Allylic Oxidation of Methyl 2-Alkenoates

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Allylic oxidation of methyl 2-alkenoates with chromium trioxide in a mixture of acetic anhydride and acetic acid afforded methyl 4-oxo-2-alkenoates.

The allylic oxidation of cycloalkenes to cycloalkenones with chromium trioxide in acetic acid has been reported.[1] However, the oxidation of methyl 2-alkenoates with the above reagent has not yet been reported.

We wish to report the allylic oxidation of methyl 2-alkenoates with a modified reagent prepared from chromium trioxide in a mixture of acetic anhydride and acetic acid. This reagent has the advantage that it is readily available and the reaction is rapid and efficient. The resulting product gave methyl 4-oxoalkanoates, which can be converted into cyclopentenones,[2] by reduction with zinc in acetic acid[3] or titanium trichloride.[4]

The methyl 2-alkenoates (**1a**—**f**) were prepared by a Wittig reaction using methoxycarbonylmethylenetriphenylphosphorane[5] of the corresponding aldehydes in good yields.

When methyl 2-decenoate (**1a**) was treated by the chromium trioxide–(pyridine)$_2$–dichloromethane system[6] or *t*-butyl chromate reagent[7] under several reaction conditions, the oxidation product was not obtained. On the other hand, **1a** was more slowly oxidized with chromium trioxide in acetic acid to give methyl 4-oxo-2-decenoate (**2a**). The addition of acetic anhydride to the above solution, however, resulted in a rapid oxidation. Consequently, the oxidation of **1a** was carried out in a mixture of acetic anhydride and glacial acetic acid (1:2) with chromium trioxide.

The oxidation of **1a** for 50 min with chromium trioxide in acetic anhydride and acetic acid (1:2) containing 1:1, 1.5:1, 3:1, 3.5:1, and 5:1 molar ratios of chromium trioxide to **1a** gave conversions to **2a** of 10, 20, 38, 57, and 80%, respectively. It is clear from the data that 5 mol equivalents of the reagent are required for complete conversion to ketone. With less than the 5:1 molar ratio extremely slow oxidation occurs.

Preparation of methyl 4-oxo-2-alkenoates (**2a**—**f**) was carried out by this method (Table 1).

The reagent was prepared by addition of chromium trioxide (50 mmol) in small portions to a mixture of acetic anhydride and glacial acetic acid under ice-cooling. Into the solution of the above reagent, methyl 2-alkenoates (**1a**—**f**) (10 mmol) were added with stirring. The optimal conditions for formation of methyl 4-oxo-2-alkenoates (**2a**—**f**) with minimum recovery of starting material were maintained by keeping a temperature at 15—25 °C for moderate times; if the temperature was allowed to rise to 30 °C, the desired product was obtained in a poor yield in the same reaction period. It was determined by gas chromatography that methyl 4-oxo-2-alkenoates (**2a**—**f**) were the sole reaction products.

Table 1. Allylic oxidation of methyl 2-alkenoates (**1**) with chromium trioxide

$$R\text{-}CH_2\text{-}CH{=}CH\text{-}COOCH_3 \xrightarrow[Ac_2O\text{-}AcOH]{CrO_3} R\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH{=}CH\text{-}COOCH_3$$

(**1**) (**2**)

Substrate	R	Molar ratio of **1** : CrO_3	Time (min)	Product (% yield)[a,b]
1a	n-C_6H_{13}	1 : 1	50	**2a** 10
1a	n-C_6H_{13}	1 : 1.5	50	**2a** 20
1a	n-C_6H_{13}	1 : 3	50	**2a** 38
1a	n-C_6H_{13}	1 : 3.5	50	**2a** 57
1a	n-C_6H_{13}	1 : 5	50	**2a** 80
1b	C_2H_5	1 : 5	30	**2b** 50
1c	n-C_3H_7	1 : 5	30	**2c** 72
1d	n-C_4H_9	1 : 5	40	**2d** 77
1e	n-C_5H_{11}	1 : 5	40	**2e** 86
1f	$CH_3OOC(CH_2)_7$	1 : 5	60	**2f** 78

a) Isolated yields. b) The products were gas chromatographically pure (>99%).

In each case the product was the conjugated unsaturated ketone in which the double bond is located in its original position. Also, the fact that methyl 11-methoxycarbonyl-2-undecenoate (**1f**) gave only the corresponding 4-oxo-2-undecenoate (**2f**) [IR, 1740, 1710 cm^{-1}; NMR δ 3.63, 3.79 (each 3H, s), 2.24, 2.60 (each 2H, br t, J=7 Hz), 6.53, 7.02 (each 1H, d, J=16 Hz) ppm] shows that the methylene group next to the double bond is selectively oxidized.

On the other hand, the oxidation of 3-alkene-2-ones with chromium trioxide under the same conditions gave 3-alkene-2,5-diones in poor yields (26—34%) (n-C_7—n-C_{11}), along with aliphatic acids resulting from cleavage of the double bond in the original ketones.

The resulting **2a**—**f** were easily reduced with titanium trichloride[4] to give methyl 4-oxoalkanoates (**3a**—**f**) in good yields. They are key intermediates for the preparation of cyclopentenone derivatives.[2] From the above results, the syntheses of **3a**—**f** can be achieved in three steps from the corresponding aliphatic aldehydes in moderate yields.

Table 2. Characteristics of methyl 4-oxo-2-alkenoates (**2a—e**)

Compd	Bp, °C/Torr	Mp, °C	Mass, *m/e*	IR, cm^{-1}	^{1}H-NMR, δ ppm
2a	135.0—136.0/13	44.0—46.5	198 (M^+) 167 128 113	1735 1710 1175	3.78 (3H, s) 6.53 (1H, d, J=16 Hz) 7.01 (1H, d, J=16 Hz)
2b	80.0—81.5/16.5	33.5—35.0	142 (M^+) 128 113 111	1735 1710 1175	3.82 (3H, s) 6.57 (1H, d, J=16 Hz) 7.05 (1H, d, J=16 Hz)
2c	103.0—105.0/13	38.0—39.5	156 (M^+) 128 125 113	1735 1710 1175	3.82 (3H, s) 6.55 (1H, d, J=16 Hz) 7.03 (1H, d, J=16 Hz)
2d	115.0—116.0/10.5	35.5—37.0	170 (M^+) 139 128 113	1735 1705 1175	3.82 (3H, s) 6.53 (1H, d, J=16 Hz) 7.02 (1H, d, J=16 Hz)
2e	126.0—126.5/12	46.0—47.5	184 (M^+) 153 128 113	1735 1705 1170	3.78 (3H, s) 6.50 (1H, d, J=16 Hz) 6.98 (1H, d, J=16 Hz)

Table 3. Semicarbazones of methyl 4-oxo-2-alkenoates (**2a—f**)

Compd	Mp, °C[a]	Formula	Found (Calcd), (%)		
			C	H	N
2a	128.5—130.0	$C_{12}H_{21}O_3N_3$	56.35 (56.45)	8.32 (8.29)	16.61 (16.46)
2b	149.0—149.5	$C_8H_{13}O_3N_3$	48.40 (48.23)	6.64 (6.58)	21.21 (21.10)
2c	162.5—164.0	$C_9H_{15}O_3N_3$	50.85 (50.69)	7.14 (7.09)	19.93 (19.71)
2d	150.0—151.5	$C_{10}H_{17}O_3N_3$	53.11 (52.85)	7.61 (7.54)	18.68 (18.49)
2e	125.0—126.5	$C_{11}H_{19}O_3N_3$	54.73 (54.75)	7.89 (7.94)	17.50 (17.41)
2f	97.0— 99.0	$C_{15}H_{25}O_5N_3$	55.08 (55.03)	7.70 (7.70)	12.56 (12.84)

a) All the semicarbazones were purified by recrystallization from methanol.

Experimental

Boiling points are uncorrected and melting points were determined on a Yanagimoto micro hot-stage and are uncorrected. The mass spectra were determined on a Hitachi RMS-4 mass spectrometer at 70 eV. The IR spectra were recorded with a Hitachi EPI-G3 grating spectrometer. All ^{1}H-NMR spectra were measured in a CCl_4 solution using a Varian T-60 NMR spectrometer with TMS as an internal standard. The GLC was carried out on a Shimadzu GC-4B, with SE-30 (2%) (3 mm×2 m) and at a temperature 140 °C, unless otherwise noted.

*Preparation of Methyl 2-Alkenoates (**1a—f**).* To a solution of methoxycarbonylmethylenetriphenylphosphorane[5] (22 mmol) in anhydrous benzene (*ca.* 60 ml), was added an appropriate aldehyde (20 mmol) in anhydrous benzene (*ca.* 5 ml) under nitrogen atmosphere. The solution was refluxed for 6 h and then cooled to room temperature. After evaporating the solvent in a reduced pressure, hexane was added to give precipitates. The precipitates were collected by filtration and washed with hexane. The combined solvents were evaporated and the resulting residue was distilled under reduced pressure. Yield; **1a**, 82% (bp 126—128 °C/14 Torr); **1b**, 91% (bp 63—65 °C/16 Torr); **1c**, 90% (bp 77—79 °C/16 Torr); **1d**, 78% (bp 103—104 °C/24 Torr); **1e**, 85% (bp 108—109 °C/12 Torr). The structures of **1a—e** were confirmed by examining their mass, IR, and NMR spectra.

*Methyl 11-Methoxycarbonyl-2-undecenoate (**1f**)*: Yield, 97% [from methyl 9-formylnonanoate (bp 122 °C/3 Torr)[8]]. Bp 152—154 °C/2 Torr; MS *m/e* 256(M^+), 225, 157, 87; IR 1745, 1735, 1665, 1180, 1145 cm^{-1}; NMR δ 1.33 (12H, br s), 1.98—2.45 (4H, m), 3.60, 3.65 (each 3H, s), 5.70 (1H, dt, J=16, 1.5 Hz), 6.84 (1H, dt, J=16, 7 Hz).

General Oxidation Procedure. The reagent was prepared by addition of chromium trioxide (50 mmol) in small portions to a mixture of acetic anhydride (12.5 ml) and glacial acetic acid (25 ml), followed by dilution with benzene (25 ml) under ice-cooling. Into the solution of the above reagent, **1** (10 mmol) in benzene (5 ml) was added dropwise with stirring. The reaction temperature was kept below 20 °C. The methyl 2-alkenoates were consumed in moderate times (the times required are shown in the Table 1) as confirmed by TLC. The reaction mixture was diluted with water, neutralized with aqueous sodium hydroxide solution, and extracted with ether. After being dried over anhydrous sodium sulfate, the extract was concentrated and the resulting residue was distilled under reduced pressure or crystallized from hexane to give **2** (Tables 1, 2, 3, and below).

*Methyl 11-Methoxycarbonyl-4-oxo-2-undecenoate (**2f**)*: Mp 54—55 °C (colorless needles from hexane); MS *m/e* 239 (M−31), 157, 128, 113; IR 1740, 1710, 1175 cm^{-1}; NMR δ 1.12—1.95 (10H, br s), 2.24, 2.60 (each 2H, br t, J=7 Hz), 3.63, 3.79 (each 3H, s), 6.53, 7.02 (each 1H, d, J=16 Hz). GLC: temperature program: 5 °C/min, from 150 to 200 °C. Found: C, 62.19; H, 8.40%. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20%.

*Reduction of Methyl 4-Oxo-2-alkenoates (**2a—f**).* Into a solution of **2** (3.5 mmol) in acetone (*ca.* 20 ml) cold titanium trichloride aqueous solution (20%, 8 mmol) was added under nitrogen atmosphere. The mixture was stirred for 40 min at room temperature, then poured into 50 ml of brine, and extracted with ether. The extract was concentrated and the residue was chromatographed on a silica gel column, eluting with ethyl ether–hexane (1 : 1). Yield, **3a**, 91% (M^+ *m/e* 200); **3b**, 88% (M^+ *m/e* 144); **3c**, 93% (M^+ *m/e* 158); **3d**, 90% (M^+ *m/e* 172); **3e**, 87% (M^+ *m/e* 186); **3f**, 87% (M^+ *m/e* 272). The structures of **3a—f** were confirmed by examining their IR and NMR spectra.

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