The Substitution Reaction of 2-Aralkylthio-1-alkenyl and 2-Alkylsulfinyl-1-alkenyl Ketones with Alkoxides: Preparation of 2-Alkoxy-1-alkenyl Ketones

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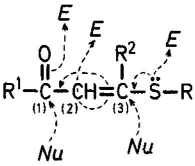
2-Aralkylthio-1-alkenyl ketones **1** are interesting and useful intermediates for the synthesis of a variety of compounds[1] as they possess reactive sites for nucleophilic attack at C-1 and C-3 and for electrophilic attack at the carbonyl O-atom, C-2, and the sulfur atom as shown below.



E = electrophile
Nu = nucleophile

2-Alkylsulfinyl-1-alkenyl ketones **2** are also of interest. We have previously described the reaction of **1** with sodium borohydride or lithium aluminium hydride leading to the smooth reductive elimination of the *S*-function to afford 1-alkenyl ketones[2], and the preparation of 2-amino-1-alkenyl ketones by reaction of ketones **1** or **2** with amines[3]. Relatively few data have hitherto been reported on the reaction of **1** or **2** with alkoxides[4]. We describe here the substitution reaction[5] of 2-aralkylthio-1-alkenyl ketones **1** and 2-alkylsulfinyl-1-alkenyl ketones **2** with alkoxides **3** which provides a new synthesis of 2-alkoxy-1-alkenyl ketones **4** under mild conditions. Compounds **4** are usually prepared from the sodium salts of β-dicarbonyl compounds and alkyl halides[6], β-diketones and alkyl orthoformates[7], β-diketones and diazomethane[8], and 2-chloro-1-alkenyl ketones and alkoxides[9].

Treatment of **1a–f** with **3** in the corresponding alcohol or alcohol/benzene at ambient temperature affords **4** in moderate yields. However, from the reaction of **1a** with *t*-butoxide and **1f** with methoxide the starting ketones **1** were recovered almost quantitatively. Furthermore, in the case of ketone **1d** with methoxide, 3,3-dimethoxy-1-phenylpropan-

Table 1. Preparation of 2-Alkoxy-1-alkenyl Ketones **4**

Starting Ketone	R¹	R²	R³	Alkoxide **3**	Solvent	Conditions	Yield [%]	Other Product (Yield [%])	Recovery of **1** or **2** [%]
1a	C_6H_5	CH_3	C_2H_5	$NaOCH_3$	CH_3OH	r.t., 16 h	78		10
2a	C_6H_5	CH_3	C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 1 h	90		trace
1a	C_6H_5	CH_3	C_2H_5	$NaOC_2H_5$	C_2H_5OH	r.t., 15 h	75		9
1a	C_6H_5	CH_3	C_2H_5	KOC_3H_7-*i*	*i*-C_3H_7OH	r.t., 15 h	75		10
1a	C_6H_5	CH_3	C_2H_5	KOC_4H_9-*t*	*t*-C_4H_9OH	reflux, 20 h	—		90
2a	C_6H_5	CH_3	C_2H_5	KOC_4H_9-*t*	*t*-C_4H_9OH/C_6H_6	r.t., 6 h	—		trace
1a[a]	C_6H_5	CH_3	C_2H_5	KOH	CH_3OH	r.t., 15 h	55	C_6H_5—CO—CH_2—CO—CH_3 (21)	21
1b	C_6H_5	CH_3	C_6H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 15 h	75		trace
1b	C_6H_5	CH_3	C_6H_5	KOC_3H_7-*i*	*i*-C_3H_7OH/C_6H_6	r.t., 15 h	74	C_6H_5SH (2)	15
1b[a]	C_6H_5	CH_3	C_6H_5	KOH	CH_3OH	r.t., 15 h	26	C_6H_5—CO—CH_2—CO—CH_3 (17)	49
1c	C_6H_5	C_6H_5	C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 15 h	27	C_6H_5—CO—CH_2—CO—C_6H_5 (65)	trace
2c	C_6H_5	C_6H_5	C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 6 h	32	C_6H_5—CO—CH_2—CO—C_6H_5 (52)	trace
1d	C_6H_5	H	C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 20 h	—	**5** (95)	trace
1d	C_6H_5	H	C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	0 °C, 1 h	trace	**5** (56)	28
1d	C_6H_5	H	C_2H_5	KOC_3H_7-*i*	*i*-C_3H_7OH/C_6H_6	r.t., 15 h	trace	C_6H_5—CO—CH_2—CH(OC_3H_7-*i*)$_2$ (trace)	25
1e	CH_3	C_6H_5	C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 6 h	50	C_6H_5—CO—CH_2—CO—CH_3 (16)	30
1f	—CH_2—C$(CH_3)_2$—CH_2—		C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 20 h	—		95
2f	—CH_2—C$(CH_3)_2$—CH_2—		C_2H_5	$NaOCH_3$	CH_3OH/C_6H_6	r.t., 6 h	84		trace

[a] The starting ketone **1** was stirred in methanol in the presence of potassium hydroxide.

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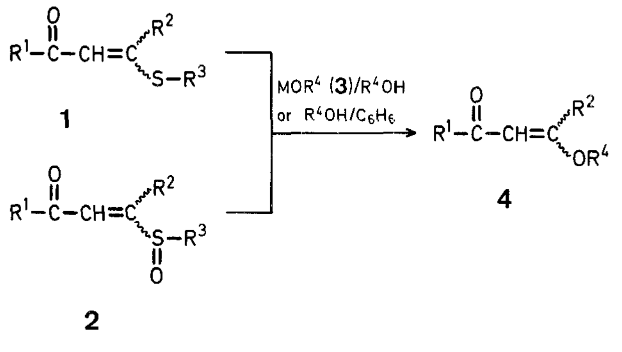
Table 2. Data of 2-Alkoxy-1-alkenyl Ketones 4 and β-Keto Acetal 5

Product R^1	R^2	R^4	b.p. [°C]/ torr[a]	Molecular formula[b] or Lit. b.p. [°C]/torr	I.R. (film) ν [cm⁻¹]	N.M.R. ($CDCl_3$) δ [ppm]
C_6H_5	CH_3	CH_3	130°/2	154–155°/16[10]	3060, 1660, 1585, 1205, 1060, 775, 675	2.39 (s, 3H); 3.73 (s, 3H); 6.11 (s, 1H); 7.3–7.6 (m, 3H); 7.7–8.0 (m, 2H)
C_6H_5	CH_3	C_2H_5	105°/2	162–164°/13[7]	3060, 1660, 1585, 1205, 1060, 775, 705, 675	1.37 (t, 3H); 2.41 (s, 3H); 3.97 (q, 2H); 6.13 (s, 1H); 7.3–7.6 (m, 3H); 7.8–8.0 (m, 2H)
C_6H_5	CH_3	C_3H_7-*i*	105°/2	$C_{13}H_{16}O$ (188.3)	3070, 1660, 1590, 1200, 1035, 780, 710, 680	1.35 (d, 6H); 2.40 (s, 3H); 4.57 (sept, 1H); 6.13 (s, 1H); 7.25–7.55 (m, 3H); 7.75–7.9 (m, 2H)
C_6H_5	C_6H_5	CH_3	130°/1	$C_{16}H_{14}O$ (222.3)	3060, 1650, 1590, 1190, 1045, 1020, 760, 690	3.91 (s, 3H); 6.19 (s, 1H); 7.2–7.65 (m, 8H); 7.8–8.0 (m, 2H)
CH_3	C_6H_5	CH_3	105°/2	$C_{11}H_{12}O$ (160.2)	3060, 3030, 1705, 1600, 1490, 1080	1.93 (s, 3H); 3.80 (s, 3H); 5.61 (s, 1H); 7.3–7.5 (m, 5H)
$-CH_2-C(CH_3)_2-CH_2-$		CH_3	90°/2	136°/20[8]	2960, 2875, 1655, 1610, 1225, 1015	1.07 (s, 6H); 2.22 (s, 2H); 2.28 (s, 2H); 3.70 (s, 3H); 5.37 (s, 1H)
5			116°/2	111–111.5°/2[11]	3070, 1685, 1600, 750, 690	3.27 (d, 2H, *J* = 5.5 Hz); 3.40 (s, 6H); 5.00 (t, 1H, *J* = 5.5 Hz); 7.25–7.6 (m, 3H); 7.8–8.05 (m, 2H)

[a] Kugelrohr – bath temperature.

[b] Satisfactory microanalyses obtained: C ±0.33, H ±0.25.



2-one (**5**) was obtained in 95% yield and 3-methoxy-1-phenylprop-2-en-1-one (**4d**) could not be obtained even at 0 °C. 3-Methoxy-1-phenylbut-2-en-1-one (**4a**) was also obtained by treatment of **1a, b** with potassium hydroxide in methanol. On the other hand, treatment of **2a, c, f** with methoxide in methanol/benzene at room temperature affords **4** in higher yield than that of **1** and methoxide.

From the results listed in Table 1 it can be seen that the C-3 substitution reaction of **2** with alkoxide proceeds under milder condition than that of **1** with alkoxides.

Known compounds **4** were identified by comparison with authentic samples[7,8,10]. The structures of new compounds **4** were established by microanalyses, I.R., and N.M.R. spectra (Table 2).

2-Alkoxy-1-alkenyl Ketones 4 from 2-Aralkylthio-1-alkenyl Ketones 1 and Alkoxides 3; General Procedure:

To a solution of the alkoxides **3** [sodium (1.2–2.0 mmol) or potassium (1.2–2.0 mmol) and the corresponding alcohol (5 ml)] in alcohol is added slowly a solution of the ketone **1** (1 mmol) in the same alcohol (5 ml) or benzene (5 ml). After the mixture has been stirred for 5–20 h, the reaction mixture is poured into water (10 ml) and extracted with dichloromethane (2 × 20 ml). The extract is washed with 5% aqueous hydrochloric acid (1 × 40 ml), water (1 × 40 ml), and then dried with anhydrous magnesium sulfate. After removal of the solvent, the residual oil is chromatographed on a silica gel column with benzene/ethyl acetate (19:1) to give the ketone **4**, together with starting material and other products.

2-Alkoxy-1-alkenyl Ketone 4 from 2-Aralkylthio-1-alkenyl Ketones (1) and Potassium Hydroxide in Methanol; General Procedure:

To a solution of potassium hydroxide (~50 mg) in methanol (10 ml) is added a solution of **1** (1 mmol) in methanol (5 ml). The mixture is stirred for 15 h at room temperature, then poured into water (20 ml), and extracted with dichloromethane (2 × 25 ml). The extract is washed with 5% aqueous hydrochloric acid (1 × 30 ml), water (1 × 30 ml), and dried with anhydrous magnesium sulfate. After removal of the solvent, the residual oil is chromatographed on a silica gel column with benzene/ethyl acetate (19:1) to give the ketone **4** and other products.

2-Alkoxy-1-alkenyl Ketones 4 from 2-Alkylsulfinyl-1-alkenyl Ketones 2 with Alkoxides 3; General Procedure:

To a solution of the alkoxide **3** [sodium (1.2–2.0 mmol) or potassium (1.2–2.0 mmol) and corresponding alcohol (5 ml)] in alcohol is added slowly a solution of ketone **2** (1 mmol) in benzene (5 ml). After the mixture has been stirred for several hours, the reaction mixture is poured into water (20 ml) and extracted with benzene (2 × 20 ml). The benzene solution is washed with 5% aqueous hydrochloric acid (1 × 40 ml), water (1 × 40 ml), and dried with anhydrous magnesium sulfate. After removal of the solvent, the residual oil is chromatographed on a silica gel column with benzene/ethyl acetate (19:1) to give the ketone **4**, accompanied by the starting material and other products.

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