Enol Silyl Ethers and their Use for the Synthesis of α-Halo-α,β-unsaturated Carbonyl Compounds

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Carbon-chain homologation and ring enlargement by addition of dihalomethylene to C=C double bonds and subsequent thermal or chemical ring cleavage of the dihalocyclopropane formed are well-known reactions[1]. When applied to enol ethers[2,3,4], enol acetates[5], or enamines derived from carbonyl compounds[6], this carbon-chain homologation reaction leads to the formation of homologous α-halo-α,β-unsaturated carbonyl compounds. However, the results obtained using enol ethyl ethers of aliphatic[2] and alicyclic[3] ketones vary considerably and are dependant on the structure of the ketone, on the dihalocarbene used, and on the experimental conditions.

In the present communication, we show that the preparation of α-halo-α,β-unsaturated carbonyl compounds according to the above-mentioned reaction sequence can be considerably improved by using enol silyl ethers (2) instead of enol ethyl ethers. Enol trimethylsilyl ethers (2) are usually better accessible than other enol ethers; this is particularly the case when, starting from an unsymmetric ketone, only one of the possible two isomeric enol ethers is required. The reaction of the enol silyl ethers with dihalocarbenes affords 1,1-dihalo-2-siloxycyclopropanes (3) in good yields. Compounds 3 readily undergo elimination of halotrimethylsilane to give α-halo-α,β-unsaturated carbonyl compounds (4) in high yields and in a fast reaction.

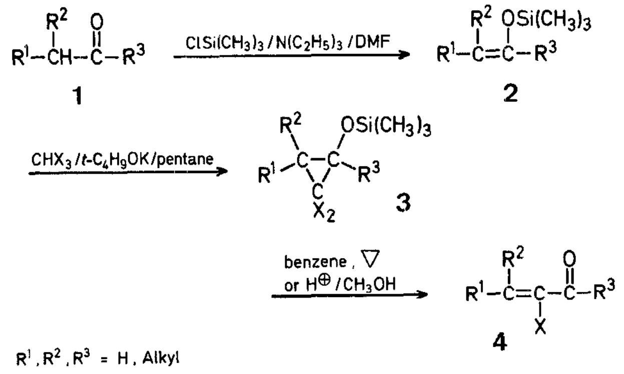
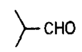
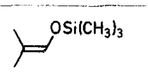
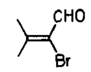
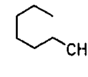
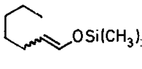
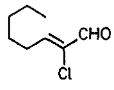
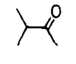
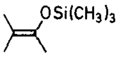
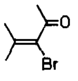
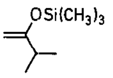
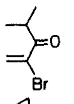
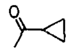
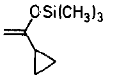
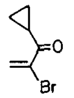
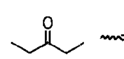
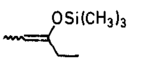
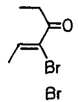
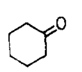
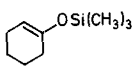
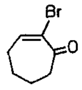
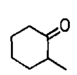
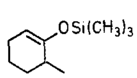
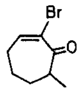
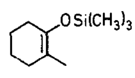
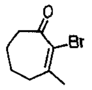


Table 1. α-Halo-α,β-unsaturated Carbonyl Compounds (4) from Aldehydes or Ketones (1) via Enol Silyl Ethers (2) and 2,2-Dihalo-1-trimethylsiloxycyclopropanes (3)

1		2[a]	3[b] Yield [%]	4[c] Formula	Yield[d] [%]	b.p./15 torr
a			70		63	78–80°
b			75		64	110–112
c			85–95		62	66–68°
c′			85–95		68	58–60[c]
d			85–95		86	64–66[c]
e			84		82	66–68°
f			85–95		90	95–97°
g			40		40[g]	
g′			40		49[g]	

[a] Compounds 2 were prepared from 1, chlorotrimethylsilane, and triethylamine in dimethylformamide according to the general method described in Ref.[8,9]. The enol silyl ethers 2c and 2g′, obtained from methyl isopropyl ketone and 2-methylcyclohexanone, respectively, were easily isolated by careful fractionating distillation; the corresponding isomers 2c′ and 2g were obtained from the same ketones by reaction with lithium diisopropylamide in dimethoxyethane, followed by the addition of chlorotrimethylsilane according to Ref.[8,9].

[b] The conversion 2→3 was performed using trihalomethane/potassium t-butoxide in pentane according to the general technique described in Ref.[7].

[c] The conversion 3→4 with elimination of halotrimethylsilane was achieved by refluxing in benzene for 5 h (in toluene for 3b→4b), or by allowing compounds 3 to stand in acidified methanol at room temperature for 25 h. In the cases 3d, 3g, and 3g′, the rearrangement began during evaporation of the solvent.

[d] Compounds 4a–f were purified by distillation, showed molecular-ion peaks in the mass spectra, and gave satifactory elemental analyses (Cl or Br ± 1%).

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[f] see Ref.[3].

[g] Compounds 4g and 4g′ were isolated from the crude reaction products by column chromatography on silica gel using pentane/ether (3 : 1) as eluent.

The products 4 thus obtained were isolated by distillation. Their structures as 2-halo-2-alkenals (4, $R^3 = H$) and 1-halo-1-alkenyl ketones (4, R^3 = alkyl), respectively, were confirmed

Table 2. Spectral Data of α-Halo-α,β-unsaturated Carbonyl Compounds (**4**)

4	I.R. (film) [cm^{-1}] $\delta_{C=C-H}$	δ_{CO-H}	$\nu_{C=O}$	$\nu_{C=C}$	^{1}H-N.M.R. (CCl$_4$, 60 MHz) δ [ppm]
a		2730	1680	1600	9.67 (s, 1H), 2.33 (s, 3H), 2.17 (s, 3H)
b	3020	2725	1697	1607	9.30 (s, 1H), 6.90 (t, 1H, $J=6$ Hz), 2.49 (q, 2H, $J=6$ Hz), 1.9–1.1 (broad, 9H, with a triplet at 0.91)
c			1680	1590	2.38 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H)
c′	3015		1690	1595	6.79 (d, 1H, $J=3$ Hz), 6.32 (d, 1H, $J=3$ Hz), 3.34 (q, 1H, $J=6$ Hz), 1.16 (d, 6H, $J=6$ Hz)
d	3090		1672	1595	6.73 (d, 1H, $J=3$ Hz), 6.17 (d, 1H, $J=3$ Hz), 1.3–0.6 (broad, 5H)
e	3080		1690	1615	7.22 (q, 1H, $J=5$ Hz), 2.24 (q, 1H, $J=6$ Hz), 1.97 (d, 3H, $J=5$ Hz), 1.10 (t, 3H, $J=6$ Hz)
f	3035		1680	1600	7.25 (t, 1H, $J=6$ Hz), 2.8–2.1 (broad, 4H), 2.1–1.7 (broad, 4H)
g	3020		1682	1595	7.15 (t, 1H, $J=6$ Hz), 3.05–2.15 (broad, 3H), 2.15–1.3 (broad, 4H), 1.15 (d, 3H, $J=6,5$ Hz)
g′			1670	1590	2.8–2.4 (broad, 4H), 2.19 (s, 3H), 2.0–1.6 (broad, 4 H)

by spectral methods. The bromocycloheptenone **4g** isomerizes on distillation (the C=C double bond is shifted to the α′,β′-position with reference to the carbonyl group); compound **4g** can, however, be purified by column chromatography on silica gel. The same applies to compound **4g′**. In both cases, the yields were lower than the yields of the other products **4** which were purified by distillation.

The enol silyl ethers **2b** and **2e** are mixtures of the *Z* and *E* isomers; nevertheless, the corresponding products **4b** and **4e** consist of only one isomer which has probably the *trans* structure.

To our knowledge, the α-halo-α,β-unsaturated carbonyl compounds listed in Table 1 are hitherto still unknown or have only been incompletely described.

3-Bromo-4-oxo-2-hexene (4e):

3-Trimethylsiloxy-2-pentene (**2e**): This compound is prepared from 3-pentanone, chlorotrimethylsilane, and triethylamine in dimethylformamide in accordance with the procedure reported in Ref.[8] yield: 91%; b.p. 135–138°/760 torr.

2,2-Dibromo-1-ethyl-3-methyl-1-trimethylsiloxycyclopropane (**3e**): Bromoform (25.3 g, 0.10 mol) is added, over a period of 1 h, to a stirred mixture of the enol silyl ether **2e** (15.8 g, 0.10 mol) and potassium *t*-butoxide (12 g, 0.106 mol) in pentane (100 ml) at −10°. The mixture is then allowed to warm to room temperature, stirring is continued for 3 h, and the mixture taken up in water. The organic layer is separated, dried with sodium sulfate, and the solvent removed under vacuum. The residual oil consists of practically pure (by N.M.R.) **3e**; yield: 27.7 g (84%).

3-Bromo-4-oxo-2-hexene (**4e**): The cyclopropane derivative **3e** (16.5 g, 0.05 mol) is refluxed in benzene (150 ml) for 5 h. The benzene is evaporated and the residual oil distilled in vacuo; yield: 7.25 g (82%); b.p. 66–68°/15 torr.

The same result (rearrangement-elimination) is obtained by heating a solution of the cyclopropane **3e** (16.5 g) in a boiling 80:20 mixture (150 ml) of methanol and water for 3 h, or by adding commercial hydrochloric acid (2–3 ml) to the same reaction mixture and allowing it to stand at room temperature for 24 h. The product is isolated by dilution with water, extraction, etc. as described above.

C_6H_9BrO (177.0) M.S.: $m/e=178$ (M$^+$), 176.

I.R. (film): $\nu_{max}=1690$ (C=O), 1615 (C=O) cm^{-1}.

^{1}H-N.M.R. (CCl$_4$): $\delta=7.22$ ppm (q, 1 H, $J=5$ Hz).

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