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ALKYLATION VIA TRIS(DIALKYLAMINO)SULFONIUM ENOLATES[1]

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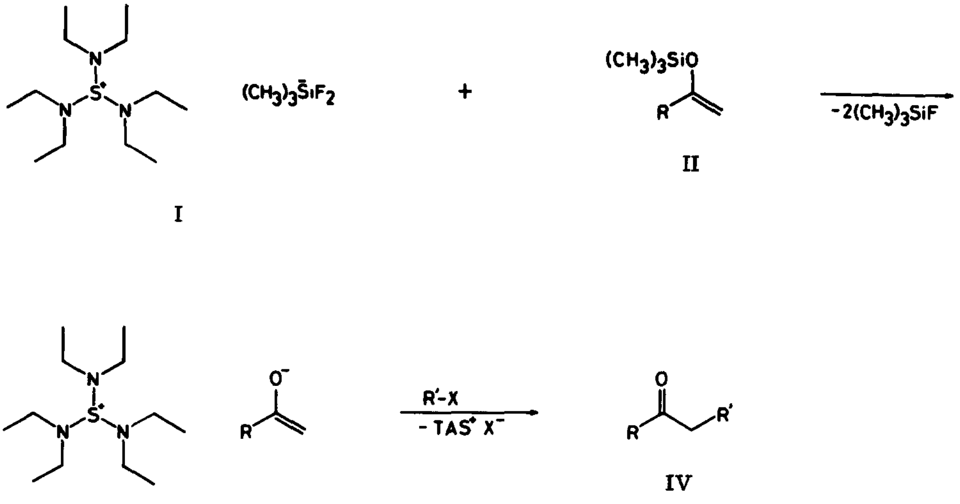
Summary: Tris(dialkylamino)sulfonium enolates generated from tris(diethylamino)sulfonium difluorotrimethylsiliconate and enol silyl ethers are readily alkylated by various alkyl halides under mild conditions.

Recently we have demonstrated that reaction of tris(diethylamino)sulfonium (TAS) difluorotrimethylsiliconate (I) and an enol silyl ether II in THF produces the TAS enolate, III, in which the charged moieties have negligible interactions.[1] Described herein is a mild procedure for alkylation of III generated in situ from I (a fluoride ion source)[2,3] and a variety of enol silyl ethers. The unsolvated fluoride and enolate ions under such conditions can behave as naked, supernucleophilic agents[4] and the overall C-alkylation reaction, II → IV, is accomplished at -78 to -30 °C.



I

II

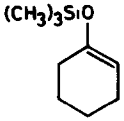
III

IV

Benzylation of 1-trimethylsiloxycyclohexene (V) would be illustrative. Under argon atmosphere, a solution of I (5.0 mmol) in THF (5 ml) was added to a mixture of V (4.9 mmol) and benzyl bromide (5.9 mmol) in THF (7.5 ml) maintained at -78 °C. The resulting mixture was kept at the same temperature for 3 h, diluted with hexane (100 ml), and treated with water. The organic layer was dried, concentrated, and chromatographed on silica gel to give 2-benzylcyclohexanone in 72% yield.

In a similar manner, a variety of reactive alkylating agents could be used. Some examples are given in Table I. No or very little dialkylation products were obtained.[5] The reaction is regiospecific with respect to enol silyl ether substrates. Thus each of the enol silyl ethers VII and VIII was benzylated only at the C-2 position; no crossover of the products was observed.

It should be worth pointing out that neither cyclopropylcarbinyl nor 5-hexenyl as entering group rearranges during the alkylation. The fluoride ion promoted reaction of IX and cyclo-



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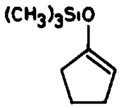

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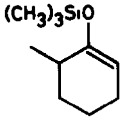

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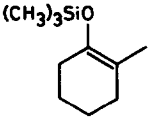

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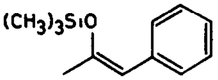

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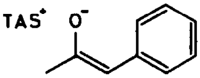

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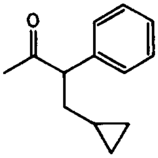

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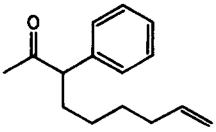

XII

Table I. Fluoride Ion Promoted Alkylation of Enol Silyl Ethers[a]

enol silyl ether	alkylating agent (equiv)	reaction conditions		% yield of[b] product
		I, equiv	temp, °C (time, h)	
V	CH_3I (1.5)	1.2	-78 (4)	95[c]
V	n-C_4H_9I (1.2)	1.1	-30 (3)	59
V	$C_6H_5CH_2Br$ (1.2)	1.0	-78 (3)	72
V	$C_6H_5CH{=}CHCH_2Br$ (1.2)	1.0	-78 (2.5)	61
V	$BrCH_2COOCH_3$ (1.2)	1.0	-78 (2)	83
VI	$C_6H_5CH_2Br$ (1.2)	1.2	-78 (4)	82[d]
VI	$CH_2{=}CHCH_2Br$ (1.2)	1.2	-78 (4)	60[d]
VII	$C_6H_5CH_2Br$ (1.2)	1.0	-78 (3)	66[e]
VIII	$C_6H_5CH_2Br$ (1.2)	1.0	-78 (3)	60
IX	CH_3I (1.3)	1.0	-78 (0.25)	89[f]
IX	cyclo-$C_3H_5CH_2I$ (1.3)	1.0	-74 (7)	83[c]
IX	cyclo-$C_3H_5CH_2I$ (1.3)	1.0	-74 (12)[g]	51[c]
IX	$CH_2{=}CH(CH_2)_4I$ (1.0)	1.0	-78 (4) + -40 (0.5)	91[c]

[a] Unless otherwise stated, reaction was carried out in THF. [b] Isolated yield. [c] Determined by GC analysis. [d] Trace amounts of dialkylated products were detected by GC—MS analysis. [e] cis/trans = 1:5. [f] Determined by NMR analysis. [g] Haxamethylphosphoric triamide (10 equiv) was added to the reaction mixture.

propylcarbinyl iodide in THF or a THF—hexamethylphosphoric triamide mixture led to only XI. Careful examination of the reaction mixtures revealed no detectable 3-butenylated product. 5-Hexenyl moiety did not rearrange either. Reaction of the enolate X (either in situ generated or isolated by an evacuation technique[1]) and 5-hexenyl iodide gave solely XII; cyclization products possessing cyclopentylcarbinyl group were not formed. Therefore the present alkylation reaction, though proceeding through naked enolated species, does not involve non-geminate, free radicals formed via electron-transfer processes,[6] but is interpreted in terms of a classical S_N2-type mechanism.[7]

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reaction mechanism are also acknowledged.

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