Simultaneous Control of Regio- and Stereoselectivity in the Reaction of Pentadienyltin
by the Lewis Acid-Coordination to Its Ethereal Functionality

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By the $TiCl_4$-coordination to the ethereal functionality on the pentadienyltin, its
addition to aldehydes was controlled to proceed at its γ-position with high regioselectivity,
in contrast to the usual ε-selectivity of dienyltins and -silanes. High *syn,syn*-stereoselec-
tivity was simultaneously realized as an asymmetric induction from the tin reagent.

Pentadienylmetals are now occupying an important position in synthetic and theoretical chemistry.[1] They
can provide a way to introduce C_5 units, pentadienyl groups, nucleophilically into various electrophiles. In addi-
tion, since they are π-extended homologs of allylmetals, their reactivity is of interest. However, study on the
control of their selective reaction has been scarce so far.[2] Herein we describe one of the most synthetically use-
ful pentadienylmetals, pentadienyltin (PDT), was added regioselectively at its γ-position to aldehydes by the
Lewis acid-coordination to an ethereal functionality on the PDT. Moreover, highly stereoselective addition was
simultaneously realized.

As a coordinatively regio- and stereogenic functionality on PDT, we employed methoxyethyl group for its
facile availability.[3] Thus, racemic (Z)-2-(1-methoxyethyl)-2,4-pentadienyltrimethyltin (2) was applied to the re-
action with aldehydes (1).[4] Three types of regioisomeric products 3, 4, and 5 were obtainable (Scheme 1).
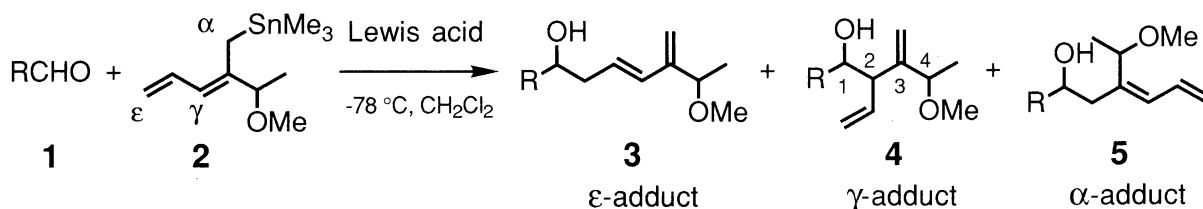
Scheme 1.

As previously reported, dienyltins[5] as well as dienylsilanes[6] are known to usually react at their ε-posi-
tion. This regioselectivity at the terminal position of the conjugated system is parallel to that of allylic tins and
silanes. Along this line, PDT 2 also gave the corresponding ε-adduct 3 preferentially by the use of $BF_3 \cdot OEt_2$ as
shown in Table 1.

On the contrary, a dramatic contrast to the above in regioselectivity was observed as summarized in Table
2, when we applied another popular Lewis acid, $TiCl_4$, to the present reaction. In our experiment here, about

Table 1. BF$_3$·OEt$_2$-mediated Reaction

Entry	Aldehyde / R	Product distribution			Combined yield / %
		3	4a)	5	
1	n-C$_9$H$_{19}$	84	6	10	67
2	cyclo-C$_6$H$_{11}$	81	10	9	100
3	C$_6$H$_5$	55	20	25	74
4	p-MeO$_2$CC$_6$H$_4$	78	22	0	92
5	p-O$_2$NC$_6$H$_4$	70	24	6	76

a) About 90% of the γ-adduct was a syn, anti-isomer like **4C** in Scheme 2. Also see the text.

Table 2. TiCl$_4$·OEt$_2$-mediated Reaction

Entry	Aldehyde / R	Product distribution			Combined yield / %
		3	4a)	5	
1	n-C$_9$H$_{19}$	7	89	4	52
2	cyclo-C$_6$H$_{11}$	26	67	7	51
3	p-MeC$_6$H$_4$	5	95	trace	56
4	C$_6$H$_5$	0	100	0	61
5	p-ClC$_6$H$_4$	0	100	0	64
6	p-MeO$_2$CC$_6$H$_4$	0	100	0	100
7	p-O$_2$NC$_6$H$_4$	7	93	0	100
8	o-FC$_6$H$_4$	6	94	0	86
9	o-ClC$_6$H$_4$	70	30	trace	61

a) Exclusively one diastereoisomer (syn, syn-isomer like **4A** in Scheme 2) among four possibles was formed. Also see the text.
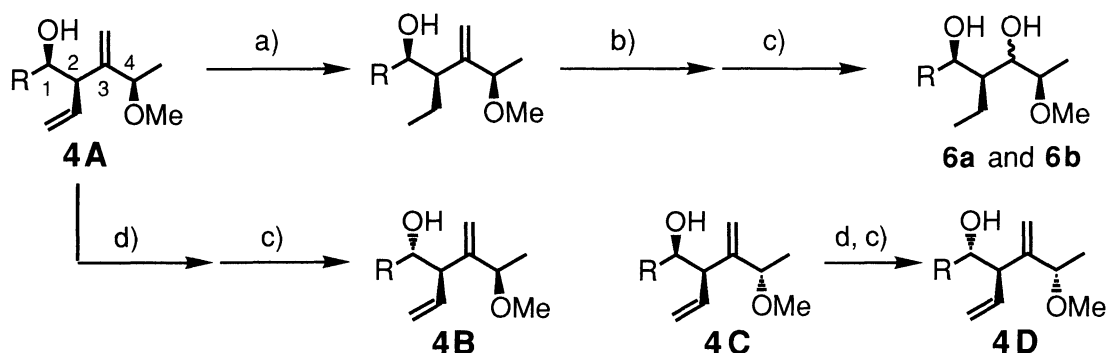
Scheme 2. Reagents: R = p-O$_2$NC$_6$H$_4$; a) p-MeC$_6$H$_4$SO$_2$NHNH$_2$; b) NaIO$_4$, OsO$_4$; c) NaBH$_4$; d) Jones reagent.

Fig. 1. Structure of **6a**.
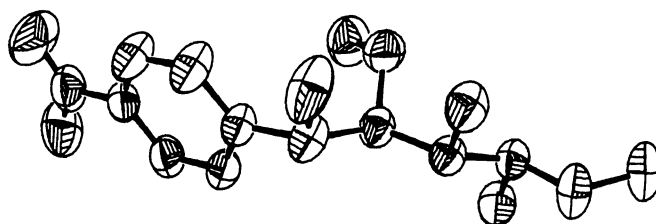
two equivalents of ethyl ether was added to TiCl4 to suppress transmetalation reaction[7] which complicated the addition reaction. In most instances, extremely high γ-selectivity was realized,[8] though decreased γ- and opposite ε-selectivities were obtained when the applied aldehydes were sterically crowded (entries 2 and 9).

More interestingly, the γ-adduct 4 obtained from the TiCl4-mediated reaction was found to consist of a single diastereoisomer detectable among the four possibles; extremely high stereoselectivity (concerning the two newly generated stereocenters) was realized along with high regioselectivity. Its relative configuration was determined as follows. Compound 4A afforded from entry 7 in Table 2 was converted to a pair of diols 6a and 6b by the series of reactions depicted in Scheme 2. Fortunately, because the one isomer 6a was crystallized, X-ray crystal analysis became available.[9] As a result, the configurational structure of 6a was determined to be all syn as shown in Fig. 1, which thus indicated the parent γ-adduct 4A had a 1,2-syn, 2,4-syn-configuration.[10]

Another diastereoisomer of 4 was selectively obtained from 4A by the procedure shown in Scheme 2 (Jones oxidation and reduction) as the C-1 isomer (1,2-anti) 4B as was expected from Cram's rule. In addition, the major γ-adduct 4C in the BF3-mediated reaction (Table 1, entry 5) was found to differ from the above isomers 4A and 4B. Together with the fact that 4C could be also isomerized at C-1 to the Cram product (1,2-anti) 4D by the oxidation-reduction procedure, the configurations of 4C and 4D were confirmed to be 1,2-syn, 2,4-anti and 1,2-anti, 2,4-anti, respectively.[10] Thus, the all four possible diastereoisomers were spectroscopically identified. Regarding this as a criteria, other TiCl4-mediated and BF3-mediated γ-adducts were concluded to have the same syn, syn- and syn,anti-configurations,[10] respectively, from comparison of ^{1}H NMR spectra of 4.
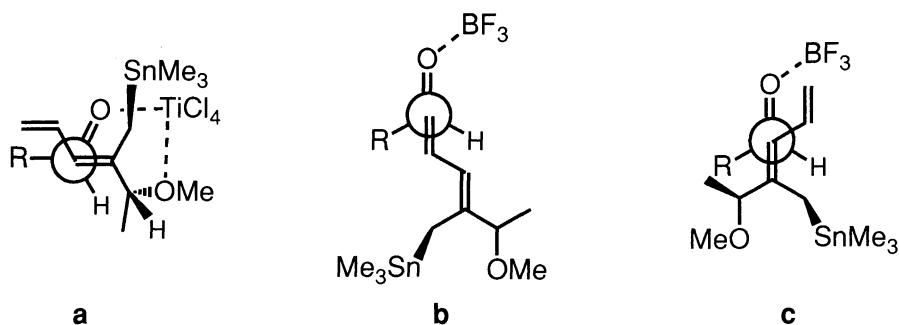

Fig. 2. Transition state models.

The high γ- and syn, syn-selectivity by TiCl4 can be rationalized by its coordination mode. TiCl4, having two acceptor sites, is expected to bind 1 and 2 by coordination to the oxygen functionalities of the both reagents (Fig. 2a), so is favored the reaction at the nearer position to the coordinative methoxyl group. But when R is bulky, the steric repulsion between R and the vinyl group becomes so severe as to decrease the γ-selectivity. The high syn, syn-stereoselectivity can be also attributed to the rigid cyclic transition complex, which is consistent with that we have already proposed in the stereodivergent reaction of an allylic silane.[11] On the other hand, since BF3 has only one acceptor site, it can not experience such a cyclic transition state but extended acyclic one (Fig. 2b). Therefore, the ε-adduct is favored from the steric demand. The syn, anti-selectivity of the γ-adduct by the BF3-mediation can be also explained by the acyclic transition state (Fig. 2c).[11] Furthermore, the following results support the importance of the Lewis acid-coordination. When (Z)-2-isopropylpentadienyltin[1a] was allowed to react with p-nitrobenzaldehyde, a significant amount of the ε-adduct was formed even by the use of TiCl4 and the stereoselectivity of the γ-adduct was decreased.[12] This is reasonable because the isopropyl group is non-coordinative but sterically similar in size to the methoxyethyl group.

From above all, very high level of simultaneous control of regio- and stereochemistry in the pentadienyl system was realized. This is the first example for such a coupled control from an organometalic reagent, though a few instances of stereocontrol alone are known.[11, 13] Because the introduced diene moiety can be converted to other functional groups (e.g. Scheme 2), this methodology may be valuable for the stereoselective synthesis of acyclic compounds with many chiral centers.

References

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2)   For recent example, Y. Nishigaichi and A. Takuwa, *Chem. Lett.*, **1990**, 1575.

3)   PDT **2** was prepared by the reaction of 3-butyn-2-ol and allylzinc bromide to give dienol followed by methylation (MeI, KOH) and stannylation (n-BuLi, Me$_3$SnCl). Y. Naruta, Y. Nishigaichi, and K. Maruyama, *J. Org. Chem.*, **53**, 1192 (1988); *J. Chem. Soc., Perkin Trans. 1*, **1991**, 831. See also Ref. 1a.

4)   Typical experimental procedure: to a mixture of an aldehyde (0.2 mmol) and a Lewis acid (0.4 mmol) in CH$_2$Cl$_2$ (5 ml) was added PDT **2** (0.3 mmol) at -78 °C followed by stirring for 2 h at the temperature. The reaction was then quenched with water and the products were purified by TLC. The product distribution was determined by ^{1}H NMR (270 MHz) spectroscopy.

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8)   When one equivalent of TiCl$_4$ was used, somewhat lower γ-selectivity was observed (R = C$_6$H$_5$; **3** : **4** : **5** = 4 : 85 : 11; 55% yield), though the stereoselectivity of **4** remained high. Thus, two equivalents should be required because added Et$_2$O deactivates TiCl$_4$.

9)   Crystallographic data for **6a**: C$_{14}$H$_{21}$O$_5$N, FW = 283.32, monoclinic, space group $P2_1/n$, a = 15.202(2) Å, b = 12.925(1) Å, c = 7.642(1) Å, β = 99.82(1)°, V = 1479.6(3) Å^3, Z = 4, D_c = 1.272 g·cm^{-3}, D_m = 1.270(3) g·cm^{-3}, R = 0.070, 1878 reflections.

10) The present result on the stereoselectivity is indeed conflict with that previously reported for the reaction of (Z)-2-(methoxymethyl)pentadienyltin where the *anti*-γ-adduct was said to be selectively yielded by the use of BF$_3$·OEt$_2$. From our reexamination and comparison with the present result, the previous report should be corrected to have afforded *syn*-γ-adduct. Accordingly, the transition state mentioned there should be also corrected. Y. Naruta, Y. Nishigaichi, and K. Maruyama, *Chem. Lett.*, **1988**, 225. See also Ref. 14.

11) Y. Nishigaichi, A. Takuwa, and A. Jodai, *Tetrahedron Lett.*, **32**, 2383 (1991)

12) The product distribution was ϵ : γ : α = 45 : 44 : 11 with a combined yield of 48%. For the γ-adduct, *syn* : *anti* = 8 : 2. For the reason of this rather high distribution of the γ-adduct, see Ref. 14.

13) J. Yamada, H. Abe, and Y. Yamamoto, *J. Am. Chem. Soc.*, **112**, 6118 (1990); B. M. Trost and H. Urabe, *J. Org. Chem.*, **55**, 3982 (1990); K. Tanaka, H. Yoda, Y. Isobe, and A. Kaji, *ibid.*, **51**, 1856 (1986).

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