STEREOCHEMISTRY OF THE ENOLATE FROM METHYL PHENYLACETATE

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Abstract: Deprotonation of methyl phenylacetate with lithium diisopropylamide in tetrahydrofuran followed by trapping with trimethylsilyl chloride afforded an 81:19 mixture of *E*- and *Z*-silyl ketene acetals in agreement with a prediction by the calculation by Dauben. The *E*-silyl ketene acetal was readily isomerized to *Z*-isomer in the presence of LiCl and HMPA in THF.

Lithium ester enolates are of great importance as reactive intermediates in synthetic organic chemistry particularly in ester enolate Claisen rearrangement, where the stereochemistry of the enolates dictates the stereochemical outcome of the product.¹ Because of the low stability of ester enolates, their stereochemistries have not been determined directly,² but indirectly assigned by trapping them as the corresponding silyl ketene acetals.^{1,4-7} The validity of this method has been confirmed with *t*-butyl propionate by X-ray structure determinations of its lithium enolate³ and the corresponding ketene silyl acetal.⁸ Thus, silylation of lithium ester enolates is reasonably believed to proceed without isomerization of the double bond geometry. Extensive studies by Ireland *et al*¹ demonstrated that the stereochemistry of the ester enolates could be successfully controlled by changing the solvent system. Thus, ester 1 afforded (*E*)-silyl ketene acetal 4 as a major product via (*Z*)-enolate 2 when lithium diisopropylamide (LDA) was used for deprotonation in tetrahydrofuran (THF), while in THF-23% hexamethylphosphoric triamide (HMPA) predominant formation of (*Z*)-silyl ketene acetal 5 was observed (Scheme I).

Scheme I



The molecular mechanics model proposed by Moreland and Dauben⁹ supported the experimental results on the Z:E enolate ratios from the kinetic deprotonation of esters with LDA in THF or THF-HMPA.

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The only inconsistency between the experimental results and the calculation is that observed with methyl phenylacetate (1; $R^1 = C_6H_5$, $R^2 = CH_3$), which afforded (Z)-isomer 5 ($R^1 = C_6H_5$, $R^2 = CH_3$) predominantly even in THF alone (a 71 : 29 ratio of (Z)- to (E)-silyl ketene acetals).¹ The calculations predicted that the (E)-silyl ketene acetal would be energetically favored in contrast to the ratio actually observed. In connection with other studies,¹⁰ we investigated the enolate formation of methyl phenylacetate in detail. Here, we report that the prediction from the calculation was correct and the predominant formation of (Z)-isomer 5 ($R^1 = C_6H_5$, $R^2 = CH_3$) in THF was not a result of kinetic formation of the enolate but of an involvement of a thermodynamic equilibrium between (E)- and (Z)-silyl ketene acetals under the reaction conditions and/or during the work-up procedure.

The reactivity of t-butyldimethylsilyl chloride (TBSCl) toward the lithium enolate of methyl phenylacetate (6) is too low to provide the corresponding ketene acetals without HMPA,¹ while HMPA is unnecessary for the formation of the corresponding trimethylsilyl ketene acetals 7.¹¹ We examined the stereochemistry and the *E*:*Z* ratio of the silyl ketene acetals of methyl phenylacetate (6) using trimethylsilyl chloride (TMSCl) as a silylating agent to avoid the effect of HMPA. The ratio of (*E*)- to (*Z*)-silyl ketene acetals 7 obtained by the standard procedure in THF¹² was determined to be 81:19 by 400 MHz ¹H NMR spectrum in CDCl₃. The *E*:*Z* ratio observed by trapping with TMSCl was totally reversed to that with TBSCl reported by Ireland *et al.*¹³ The (*E*)- to (*Z*)-silyl ketene acetal ratio changed to 6:94 on addition of HMPA just before the work-up.¹⁴ These findings suggested an equilibrium between silyl ketene acetals (*E*)-7 and (*Z*)-7 in favor of (*Z*)-7. Deprotonation in THF-HMPA led to a 9:91 ratio of (*E*)- and (*Z*)-silyl ketene acetals 7, which agrees with the reported results.¹⁵ Stereochemistries of (*E*)-7 and (*Z*)-7 were determined by the nuclear Overhauser effect measurement as shown in Scheme II.

Scheme II



In order to confirm the equilibrium between (E)-7 and (Z)-7, ¹H NMR spectra of an isolated mixture¹¹ of (E)-7 and (Z)-7 were measured in THF-dg under a variety of conditions. The pertinent results are compiled in Table I. Silyl ketene acetals (E)-7 and (Z)-7 are stable under coexistence with diisopropylamine, HMPA, or both (entries 2, 3, or 4, respectively). Lithium chloride was found to promote an isomerization of silyl ketene acetal (E)-7 to (Z)-7. A 75:25 ratio of (E)- to (Z)-silyl ketene acetals 7 with LiCl, for about 51 h at 20°C, led to an 11:89 ratio of (E)-7 to (Z)-7, (entries 5-7), which is the same as that

obtained by the deprotonation with LDA in THF-HMPA. The equilibrium between (E)-7 and (Z)-7 was facilitated dramatically by addition of HMPA (entries 8-12).¹⁶ These findings clearly indicate the existence of a thermodynamic equilibrium between (E)-7 and (Z)-7. Though the E:Z isomerization in aliphatic silyl ketene acetals 4 and 5 has been reported to be readily achieved with HgBr₂/TMSBr,¹⁷ trialkylammonium perchlorates,¹⁸ CF₃COCF₃ or CF₃COCH₃,¹⁹ or CsF,¹⁹ what is unprecedented is the finding that suggests isomerization in (E)- and (Z)-silyl ketene acetals under reaction conditions and/or during the work-up procedure.

	entry	Of	iginal ratio	additive (mmol)	time	final ratio	
		7:6	(E)- 7 : (Z)- 7			7:6	(E)-7 : (Z)-7
	1	>10:1	76 : 24	none	48 h	6:1	74 : 26
	2	6:1	73 : 27	ⁱ Pr ₂ NH ₂ (0.29)	13 h	5:1	72 : 28
	3	>10 : 1	71 : 29	HMPA (0.23)	7.5 h	>10:1	70 : 30
	4	5:1	69:31	ⁱ Pr ₂ NH ₂ (0.29)	17 h	4:1	67 : 33
				HMPA (0.23)			
	5	>10:1	75 : 25	LiCl (0.12)	40 min	4:1	65 : 35
	6				12 h	4:1	26 : 74
	7				39 h	4:1	11:89
	8	>10:1	72 : 28	HMPA (0.06)	5 min	7:1	69 : 31
				LiCl (0.04)			
	9				15 min	7:1	64 : 36
	10				65 min	7:1	48 : 52
	11				4 h	7:1	30 . 70
	12				<u>8 h</u>	7:1	15 : 85

Table I. The change of the ratio of (E)-7 : (Z)-7 at 20 °C.^a

^aA mixture of silyl ketene acetals 7 (0.35 mmol) in THF-d₈ (0.5 mL).

In conclusion, the present studies demonstrated that the unusual results, previouly reported by Ireland *et al*¹ involving the predominant formation of (Z)-silyl ketene acetal 5 ($R^1 = C_6H_5$, $R^2 = CH_3$) were not due to kinetic deprotonation of methyl phenylacetate (6) in THF but to the equilibrium between the resulting (*E*)- and (*Z*)-silyl ketene acetals. The present results do not affect previous conclusions¹ on the determination of the stereochemistries of (*E*)- and (*Z*)-enolates of aliphatic esters based on experiments in which they had been converted into TBS ketene acetals.

References

 (a) Ireland, R. E.; Willard, A. K. Tetrahedron Lett., 1975, 3975.
 (b) Ireland, R. E.; Mueller, R. H.; Willard, A. K. J. Am. Chem. Soc. 1976, 98, 2868.
 (c) Ireland, R. E.; Wipf, P.; Armstrong, III, J. D. J. Org. Chem. 1991 56, 650.

- (2) The structures of lithium enolates of *t*-butyl propionate, *t*-butyl 2-methylpropionate, and methyl 3,3dimethylbutanoate have been determined by X-ray analyses.⁴
- (3) Seebach, D.; Amstutz, R.; Laube, T.; Schweizer, W. B.; Dunitz, J. D. J. Am. Chem. Soc. 1985, 107, 5403.
- (4) Chan, T. H.; Aida, T.; Lau, P. W. K.; Gorys V.; Harpp, D. N. Tetrahedron Lett. 1979, 4029.
- (5) Corey, E. J.; Gross, A. W. Tetrahedron Lett. 1984, 25, 495.
- (6) Misumi, A.; Iwanaga, K.; Furuta, K.; Yamamoto, H. J. Am. Chem. Soc. 1985, 107, 3343.
- (7) Kanemasa, S.; Nomura, M.; Wada, E. Chem. Lett. 1991, 1735.
- (8) Babston, R. E.; Lunch, V.; Wilcox, C. S. Tetrahedron Lett. 1989, 30, 447.
- (9) Moreland, D. W.; Dauben, W. G. J. Am. Chem. Soc. 1985, 107, 2264.
- (10) (a) Fuji, K.; Node, M.; Tanaka, F.; Hosoi, S. Tetrahedron Lett. 1989, 30, 2825. (b) Fuji, K.;
 Node, M.; Tanaka, F. Tetrahedron Lett. 1990, 31, 6553
- (11) Anisworth, C.; Chen, F.; Kuo, Y. J. Organometal. Chem. 1972, 46, 59.
- (12) Methyl phenylacetate (6) (0.5 mmol) was added at -78 °C to a solution of LDA (0.6 mmol) in THF (2 mL) and the mixture was diluted with THF (2 mL) followed by stirring for 30 min at the same temperature. After addition of TMSCI (2.0 mmol), the mixture was stirred for another 1 h at -78 °C, and then the cooling bath was removed. The volatile material was distilled off under reduced pressure to give a crude mixture of (E)- and (Z)-silyl ketene acetals 7, the ¹H NMR specturm of which showed almost a 100% conversiton.
- (13) A 29:71 mixture of (E)- and (Z)-silyl ketene acetals was obtained. See ref. 2.
- (14) The same procedure as that in ref. 13 except for addition of HMPA (2.5 mmol) just before evaporation of the volatile material.
- (15) A 5:95 mixture of (E)- and (Z)-silyl ketene acetals was obtained. See ref. 2.
- (16) The ratio of 4 ($R^1 = CH_3$, $R^2 = C_2H_5$) to 5 ($R^1 = CH_3$, $R^2 = C_2H_5$) was reported to change from 70:30 to 61:39 on warm up from -78 °C to room temperature in the presence of HMPA, LiCl, and LDA due to significant decomposition of the (*E*)-isomer (ref. 2c).
- (17) Burlachenko, G. S.; Manukina, T. A.; Baukov, Y. I. J. Organometal. Chem. 1971, 33, C59.
- (18) Wilcox, C. S.; Babston, R. E. J. Org. Chem. 1984, 49, 1451.
- (19) Adam, W.; Wang, X. J. Org. Chem. 1991, 56, 7244.

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