

## Diastereo- and Regio-selective Aldol Condensation by Trapping Dienolates with Tin

Yoshinori Yamamoto,\* Satoshi Hatsuya, and Jun-ichi Yamada

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

Although the reaction of dienolate (1) with aldehydes is frequently lacking in regio- and diastereo-selectivity, the  $\gamma$ -tin substituted derivatives (5), easily obtainable from (1), give (3) and (4) diastereoselectively by controlling the reaction conditions.

Despite rapid progress in aldol chemistry during the past decade,<sup>1</sup> the problem of diastereo- and regio-selectivity in the reaction of the dienolate (1) with aldehydes remains unsolved. The reaction of (1) with aldehydes at higher temperatures under thermodynamically controlled conditions leads to the  $\gamma$ -adduct (2), and in turn (2').<sup>2</sup> At lower temperatures under kinetically controlled conditions,  $\alpha$ -regioselective carbon-carbon bond formation is realized. Unfortunately, however, the diastereoselectivity is low and frequently a mixture of (3) and (4) is produced (Scheme 1).<sup>2</sup> In this communication we report a method of trapping dienolates with tin to provide a solution to some of these problems.

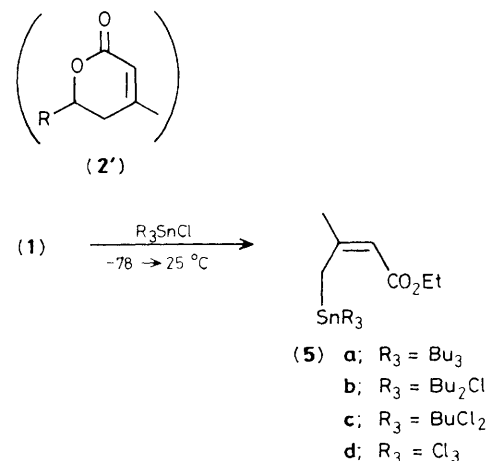
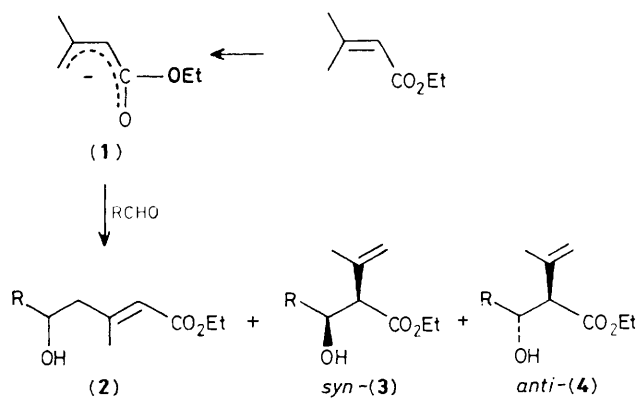
The reaction of (1) with  $R_3SnCl$  gave (5) in an essentially quantitative yield (Scheme 1). The tin intermediate was stable enough to isolate through Kugelrohr distillation. Compound (5) (*Z*-isomer) was always contaminated with small amounts of the (*E*)-isomer. The results of the reactions of (5) with representative aldehydes under the influence of Lewis acids or  $Bu_4NF$  are summarized in Table 1.

The  $BF_3$ - and  $ZnBr_2$ -mediated reactions of (5a-c) with aldehydes at  $-78^\circ C$  produced the *anti* adduct (4) either exclusively or predominantly (entries 1, 4-8, and 10). Use of  $TiCl_4$  gave a mixture of (3), (4), and the  $\gamma$ -products (entry 2). Although the  $F^-$  mediated reactions of (5b-d) at  $-78^\circ C$  afforded again (4) either exclusively or predominantly (entries 9, 12, and 14), the same reaction of (5a) gave (3) preferentially (entry 3). Further, (5c) and (5d) reacted with benzaldehyde at room temperature without Lewis acids or  $Bu_4NF$  assistance

(entries 11 and 13), presumably owing to the increased Lewis acidity of these tin chlorides.<sup>3†</sup>

The above observations on diastereoselectivity are different from the recent results on  $\gamma$ -silylated  $\alpha,\beta$ -unsaturated amides reported by Snieckus and coworkers.<sup>4</sup> The  $TiCl_4$ -mediated reaction of the silylated analogue produces the corresponding *syn* derivatives, while the  $F^-$  mediated reaction does not produce good diastereoselectivity.<sup>4</sup> The present diastereoselectivity can be explained as shown in Scheme 2.

The Lewis acid mediated reaction proceeds through the acyclic transition state (6), as proposed previously,<sup>5</sup> to produce the *anti* alcohol [*anti*-(4)] regardless of the geometry of the double bond. Without Lewis acids (entries 11 and 13), the (*Z*)-allylic stannanes (5c,d) again produce (4) via a six-membered cyclic transition state. The reaction of  $Bu_4NF$



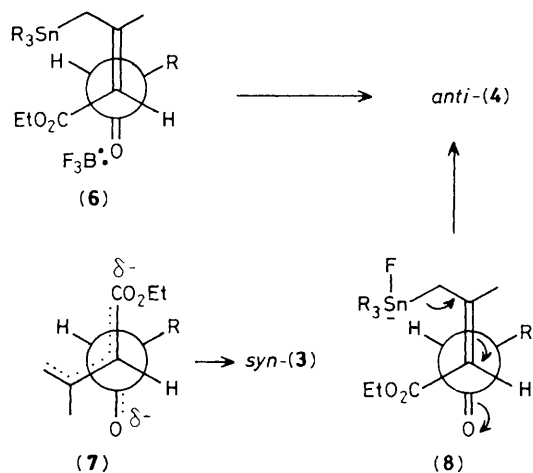
Scheme 1

Table 1. Regio- and diastereo-selective reaction of (5) with aldehydes.<sup>a</sup>

Entry	Tin	Aldehyde	Additive	Product ratio <sup>b</sup>			Total yield <sup>b,c</sup> /%
				(3)	(4)	(2)	
1	(5a)	PhCHO	$BF_3 \cdot OEt_2$	—	100	—	100
2	(5a)	PhCHO	$TiCl_4$	22	34	44	100
3	(5a)	PhCHO	$Bu_4NF$	72	28	—	65
4	(5a)	EtCHO	$BF_3 \cdot OEt_2$	—	100	—	34
5	(5a)	$(Et)_2CHCHO$	$BF_3 \cdot OEt_2$	—	100	—	40
6	(5a)	$PhCH=CHCHO$	$BF_3 \cdot OEt_2$	16	84	—	69
7	(5b)	PhCHO	$BF_3 \cdot OEt_2$	—	100	—	33
8	(5b)	PhCHO	$ZnBr_2$	—	100	—	52
9	(5b)	PhCHO	$Bu_4NF$	—	100	—	65
10	(5c)	PhCHO	$BF_3 \cdot OEt_2$	—	100	—	30
11	(5c)	PhCHO	None	—	100	—	70
12	(5c)	PhCHO	$Bu_4NF$	—	100	—	30
13	(5d)	PhCHO	None	16	48	37	100
14	(5d)	PhCHO	$Bu_4NF$	22	78	—	100

<sup>a</sup> All reactions were carried out on 1 mmol scale at  $-78^\circ C$ , except entries 11 and 13 where the reactions were carried out at room temperature.  $CH_2Cl_2$  (entries 1,2, 4-8, 10,11, and 13) or tetrahydrofuran (entries 3,9,12, and 14) solvent was used. <sup>b</sup> Determined by  $^1H$  n.m.r. analysis. <sup>c</sup> When the yield was low, the self-condensation of (5) took place and the aldehyde was recovered.

† The structures of (2)–(4) were unambiguously determined by comparison with authentic materials (ref. 2a).



Scheme 2

with (5a) may give the naked dienolate, in which the negative charge will be localized at the ester function. Accordingly, the reaction proceeds through (7) which is the most stable intermediate from both steric and electronic points of view,

resulting in the predominant formation of (3). The reaction of  $\text{Bu}_4\text{NF}$  with (5b—d) may afford the ate complex owing to the strong electron withdrawing effect of the Cl atom. Thus, (8) must be the most stabilized transition state, leading to (4). In conclusion, this work provides not only a regio- and diastereo-selective aldol methodology for dienolates, but also opens up the argument whether a naked anion is involved in  $\text{F}^-$ -mediated reactions.

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