The Substitution Reaction of 2-Alkylthio-1-alkenyl and 2-Alkylsulfinyl-1-alkenyl Ketones with Amines: Preparation of 2-Amino-1-alkenyl Ketones

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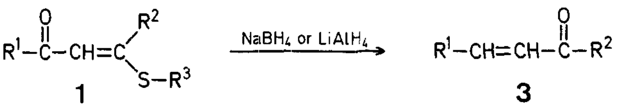
2-Alkylthio-1-alkenyl ketones (**1**) and 2-alkylsulfinyl-1-alkenyl ketones (**2**) are useful intermediates for the synthesis of a variety of compounds[1]. They possess reactive sites for nucleophilic attack at C-1 and C-3 and for electrophilic attack at the carbonyl *O*-atom and at C-2. We have previously described the reaction of **1** with sodium borohydride or lithium aluminum hydride, which are nucleophiles; these reactions lead to the smooth reductive elimination of the S-function to afford 1-alkenyl ketones (**3**)[2].



We have now investigated the reactions of ketones **1** and **2** with amines (**5**) as nucleophiles. Relatively few data have hitherto been reported on the reaction of compounds **1** with amines[1]. We describe here the substitution reactions of 2-alkylthio-1-alkenyl ketones (**1**) and 2-alkylsulfinyl-1-alkenyl ketones (**2**) with amines (**5**) which provide a synthesis of 2-amino-1-alkenyl ketones (**4**) under mild conditions. Although several syntheses of compounds **4** have hitherto been described, only little attention has been paid to the reaction of compounds **1** or **2** with amines[3,4]. Compounds **4** are usually prepared from 2-chloro-1-alkenyl ketones and amines; however, the synthesis of the 2-chloro-1-alkenyl ketones is difficult, in particular, when a further substituent is at C-3, and these compounds are generally unstable[4].

Treatment of 2-alkylthio-1-alkenyl ketones (**1a–d**) with primary or secondary amines (**5**) in benzene at room temperature or higher temperature (100 °C) affords 2-amino-1-alkenyl ketones (**4**) in moderate yields. However, from the reactions of ketone **1a** with diethylamine and of **1c** with aniline the starting ketones **4** were recovered quantitatively.

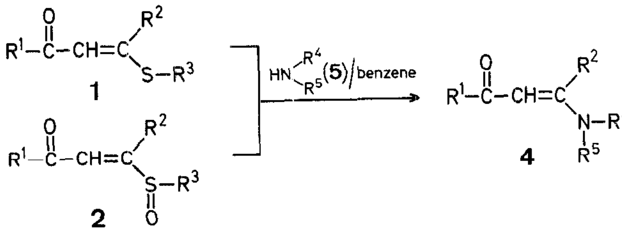


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Table 1. Preparation of 2-Amino-1-alkenyl Ketones (**4**)

Starting Ketone	R^1	R^2	R^3	R^4	R^5	Conditions	Yield [%]	Recovery of **1** or **2** [%]
1a	C_6H_5	CH_3	C_2H_5	n-C_3H_7	H	r.t., 15 h	36	64
1a	C_6H_5	CH_3	C_2H_5	C_6H_5	H	r.t., 15 h	55	45
1a	C_6H_5	CH_3	C_2H_5	$-(CH_2)_2-O-(CH_2)_2-$		r.t., 15 h	85	trace
2a	C_6H_5	CH_3	C_2H_5	$-(CH_2)_2-O-(CH_2)_2-$		r.t., 3 h	99	trace
1a	C_6H_5	CH_3	C_2H_5	CH_3	CH_3	r.t., 15 h	65	trace
2a	C_6H_5	CH_3	C_2H_5	CH_3	CH_3	r.t., 1 h	95	trace
1a	C_6H_5	CH_3	C_2H_5	C_2H_5	C_2H_5	reflux, 10 h	—	quantitative
2a	C_6H_5	CH_3	C_2H_5	C_2H_5	C_2H_5	r.t., 2 h	93	trace
1b	C_6H_5	H	C_2H_5	C_6H_5	H	r.t., 15 h	76	trace
1b	C_6H_5	H	C_2H_5	CH_3	CH_3	r.t., 15 h	90 (88)[b]	trace
1c	C_6H_5	C_6H_5	C_2H_5	C_6H_5	H	100 °C[a], 10 h	—	quantitative
2c	C_6H_5	C_6H_5	C_2H_5	C_6H_5	H	r.t., 5 h	65	30
1c	C_6H_5	C_6H_5	C_2H_5	$-(CH_2)_2-O-(CH_2)_2-$		reflux, 10 h	95	trace
2c	C_6H_5	C_6H_5	C_2H_5	$-(CH_2)_2-O-(CH_2)_2-$		r.t., 5 h	80	trace
1d	CH_3	CH_3	n-C_4H_9	C_6H_5	H	reflux, 10 h	25	55
1d	CH_3	CH_3	n-C_4H_9	$-(CH_2)_2-O-(CH_2)_2-$		reflux, 5 h	30	70
1d	CH_3	CH_3	n-C_4H_9	$-(CH_2)_2-O-(CH_2)_2-$		100 °C[a], 5 h	80	8

[a] In a sealed tube.

[b] Yield obtained from 1-chloro-3-oxo-3-phenylpropene and dimethylamine[4].

Table 2. Data of 2-Amino-1-alkenyl Ketones (**4**)

R^1	R^2	R^4	R^5	m.p. or b.p./torr [°C]	Molecular formula[a] or m.p. reported	I.R. ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
C_6H_5	CH_3	H	n-C_3H_7	b.p. 120°/2[b]	$C_{13}H_{17}NO$ (203.3)	1610, 1545, 755, 695	1.02 (t, 3H); 1.4–1.9 (m, 2H); 2.05 (s, 3H); 3.25 (q, 2H); 5.65 (s, 1H); 7.2–7.5 (m, 3H); 7.7–8.0 (m, 2H); 11.5 (br s, 1H)
C_6H_5	CH_3	H	C_6H_5	m.p. 105–106°	$C_{16}H_{15}NO$ (237.3)	1615, 1540, 750, 690	2.15 (s, 3H); 5.88 (s, 1H); 7.2–7.6 (m, 8H); 7.8–8.0 (m, 2H); 13.15 (br s, 1H)
C_6H_5	CH_3	$-(CH_2)_2-O-(CH_2)_2-$		m.p. 141.5–142.5°	$C_{14}H_{17}NO_2$ (231.3)	1605, 1530, 760, 690	2.61 (s, 3H); 3.35–3.45 (m, 4H); 3.7–3.8 (m, 4H); 5.86 (s, 1H); 7.3–7.45 (m, 3H); 7.8–7.9 (m, 2H)
C_6H_5	CH_3	CH_3	CH_3	m.p. 45–46°	$C_{12}H_{15}NO$ (189.3)	1605, 1540, 760, 700	2.62 (s, 3H); 3.00 (s, 6H); 5.63 (s, 1H); 7.2–7.5 (m, 3H); 7.7–8.0 (m, 2H)
C_6H_5	CH_3	C_2H_5	C_2H_5	b.p. 110°/2[b]	$C_{14}H_{19}NO$ (217.3)	1615, 1530, 765, 705	1.22 (t, 6H); 2.67 (s, 3H); 3.37 (q, 4H); 5.73 (s, 1H); 7.2–7.6 (m, 3H); 7.7–8.0 (m, 2H)
C_6H_5	H	H	C_6H_5	m.p. 139–140°	m.p. 140–141°[4]	1620, 1545, 740, 680	6.01 (d, 1H, J=7.8 Hz); 7.05–7.6 (m, 9H); 7.85–8.0 (m, 2H); 12.15 (br s, 1H)
C_6H_5	H	CH_3	CH_3	m.p. 92–94°	m.p. 90–91°[4]	1640, 1540, 760, 705	3.00 (s, 6H); 5.68 (d, 1H, J=13.5 Hz); 7.78 (d, 1H, J=13.5 Hz); 7.25–7.5 (m, 3H); 7.8–8.0 (m, 2H)
C_6H_5	C_6H_5	H	C_6H_5	m.p. 101–102°	m.p. 102–103°[5]	1600, 1575, 765, 750, 700, 690	6.08 (s, 1H); 6.7–7.5 (m, 13H); 7.9–8.0 (m, 2H); 12.9 (br s, 1H)
C_6H_5	C_6H_5	$-(CH_2)_2-O-(CH_2)_2-$		m.p. 94–95°	m.p. 92–93°[5]	1660, 1600, 1525, 765, 705	3.2–3.35 (m, 4H); 3.65–3.8 (m, 4H); 6.00 (s, 1H); 7.2–7.45 (m, 8H); 7.75–7.9 (m, 2H)
CH_3	CH_3	H	C_6H_5	m.p. 101.5–103°	m.p. 103°[4]	1600, 1565, 765, 750, 700	1.99 (s, 3H); 2.10 (s, 3H); 5.19 (s, 1H); 7.1–7.4 (m, 5H); 12.46 (br s, 1H)
CH_3	CH_3	$-(CH_2)_2-O-(CH_2)_2-$		b.p. 112°/2[b]	$C_9H_{15}NO_2$ (169.2)	1630, 1550	2.09 (s, 3H); 2.47 (s, 3H); 3.25–3.36 (m, 4H); 3.68–3.79 (m, 4H); 5.42 (s, 1H)

[a] The microanalyses were in satisfactory agreement with the calculated values (except for the last compound listed; C, +0.43): C, ±0.32; H, ±0.12; N, ±0.27.

[b] Kugelrohr temperature.

On the other hand, the reaction of the 2-alkylsulfinyl-1-alkenyl ketones **2a, c** with several amines in benzene at room temperature affords the corresponding ketones **4** in good yields.

From the results listed in Table 1 it can be seen that the reaction of compounds **2** with amines proceeds under milder conditions than that of compounds **1** with amines.

Known compounds **4** were identified by comparison with authentic samples[4,5,6]. The structure of new compounds **4** was established by microanalyses, I.R., and ^{1}H-N.M.R. spectra.

2-Amino-1-alkenyl Ketones (4) from 2-Alkylthio-1-alkenyl Ketones (1) and Amines (5); General Procedure:

A solution of the ketone **1** (1 mmol) and the amine **5** (1.2 mmol) in benzene (30 ml) is stirred for 5–15 h at room temperature or at reflux temperature or heated at 100 °C in a sealed tube (see Table 1). The reaction mixture is then poured into dilute hydrochloric acid (30 ml) and the resultant mixture extracted with benzene (2 × 30 ml). The extract is washed with water (1 × 50 ml), dried with magnesium sulfate, and evaporated. The residual product is purified by distillation or recrystallization from methanol.

2-Amino-1-alkenyl Ketones (4) from 2-Alkylsulfinyl-1-alkenyl Ketones (2) and Amines (5); General Procedure:

A solution of the ketone **2** (1 mmol) and the amine **5** (1.2 mmol) in benzene (30 ml) is stirred for 1–5 h at room temperature (see Table 1), and is then poured into dilute hydrochloric acid (30 ml). The mixture is extracted with benzene (2 × 30 ml), the extract washed with water (1 × 50 ml), dried with magnesium sulfate, and evaporated. The residual product is purified by distillation or recrystallization from methanol.

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