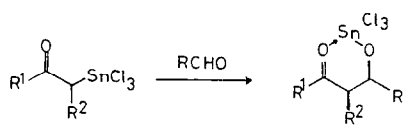
Tetrahedron Letters,Vol.24,No.32,pp 3347-3350,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

ERYTHRO SELECTIVE ALDOL REACTION OF α-TRICHLOROSTANNYL KETONES

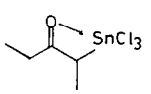
Eiichi NAKAMURA and Isao KUWAJIMA*
Department of Chemistry, Tokyo Institute of Technology
Meguro, Tokyo 152, Japan

Summary: The aldol reaction of α-stannyl ketones with aromatic and aliphatic aldehydes is highly (up to 95%) erythro selective.

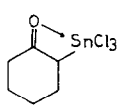
Metal cations of a highly Lewis acidic character are an emerging class of "tools" in organic synthesis. Such concept has been particularly useful in aldol chemistry; the metal is considered to stabilize and tighten the chair-formed chelated transition state, and enhance the stereoselectivity of the reaction.[1] This expectation has been amply rewarded in the chemistry of boron enolates,[2] but controversial situations have been noted recently in some other cases.[1b] For instance, the aldol reactions of tin, zirconium, and titanium enolates exhibit an unprecedented stereoselectivity, the erythro preference irrespective of the enolate geometry.[3] It is entirely possible that these reactions do not proceed via the usual chair transition state, and in fact we have shown that at least one of them involves the boat transition state.[3] We now report the highly erythro-selective aldol reaction of α-trichlorostannyl ketones 1 (eq 1), which indicates yet another possibility that the erythro-selectivity also arises from the reaction of α-metallo ketones. Lewis acid catalyzed reaction of α-silyl[4] and α-mercurio ketones[5] has already been reported to be erythro selective.



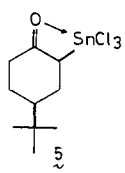
1 2 (1)



3



4



5

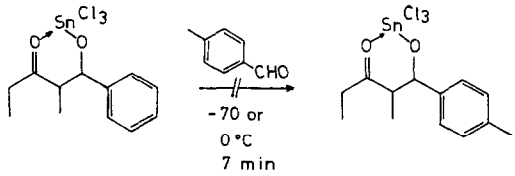
The stannyl ketones 3—5 were prepared from the corresponding enol silyl ethers by the method that we just reported.[6] The aldol reaction proceeded rapidly at a low temperature with high kinetic erythro selectivity (Table 1).[7] Relatively rapid equilibration of the aldolate 2 was rather unexpected. The

benzaldehyde adducts equilibrate faster than the adducts obtained from aliphatic aldehydes (entries 1—8). Interestingly, neither the exchange of the aldehydes nor polycondensation occurred, when a second aldehyde was added to the preformed aldolate (eq 2). The presence of excess $SnCl_4$ does not greatly affect either the kinetic selectivity or the rate of the equilibration (entries 9 and 10). The stannyl ketone slowly reacts with a benzaldehyde acetal, but the reaction is stereo-random (entry 16).

Table 1. Erythro Selective Aldol Reaction of α-Stannyl Ketones[a]

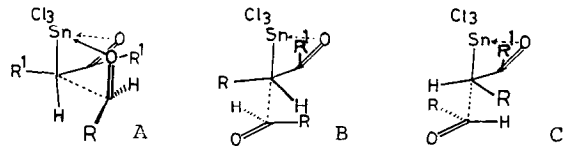
Entry	Stannyl ketone	Aldehyde	Temp °C	Time	Conc.[b] M	Erythro:[c] threo	% yield[c]
1	3	PhCHO	-70	5 sec	0.1	95:5	54
2	3	PhCHO	-70	1 min	0.1	91:9	61
3	3	PhCHO	-70	1 h	0.1	85:15	65
4	3	PhCHO	-70 0	15 min 10 min	0.1	61:39	76
5	3	n-PrCHO	-70	5 sec	0.1	95:5[d]	56
6	3	n-PrCHO	-70	1 h	0.1	89:11[d]	52
7	3	i-PrCHO	-70	5 sec	0.1	87:13[e]	34
8	3	i-PrCHO	-70	1 h	0.3	85:15[e]	53
9	3 + $SnCl_4$[f]	PhCHO	-70	5 sec	0.1	95:5	40
10	3 + $SnCl_4$[f]	PhCHO	-70	1 h	0.1	92:8	41
11	4	PhCHO	-70	5 sec	0.1	93:7	80[g]
12	4	n-PrCHO	-70	7 min	0.05	95:5[e]	73
13	5	PhCHO	-70	1 min	0.3[h]	[82:18 cis 82:18 trans][i]	10[h] 10
14	5	PhCHO	-70	5 sec	0.1	[87:13 cis 81:19 trans][i]	36 21
15	5	PhCHO	-70	5 sec	0.01	[87:13 cis 74:26 trans][i]	45 38
16	3	$PhCH(OMe)_2$	-70	1 h	0.1	47:53 or 53:47	50

a: About 1—1.2 equiv of the stannyl ketone prepared in situ was used in methylene chloride. b: Approximate concentration of the aldehyde. c: The ratio and the yield were determined by ^1H NMR using an internal standard, unless otherwise noted. The stereochemistry is based on ^1H NMR (ref 1). GLC analysis was perfomed on fused silica capillary columns. d: OV-101, 20 m. e: PEG-20M, 20 m. f: $SnCl_4$ (ca. 1.5 equiv to the aldehyde) was present in the mixture, causing precipitation of white solid. g: Isolated yield. h: Low yield is due to the insolubility of the 1/aldehyde complex; the effective concentration of the reactants may be therefore lower. i: The cis and the trans products refer to the 1,4-cis- and trans-cyclohexanone adducts, respectively.



(2)

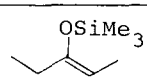
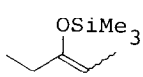
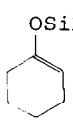
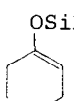
Scheme 1.



The reaction of 5 gave a mixture of the cis and the trans isomers, both in excess of the erythro diastereomers (entries 13--15).[3,8] These isomers may have resulted from the cleavage of the carbon-tin bond with retention and inversion of the stereochemistry. Three rationales to account for the results are suggested in Scheme 1. The stereochemistry concerning the carbon-metal bond cleavage constitutes the unique problem in the reactions of α-metallo ketones and should be the subject of further studies.

As an extention of the present studies, the stereochemistry of the reaction of enol silyl ethers with an MX_n/aldehyde complex was examined (Table 2). The kinetic diastereoselectivity is distinctively different from that found for the α-stannyl ketones or the titanium enolates.[3] The Mukaiyama aldol reaction[8] at low temperatures therefore does not involve the silicon-metal exchange[8b] before the crucial C-C bond formation, as has often been alluded to.[1a, b]

Table 2. Stereochemistry of the MX_n-Mediated Aldol Reaction of Enol Silyl Ethers and Benzaldehyde[a]

Entry	Enol silyl ether	MX_n	Erythro: threo
1		$SnCl_4$	62:38[b]
2		$TiCl_4$	50:50[c]
3		$TiCl_4$	25:75[d]
4		$SnCl_4$	24:76[d]
5		$TiCl_4$	14:32 cis[e,f] 14:40 trans
6		$SnCl_4$	12:35 cis[b,f] 18:35 trans

a: The reaction was performed at -70 °C in a 0.1—0.4 M methylene chloride solution, using the preformed benzaldehyde/MX_n complex (ref 8). b: Kinetic selectivity at -70 °C, 1 min. c: Ref 9. d: Ref 8. e: The reaction was performed at -70 to 20 °C. f: See note i in Table 1.

References and Notes

1. (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. Topics in Stereochemistry, 1982, 13, 1. (b) Heathcock, C. H. "Asymmetric Synthesis"; Vol. 2.; Morrison, J. D., Ed.; Academic Press: New York, 1983; Chapter 2. (c) Mukaiyama, T. Org. Reactions, 1982, 28, 203.
2. (a) Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. J. Am. Chem. Soc. 1981, 103, 3099. (b) For an impressive demonstration of the power of the aldol reaction, see Masamune, S.; Imperiali, B.; Garvey, D. S. J. Am. Chem. Soc. 1982, 104, 5528, and ref therein.
3. Nakamura, E.; Kuwajima, I.; preceeding communication and ref 8 therein.
4. Kuwajima, I.; Inoue, T.; Sato, T. Tetrahedron Lett. 1978, 4887. The erythro selectivity observed here albeit moderate is general; Inoue, T.; Ph.D thesis: Tokyo Institute of Technology, 1980.
5. Yamamoto, Y.; Maruyama, K. J. Am. Chem. Soc. 1982, 104, 2323.
6. Nakamura, E.; Kuwajima, I. Chem. Lett. 1983, 59. 1-Methyl-2-(trimethylsiloxy)-1-cyclohexene is inert to $SnCl_4$.
7. A solution of 4 (ca. 0.2 mmol) in 2 ml of methylene chloride was prepared from $SnCl_4$ (81 μl, 0.70 mmol) and the enol silyl ether of cyclohexanone (85 mg, 0.50 mmol) at 20 °C. To this solution was added benzaldehyde (21 mg, 0.20 mmol) at -70 °C. After 5 sec, water was added at once, and usual workup was performed to obtain the crude aldol (36 mg) as a crystaline solid (e:t = 95:5), from which 33 mg (80%) of the erythro aldol was obtained. A separate run under ^1H NMR monitoring indicated the absence of the participation of chlorotrimethylsilane, a side product of the stannyl ketone-forming reaction, in the subsequent aldol reaction.
8. (a) Mukaiyama, T.; Banno, K.; Narasaka, K. J. Am. Chem. Soc. 1974, 96, 7503. (b) Mukaiyama, T.; Narasaka, K.; Banno, K. Chem. Lett. 1973, 1011.
9. Yamamoto, Y.; Maruyama, K. Tetrahedron Lett. 1980, 4607.

(Received in Japan 19 April 1983)