Diastereoselective Reactions of Pyruvates with But-2-enyl Organometallic Compounds. Stereocontrol at the Tertiary Carbon Centre

Yoshinori Yamamoto,* Toshiaki Komatsu, and Kazuhiro Maruyama

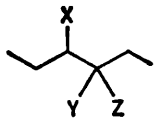
Department of Chemistry, Faculty of Science, Kyoto University, Kyoto 606, Japan

The reaction of pyruvates (**3**) with but-2-enyl-9-borabicyclo[3.3.1]nonane (**2a**) or its α-silyl and α-stannyl substituted derivatives (**10**) produced the *threo*-isomer [(**4**) or (**11**), respectively] stereoselectively; the latter reaction was applied to the synthesis of *cis*-crobarbatic acid (**14**).

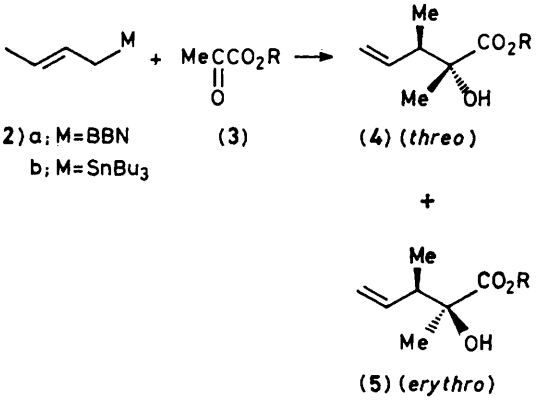
Diastereocontrol between two adjacent substituents in the acyclic system (**1**) is a problem of pressing concern in organic synthesis.[1] Such stereocontrol between X = C≡ and Y = O– (Z = H) is achieved by various methods.[1] Recently we reported stereocontrol between X = heteroatom, *e.g.* Si≡, O–, S–, or Se–, and Y = O– (Z = H) using heterosubstituted allylic carbanions.[2] This method provides stereochemical control at the secondary carbon centre (Z = H) (**1a, b**). In spite of the fact that the synthesis of a number of important natural products requires stereochemical control at the tertiary carbon centre, the methodology for such control is very inadequate in comparison with that for the secondary carbon centre.[3] We now report such stereocontrol (**1c**, X = Z = C≡, Y = O–) *via* the reaction of pyruvates with but-2-enyl organometallic compounds.

First, the reaction of pyruvates (**3**) with but-2-enyl-9-borabicyclo[3.3.1]nonane (but-2-enyl-BBN) (**2a**) or but-2-enyltributyltin (**2b**) was examined, and the results are summarized in Table 1. By increasing the steric bulk of the ester groups, the *threo*-isomer[4] (**4**) can be obtained either predominantly or exclusively *via* the reaction with (**2a**). On the other hand, the stereoselective synthesis of the *erythro*-isomer (**5**) is difficult, and the best result so far obtained is *ca.* 60% *via* the reaction with (**2b**). These stereochemical features can be explained by the transition-state geometries shown in Scheme 1. In the six-membered chair transition state from (**2a**), (**6**) gives (**4**) and (**7**) produces (**5**). Increase of the steric bulk of R destabilizes (**7**) relative to (**6**) owing to the CO_2R–L interaction. On the other hand, the but-2-enyltributyltin–BF_3 reaction proceeds *via* an acyclic transition state.[5] With a small R group (**8**) is only slightly stabilized relative to (**9**), and with a large R group this is reversed. Thus, the reaction *via* (**2b**) results in low selectivity.

Next, we examined the reaction of (**3**) with α-silyl or α-stannyl substituted but-2-enyl-BBN (**10a, b**).[6] Interestingly, even methyl pyruvate produced the *threo-cis*-isomer (**11b**) as



(**1**) **a**; X = C≡, Y = O–, Z = H
b; X = heteroatom, Y = O–, Z = H
c; X = Z = C≡, Y = O–

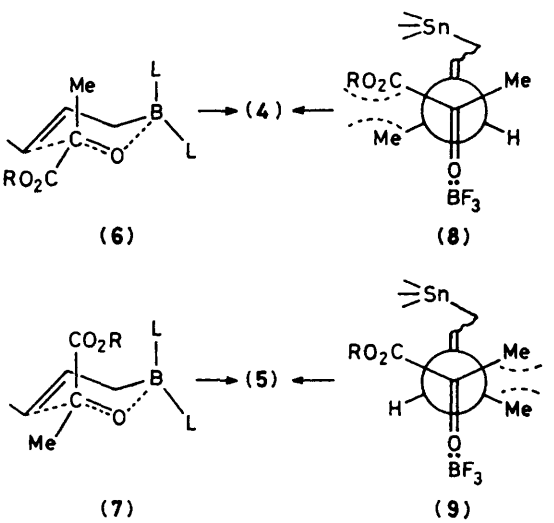


BBN = 9-borabicyclo[3.3.1]nonan-9-yl.

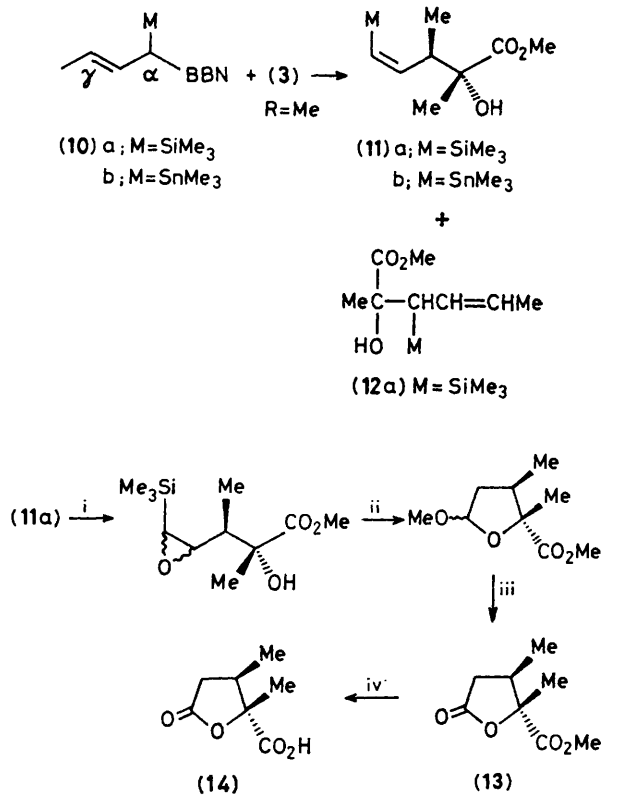
Table 1. Reaction of (**3**) with but-2-enyl organometallic compounds (**2**).[a]

But-2-enyl organometallic compound	Pyruvate (**3**) (R =)	Product ratio, %[b] *threo*-(**4**)	*erythro*-(**5**)
(**2a**)	Me	73	27
	Me_3CCH_2	85	15
	$PhCH_2$	80	20
	Ph	90	10
	2,6-Bu^t_2-4-Me-C_6H_2	*ca.* 100	—
(**2b**)	Me	60	40
	Me_3CCH_2	54	46
	$PhCH_2$	50	50
	2,6-Me_2-C_6H_3	43 (35)[c]	57 (65)[c]

[a] Compound (**2a**) (1 mmol) was added to a dry diethyl ether solution of (**3**) (1 mmol) at −78 °C under N_2. The reaction mixture was allowed to reach room temperature, and then quenched with aminoethanol (2 mmol)–MeOH (0.5 ml). The reaction of (**3**) with (**2b**) (1 mmol) in the presence of BF_3·OEt_2 (2 mmol) was carried out as described previously.[5] [b] The ratio of *threo/erythro* was determined by ^1H n.m.r. analysis of the reaction mixture. The doublet methyl protons (CH_3CH) of (**4**) always appeared at lower field (*ca.* δ 0.03—0.14) than those of (**5**). For the structure determination, see footnote †. Total yields were in the range 89—96% with (**2a**) and 84—88% with (**2b**). [c] $EtAlCl_2$ was used in place of BF_3·OEt_2 as the Lewis acid.



Scheme 1. Transition-state geometry.



Scheme 2. i, *m*-Chloroperbenzoic acid–CH_2Cl_2, 95%; ii, $BF_3 \cdot OEt_2$–MeOH, 90%; iii, CrO_3–H_2SO_4, acetone, 80%; iv, LiOH, MeOH–H_2O.

a single product from the reaction of (**10b**). Unfortunately, the reaction of (**10a**) was accompanied by the formation of the α-adduct (**12a**); (**11a**/**12a**) = 63/37 with Bu^nLi as base.[6] The *threo-cis*-adduct (**11a**) was easily separated from (**12a**) by silica gel column chromatography, and converted into *cis*-crobarbatic acid methyl ester (**13**) *via* the procedure of Magnus.[7] The usual hydrolysis produced the corresponding acid (**14**) (Scheme 2). The structure of (**13**) [and in turn (**14**)] was determined by comparison with an authentic material prepared using the literature procedure [*trans*-/*cis*-(**13**) = 10/1].[8]† Both g.l.c. and ^1H n.m.r. examination revealed that the *trans*-isomer was not contained in our sample (**13**); ^1H n.m.r. δ (CCl_4, Me_4Si), *cis*-isomer, 1.15 (d, *J* 7 Hz, 3H), 1.51 (s, 3H), 2.0—2.4 (m, 1H), 2.5—3.0 (m, 2H), 3.77 (s, 3H); *trans*-isomer, 1.05 (d, *J* 6.5 Hz, 3H), 1.60 (s, 3H), 2.2—2.8 (m, 3H), 3.82 (s, 3H). Since the synthetic procedure for the *trans*-isomer is well known,[8] both isomers of crobarbatic acid are now available. This is especially important for the synthesis of various pyrrolizidine alkaloids and related compounds.[8a]

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† Protodesilylation or protodestannylation of (**11**) followed by hydrolysis produced *threo*-(**4**) (R = H). The reaction products [(**4**) and (**5**)] of Table 1 were converted into the corresponding acids by hydrolysis and compared with an authentic *threo*-isomer.