α-Trialkylsilylketones from α-Bromoketones: Utilization of a 1,3-O to C Silyl Migration

Paul Sampson and David F. Wiemer*†

Department of Chemistry, University of Iowa, Iowa City, IA 52242, U.S.A.

A new route from α-bromoketones to α-trialkylsilylketones has been developed which demonstrates the viability of halogen–metal exchange *vis-a-vis* nucleophilic attack at silicon, even with the unhindered trimethylsilyl group.

Despite the established utility of α-silylketones in organic synthesis, few general methods are available for their preparation.[1—4] Kuwajima[2] demonstrated the synthesis of α-trialkylsilylketones from α-phenylselenoketones, involving an O to C silyl migration in a trialkylsiloxyvinyl lithium intermediate. However, this approach was investigated only with sterically hindered silyl groups, and required the synthesis and use of toxic organoselenium intermediates. Corey and Rucker[3] employed a silyl migration from oxygen to the allylic position

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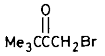
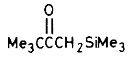
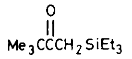
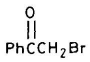
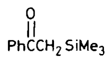
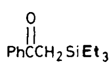
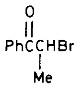
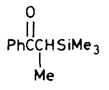
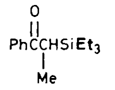
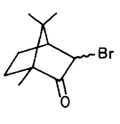
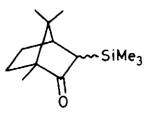
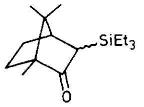
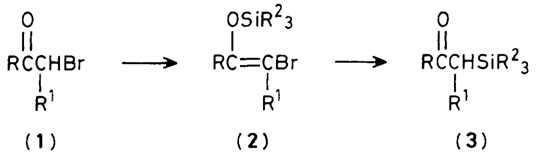
Table 1. Synthesis of α-trialkylsilylketones.

Entry	α-Bromoketone	α-Trialkylsilylketone	Yield/%
1	 $\mathrm{Me_3C}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2Br}$	 $\mathrm{Me_3C}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2SiMe_3}$	68[a]
2	"	 $\mathrm{Me_3C}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2SiEt_3}$	67[a]
3	 $\mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2Br}$	 $\mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2SiMe_3}$	51[a]
4	"	 $\mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2SiEt_3}$	62[b]
5	 $\mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\underset{\mathrm{Me}}{\underset{\|}{\mathrm{C}}}\mathrm{HBr}$	 $\mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\underset{\mathrm{Me}}{\underset{\|}{\mathrm{C}}}\mathrm{HSiMe_3}$	6[c]
		$\mathrm{PhC{\equiv}CMe}$	83[c]
6	"	 $\mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\underset{\mathrm{Me}}{\underset{\|}{\mathrm{C}}}\mathrm{HSiEt_3}$	8[c]
		$\mathrm{PhC{\equiv}CMe}$	80[c]
7			80[a,d,e]
8	"		78[b,d,f]

[a] Isolated yield after distillation. [b] Isolated yield after flash chromatography. [c] Yield by g.c. [d] Rearrangement occurs upon warming to room temperature. [e] Isolated as a 50 : 50 ratio of epimers. [f] Isolated as a 60 : 40 ratio of epimers.

of a silyl enol ether anion in their approach to α-trialkylsilylketones. However, this approach required an α′-hydrogen, and α-trimethylsilylketones could not be made, presumably owing to nucleophilic attack on the silicon centre. Kowalski and coworkers[4] have demonstrated the feasibility of forming dilithiated species from α-bromoketones, which then afford C-silylated products upon treatment with chlorotrialkylsilanes, but this approach requires the use of t-butyl-lithium. It appeared that the readily available trialkylsiloxyvinyl bromides (**2**) could be used to overcome the problems inherent in the approaches of Kuwajima, Corey, and Kowalski, if halogen–metal exchange were faster than nucleophilic attack upon the silicon centre. It is.

Our reaction sequence is outlined in Scheme 1. When an α-bromoketone (**1**) is treated with lithium hexamethyldisilazide at −78 °C, addition of a chlorotrialkylsilane and warming to room temperature results in formation of the expected trialkylsiloxyvinyl bromide (**2**) *in situ*. After cooling this solution to −78 °C again, addition of two equivalents of n-butyl-lithium results in halogen–metal exchange, whereupon rapid O to C silyl migration occurs. The final reaction products (**3**) are obtained, following addition of aqueous ammonium chloride, by distillation, or, with the more stable triethylsilyl compounds, by flash chromatography (see Table 1).‡



Scheme 1

The synthesis of α-trimethyl- and α-triethylsilylketones derived from primary α-bromoketones proceeds in reasonably good isolated yield (Table 1, entries 1—4). Only low yields of α-silylketones were found with α-bromopropiophenone (entries 5 and 6). The major product, prop-1-ynylbenzene, is not unreasonable, given the precedents for rapid elimination of siloxide (*cf.* the Peterson olefination[5]). With a secondary α-bromoketone where formation of the corresponding acetylene is not possible, the desired α-silylketones are produced in good yield (entries 7 and 8).

In conclusion, a new and facile method has been developed for the preparation of at least primary and some secondary α-trialkylsilylketones from α-bromoketones. By utilizing the susceptibility of vinyl bromides to halogen–metal exchange, O to C migration of the trimethylsilyl group has been demonstrated. Additional advantages over current methods of α-trialkylsilylketone formation include the ready availability and relative ease of handling of all necessary starting materials and reagents.

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References

1 For some alternative approaches to α-trialkylsilylketones, *cf.* M. Obayashi, K. Utimoto, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 2646, and references cited therein; I. Fleming and A. Pearce, *J. Chem. Soc., Perkin Trans. 1*, 1981, 251; D. E. Seitz and A. Zapata, *Synthesis*, 1981, 557; I. Kuwajima, T. Inoue, and T. Sato, *Tetrahedron Lett.*, 1978, 4887.
2 I. Kuwajima and R. Takeda, *Tetrahedron Lett.*, 1981, **22**, 2381.
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5 (a) E. Colvin, 'Silicon in Organic Synthesis,' Butterworths, London, 1981; (b) E. Colvin, *Chem. Soc. Rev.*, 1978, **7**, 15; (c) I. Fleming, *Chem. Soc. Rev.*, 1981, **10**, 83.

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‡ Caution should be observed when examining these reactions by g.c., since thermal rearrangement of the α-silylketones to the corresponding silyl enol ethers can occur at typical injector port temperatures (ref. 5a).