A Convenient Synthesis of 2-Substituted Ethyl 4-Oxo-*trans*-2-alkenoates

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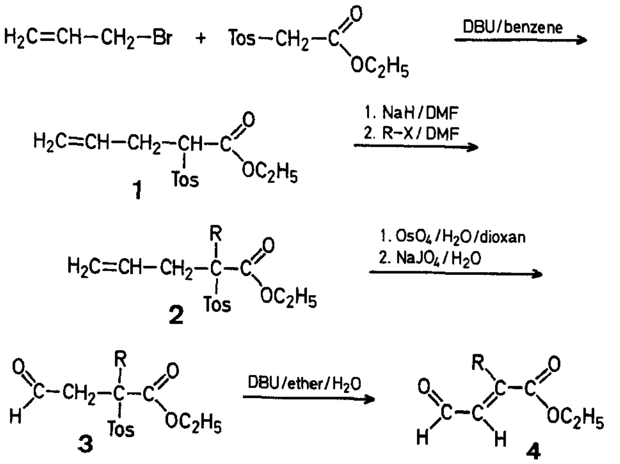
A simple method was required for the synthesis of 2-substituted alkyl 4-oxo-*trans*-2-alkenoates from readily available starting materials. The method described by Slotter and Eppner[1] involves the selective ozonolysis of alkyl 1,4-dieneoates prepared by a Wittig reaction.

Ono et al.[2] recently described a method for the monoalkylation of ethyl tosylacetonitrile using 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) as catalyst. I found that this method works equally well for the monoalkylation of ethyl tosylacetate with allyl bromide. The resulting ethyl 2-tosyl-4-pentenoate (**1**) can be further alkylated with 1-bromo- or 1-iodoalkanes to give ethyl 2-alkyl-2-tosyl-4-pentenoates (**2**). Oxidative cleavage[3] of the C=C double bond in **2** with osmium tetroxide/sodium periodate affords ethyl 2-alkyl-4-oxo-2-tosylbutanoates (**3**) which can be detosylated to give ethyl 4-oxo-*trans*-2-butenoates (**4**) by treatment with DBU[4] in wet ether.



0039-7881/79/0232-0139 $ 03.00

Table 1. Ethyl 2-Alkyl-2-tosyl-4-pentenoates (**2**)

2	R	Yield [%]	b.p./torr	Molecular formula[a]	I.R. (thin film) [cm^{-1}] ν_{COOR}	$\nu_{C=C}$	$\nu_{C_6H_4}$	ν_{-SO_2-}	^{1}H-N.M.R. δ [ppm] H$_{arom}$
a	C_2H_5	84	200°/3.5	$C_{16}H_{22}O_4S$ (310.4)	1745	1650	1604	1325 1155	7.65 (d, J=8 Hz); 7.25 (d, J=8 Hz)
b	n-C_3H_7	80	200°/2.3	$C_{17}H_{24}O_4S$ (324.4)	1745	1650	1604	1325 1155	7.65 (d, J=8 Hz); 7.25 (d, J=8 Hz)
c	n-C_4H_9	80	215°/2.4	$C_{18}H_{26}O_4S$ (338.4)	1745	1650	1604	1325 1155	7.65 (d, J=8 Hz); 7.25 (d, J=8 Hz)
d	n-C_5H_{11}	87	216°/2.1	$C_{19}H_{28}O_4S$ (352.5)	1745	1650	1604	1325 1155	7.65 (d, J=8 Hz); 7.25 (d, J=8 Hz)
e	n-C_6H_{13}	83	225°/1.8	$C_{20}H_{30}O_4S$ (366.5)	1745	1650	1604	1325 1155	7.65 (d, J=8 Hz); 7.25 (d, J=8 Hz)

[a] The microanalyses showed the following maximum deviations from the calculated values: C (except for **2a**, **d**), ±0.30; H, ±0.26. **2a**: C, −0.41; **2d**: C, −0.47.

Table 2. Ethyl 2-Alkyl-4-oxo-*trans*-2-butenoates (**4**)

4	R	Yield[a] [%]	b.p./torr	m.p. of 2,4-DNP	Molecular formula[b]	I.R. (thin film) [cm^{-1}] $\nu_{C=C}$	$\nu_{C=O}$	ν_{COOR}	^{1}H-N.M.R. δ [ppm] 4-H, 3-H
a	C_2H_5	27	95°/2.6	155°	$C_8H_{12}O_3$ (156.2)	1630	1695	1730	10.11, 6.63 (J=8 Hz)
b	n-C_3H_7	32	109°/3.3	142°	$C_9H_{14}O_3$ (170.2)	1630	1695	1730	10.08, 6.65 (J=8 Hz)
c	n-C_4H_9	41	132°/4.5	138°	$C_{10}H_{16}O_3$ (184.2)	1630	1695	1730	10.08, 6.65 (J=8 Hz)
d	n-C_5H_{11}	51	127°/1.5	118°	$C_{11}H_{18}O_3$ (198.3)	1630	1695	1730	10.08, 6.64 (J=8 Hz)
e	n-C_6H_{13}	47	160°/4.0	108°	$C_{12}H_{20}O_3$ (212.3)	1630	1695	1730	10.11, 6.65 (J=8 Hz)

[a] Yield of purified aldehyde.

[b] The microanalyses of the 2,4-dinitrophenylhydrazones of **4** were in satisfactory agreement with the calculated values; maximum deviation: C, ±0.36; H, ±0.08; N, ±0.27.

Product **4** can be easily and quickly separated from more polar impurities by low-temperature distillation (Kugelrohr), under reduced pressure. The ^{1}H-N.M.R. spectrum shows that in each case the product contains only the *trans* isomer. The aldehyde proton appears as a sharp doublet centered at $\delta = 10.1$ ppm ($J = 8$ Hz), and the vinyl proton as a sharp doublet centered at $\delta = 6.7$ ppm ($J = 8$ Hz). It was noted that the use of triethylamine in benzene as a base for the elimination step resulted in the formation of a 5:3 mixture of the *trans* and *cis* isomers of **4**. The ^{1}H-N.M.R. spectrum of the *cis* compound shows the signal of the aldehyde proton at higher field at $\delta = 10.0$ ppm ($J = 8$ Hz). The vinyl proton appears also at higher field at $\delta = 6.0$ ppm. In addition, the vinyl proton of the *cis* isomer is also coupled with the allylic methylene group, while such coupling is not observed for the *trans* compound.

Ethyl 2-Tosyl-4-pentenoate (1):

Allyl bromide (10.16 g, 84 mmol) is added dropwise, over a 15 min period, to a stirred solution of ethyl tosylacetate (12.25 g, 51 mmol) and DBU (12.77 g, 84 mmol) in benzene (120 ml). The mixture is stirred at room temperature for 90 min, then diluted with benzene (100 ml), and washed with 5% hydrochloric acid (3 × 20 ml) and water (3 × 20 ml). The organic solution is dried with sodium sulfate, the solvent removed under reduced pressure, and the residue distilled in vacuo; yield: 14.03 g (97%); b.p. 178°/0.6 torr.

$C_{14}H_{18}O_4S$	calc.	C 59.56	H 6.43
(282.3)	found	58.98	6.48

I.R. (thin film): $\nu_{max} = 1745$ ($COOC_2H_5$); 1650 (C=C); 1605 (benzene ring); 1325, 1155 cm^{-1} ($-SO_2-$).

^{1}H-N.M.R. (CCl_4): $\delta = 7.7$ (d, 2H$_{arom}$, $J = 8$ Hz); 7.3 (d, 2H$_{arom}$, $J = 8$ Hz); 5.9–5.4 (m, 1H, $-C\underline{H}=$); 5.3–4.8 (m, 2H, $=C\underline{H}_2$); 4.2–3.7 (m, 3H, $-C\underline{H}_2-O$ + $O=C-C\underline{H}-SO_2-$); 2.9–2.55 (m, 2H, $-C\underline{H}_2-C=C$); 2.45 (s, 3H, $C_6H_4-C\underline{H}_3$); 1.1 ppm (t, 3H, $-CH_2-C\underline{H}_3$).

Ethyl 2-Alkyl-2-tosyl-4-pentenoates (2); General Procedure:

To dry dimethylformamide (30 ml) is added ethyl 2-tosyl-4-pentenoate (**1**; 4.24 g, 15 mmol). The mixture is stirred and sodium hydride (0.36 g, 15 mmol) is added in small portions over a 10 min period. Then, a solution of the alkyl halide (15 mmol) is added dropwise with stirring. The resultant dark solution is allowed to stand at room temperature overnight, then diluted with ether (250 ml), washed with water (3 × 25 ml), and dried with sodium sulfate. The solvent is evaporated and the residual product distilled in vacuo (see Table 1).

Ethyl 2-Alkyl-4-oxo-2-toxylbutanoates (3); General Procedure:

To dioxan (50 ml, freshly distilled from $LiAlH_4$) is added water (1.5 ml) and the ethyl 2-alkyl-2-tosyl-4-pentenoate (**2**; 12.9 mmol). To this solution, osmium tetroxide (176 mg, 0.7 mmol) is added and the mixture is stirred for 15 min in the dark. A solution of sodium metaperiodate ($NaJO_4$; 5.52 g, 25.8 mmol) in water (50 ml) is added with stirring, during a 1 h period, in the dark, and stirring is continued for 3 h at room temperature. The solid material is filtered off and washed with ether. Ether (200 ml) is added to the filtrate. The organic phase is washed with 10% aqueous sodium sulfide nonahydrate (4 × 20 ml) and water (3 × 20 ml), and is dried with sodium sulfate. The ether is removed

$H_2C{=}CH-$	$-CH_2-O-$	$-C_6H_4-C\underline{H}_3$
6.2-5.5(m); 5.3-4.8(m)	4.05(q, $J = 7$ Hz)	8.4 (s)
6.2-5.5(m); 5.3-4.8(m)	4.05(q, $J = 7$ Hz)	8.4 (s)
6.2-5.5(m); 5.3-4.8(m)	4.05(q, $J = 7$ Hz)	8.4 (s)
6.2-5.5(m) 5.3-4.8(m)	4.05(q, $J = 7$ Hz)	8.4 (s)
6.7-5.5(m); 5.3-4.8(m)	4.05(q, $J = 7$ Hz)	8.4 (s)

under reduced pressure to give the crude ester **3** which is used in the next step without further purification; yields: 51-69%.

Ethyl 2-Alkyl-4-oxo-*trans*-2-butenoates (4); General Procedure: The crude ester **3** (8.95 mmol) is dissolved in wet ether (150 ml). To this solution is added a solution of DBU (1.363 g, 8.95 mmol) in ether (50 ml). The resulting mixture is stirred for 2 h at room temperature, and then washed with 5% hydrochloric acid (2 × 20 ml), 5% aqueous sodium hydrogen carbonate (2 × 20 ml), and water (3 × 20 ml). The ether solution is dried with sodium sulfate and the solvent removed under reduced pressure. The crude product **4** is purified by Kugelrohr distillation (see Table 2).

For microanalysis, compounds **4** were converted to their 2,3-dinitrophenylhydrazones.

The author acknowledges the assistance of Dr. T. Griffith, Mr. C. Mallard and Mr. K. Pringnitz for recording the N.M.R. spectra, and for doing the elemental analyses.

Received: April 18, 1978
(Revised form: August 31, 1978)

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0039-7881/79/0232-0141 $ 03.00