The *threo*-Selective Reaction of But-2-enyl Organometallic Compounds with Ethylidenemalonates and Related Compounds

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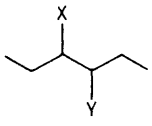
The reaction of diethyl ethylidenemalonate (**3**) with 9-but-2-enyl-9-borabicyclo[3.3.1]nonane and but-2-enyltitanium reagents produces the *threo*-adduct (**4**) predominantly in a ratio of 9 : 1; similarly, the reaction of ethyl α-cyanocrotonate (**5**) with but-2-enyl-titanium, -zirconium, and -magnesium reagents gives the *threo*-adduct (**6**) preferentially in a ratio of 4 : 1.

The diastereofacial control between two adjacent substituents in the acyclic system (**1**) continues to be of current importance in organic synthesis. Although such stereocontrol between X = C≡ and Y = heteroatoms (**1b**) or between X = Y = heteroatoms (**1c**) may be achieved by various excellent methods,[1] the method for diastereofacial control between two adjacent alkyl groups, *e.g.*, (**1a**), seems to be inadequate[2] despite frequent occurrence of such a stereo-defined unit in important natural products.[3] We report that the reaction of but-2-enyl organometallic compounds (**2**) with ethylidenemal-



(1)

a; X = Y = Me

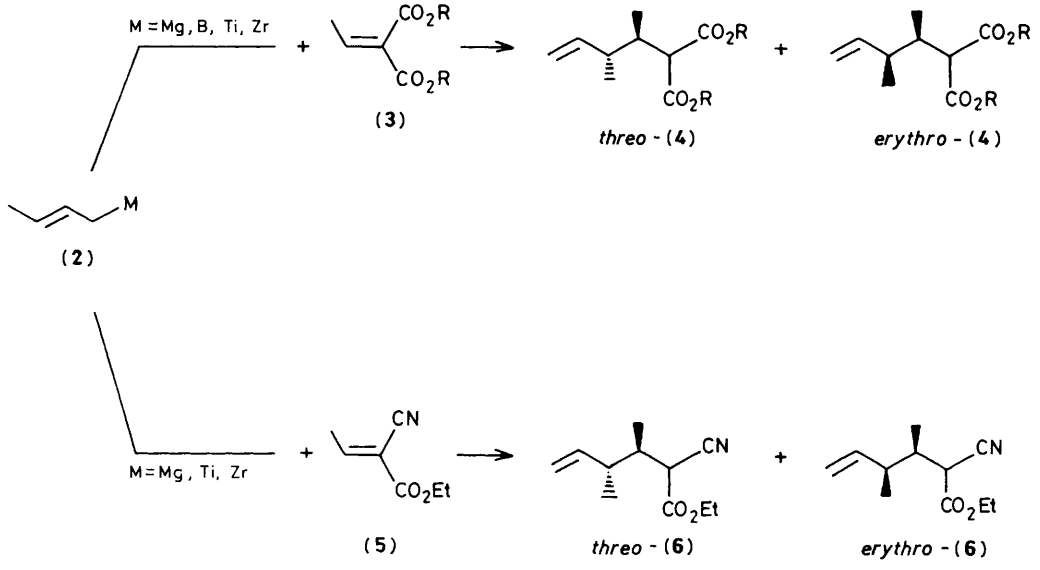
b; X = C≡, Y = O, N

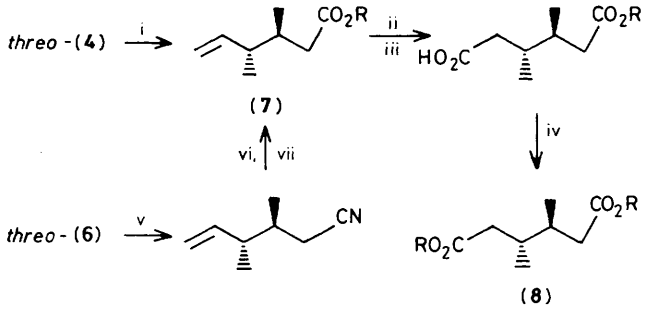
c; X = Y = O, N

Table 1. *threo*-Selective reaction of (2) with (3).[a]

Entry	(2), M	(3), R	Reaction conditions Temp./°C	Time/h	Product ratio *threo* : *erythro*-(4)
1	MgCl	Me	−78	0.5	60:40
2	MgCl	Et	−78	0.5	60:40
3	MgCl	Pr^i	−78	0.5	60:40
4	9-BBN[c]	Me	25	12	80:20
5	9-BBN[c]	Et	25	12	90:10
6	9-BBN[c]	Pr^i	25	12	85:15
7	$Ti(OPr^i)_3$	Me	−78→0	1	75:25
8	$Ti(OPr^i)_3$	Et	−78→0	1	90:10
9	$Ti(OPr^i)_3$	Pr^i	−78→0	1	85:15
10	$ZrCp_2Cl$[c]	Et	0→25	1	80:20

[a] All reactions were carried out on a 1 mmol scale under N_2 atmosphere. Compound (3) was added to an ether solution of (2) prepared by the reported procedure,[4] and the resulting mixture was stirred under the conditions stated. Total yields were in the range 80—95%. [b] By ^1H n.m.r. anlaysis. [c] 9-Borabicyclo[3.3.1]nonan-9-yl; Cp = cyclopentadienyl.





Scheme 1. i, Me_4NOAc–hexamethylphosphoramide, 110 °C, 10 h, 90%; ii, $BH_3{\cdot}SMe_2$–tetrahydrofuran, then $NaOH–H_2O_2$, 92%; iii, $CrO_3–H_2SO_4$–acetone, 80%; iv, ROH–tosyl-OH–C_6H_6, reflux, 10 h, 90%; v, NaCl–H_2O–dimethyl sulphoxide, 150 °C, 1 h, 80%; vi, 5 M KOH–$HOCH_2CH_2OH$, 120 °C, 2 h; vii, EtOH–tosyl-OH–C_6H_6, reflux, 10 h, 78%.

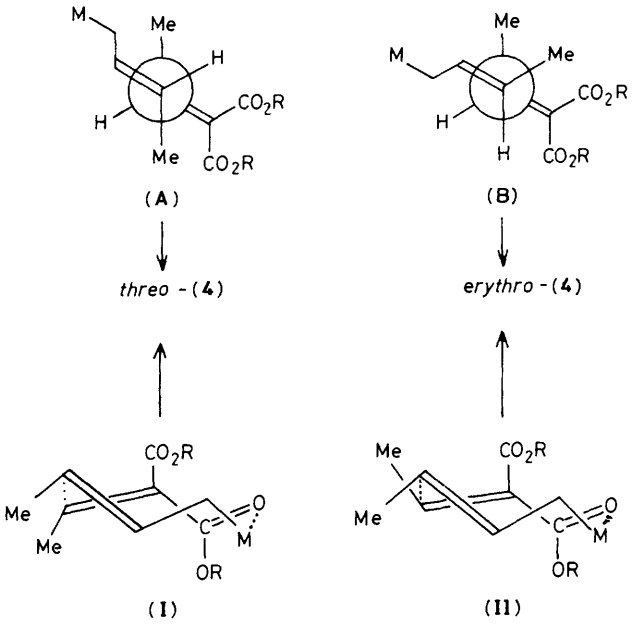
onates (3) provides the *threo*-adduct (4) predominantly. The results are summarized in Table 1.

The reaction with 9-but-2-enyl-9-borabicyclo[3.3.1]nonane or but-2-enyltitanium tri-isopropoxide produces the *threo*-adduct with high diastereoselectivity (up to 9 : 1 ratio) (entries 5 and 8), while the reaction with but-2-enylmagnesium chloride results in low selectivity[5] (entries 1—3). The steric bulk of the ester group does not exert a strong influence upon the selectivity.

The structure of (4; R = Et) was determined as shown in Scheme 1. Decarboxylation of *threo*-(4; R = Et) produced (7; R = Et). Hydroboration–oxidation of (7; R = Et), followed by oxidation with CrO_3 gave the corresponding acid which was converted into the ester (8; R = Et). Comparison (^{13}C n.m.r.) with an authentic sample[3a] indicated the *threo* structure. The structure of *erythro*-(4; R = Et) was confirmed by a similar procedure.

The *threo*-selectivity can be explained by either an acyclic or an eight-membered cyclic transition state. Although two possible conformations, crown and boat–chair, are conceivable in the eight-membered transition state, the former is generally more stable than the latter.[6] In the crown conformations, it seems that (I) is destabilized in comparison with (II) owing to the pseudo-axial Me group. Further, the comparative stabilities of (I) and (II) should be sensitive to variations of size in the alkoxycarbonyl groups, which is not observed (Table 1). Therefore, the reaction must proceed through the acyclic transition state, in which it is clear that (A) is more stable than (B) for steric reasons.

We also examined the reaction with ethyl α-cyanocrotonate



(**5**).† Here again, (**2**) [M = MgCl, $Ti(OPr^i)_3$, and $ZrCp_2Cl$] gave *threo*-(**6**) predominantly, *threo* : *erythro* ratio 80 : 20. The selectivity in the reaction of the but-2-enylmagnesium reagent with (**5**) is greater than that with (**3**). Reaction did not take place with but-2-enyl-9-BBN and the desired adduct could not be obtained.

† The geometry of (**5**) was determined by the carbon–vinyl proton coupling constant ($^3J_{CH}$); $^3J_{CN-H}$ 13.7 and $^3J_{CO-H}$ 3.5 Hz.

The stereochemistry of (**6**) was determined in a similar manner to that of (**4**) (Scheme 1). Decarboxylation of *threo*-(**6**) followed by hydrolysis–esterification produced (**7**).

The present work thus provides a new method for preparing the *threo*-selective carbon framework (**1a**). Although the precise mechanism of the *threo*-selectivity is not clear at present, it should be noted that the Lewis acid-mediated addition of (*E*)-1,4-bistrimethylsilylbut-2-ene to α,β-ethylenic acyl cyanides produces the *erythro*-adduct predominantly.[7]

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References

1 For example, *Tetrahedron Symp.* No. 16, ed. T. Mukaiyama, 1984, vol. 40, and references cited therein.
2 The previous methods for this stereocontrol are primarily based on intramolecular reactions, such as ester enolate and thio Claisen rearrangements. For example, see R. E. Ireland and M. D. Varney, *J. Am. Chem. Soc.*, 1984, **106**, 3668; Y. Tamaru, Y. Furukawa, M. Mizutani, O. Kitao, and Z. Yoshida, *J. Org. Chem.*, 1983, **48**, 3631; P. Beslin, P. Metzner, Y. Vallée, and J. Vialle, *Tetrahedron Lett.*, 1983, 3617.
3 For faranal, see (a) R. Baker, D. C. Billington, and N. Ekanayake, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1387; (b) D. W. Knight and B. Ojhara, *Tetrahedron Lett.*, 1981, 5101. For ikarugamycin, see (c) M. J. Kurth, D. H. Burns, and M. J. O'Brien, *J. Org. Chem.*, 1984, **49**, 733. For steroid side chains, see (d) T. Gebreyesus and C. Djerassi, *Tetrahdron Lett.*, 1982, 4427.
4 Y. Yamamoto and K. Maruyama, *Heterocycles*, **18**, 1982, 357 and references cited therein.
5 For the reaction of isopropylidenemalonates with Grignard reagents, see G. A. Holmberg and R. Sjoholm, *Acta. Chem. Scand.*, 1970, **24**, 3490.
6 See ref. 4 and N. L. Allinger, *J. Am. Chem. Soc.*, 1959, **81**, 5727.
7 D. El-abed, A. Jellal, and M. Santelli, *Tetrahedron Lett.*, 1984, 1463.