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α-CHLOROACYLTRIMETHYLSILANES AS α-TRIMETHYLSILYLACYL EQUIVALENTS. SPECIFIC C-ACYLATION OF ENOLATES

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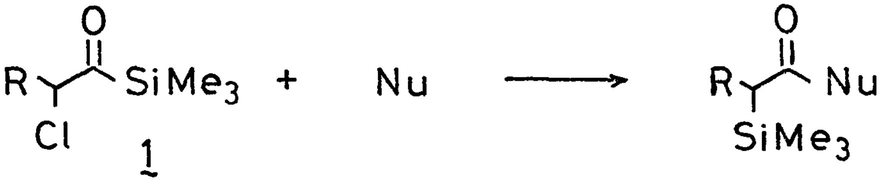
Summary: α-Chloroacyltrimethylsilanes have been employed as α-trimethylsilylacyl equivalents in the reaction with enolate anions and have yielded the corresponding C-acylated products selectively.

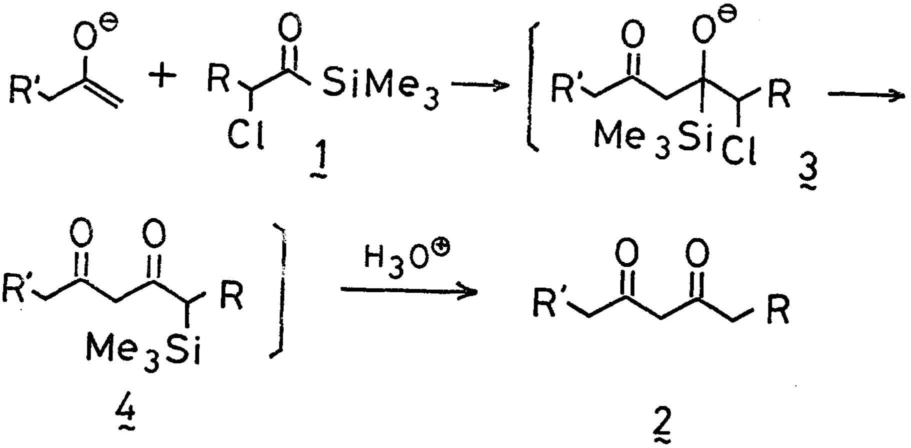
In a past decade, a remarkable progress has been achieved on the chemistry of enolate anions.[1] Based on new concepts, various methods have been developed for alkylation[2] and aldol reactions[3] with high regioselectivity. However, problems have still remained undissolved on the acylation reactions;[4] especially synthetic procedures for specific C-acylation usually involves a lot of difficulties.[5]

We have recently reported that α-chloroacyltrimethylsilanes 1[6] are employable as α-trimethylsilylacyl equivalents in the reactions with various nucleophiles such as Grignard reagents[6b] or alkoxides[7] as shown in the following equation.



In the present paper, we wish to describe reactions of 1 with enolates, which should afford a highly efficient method for specific C-acylation to give unsymmetrically substituted 1,3-dicarbonyl compounds. Our hypothesis for examining the reactions was that, depending on the effect of trimethylsilyl group, carbonyl of the acyltrimethylsilane might be a quite soft electrophile enough to react on the carbon sites of enolates preferentially.[8] Removal of chloride ion from the resulting adduct 3 followed by rearrangement of silyl group would afford the corresponding C-acylated products.

As expected, it has been established that ketone enolates usually react with α-chloroacyltrimethylsilane 1 under mild reaction conditions to give the corresponding 1,3-dicarbonyl compounds 2[9] without any formation of O-acylated products. For effecting such kind of transformation, the following two procedures have been examined. For quenching the generated active methylene or methyne group of the product, two equivalents of an enolate generated by LDA were used in the reaction with 1(1 eq) in method (A), and two equivalents of lithium 1,1-bis(trimethylsilyl)-3-methylbutoxide (LiBTSMB)[10] were employed in an equimolar reaction of a ketone with 1 for generation of the enolate[11] and for avoiding a waste of the enolate in method (B).



As shown in the Table, the corresponding 1,3-dicarbonyl compounds 2 could be isolated in good to excellent yield. Method (A) usually affords better results as compared with method (B). However, with methyl ketones,[11a] the products 2 could be obtained in satisfactory yield by method (B) without any expense of the starting ketones.

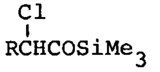
$$\text{Ketone (2 eq)} \xrightarrow{\text{LDA (2 eq)}} \xrightarrow{1} \xrightarrow{H_3\overset{+}{O}} 2 \quad \text{Method (A)}$$

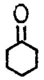
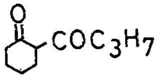
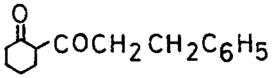
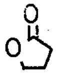
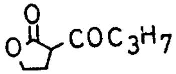
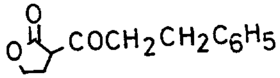
$$\text{Ketone (1 eq)} \xrightarrow{\text{LiBTSMB (2 eq)}} \xrightarrow{1} \xrightarrow{H_3\overset{+}{O}} 2 \quad \text{Method (B)}$$

The following examples are representative.

(Method A). 3-Pentanone (86 mg, 1.0 mmol) was treated with LDA (1 eq) in THF (4 ml) at -78°C for 30 min. To the resulting solution was added THF (4 ml) solution of 2-chloro-3-phenylpropionyltrimethylsilane (121 mg, 0.50 mmol) at 0°C and it was stirred for 30 min at that temperature. Acidic work up[12] of the reaction mixture followed by separation with tlc afforded 1-phenyl-4-methyl-3,5-heptanedione (101 mg, 93%).

(Method B). 4-Phenyl-2-butanone (148 mg, 1.0 mmol) was treated with LiBTSMB (2.05 mmol) in THF (4 ml) for 2 hr at -40°C. Then, THF (2 ml) solution of 2-chloro-3-phenylpropionyltrimethylsilane (241 mg, 1.0 mmol) was added and it was stirred for 3 hr at -40°C. Acidic work up of the reaction mixture and purification by tlc gave 1,7-diphenyl-3,5-heptanedione (230 mg, 82%).

Table. Reactions of Enolates with α-Chloroacyltrimethylsilane 1,  $R\overset{Cl}{C}HCOSiMe_3$.

Ketone	R of 1	Product	Yield,% (Method)
$C_2H_5COC_2H_5$	$C_6H_5CH_2$	$C_6H_5CH_2CH_2COCH(CH_3)COC_2H_5$	93(A)
$C_4H_9COC_4H_9$	C_2H_5	$C_3H_7COCH(C_3H_7)COC_4H_9$	78(A)
	$C_6H_5CH_2$	$C_6H_5CH_2CH_2COCH(C_3H_7)COC_4H_9$	94(A)
$C_6H_5COCH_3$	$C_6H_5CH_2$	$C_6H_5CH_2CH_2COCH_2COC_6H_5$	98(A), 87(B)
$(CH_3)_2CHCOCH_3$	$C_6H_5CH_2$	$C_6H_5CH_2CH_2COCH_2COCH(CH_3)_2$	80(B)
$C_6H_5CH_2CH_2COCH_3$	C_2H_5	$C_3H_7COCH_2COCH_2CH_2C_6H_5$	74(B)
	$C_6H_5CH_2$	$C_6H_5CH_2CH_2COCH_2COCH_2CH_2C_6H_5$	82(B)
	C_2H_5		75(A)
	$C_6H_5CH_2$		79(A)*
	C_2H_5		75[a)]
	$C_6H_5CH_2$		87(A)

a) The reaction was carried out in the presence of LDA (1 eq) and LiBTSMB (1 eq) at -20°C for 5 hr.

References and Notes

1) M. E. Jung, Tetrahedron, **32**, 3 (1976); J. d'Angelo, ibid., **32**, 2979 (1976).

2) See, for example, I. Kuwajima and E. Nakamura, J. Am. Chem. Soc., **97**, 3257 (1975); E. S. Binkley and C. H. Heathcock, J. Org. Chem., **40**, 2156 (1975).

3) G. Stork, G. A. Kraus, and G. A. Garcia, J. Org. Chem., **39**, 3459 (1974); G. Stork and J. d'Angelo, J. Am. Chem. Soc., **96**, 7114 (1975); T. Mukaiyama, T. Sato, S. Suzuki, T. Inoue, and H. Nakamura, Chemistry Lett., 95 (1976); I. Kuwajima, T. Sato, M. Arai, and N. Minami, Tetrahedron Lett., 1817 (1976); R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura, and M. Shimizu, J. Am. Chem. Soc., **99**, 1265 (1977); K. Maruoka, S. Hashimoto, Y. Kitagawa, H. Yamamoto, and H. Nozaki, ibid., **99**, 7705 (1977); I. Kuwajima, T. Inoue, and T. Sato, Tetrahedron Lett., 4887 (1978).

4) H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, Menlo Park, Calif., 1972, pp 734-816.

5) Recently, successful C-acylation of enolates has been reported; A. K. Beck, M. S. Hoekstra, and D. Seebach, Tetrahedron Lett., 1187 (1977), and references cited therein.

6) a) I. Kuwajima, T. Abe, and N. Minami, Chemistry Lett., 993 (1976); b) T. Sato, T. Abe, and I. Kuwajima, Tetrahedron Lett., 259 (1978).

7) I. Kuwajima, K. Matsumoto, and T. Inoue, Chemistry Lett., 419 (1979).

8) T.-L. Ho, "Hard and Soft Acids and Bases Principle in Organic Chemistry", Academic Press, 1977.

9) If desired, the product appears to be isolated as the silylated form **4**. For example, $C_6H_5COCH_2COCH(SiMe_3)CH_3$ could be obtained in 88% yield by the reaction of 2-chloropropionyltrimethylsilane with acetophenone enolate (2 eq). nmr (CCl_4): δ 0.07 (s, 9H), 1.23 (d, J = 7 Hz, 3H), 2.20 (q, J = 7 Hz, 1H), 5.90 (s, 1H), 7.2∿7.9 (m, 5H), 16.4 (br, 1H). ir(neat): 1600, 1570, 1250, and 845 cm^{-1}.

10) I. Kuwajima, T. Sato, N. Minami, and T. Abe, Tetrahedron Lett., 1591 (1976); I. Kuwajima, N. Minami, T. Abe, and T. Sato, Bull. Chem. Soc. Jpn., **51**, 2391 (1978).

11) a) I. Kuwajima, T. Sato, M. Arai, and N. Minami, Tetrahedron Lett., 1817 (1976); b) I. Kuwajima, N. Minami, and T. Sato, ibid., 2253 (1976).

12) The products have been generally isolated after removal of trimethylsilyl group, since it has usually been quite difficult to assign the attached position of silyl group definitly by spectral data.

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