Tetrahedron Vol 40, No. 12, pp. 2303 to 2308, 1984
Printed in Great Britain.

0040-4020/84 $3.00 + .00

[2,3]-WITTIG SIGMATROPIC REARRANGEMENT OF CROTYL PROPARGYL ETHER SYSTEM

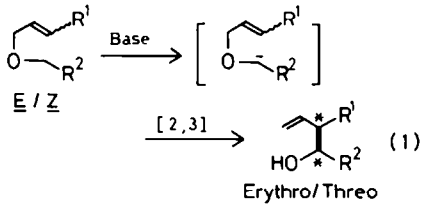
AN EMERGING TOOL FOR CONTROL OF ACYCLIC STEREOCHEMISTRY

KŌICHI MIKAMI, KEN-ICHI AZUMA and TAKESHI NAKAI*
Department of Chemical Technology, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

(*Received in Japan* 14 *July* 1983)

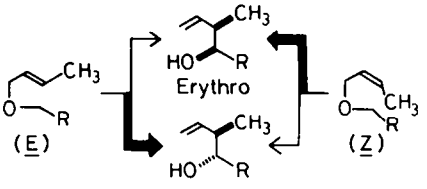
Abstract—The [2,3]-Wittig rearrangement of properly designated (*E*)- and (*Z*)-crotyl propargyl ether system has been shown to exhibit a remarkably high degree of *threo*- and *erythro*-selection, respectively, and the stereochemical outcomes are discussed on mechanistic grounds. Some useful transformations of the rearrangement product are also described within the context of the formal total synthesis of (±)-oudemansin. Further, the high level of diastereoselection is maintained in the reaction of the α-methylcrotyl counterparts, together with the exclusive formation of the (*E*)-olefinic bond.

The greatest effort in the area of acyclic stereocontrol has been devoted to the development of methodologies for diastereoselective synthesis of β-methyl alcohols, an important class of compounds for natural product synthesis. The aldol-type reactions using properly designed enolates and allylic organometallics have reached impressive levels of success.[1] In principle, on the other hand, the [2,3]-Wittig sigmatropic rearrangement as formulated in eqn (1) should constitute a general alternative strategy. However, there has existed no [2,3]-Wittig variant which exhibits a synthetically useful level of diastereoselection except for one case: the Wittig process of (*Z*)-crotyl benzyl ether showing nearly 100% of erythro-selectivity.[2] The major problem confronting the implementation of such strategy is, of course, associated with the stereochemical aspect of the [2,3]-Wittig process which remains largely unexplored.[3]



(1)

Over the past few years we have been directing considerable effort toward the development of the [2,3]-Wittig rearrangement into a new, basic strategy for acyclic stereocontrol.[4,5] Recently we described the stereoselection in several [2,3]-Wittig variants of crotyl allyl ether systems (**1**), where various vinylic groups act as the substituent (R) on the carbanion terminus (Scheme 1).[6] Although the observed degrees in these variants are only 70–85% and not high enough for synthetic use, we observed a significant stereochemical trend: *the* (E)- *and* (Z)-*substrate exhibit* threo- *and* erythro-*selection, respectively, the degrees depending upon the kind of* R. Thus, our attention was focused on search for the key R leading



1, R = $CH{=}CH_2$, $C(CH_3){=}CH_2$, $C(SiMe_3){=}CH_2$, CH=CH-Ph
2, R = C≡CH, C≡C-$SiMe_3$, C≡C-CH_3

Scheme 1.

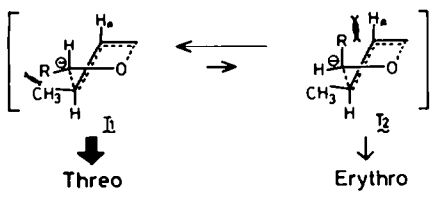
to an enhanced selectivity based on pertinent analysis of our transition-state model.[6b] Herein we report that the use of *modified* ethynyl group as the key R remarkably enhances the level of diastereoselection.[7] The significant features of the present variant of crotyl propargyl ether system (**2**) are twofold: (a) it is possible to attain an extremely high level of either diastereoselection through the proper combination of the geometry with the ethynyl group in substrate employed, and (b) the rearrangement product possesses the unique multifunctionality equipped for further synthetic elaboration. The latter feature is now highlighted in the formal total synthesis of (±)-oudemansin.

RESULTS AND DISCUSSION

[2,3]-*Wittig rearrangement of crotyl propargyl ether system*

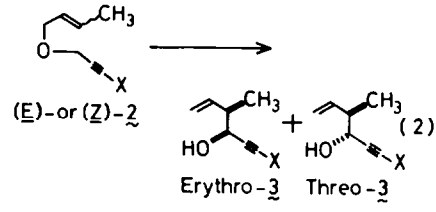
At the outset, we anticipated that the use of ethynyl group as the key R could provide a higher diastereoselectivity than that of vinyl group based on the following considerations of the transition-state geometries. In the case of (*E*)-substrates, for instance, the pseudo-gauche repulsion between R and CH_3 in the preferred T_1 (relative to T_2 suffering the pseudo-1,3-diaxial repulsion between R and H_β) would be diminished by changing R from vinyl to ethynyl, thus leading to an enhanced *threo*-selectivity (Scheme 2).

Thus, we selected the geometric pairs of the three propargyl ether systems (**2a**, **2b** and **2c**) as substrates, and examined the diastereoselection in their rear-



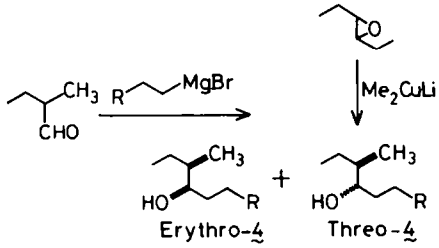
Scheme 2.

rangements (eqn (2)). The propargyl ether **2a** (X = H) was readily prepared by reaction of a geometrically-defined crotyl alcohol with propargyl bromide using the phase-transfer technique. The silylated ether **2b** (X = $SiMe_3$) and the methylated ether **2c** (X = CH_3) were prepared from the corresponding **2a** on successive treatment with ethylmagnesium bromide and chlorotrimethylsilane or iodomethane, respectively.



a, X=H ; b, X= $SiMe_3$; c, X = CH_3

The carbanion rearrangement of these substrates was carried out under the standard conditions as follows. A commercial solution of butyllithium in hexane was added to a substrate solution in THF (1.0 ml/1.0 mmol) at −85°, and stirred at that temperature for several hours. The resulting mixture was allowed to warm to 0° and quenched with aqueous ammonium chloride. Usual extractive workup followed by distillation afforded a diastereomeric mixture of the corresponding [2,3]-shifted product (**3**). In the rearrangement of **2a**, two equivalents of butyllithium was required. In the case of **2b**, on the other hand, the rearranged mixture was directly proto-



a, R=H, b, R=CH_3

Scheme 3.

desilylated to **3a** with cesium fluoride (0.03 equiv) in aqueous methanol. The diastereomeric ratio for these products was determined by GC analysis (PEG 20 M) and/or NMR analysis with the aid of a NMR shift reagent. The stereochemistry of these diastereomers was unequivocally assigned through NMR and GC comparisons of their hydrogenation products (**4**) with an authentic *threo*-isomer and/or an authentic *erythro*-rich mixture independently prepared as depicted in Scheme 3. *Threo*-**4a** was prepared by reaction of *trans*-3,4-epoxybutane with lithium dimethylcuprate. The *erythro*-rich **4a** and **4b** were obtained by reaction of 2-methylbutanal with ethyl or propyl Grignard reagent, respectively,[8] where the stereochemistry of the major diastereomer can be predicted by the Cram's rule.[9] The *erythro*/*threo* ratios thus obtained are summarized in Table 1.

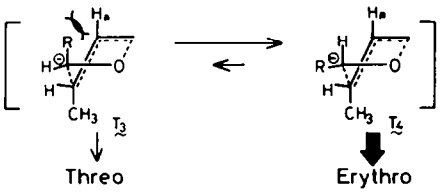
Inspection of the data in Table 1 reveals several significant stereochemical features of the present modifications. (1) (*E*)-**2a** exhibits an extremely high *threo*-selectivity as expected, whereas (*Z*)-**2a** shows a comparable *erythro*-selectivity to that of the allyl counterpart (**1a**). (2) Of the most significance is the remarkable enhancement of *erythro*-selectivity by the introduction of the silyl group (entry 3); surprisingly enough, the observed degree slightly exceeds the geometric purity of the substrate used. (3) Unexpectedly, (*E*)-**2b** shows the opposite sense of stereoselection to that of (*E*)-**2a** and -**2c**, though the degree is moderate; this anomaly is apparently responsible for the exceedingly high *erythro*-selectivity observed

Table 1. Diastereoselection in the [2,3]-Wittig process of ether **2**

Entry	Substrate (geometric purity)[a]	Erythro : Threo[b]	Distilled yield[c] (GC yield)
1	(Z)-**2a**, X=H (98%)	88 : 12 (90 : 10)	56% (76%)
2	(E)-**2a** (93%)	7 : 93 (1 : 99)	72%
3	(Z)-**2b**, X=$SiMe_3$ (93%)	98 : 2 (100 : 0)	74%
4	(E)-**2b** (93%)	75 : 25 (73 : 27)	72%
5	(Z)-**2c**, X=CH_3 (98%)	98 : 2 (100 : 0)	55% (74%)
6	(E)-**2c** (93%)	8 : 92 (1 : 99)	65% (78%)
7[d]	(Z)-**1a**, R=CH=CH_2 (95%)	(92 : 8)	88%
8[d]	(E)-**1a** (93%)	(16 : 84)	81%

[a] Refers to the geometric purity of the starting crotyl alcohol.

[b] Values in parentheses refer to the calculated values based on 100% of geometric purity. [c] Not optimized yet. [d] Cited from ref 6a.



Scheme 4.

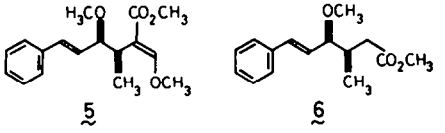
with (*Z*)-**2b**. (4) (*Z*)- and (*E*)-**2c** exhibit an enhanced *erythro*- and *threo*-selectivity, respectively; the both degrees are nearly equal to the geometric purities of the substrates employed.

While these stereochemical features have obvious applications in synthesis, let us discuss them on mechanistic grounds. The increased *threo*-selectivity of (*E*)-**2a** and -**2c** is explicable in terms of the decreased *gauche*-repulsion in the preferred transition state (T_1) as expected above (Scheme 2). The great enhancement of *erythro*-selectivity by the introduction of the silyl group can be rationalized in terms of the increased 1,3-repulsion of $R \leftrightarrow H_\beta$ relative to that for (*Z*)-**2a** (Scheme 4). A similar argument could be extended to account for the enhanced *erythro*-selectivity observed with (*Z*)-**2c**. On the other hand, the unusual *erythro*-selection observed in entry 4 is best explained by assuming that the *gauche*-repulsion of $R \leftrightarrow CH_3$ in T_1 prevails over the 1,3-repulsion of $R \leftrightarrow H_\beta$ in T_2, thus leading to *erythro*-selection (Scheme 2).

The degrees of control over the relative stereochemistry of the β-methyl alcohol unit enormously expand the potential of the present [2,3]-Wittig modifications and provide the synthetic chemist with a new, powerful tool with which to attack the current problem of acyclic stereocontrol. The ability to attain an extremely high degree of either diastereoselectivity and the simplicity of the procedure, coupled with the specific functionality pattern present in the product, place the present [2,3]-Wittig methodology in a unique position among methods for acyclic stereocontrol.

Application to the formal total synthesis of (±)*-oudemansin*

In order to illustrate the synthetic utility of the newly developed [2,3]-Wittig variant, our efforts were next directed toward the total synthesis of oudemansin (**5**), an antibiotic isolated from mycelial cultures of *Oudemansiella mucida* exhibiting strong antifungal activities.[10] To this end, we have now investigated the stereocontrolled transformation of *erythro*-**3a** obtained above to ester **6** which has recently been established as an excellent precursor of (±)-**5** in the first total synthesis by Oishi *et al.*[11] The precursor **6**



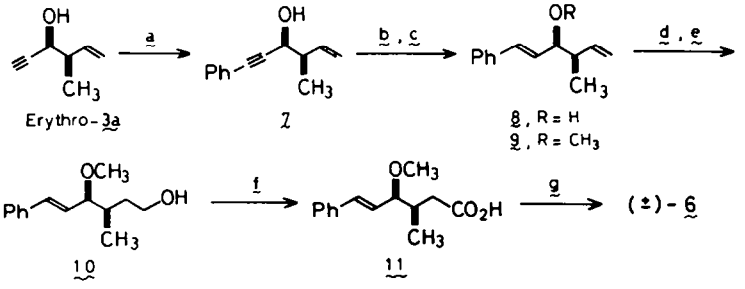
5 **6**

contains an (*E*)-styril and erythro–CH(OMe)–CH(Me)- units in its structure. Scheme 5 outlines the synthetic sequence in which the specific multifunctionality of **3a** is fully exploited.[12]

Thus, **3a** (98% erythro) obtained from (*Z*)-**2b** was first converted to alcohol **7** in 80% yield according to the Hagiwara's method[13] reported for palladium catalysed phenylation of acetylenes. We found that ultrasonic irradiation on the reaction vessel facilitated the phenylation process. The reaction was proved to proceed without appreciable epimerisation, while a similar reaction of the methyl ether of **3a** led to epimerisation to some extents. Reduction of **7** with lithium alminum hydride gave the (*E*)-cinnamylic alcohol **8**[14] which was converted to the methyl ether **9** (64% overall yield from **7**). Hydroboration of **9** with 9-BBN (9-borabicyclo[3.3.1]nonane) followed by oxidation afforded 68% yield of the methoxy alcohol **10** with 93% of erythro-purity (by NMR assay). The use of diborane in place of 9-BBN resulted in considerable epimerisation (*ca* 30%). Oxidation of **10** to acid **11** followed by esterification furnished the desired ester **6** in 68% yield. Since **6** has been converted to **5** in two steps,[11] the present synthesis of (±)-**6** constitutes a new formal total synthesis of (±)-oudemansin.

[2,3]-Wittig rearrangement of α-methylcrotyl propargyl ether system

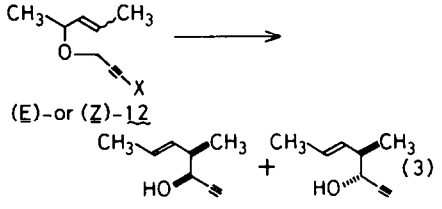
In order to expand the scope of synthetic utility of the highly diastereoselective [2,3]-Wittig modifications, we further examined the stereoselection in the synthetically more interesting variants (**12**) involving α-methylcrotyl as the migrating allylic moiety, in which an additional problem of stereo-



[a] PhI, $(Ph_3P)_2PdCl_2$/CuI, Et_2NH. [b] $LiAlH_4$, THF, refl., [c] NaH/CH_3I, THF, refl.
[d] 9-BBN, THF, 0°, [e] H_2O_2, aq. NaOH, 0°, [f] O_2/PtO_2, aq. $NaHCO_3$, 90-100°; [g] CH_2N_2, Et_2O

Scheme 5.

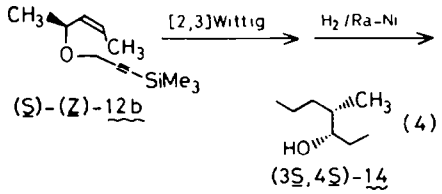
selectivity arises concerning the newly formed double bond (*E*/*Z*) (eqn (3)). We first found that the carbanion rearrangement of (*E*)-**12a** (X = H) under the standard conditions exhibited 88% *threo*-selectivity, together with *the exclusive formation of the* (E)-*double bond* in either diastereomer (by IR and ^{13}C NMR analysis). The use of THF alone as the solvent increased the *threo*-selectivity to 91%, although the degree is still lower than that observed with (*E*)-**2a**. In contrast, the rearrangement of (*Z*)-**12b** (X = $SiMe_3$) in THF alone was found to exhibit an extremely high *erythro*-selectivity which is essentially the same as that observed with (*Z*)-**2b**. Again the double bond in the product possesses exclusively *E* geometry.



(E)-12a, X=H (99% E)	9	:	91
	(12	:	88)*
(Z)-12b, X=SiMe$_3$ (97% Z)	99	:	1

* In THF/hexane (1 : 1)

Finally, it is worthwhile to note that hydrogenation of (*E*)-*erythro*-**13** thus obtained afforded *erythro*-4-methyl-3-heptanol (**14**) of which the (3*S*,4*S*)-isomer is known as an aggregation pheromone of the smaller European elm bark beetle (*Scolytus multistriatus*).[15,16] Quite recently, we have found that an *asymmetric* version using (*S*)-(*Z*)-**12b** (98% ee) as the substrate proceeds with an extremely high enantiospecificity, eventually furnishing an optically active phermone (3*S*,4*S*)-(−)-**14** (98% ee) (eqn (4)).[17] The result of the *asymmetric* [2,3]-Wittig rearrangement will be reported shortly.



EXPERIMENTAL

B.ps are uncorrected. IR spectra were recorded on a JASCO A-102 spectrometer. NMR spectra were taken on a Varian EM-390 spectrometer and are reported in ppm down field from internal TMS. GC analyses were run on a Shimazu GC-3BT chromatograph by using helium as the carrier gas (1 kg/cm^2) and a 3 mm × 3 m column (20% PEG 20 M on Chromosorb W (60–80 mesh)) at the indicated temp. THF was dried by distillation from LAH immediately prior to use. All reactions involving organometallic reagents were performed under an inert atmosphere. BuLi was used as a soln in hexane (*ca* 1.3 M) purchased from Ventron Co. The term "usual workup", which is used in the following experimental section, refers to the following product isolation procedure: dilution of the reaction mixture with ether and water, successive extraction with ether and brine; treatment of the organic extracts with anhyd $MgSO_4$; and the solvent removal under reduced pressure. The term "chemical purity" stands for the freedom of a stereoisomeric mixture of the indicated compound from contaminants.

Crotyl propargyl ether (**2a**). Propargyl bromide (45.0 g, 0.38 mol) was added dropwise to a rigorously stirred mixture of crotyl alcohol (93% *E* by GC assay) (21.0 g, 0.29 mol), n-Bu_4NHSO_4 (5.5 g, 0.015 mol), NaOH (46.0 g, 1.17 mol), and water (15 ml) at 20–30°, and the resulting mixture was stirred overnight at room temp. The solid formed was filtered off. Usual workup of the filtrate followed by distillation gave ether (*E*)-**2a** (28.3 g, 88%): b.p. 65–67°/58 mmHg (>95% chemical purity by GC assay); IR (neat) 3300, 2110, 1675, 1110, 970 cm^{-1}; NMR (CCl_4) δ 1.77 (d, J = 6.0 Hz, 3H), 2.27 (t, J = 4.5 Hz, 1H), 3.90 (d, J = 6.0 Hz, 2H), 4.03 (d, J = 4.5 Hz, 2H), 5.30–5.90 (m, 2H).

A similar reaction of crotyl alcohol (98% *Z*) (43 mmol) with propargyl bromide (56 mmol) gave (*Z*)-**2a** (3.6 g, 76%): b.p. 60–66°/50 mmHg (>95% chemical purity by GC assay); NMR (CCl_4) δ 1.73 (d, J = 6.0 Hz, 3H), 2.37 (t, J = 3.0 Hz, 1H), 3.97–5.23 (m, 4H), 5.27–5.83 (m, 2H).

Crotyl γ-trimethylsilylpropargyl ether (**2b**). To a soln of EtMgBr (0.15 mol) in THF (100 ml) was added a soln of the (*Z*)-**2a** (11.0 g, 0.10 mol) in THF (50 ml) at 0–5° with stirring, and the mixture was stirred for 3 hr at 20–25°. Chlorotrimethylsilane (19 ml, 0.15 mol) was added dropwise to the resulting mixture at 0–5° over 20 min, and stirred at 20–25° for 10 hr. Usual workup followed by distillation gave the silylated ether (*Z*)-**2b** (16.5 g, 90%): b.p. 65–68°/3 mmHg (98% chemical purity by GC assay); IR (neat) 2160, 1250, 840, 760, 700 cm^{-1}; NMR (CCl_4) δ 0.18 (s, 9H), 1.66 (d, J = 5.4 Hz, 3H), 4.00 (s, 2H), 4.03 (d, J = 4.8 Hz, 2H), 5.23–5.82 (m, 2H).

A similar reaction of the (*E*)-**2a** with Me_3SiCl gave (*E*)-**2b** (5.77 g, 90%): b.p. 107–111°/35 mmHg (>95% chemical purity by GC assay); NMR (CCl_4) δ 0.07 (s, 9H), 1.63 (d, J = 5.4 Hz, 3H), 3.90 (d, J = 5.7 Hz, 2H), 4.03 (s, 2H), 5.23–5.82 (m, 2H).

Crotyl 2-butynyl ether (**2c**). A soln of the (*E*)-**2a** (25.3 g, 0.23 mol) in THF (65 ml) was treated with a soln of EtMgBr (0.39 mol) in THF (80 ml) in the predescribed manner. To the resulting mixture was added a soln of CH_3I (24.3 ml, 0.39 mol) in THF (95 ml) at 0–5° over 30 min, and refluxed for 3 hr. Usual workup followed by distillation afforded (*E*)-**2c** (24.0 g, 84%): b.p. 112–115°/80 mmHg (>95% chemical purity by GC assay); IR (neat) 2230, 1675, 1100, 1140, 1070, 970 cm^{-1}; NMR (CCl_4) δ 1.73 (d, J = 6.0 Hz, 3H), 1.82 (t, J = 3.0 Hz, 3H), 3.80–4.13 (m, 4H), 5.27–5.93 (m, 2H).

A similar reaction of the (*Z*)-**2a** with CH_3I gave (*Z*)-**2c** (1.7 g, 81%): b.p. 50–56°/10 mmHg (>95% chemical purity by GC assay); NMR (CCl_4) δ 1.67 (d, J = 6.0 Hz, 3H), 1.83 (t, J = 3.0 Hz, 3H), 3.90–4.17 (m, 4H), 5.27–5.83 (m, 2H).

Rearrangement of (E)- *and* (Z)-**2a**. A soln of n-BuLi in hexane (160 ml, 208 mmol) was added dropwise to a cold (−85°C) soln of the (*E*)-**2a** (8.80 g, 80.0 mmol) (in an EtOH/liquid N_2/dry icebath). The resulting mixture was stirred at that temp for 8 hr, allowed to warm to 0° (*ca* 5 hr), and quenched with saturated NH_4Cl (50 ml). Usual workup followed by distillation afforded a diastereomeric mixture of the rearranged alcohol **3a** (6.32 g, 72%) as an oil: b.p. 52–53°/10 mmHg; IR (neat) 3500, 3300, 1645, 1000, 920 cm^{-1}; NMR (CCl_4) δ 1.10 (d, J = 7.2 Hz, 3H), 2.10–2.63 (m, 1H), 2.32 (d, J = 2.3 Hz, 1H), 4.13 (dd, J = 5.4 and 2.3 Hz, 1H), 4.97–5.28 (m, 2H), 5.82 (ddd, J = 17.3, 10.1 and 7.5 Hz, 1H); GC (130°) t_R = 25 and 28 min (7:93). On addition of $Eu(fod)_3$ (8 mg) to solution of **3a** in CCl_4 (7.6 mg in 0.3 ml) the doublet at δ 1.10 was changed into the two

doublets at δ 1.88 and 2.13 (relative intensity = 1:13); the NMR ratio was identical with the GC ratio.

A similar rearrangement of the (*Z*)-**2a** (8 mmol) with n-BuLi (20 mmol) afforded a diastereomeric mixture of **3a** (0.49 g, 56%): b.p. 60–62°/15 mmHg; GC (130°) t_R = 25 and 28 min (88:12).

The structure (two-dimensional) of alcohol **3a** was confirmed by identity of its hydrogenation product (**4a**) with an authentic sample described below.

Rearrangement of (E)- *and* (Z)-**2b**. A soln of the (*Z*)-**2b** (9.12 g, 50.0 mmol) in THF (50 ml) was treated with n-BuLi (50 ml, 60.0 mmol) in the predescribed manner. To the resulting mixture was added a mixture of CsF (0.25 g, 1.67 mmol), H_2O (2.7 ml) and MeOH (4.65 ml), and the mixture was heated at 50° for 15 min. Usual workup followed by distillation gave a diastereomeric mixture of **3a** (5.5 g, 74%): GC (130°) t_R = 25 and 28 min (98:2). A similar reaction of the (*E*)-**2b** gave a stereo-mixture of **3a** (3.7 g, 72%): GC (130°) t_R = 25 and 28 min (75:25).

Rearrangement of (E)- *and* (Z)-**2c**. Treatment of a soln of the (*E*)-**2c** (0.63 g, 5.0 mmol) in THF (5.4 ml) with n-BuLi (5.4 ml, 6.5 mmol) in the predescribed manner afforded a distereomeric mixture of the rearranged alcohol **3c** (0.41 g, 65%): b.p. 62–67°/7 mmHg; IR (neat) 3360, 2230, 1640, 995, 915 cm^{-1}; NMR (CCl_4) δ 1.05 (d, J = 6.8 Hz, 3H), 1.83 (d, J = 2.3 Hz, 3H), 2.35 (ddq, J = 7.5, 6.8, and 5.7 Hz, 1H), 4.10 (dd, J = 5.7 and 2.3 Hz, 1H), 4.87–5.30 (m, 2H), 5.81 (ddd, J = 18.0, 9.9, and 7.5 Hg, 1H); GC (120°) t_R = 48 and 54 min (8:92). A similar treatment of the (*Z*)-**2c** (1.0 mmol) with n-BuLi (1.1 mmol) gave, after distillation, a stereo-mixture of **3c** (0.07 g, 55%): GC (120°) t_R = 48 and 54 min (98:2).

The structure (two-dimensional) of **3c** was confirmed by identity of its hydrogenation product (**4c**) with an authentic sample described below.

Preparation of authentic threo-**4a** *and* erythro-*rich mixtures of* **4a** *and* **4c**. Reaction of *trans*-3,4-epoxyhexane (20 mmol) with an excess of dimethyllithium cuprate via the standard procedure afforded *threo*-**4a** (76%): b.p. 45–46°/10 mmHg; IR (neat) 3350, 1100 cm^{-1}; NMR (CCl_4) δ 0.7–1.14 (m, 9H), 1.14–1.60 (m, 5H), 2.10 (s, 1H), 3.30 (dt, J = 8.4 and 4.2 Hz, 1H); GC (100°) t_R = 29.8 min (>90% chemical purity).

Reaction of 2-methylbutanal (25 mmol) with EtMgBr via the standard procedure[8] gave a diastereomeric mixture of **4a** (77%): b.p. 40–46°/10 mmHg lit[8c] 57–59°/15 mmHg); NMR (CCl_4) δ 0.71–1.14 (m, 9H), 1.14–1.60 (m, 5H), 1.58 (s, 1H), 3.13–3.50 (m, 1H). On decoupling of the multiplet at δ 1.14–1.60 the multiplet at δ 3.13–3.50 was changed to the two singlet at δ 3.30 and 3.35 (rel. intensity = 34:66); GC (100°) t_R = 28.8 (major) and 29.8 (minor). A similar reaction of 2-methylbutanal with n-PrMgBr[8] afforded a diastereomeric mixture of **4c** (94%): b.p. 83–86°/30 mmHg; GC (80°) t_R = 64 (major) and 67 (minor); *erythro*–*threo* = 66:34 (by NMR assay).

Phenylation of alcohol **3a**. To a mixture of the *erythro*-**3a** (98% *erythro*) (2.75 g, 25.0 mmol), iodobenzene (4.20 ml, 37.5 mmol), and diethylamine (60 ml) were successively added $(Ph_3P)_2PdCl_2$ (0.35 g, 0.50 mmol) and CuI (0.025 g, 0.25 mmol). The resulting mixture was stirred at 50° for 10 hr with ultrasonic irradiation (using an ultrasonic cleaner: Bransonic model 220, 50 Hz, 185 W). The solid formed was filtered off and the filtrate was concentrated *in vacuo*. The oily residue was chromatographated on silica gel (elution with 50% ether in hexane) gave the phenylated product **7** (3.71 g, 80%) as a colorless oil (>95% erythro by NMR assay): IR (neat) 3350, 1640, 1600, 1490, 1445, 1000, 915, 755, 690 cm^{-1}; NMR ($CDCl_3$) δ 1.18 (d, J = 6.9 Hz, 3H), 2.00 (br.s, 1H), 2.30–2,77 (m, 1H), 4.47 (d, J = 4.9 Hz, 1H), 5.17 (d, J = 12.0 Hz, 1H), 5.18 (d, J = 16.0 Hz, 1H), 5.92 (ddd, J = 16.0, 12.0, and 7.5 Hz, 1H), 7.10–7.57 (m, 5H). A similar reaction (without ultrasonic irradiation) of the *threo*-**3a** (93% *threo*) afforded 37% yield of the *threo*-rich mixture of **7** of which the NMR spectrum showed a doublet at δ 4.43 (J = 6.0 Hz) due to the carbinol proton for *threo*-**7**.

Reduction of alcohol **7**. A soln of **7** (5.42 g, 29 mmol) in THF (20 ml) was added to a suspension of $LiAlH_4$ (0.80 g, 21.0 mmol) in THF (30 ml) at 0°, and refluxed for 3 hr. The resulting mixture was poured to saturated Na_2SO_4. Usual workup gave **8** (4.37 g, 80%) as an oil which was used next step without purification: NMR ($CDCl_3$) δ 1.02 (d, J = 6.3 Hz, 3H), 2.10–2.60 (m, 1H), 2.93 (br. s, 1H), 4.04 (dd, J = 6.0 Hz, 1H), 5.00 (d, J = 12.3 Hz, 1H), 5.03 (d, J = 15.3 Hz, 1H), 5.60–6.27 (m, 2H), 6.50 (d, J = 16.2 Hz, 1H), 7.00–7.47 (m, 5H). The NMR spectrum was essentially identical with that of an *erythro*-rich (70% *erythro*) *of* **8** obtained via the [2,3]-Wittig process of (*Z*)-crotyl (*E*)-cinnamyl ether.[6b,14]

Methylation of alcohol **8**. A soln of **8** (3.47 g, 18.4 mmol) in THF (10 ml) was added to a suspension of NaH (0.97 g, 20.2 mmol) in THF (40 ml), and refluxed for 3 hr. To the resulting mixture was added CH_3I (4 ml) at 5–10°, and stirred overnight at 20–25°. After usual workup, the oily residue was chromatographed on silica gel to give the methyl ether **9** (3.01 g, 80%) as an oil which was subjected to the next step without further purification: IR (neat) 1100, 970, 750, 700 cm^{-1}; NMR (CCl_4) δ 1.05 (d, J = 6.3 Hz, CH_3), 3.27 (s, OCH_3), 6.50 (d, J = 15.0 Hz, PhCH = CH–).

Transformation of ether **9** *to the methoxy alcohol* **10**. To a soln of **9** (0.654 g, 3.23 mmol) in THF (15 ml) was added 9-BBN (7 ml of a 0.5 M soln in THF) at 0° over 30 min, and the mixture was stirred for additional 1.5 hr. Then the resulting mixture was treated successively with 3N NaOH (1.16 ml) and 30% H_2O_2 (1.16 ml) at 5–10°. Usual workup followed by column chromatography (silica gel, Et_2O–hexane (1:1)) gave **10** (0.484 g, 68%) as an oil: IR, (neat) 3400, 1650, 1600, 1080, 970 cm^{-1}; NMR (CCl_4) δ 0.93 (d, J = 6.3 Hz, 3H), 1.10–2.10 (m, 3H), 3.20 and 3.27 (2s, 0.21H and 2.79H (7:93)), 3.27–3.83 (m, 4H), 6.07 (dd, J = 16.2 and 9.0 Hz, 1H), 6.50 (d, J = 16.2 Hz, 1H), 7.00–7.50 (m, 5H). The use of diborane in place of 9-BBN afforded 33% of a stereomixture of **10** for which the *erythro*–*threo* ratio was found to be 2:1 (by NMR assay).

Conversion of alcohol **10** *to ester* **6**. Oxidation of **10** was performed by adaption of the reported procedure using molecular O_2.[18] A suspension of **10** (134 mg, 0.61 mmol) and PtO_2 (47 mg) in 20% $NaHCO_3$ (20 ml) was heated at 90–100° and O_2 gas was bubbled into the mixture with stirring for 50 hr. The solid was filtered off and the filtrate was diluted with ether (20 ml). The aqueous extract was acidified with 6N HCl and extracted with ether. Usual workup afforded acid **11** (56 mg, 78% based on the reacted **10**); 50% of **10** was recovered from the first organic extract: IR (neat), 3200, 1710, 970 cm^{-1}; NMR (CCl_4) δ 1.05 (d, J = 6.0 Hz, CH_3), 3.30 (s, OCH_3), 6.10 (dd, J = 15.6 and 6.6 Hz, PhCH=CH–), 6.62 (d, J = 15.6 Hz, PhCH=CH–), 10.0 (br.s, COOH). Conventional treatment of **11** with CH_2N_2 in Et_2O followed by column chromatography (silica gel, Et_2O–hexane (1:1)) furnished ester **6** (43 mg, 87%): IR (neat) 1735, 1085, 970, 750, 675 cm^{-1}; NMR (CCl_4) δ 1.00 (d, J = 6.0 Hz, 3H), 1.90–2.63 (m, 3H), 3.31 (s, 3H), 3.64 (s, 3H), 3.53–3.77 (m, 1H), 6.05 (dd, J = 15.6 and 6.6 Hz, 1H), 6.55 (d, J = 15.6 Hz, 1H), 7.06–7.60 (m, 5H). The spectral (IR and NMR) data are in agreement with the literature values.[11]

α-Methylcrotyl proaprgyl ethers (E)-**12a** *and* (Z)-**12b**. Reaction of 3-penten-2-ol (99% *E*) (2.00 g, 23.2 mmol) with propargyl bromide (46.0 mmol) in the same manner as described for **2a** gave (*E*)-**12a** (1.52 g, 53%): b.p. 70–72°/56 mmHg (>95% chemical purity by GC assay); NMR (CCl_4) δ 1.17 (d, J = 6.0 Hz, 3H), 1.68 (d, J = 6.0 Hz, 3H), 2.17 (t, J = 3.0 Hz, 1H), 3.73–4.27 (m, 3H), 5.07–5.87 (m, 2H).

A similar reaction of 3-penten-2-ol (97% *Z*) (32 mmol) gave (*Z*)-**12a** (3.1 g, 78%): b.p. 70–73°/56 mmHg; NMR (CCl_4) δ 1.17 (d, J = 6.5 Hz, 3H), 1.73 (dd, J = 6.8 and 1.5 Hz, 3H), 2.23 (t, J = 2.3 Hz, 1H), 3.80–4.23 (m, 3H), 5.13–5.93 (m, 2H). Silylation of the (*Z*)-**12a** in the same

manner as described for **2b** gave (*Z*)-**12b** (2.48 g, 98%): b.p. 65–68°/3 mmHg (>95% chemical purity by GC assay); NMR (CCl_4) δ 0.17 (s, 9H), 1.23 (d, J = 6.0 Hz, 3H), 1.67 (dd, J = 7.5 and 1.5 Hz, 3H), 3.97–4.67 (m, 3H), 5.03–5.82 (m, 2H).

Rearrangement of (E)-**12a** *and* (Z)-**12b**. A soln of the (*E*)-**12a** (1.20 g, 10.0 mmol) in THF (30 ml) was added at −85° to n-BuLi isolated by removal of the hexane from 18.6 ml (26.0 mmol) of a hexane soln. The resulting mixture was stirred at that temperature for 6 hr, allowed to warm to 0°, and quenched with 6N HCl. Usual workup followed by distillation gave a diastereomeric mixture of **13** (0.74 g, 62%): b.p. 60–65°/10 mmHg; IR (neat) 3400 (OH) and 980 cm^{-1} (trans–CH=CH–); NMR (CCl_4) δ 1.15 (d, J = 6.0 Hz, 3H), 1.77 (d, J = 4.5 Hz, 3H), 2.15–2.50 (m, 1H), 2.33 (d, J = 1.5 Hz, 1H), 4.07 (dd, J = 6.0 and 1.5 Hz, 1H), 5.17–5.77 (m, 2H); GC (150°) t_R = 19.4 and 21.8 min (9:91). The ^{13}C NMR spectrum (CCl_4) (on a JEOL FX90Q spectrometer) showed only one signal at δ 18.03 due to the CH_3 bonded to the olefinic carbon, indicating that the new double bond possesses exclusively (*E*)-geometry.

A similar treatment of the (*Z*)-**12b** (1.97 g, 10.0 mmol) with n-BuLi (13 mmol) followed by protodesilylation in the same manner as described for **3b** afforded, after distillation, 0.79 g (64%) of a diastereomeric mixture of **13**: IR (neat) 3400 and 980 cm^{-1}; ^{13}C NMR (CCl_4) δ 18.03; GC (150°) t_R = 19.4 and 21.8 min (99:1).

Conventional hydrogenation of **13** (99% *erythro*) using Raney Ni catalyst in EtOH afforded 90% of **14**: b.p. 80–85°/22 mmHg (lit 70–75°/14 mmHg for (±)-*erythro*-**14**,[16b] 99–101°/98 mmHg for (3*S*,4*S*)-**14**,[16b] and 60–65°/15 mmHg for (±)-*threo*-**14**[16d]); IR (neat) 3360, 1460, 970 cm^{-1}; NMR (CCl_4) δ 0.77 (m, 9H), 1.07–1.57 (m, 8H), 3.22–4.43 (m, 1H). The spectral (IR and NMR) data are in agreement with the literature values.[16]

Acknowledgement—This research was generously supported in part by the Kurata Foundation and the Grant-in-Aid for Special Project Research from the Ministry of Education, Science and Culture, Japan.

REFERENCES

[1]Recent reviews include: [a]D. A. Evans, J. V. Nelson and T. R. Taber, *Top. Stereochem.* **13**, 1 (1982); [b]P. A. Bartlett, *Tetrahedron* **36**, 2 (1980).

[2]V. Rautenstrauch, *J. Chem. Soc.* Chem. Commun. 4 (1970). See also: U. Schöllkopf, K. Fellenberger and M. Rizk, *Justus Liebigs Ann. Chem.* **734**, 106 (1970). In contrast, the (*E*)-counterpart has exhibited a low stereoselectivity.

[3]For a general review on the stereochemistry of [2,3]-sigmatropic rearrangements: R. W. Hoffman, *Angew. Chem.* Int. Ed. Engl. **18**, 563 (1979).

[4]For recent reviews on acyclic stereocontrol via sigmatropic rearrangements: see Ref. 1*b* and T. Nakai, K. Mikami and N. Sayo, *J. Synth. Org. Chem. Jpn.* **41**, 100 (1983).

[5]Quite recently we have reported the successful development of a highly *erythro*-selective [2,3]-Wittig variant which eventually provides 2-hydroxy-3-methyl-4-pentenoic acid derivatives: K. Mikami, K. Fujimoto and T. Nakai, *Tetrahedron Letters* **24**, 513 (1983).

[6][a]T. Nakai, K. Mikami, S. Taya and Y. Fujita, *J. Am. Chem. Soc.* **103**, 6492 (1981); [b]K. Mikami, Y. Kimura, N. Kishi and T. Nakai, *J. Org. Chem.* **48**, 279 (1983).

[7]A preliminary report of this work was presented at the 4*th Int. Conf. on Organic Synthesis* (*IUPAC*), Tokyo, 1982, No. B-I-7301.

[8][a]W. Kirmse, H.-J. Ratajczak and G. Rauleader, *Chem. Ber.* **110**, 2290 (1977); [b]N. K. Undaria, M. L. Dhanami and K. A. Thaker, *J. Instit. Chem., Calcutta* **46**, 156; *Chem. Abst.* **83**, 9079d (1975); [c]*erythro*-**4c** has been reported as a sex attractant of the ant (*Tetramorium caespitum*): J. M. Pasteels, J. C. Verhaeghe, J. C. Braekman, D. Daloze and B. Tursch, *J. Chem. Ecol.* **6**, 467 (1980); [d]For a GC study on diastereomers of **4a**, see: Y. Gault and H. Felkin, *Bull. Soc. Chim. Fr.* 742 (1965).

[9]J. D. Morrison and H. S. Mosher, *Asymmetric Organic Reactions*, Chap. 3. Prentice-Hall, New Jersey (1971).

[10]T. Anke, H. J. Hecht, G. Schramm and W. Steglich, *J. Antibiot.* **32**, 1112 (1979).

[11]T. Nakata, T. Kuwabara, Y. Tani and T. Oishi, *Tetrahedron Letters* **23**, 1015 (1982).

[12]Throughout the sequence, the stereochemistry of key intermediates was confirmed through NMR comparison with the corresponding *threo*-rich sample independently prepared from a *threo*-rich mixture of **3a**.

[13]S. Takahashi, Y. Kuroyama, K. Sonogashira and N. Hagiwara, *Synthesis* 627 (1980).

[14]Alternatively, this alcohol was obtained directly via the [2,3]-Wittig process of (*Z*)-crotyl (*E*)-cinnamyl ether; unfortunately, the rearrangement was found to exhibit only 70% of *erythro*-selection.[6b]

[15]Isolation: G. T. Pearce, W. E. Gore, R. M. Silverstein, J. W. Peacock, R. A. Cuthbert, G. N. Lanier and J. B. Simeone, *J. Chem. Ecol.* **1**, 115 (1975).

[16]For recent synthesis of the pheromone (racemic and optically active), see: [a]review: K. Mori, *The Total Synthesis of Natural Products* (Edited by J. ApSimon), Vol. 4, pp. 132. Wiley-Interscience, New York (1981); [b]M. Koreeda and Y. Tanaka, *Chem. Lett.* 1297 (1982); [c]K. Mori and H. Iwasawa, *Tetrahedron* **36**, 290 (1980); [d]G. Fráter, *Helv. Chim. Acta* **62**, 2825 (1979).

[17]N. Sayo, K. Mikami, K. Azuma and T. Nakai, *Tetrahedron Letters*, in press.

[18]K. Heyns and L. Blazejewicz, *Tetrahedron* **9**, 67 (1960).