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TEMPERATURE-DEPENDENCY OF DIASTEREOSELECTIVITY IN THE ALDOL REACTION OF TRIBUTYLSTANNYL ENOLATES WITH BENZALDEHYDE

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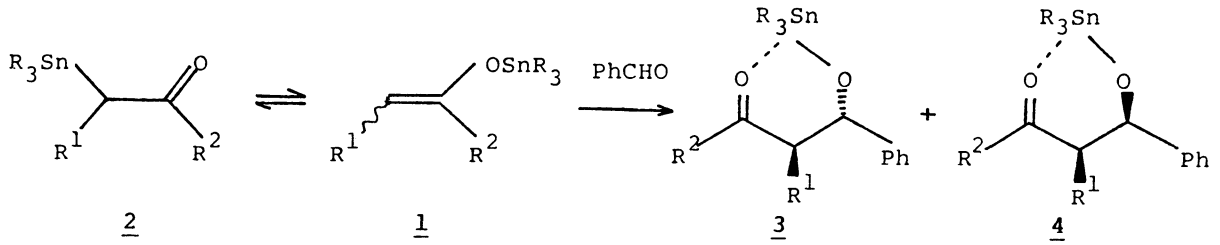
At -50°C the O-stannyl enolate reacts with benzaldehyde more quickly than the corresponding C-stannyl derivative to give predominantly *threo* adduct, which slowly isomerizes into the *erythro* isomer on warming the reaction products. At r.t. the stannyl enolate reacts rapidly to yield the *erythro* product.

Diastereoselectivity in aldol condensation of triorganostannyl enolates with aldehydes is reported to be highly dependent on reaction temperature.[1,2] At higher temperature the *erythro*[3] product forms predominantly, whereas the *threo*[3] isomer is the major product at lower temperature. This temperature-dependency of diastereoselectivity has not been rationalized explicitly. In this communication, we would like to present some experimental evidences which clarify this ambiguity. Monitoring the reaction progress of tributylstannyl enolates with benzaldehyde by ^{119}Sn and ^{1}H NMR spectroscopy[4] has revealed two novel facts. One is that the O-stannyl enolate **1** reacts more quickly than the corresponding C-stannyl derivative **2** at -50°C to give *threo* adduct **3**. Another is that **3** thus formed *slowly* isomerises into the *erythro* isomer **4** on warming the reaction product.



2 **1** **3** *(threo)* **4** *(erythro)*

a ; $R^1,R^2 = -(CH_2)_4-$
b ; $R^1,R^2 = -(CH_2)_3-$
c ; $R^1 = CH_3$, $R^2 = Ph$
d ; $R^1 = CH_3$, $R^2 = Et$

Table 1. Reaction of tributylstannyl enolates with benzaldehyde at -50°C or r.t.

Stannyl enolate	Conditions	Additional treatments	Ratio of products *threo*	*erythro*	Yield[b]
1a	-50°C/1h	none	78	22[a]	100
		r.t./7d	44	56	100
		+60°C/24h	44	56	100
	r.t./0.5h	none	22	78[a]	100
1b + **2b**	-50°C/1h	none	100	0	77
21 : 79 (-50°C)		r.t./7d	58	42	77
		+50°C/17h	50	50	77
53 : 47 (r.t.)	r.t./0.2h	none	50	50	50
		r.t./7d	50	50	100
1c	-50°C/1h	none	76	24[a]	100
		r.t./7d	70	30	100
		+60°C/20h	70	30	100
	r.t./0.5h	none	30	70	100
1d + **2d**	-50°C/1h	none	75	25	46
37 : 63 (-50°C)		r.t./7d	37	67	46
72 : 28 (r.t.)	r.t./0.5h	none	23	77	50

a) Ref. 1. b) Yields were calculated on the basis of tetrabutyltin added as an internal standard.

To a $CDCl_3$ solution of O-tributylstannyl 1-cyclohexenolate **1a**[5] was added an equimolar amount of benzaldehyde at -50°C. The ^{119}Sn NMR spectrum of the reaction mixture kept at -50°C for 30 min showed two signals at δ +111.4 and +108.3 ppm assignable to the **3a** and **4a**, respectively, whose integral ratio was 78 : 22 (Table 1). The original single peak at +104.3 ppm assigned to **1a** gradually decreased and disappeared completely after 60 min, while **3a** and **4a** were formed quantitatively. The ratio (**3a** : **4a** = 78 : 22) was maintained during 90 min at -50°C. When this mixture was warmed up to room temperature and left for a week, or when it was heated at 60°C for 24 h, the ratio of **3a** to **4a** converted to 44 : 56. This final ratio differs from the result (22 : 78)[1] in the same reaction carried out at room temperature.

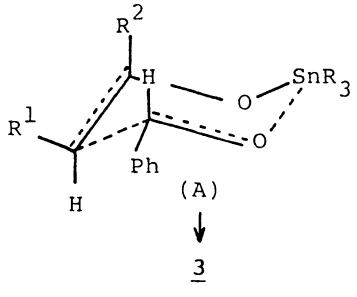
Reaction of the similar enolate of cyclopentanone[5] (**1b** : **2b** = 21 : 79 at -50°C) with benzaldehyde was conducted at -50°C. In the ^{119}Sn NMR spectra, a new peak assignable to **3b** appeared at +113.0 ppm in 10 min at the expense of the peak of **1b** at +112.7 ppm, while the signal of **2b** at +11.3 ppm slowly decreased and disappeared in 60 min.[6] No peak due to **4b** appeared after 60 min at -50°C. When the *threo* product **3b** was warmed up to room temperature, a small peak at +106.1 ppm assignable to **4b** came out. On keeping the mixture for a week at room temperature, the ratio of **3b** to **4b** converted into 58 : 42. Heating the mixture

at 50°C for 17 h resulted in a final ratio 50 : 50. When the mixture of 1b and 2b (53 : 47 at room temperature) was treated with benzaldehyde at room temperature, both 1b and 2b were consumed quickly in 10 min to give 3b and 4b in the same ratio 50 : 50 as the above isomerization results. Besides, the existence of the equilibrium between 1b and 2b could be confirmed by the temperature-dependency in the ratio of 1b to 2b.[7)]

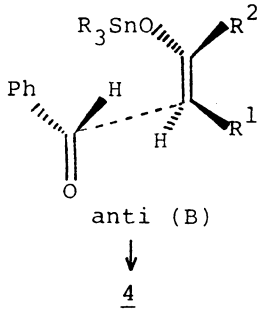
In the reaction of 1c with benzaldehyde at -50°C and room temperature, *threo* selectivity at -50°C and *erythro* selectivity at room temperature were observed respectively (Table 1).[7,8)] However, isomerization from 3c to 4c was exceedingly slow.

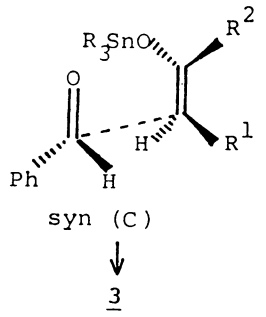
The reaction of 1d and 2d with benzaldehyde at -50°C and room temperature showed the similar results to that of the reaction of 1b and 2b (Table 1).

The *threo* selectivity at -50°C can be interpreted by the conventional *cyclic* transition state (A),[9)] a tight assemblage of the O-stannyl enolate 1 and the aldehyde under kinetic control. Since the O-stannyl enolate 1 reacts preferentially at -50°C, the C-stannyl derivative 2 can convert into more reactive 1 by the equilibrium. We could confirm that isomerization of 3 into thermodynamically more stable 4 proceeded on warming, but its rate was much slower than that of addition of 1 and 2 to the aldehyde at room temperature. Therefore, the *erythro* selectivity at a higher temperature (25°C - 45°C) can not be simply attributed to the slow isomerization from *threo* to *erythro* adducts. The *erythro* isomer 4 must be formed either from 1 through the *acyclic* transition state (B),[2,10)] or partly from 2 owing to the steric effect arising from S_E-type displacement of the C-Sn bond by the carbonyl electrophile[11)] proposed by Yamamoto and Maruyama, since 2 also will be able to react at higher temperature without the conversion. Apparent smaller ratio of *erythro* isomer (4b : 3b = 50 : 50) than an expected result in the reaction at room temperature might reflect the difference of the geometry in the acyclic transition state. Since the steric hindrance around the 3-carbon of 1b is less than that in the other enolates, we assume that the configuration (C) leading to the *threo* isomer can show the relative importance in the reaction at room temperature.



Cyclic transition state





Acyclic transition state

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References

1) S. Shenvi and J. K. Stille, Tetrahedron Lett., 23, 627 (1982).

2) Y. Yamamoto, H. Yatagai, and K. Maruyama, J. Chem. Soc., Chem. Commun., 1981, 162.

3) Recently two novel methods for specification of relative configuration in molecules with multiple chiral center have been proposed. (F. A. Carey and M. E. Kuehne, J. Org. Chem., 47, 3811 (1982); D. Seebach and V. Prelog, Angew. Chem., Int. Ed. Engl., 21, 654 (1982)). But in this communication *threo-* and *erythro-* notation is used in a sense described in the literature. (C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J. E. Sohn, and J. Lampe, J. Org. Chem., 45, 1066 (1980)).

4) Measurement by ^{1}H NMR spectroscopy showed the similar results to those by ^{119}Sn NMR spectroscopy. Details will be reported in a full paper.

5) M. Pereyre, B. Bellegarde, J. Mendelsohn, and J. Valade, J. Organometal. Chem., 11, 97 (1968).

6) In ^{119}Sn NMR spectra, the peak around +100 ppm was assigned to the O-stannyl enolate 1, since tributyltin methoxide has a peak at +107.6 ppm in $CDCl_3$. On the other hand, the C-stannyl derivatives show their absorption near that of tetrabutyltin (-12.4 ppm in $CDCl_3$).

7) K. Kobayashi, M. Kawanisi, S. Kozima, and T. Hitomi, The 47th National Meeting of the Chemical Society of Japan, 4B08 (1983).

8) Although tributylstannyl enolate of propiophenone was reported to be a mixture of C-stannyl derivative to O-stannyl enolate in a 9 : 1 ratio,[1)] we can confirm that this enolate consists of only the O-stannyl enolate 1c by the ^{119}Sn NMR spectroscopy.

9) H. O. House, D. S. Crumrine, A. Y. Teranishi, and H. D. Olstead, J. Am. Chem. Soc., 95, 3310 (1973); W. A. Kleschick, C. T. Buse, and C. H. Heathcock, *ibid.*, 99, 247, 8109 (1977); Tetrahedron Lett., 1978, 1685; P. Fellman and J. E. Dubois, *ibid.*, 1975, 1225; Tetrahedron, 34, 1349 (1978); A. I. Meyers and P. J. Reider, J. Am. Chem. Soc., 101, 2501 (1979).

10) S. Murata, M. Suzuki, and R. Noyori, J. Am. Chem. Soc., 102, 3248 (1980); Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, *ibid.*, 102, 7107 (1980); Y. Yamamoto and K. Maruyama, Tetrahedron Lett., 21, 4607 (1980); J. Mulzer, G. Bruentrup, J. Finke, and M. Zippel, J. Am. Chem. Soc., 101, 7723 (1979).

11) Y. Yamamoto and K. Maruyama, J. Am. Chem. Soc., 104, 2323 (1982).

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