212, $C_{12}H_{18}O_4$ requires 226.1205.

3.1.16. 1-Acetoxy-4-ethoxy-1-phenyl-pent-3-en-2-one 2i. (0.46 g, 58%) as a colourless oil; R_f (EtOAc/hexane 1:10) 0.90; ν_{max} (neat) 3015, 2969, 1742, 1692 cm^{-1}; δ_H (400 MHz, CDCl$_3$) (7:3 diastereoisomeric mixture) 6.84–7.56 (2×5H, m, Ph), 6.39 (2×1H, s, C*H*OAcPh), 6.33 (1H, s, C*H*=), 6.32 (1H, s, C*H*=), 3.87–3.93 (2×2H, m, MeC*H$_2$*O), 2.19 (3H, s, *Me*CO$_2$), 2.15 (3H, s, *Me*CO$_2$), 2.05 (3H, s, *Me*C=), 1.89 (3H, s, *Me*C=), 1.29–1.37 (2×3H, m, *Me*CH$_2$O); δ_C (100.6 MHz, CDCl$_3$) 205.2, 201.0, 169.9, 168.6, 159.8, 159.2, 137.4, 137.1, 135.2, 133.3, 130.8, 130.0, 129.0, 128.9, 128.7, 127.3, 127.1, 114.1, 113.9, 90.1, 81.9, 63.4, 63.2, 61.0, 21.2, 20.8, 20.0, 15.3, 15.2; HRMS (EI): M$^+$, found 262.1198, $C_{15}H_{18}O_4$ requires 262.1205.

3.1.17. 1-Acetoxy-4-ethoxy-pent-3-en-2-one 7i. (0.20 g, 35%) as a colourless oil; R_f (EtOAc/hexane 1:10) 0.83; ν_{max} (neat) 1735, 1685 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 6.44 (1H, s, C*H*=), 4.78 (2H, s, C*H$_2$*OAc), 3.92 (2H, q, *J*=7 Hz, MeC*H$_2$*O), 2.18 (3H, s, *Me*CO$_2$), 2.09 (3H, s, *Me*C=), 1.33 (3H, t, *J*=7 Hz, *Me*CH$_2$O); δ_C (100.6 MHz, CDCl$_3$) 202.4, 170.2, 159.9, 136.3, 130.8, 114.1, 69.6, 63.5, 20.8, 19.8, 15.2; HRMS (EI): M$^+$, found 186.2051. $C_9H_{14}O_4$ requires 186.0892.

3.2. General procedure for the Mn(OAc)$_3$ oxidation of α-alkoxy α,β-unsaturated ketones

A mixture of Mn(OAc)$_3$ (2.41 g, 9.0 mmol) in benzene (or corresponding solvent) (100 mL) was refluxed for 45 min. under a Dean–Stark trap, then cooled to room temperature. α-Alkoxy α,β-unsaturated ketone (3.0 mmol) was gradually added and the mixture was allowed to reflux until the dark brown colour disappeared (TLC monitoring). The reaction mixture was diluted with ethyl acetate (100 mL) and the organic phase was washed with 1N HCl (100 mL), saturated NaHCO$_3$ and brine. The organic phase was dried over MgSO$_4$ and evaporated in vacuo. The crude product was separated by flash column chromatography using ethyl acetate/hexane as eluent to afford the product.

3.2.1. 5-Acetoxy-2-ethoxy-3-methyl-5-phenyl-2-cylopentenone 9a. (0.59 g, 72%) as a colourless oil; R_f (EtOAc/hexane 1:6) 0.63; ν_{max} (neat) 1748, 1640 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.06–7.46 (5H, m, Ph), 4.15 (2H, q, *J*=7 Hz, MeC*H$_2$*O), 2.91 (1H, d, *J*=18 Hz, C*H$_a$*H$_b$-COAcPh), 2.46 (1H, d, *J*=18 Hz, CH$_a$*H$_b$*COAcPh), 2.06 (3H, s, MeCO$_2$), 2.00 (3H, s, *Me*C=), 1.21 (3H, t, *J*=7 Hz, MeCH$_2$O); δ_C (100.6 MHz, CDCl$_3$) 203.1, 169.2, 154.7, 140.2, 129.2, 129.0, 127.9, 127.3, 127.1, 90.1, 66.5, 50.0, 37.6, 21.3, 16.1, 15.3; *m/z* (EI) 216 (60), 188 (100), 173 (27), 159 (26), 145 (28), 131 (33), 118 (37), 105 (36), 103 (35), 91 (32), 77 (33%); HRMS (EI): (M−$C_2H_2O_2$), found 216.1150. $C_{16}H_{18}O_4$ requires 216.1151.

3.2.2. 5-Acetoxy-2-ethoxy-3-ethyl-5-phenyl-2-cylopentenone 9b. (0.65 g, 75%) as a colourless oil; R_f (EtOAc/hexane 1:5) 0.65; ν_{max} (neat) 3014, 1748, 1606, 1364, 1239, 738 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.26–7.46 (5H, m, Ph), 4.24–4.31 (1H, m, MeC*H$_a$*H$_b$O), 4.08–4.15 (1H, m, MeCH$_a$*H$_b$*O), 3.14 (1H, d, *J*=18 Hz, C*H$_a$*H$_b$COAcPh), 3.08 (1H, d, *J*=18 Hz, CH$_a$*H$_b$*COAcPh), 2.53 (2H, q, *J*=8 Hz, MeC*H$_2$*C=), 2.19 (3H, s, *Me*CO$_2$), 1.18–1.26 (2×3H, m, *Me*CH$_2$O, *Me*CH$_2$C=); δ_C (100.6 MHz, CDCl$_3$) 197.1, 170.0, 155.9, 149.0, 138.2, 129.0, 128.5, 127.1, 124.2, 122.5, 82.1, 66.5, 40.5, 22.0, 21.6, 15.9, 11.9; *m/z* (EI) 289 (6), 261 (30), 249 (60), 229 (100), 121 (30%);

HRMS (EI): M$^+$, found 288.3383, $C_{17}H_{20}O_4$ requires 288.1362.

3.2.3. 6-Acetoxy-2-ethoxy-6-phenyl-2-cylohexenone 9c. (0.52 g, 63%) as a colourless oil; R_f (EtOAc/hexane 1:8) 0.80; ν_{max} (neat) 3410, 2970, 1735, 1643 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.50–6.98 (5H, m, Ph), 5.39–5.44 (1H, m, C*H*═), 4.07–4.20 (2H, m, MeCH_2O), 2.15–2.27 (2H, m, CH_2), 2.05 (3H, s, *Me*CO_2), 1.98–2.02 (1H, m, CH_aH$_b$), 1.81–1.87 (1H, m, CH$_a$$H_b$), 1.35 (3H, t, *J*=7 Hz, MeCH_2O); δ_C (100.6 MHz, $CDCl_3$) 200.6, 170.3, 146.5, 144.2, 128.4, 122.6, 116.4, 115.6, 114.8, 112.5, 74.5, 62.7, 51.2, 28.8, 21.1, 15.6; *m/z* (EI) 275 (6), 269 (9), 241 (20), 177 (100), 167 (18), 135 (25%); HRMS (EI): M$^+$, found 274.1205, $C_{16}H_{18}O_4$ requires 274.3117.

3.2.4. 6-Acetoxy-2-ethoxy-2-cylohexenone 10c. (0.17 g, 28%) as a colourless oil; R_f (EtOAc/hexane 1:8) 0.66; ν_{max} (neat) 3415, 2973, 1732, 1623, 1378 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 5.77–5.80 (1H, m, C*H*═), 5.30 (1H, dd, *J*=5, 13 Hz, C*H*OAc), 3.71 (2H, q, *J*=7 Hz, MeCH_2O), 2.39–2.47 (2H, m, ═CCH_2), 2.13–2.18 (1H, m, CH_aH$_b$CHOAc), 2.10 (3H, s, *Me*CO_2), 1.99–2.08 (1H, m, CH$_a$$H_b$CHOAc), 1.29 (3H, t, *J*=7 Hz, *Me*CH_2O); δ_C (100.6 MHz, $CDCl_3$) 189.4, 170.1, 150.5, 116.6, 64.0, 29.2, 22.1, 21.2, 15.2, 14.8; *m/z* (EI) 199 (100), 157 (5), 139 (20%); HRMS (EI): M$^+$, found 198.0892. $C_{10}H_{14}O_4$ requires 198.2158.

3.2.5. 6-Acetoxy-2-ethoxy-3,5,5-trimethyl-6-phenyl-2-cylohexenone 9d. (0.56 g, 59%) as a colourless oil; R_f (EtOAc/hexane 1:14) 0.41; ν_{max} (neat) 3400, 2976, 1738, 1676 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.82–7.05 (5H, m, Ph), 3.69–3.74 (2H, m, MeCH_2O), 2.34 (1H, d, *J*=18 Hz, CH_aH$_b$CMeMe), 2.16 (1H, d, *J*=18 Hz, CH$_a$$H_b$CMeMe), 2.14 (3H, s, *Me*CO_2), 1.82 (3H, s, *Me*C═), 1.15 (3H, t, *J*=7 Hz, *Me*CH_2O), 0.99 (3H, s, *Me*MeC), 0.91 (3H, s, Me*Me*C); δ_C (100.6 MHz, $CDCl_3$) 196.5, 171.3, 155.6, 142.4, 134.1, 128.8, 128.4, 127.2, 126.2, 114.7, 110.1, 61.4, 45.1, 34.3, 21.4, 20.3, 17.9, 15.7, 14.2; HRMS (EI): M$^+$, found 316.1668. $C_{19}H_{24}O_4$ requires 316.1674.

3.2.6. 6-Acetoxy-2-ethoxy-3,5,5-trimethyl-2-cylohexenone 10d. (0.23 g, 32%) as a colourless oil; R_f (EtOAc/hexane 1:14) 0.33; ν_{max} (neat) 3417, 2988, 1730, 1632 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 5.08 (1H, s, C*H*OAc), 3.77–3.85 (1H, m, MeCH_aH$_b$O), 3.63–3.70 (1H, m, MeCH$_a$$H_b$O), 2.44 (1H, d, *J*=18 Hz, CH_aH$_b$CMeMe), 2.08 (3H, s, *Me*CO_2), 2.05 (1H, d, *J*=18 Hz, CH$_a$$H_b$-CMeMe), 1.78 (3H, s, *Me*C═), 1.14 (3H, t, *J*=7 Hz, *Me*CH_2O), 0.96 (3H, s, *Me*MeC), 0.86 (3H, s, Me*Me*C); δ_C (100.6 MHz, $CDCl_3$) 189.6, 170.7, 146.6, 142.3, 81.2, 67.8, 44.5, 37.8, 27.7, 20.2, 19.9, 18.0, 15.8; HRMS (EI): M$^+$, found 239.1281, $C_{13}H_{19}O_4$ requires 239.1284.

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