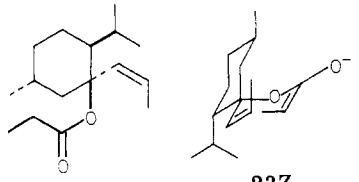
enolates derived from **12** rearrange with nearly complete transfer of chirality. To determine the sense of the chirality transfer, we converted acid **16** to *tert*-butyldiphenylsilyl ether **21** via a straightforward reaction sequence (Scheme II). Comparison of the specific rotation of **21** ($[\alpha]^{20}_D$ −3.7° ($CHCl_3$)) with that of **22**, ($[\alpha]^{20}_D$ +3.3° ($CHCl_3$)) prepared from (*S*)-2,3-dimethylbutyric acid,[21,22] established the absolute configuration at C(2) and, by extrapolation, at C(3) of **13**.

From these results we conclude that the rearrangement of ester **12** to acids **13** and **14** proceeds as outlined in Scheme III. In accord with Ireland's numerous studies,[16] enolization of **12** affords a mixture of **12Z** and **12E** in which the former predominates. Each enolate could rearrange from a number of conformations only two of which are shown in Scheme III. We suggest that rearrangement of **12Z** (**12E**) via a chair–chair transition state in which R_L occupies a pseudoequatorial site affords the observed product **13** (**14**). An examination of the chair–chair conformations of **12Z** and **12E** shown in Scheme III reveals that these menthone adducts are excellent mimics for allylic alcohols of type **2** where R_S = Me and R_L = *t*-Bu. In fact, axial substitution at the isopropyl-bearing carbon is unnecessary to produce the required difference in size between the two groups bonded to the carbinol center.

It was disappointing to find that propionate **23**, prepared



23 **23Z**

from *cis*-**11**, did not undergo Claisen rearrangement upon conversion to the corresponding enolate. We suspect that severe pseudo-1,3-diaxial interactions as shown in structure **23Z** are responsible for the decrease in rate of Claisen rearrangement relative to other processes.[23]

In summary, we have established a protocol for the preparation of configurationally pure 1,4-difunctional compounds as depicted in Scheme I. The procedure features a tertiary allylic alcohol Claisen rearrangement that proceeds with complete transfer of chirality and should be adaptable to the synthesis of a variety of compounds by varying substituents in the organometallic and esterification reagents. The sequence, however, is currently not without some operational difficulties. These difficulties are associated with the hindered nature of menthone (e.g., enolization in step A) and the derived alcohols (e.g., difficulties in derivatization and failure of simple Claisen rearrangements). Experiments that address these problems are being pursued.

Acknowledgment. This research was generously supported by a Dow Chemical U.S.A. Grant of Research Corporation.

Registry No. **5**, 14073-97-3; **8** (isomer 1), 24278-73-7; **8** (isomer 2), 24278-67-9; **9** (isomer 1), 33651-09-1; **9** (isomer 2), 33651-10-4; **10**, 33651-06-8; *cis*-**11**, 83803-21-8; *trans*-**11**, 83803-22-9; **12**, 83803-23-0; **13**, 83803-24-1; **14**, 83860-22-4; **15**, 83803-25-2; **16**, 83803-26-3; **17**, 83803-27-4; **18**, 83860-23-5; **19**, 83803-28-5; **20**, 83803-29-6; **21**, 83803-30-9; **22**, 83803-31-0; HC≡CLi, 1111-64-4; $CH_3C{\equiv}CLi$, 4529-04-8; $CH_2{=}CHMgBr$, 1826-67-1; (*E*)-$CH_3CH{=}CHMgBr$, 13154-15-9; $CH_3CH{=}CHLi$, 29283-76-9; (*Z*)-$CH_3CH{=}CHMgBr$, 13154-14-8.

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Stereochemical Consequences of Carbanion Asymmetry. An Access to 1,2-Diols

Summary: The enantiofacial discrimination of some asymmetric α-alkoxy carbanions is described, as well as an illustration of their preparative utility.

Sir: Carbon–carbon bond formation resulting from nucleophilic attack upon carbonyl compounds has played a prominent role in the evolution of organic chemistry. The means by which the stereochemical outcome of these condensations may be predictably controlled has continued to be the focus of considerable effort. Stereoselection is most often the result of facial discrimination of the carbonyl function as imposed by chirality residing in either the electrophilic (R_1*) or nucleophilic (R_2*) reaction component (Figure 1), with impressive success documented for both approaches.[1] Acceptable stereoselection is seen to result from the favorable disposition of a number of reaction parameters, including the proximity of resident chirality to the centers of reactivity, the spatial regulation of this resident chirality, as well as the nature of attendant metal species.[2] In the present study, we communicate our preliminary results in optimizing the proximity factor by arranging the coincidence of existent asymmetry with a site of reactivity. More specifically, this investigation represents initial efforts to delineate the *enantiofacial selectivity of a configurationally defined, asymmetric carbanion.*[3,4]

(20) Amide **18** was prepared from *dl-erythro*-2,3-dimethyl-4-pentenoic acid[14] [(i) $NaIO_4$, OsO_4, *t*-BuOH–H_2O; (ii) $HSCH_2CH_2CH_2SH$, HCl, $CHCl_3$; (iii) $(PhO)_2P(O)N_3$, Et_3N, (*S*)-$PhCH(NH_2)CH_3$]. Amides **18** [mp 124–125 °C, $[\alpha]^{21}_D$ −30.3° ($CHCl_3$)] and **17** [mp 141–142 °C, $[\alpha]^{21}_D$ −69.1° ($CHCl_3$)] were separable by chromatography and were easily distinguished by ^1H NMR spectroscopy: **17** ($CDCl_3$) δ 1.12 (d, *J* = 7 Hz, 3 H, CH_3), 1.18 (d, *J* = 7 Hz, 3 H, CH_3), 1.50 (d, *J* = 7 Hz, 3 H, Ar $CHCH_3$), 1.7–2.0 (m, 1 H, CH) 2.08–2.23 (m, 2 H, CH_2), 2.42 (dq, *J* = 8, 7 Hz, 1 H, CHCO), 2.83–2.95 (m, 4 H, CH_2S), 4.19 (d, *J* = 5 Hz, 1 H, CHS), 5.14 (dq, *J* = 8, 7 Hz, 1 H, CHN), 5.94 (br d, *J* = 8 Hz, 1 H, NH), 7.27 (m, 5 H, Ar H); **18** ($CDCl_3$) δ 1.02 (d, *J* = 7 Hz, 3 H, CH_3), 1.20 (d, *J* = 7 Hz, 3 H, CH_3), 1.49 (d, *J* = 7 Hz, 3 H, Ar $CHCH_3$), 1.66–2.07 (m, 3 H, CH and CH_2), 2.46–2.8 (m, 5 H, CHCO and CH_2S), 3.94 (d, *J* = 7 Hz, 1 H, CHS), 5.16 (dq, *J* = 8 Hz, 1 H, CHN), 6.08 (br d, *J* = 8 Hz, 1 H, NH), 7.27–7.36 (m, 5 H, ArH).

(21) (*S*)-2,3-Dimethylbutyric acid (91–94% ee based on reported rotation data[22]) was prepared from isovaleric acid via the method of: Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, 4233.

(22) For the absolute configuration of 2,3-dimethylbutyric acid, see: Levene, P. A.; Marker, R. E. *J. Biol. Chem.* **1935**, *111*, 299.

(23) For the sake of clarity, transition states have been represented as ground-state conformations (Scheme III, **23Z**).

(1) For recent studies: (a) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2. (b) Heathcock, C. H. *Science* **1981**, *214*, 395. (c) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357. (d) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1.

(2) For discussion addressing synthetic design, see: (a) Izumi, Y.; Tai, A. "Stereo-Differentiating Reactions"; Academic Press: New York, 1977. (b) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1976**, *10*, 175. (c) Meyers, A. I. *Pure Appl. Chem.* **1979**, *51*, 1255. (d) Evans, D. A.; Takacs, J. M.; McGee, L. R.; Ennis, M. D.; Mathre, D. J.; Bartroli, J. *Pure Appl. Chem.* **1981**, *53*, 1109. See also ref 1.

(3) For recent, related examples: (a) Williams, D. R.; Phillips, J. G.; Huffman, J. C. *J. Org. Chem.* **1981**, *46*, 4101. (b) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1982**, *104*, 2323 and references cited therein.

(4) For an interesting varient wherein the enantiofacial bias of an asymmetric *electrophile* is examined, see: Sauriol-Lord, F.; Grindley, T. B. *J. Org. Chem.* **1981**, *46*, 2831.

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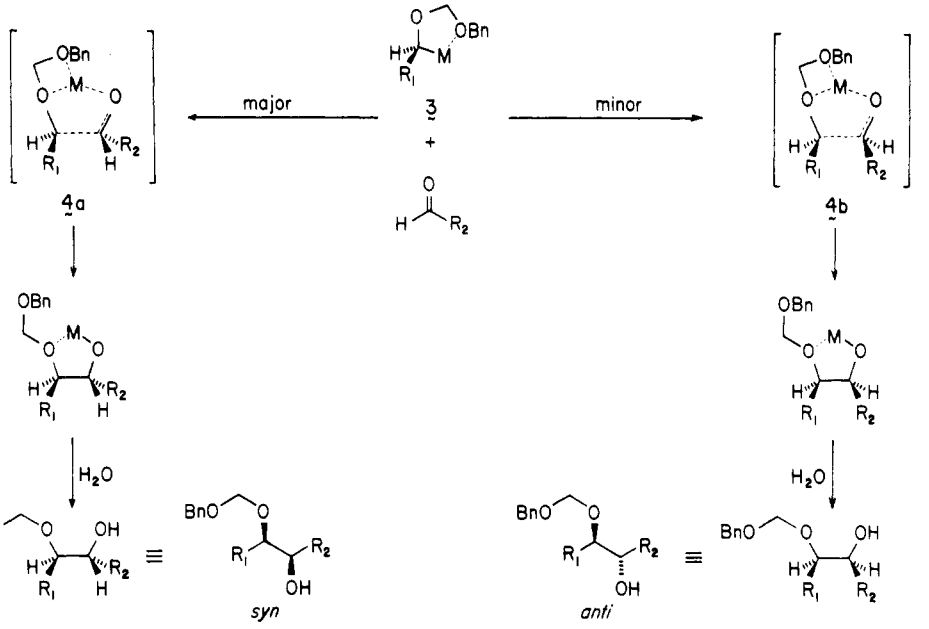
Scheme I



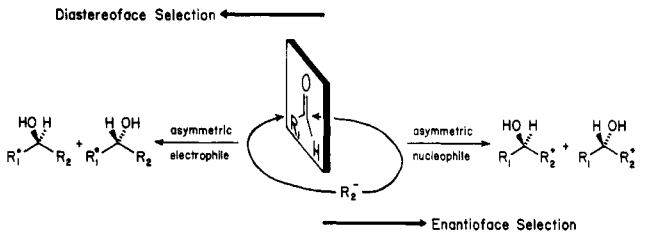
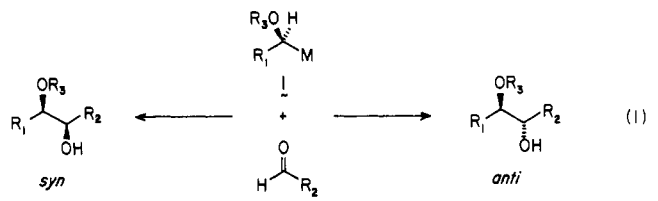


Figure 1. Facial recognition in carbonyl condensation reactions. R_1* and R_2* contain sites of asymmetry.

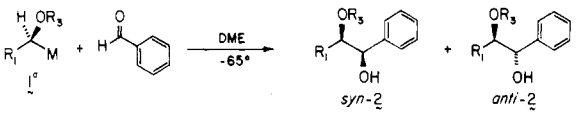
Toward this end, the stereochemical bias implicit in eq 1 was explored.[5] Previous work has demonstrated the



configurational integrity of α-alkoxyorganolithium species of type 1 (R_1 = alkyl, M = Li) in the course of accepting electrophiles with retention of configuration.[6] These asymmetric carbanions are readily accessible from the corresponding organostannane (M = $SnBu_3$) by facile exchange with *n*-butyllithium, again with retention.[6,7] To minimize reaction variables and to facilitate the analysis of stereoisomeric mixtures, benzaldehyde was chosen as a common electrophile for initial study (R_2 = Ph). The results of these condensations are presented in Table I.

Several significant trends are indicated by this data. First, with one notable exception (entry C), the syn isomer invariably predominates.[10] This diastereoselectivity be-

Table I.[5,8] Diastereoselection as a Function of the Structural Features of 1



Entry	R_1	R_3	M[b]	Yield[c]	*syn*-2 : *anti*-2[d]
A	C_2H_5	CH_2OCH_2Ph	Li[e]	75%	53 : 47
B			MgBr	77%	63 : 37
C	$CH(CH_3)_2$	CH_3	Li	96%	50 : 50
D		CH_2OCH_2Ph		95%	63 : 37
E		$CH(CH_3)OC_2H_5$		74%	68 : 32
F		$CH_2OCH_2CH_2OCH_3$		81%	55 : 45
G		$CH_2(OCH_2CH_2)_2OC_2H_5$		60%	67 : 33
H		CH_3	MgBr	82%	67 : 33
I		CH_2OCH_2Ph		84%	82 : 18
J		$CH_2OCH_2CH_2OCH_3$[e]		78%	79 : 21
K		CH_2OCH_2Ph	MgBr $Cu(OAc)_2$ (cat.)	79%	87 : 13
L	$C(CH_3)_3$	CH_2OCH_2Ph	Li[e]	65%	92 : 8
M			MgBr	65%	100 : 0

[a] These compounds prepared and condensations carried out in the manner previously described.[7] [b] M = Li prepared from M = $SnBu_3$.[7] M = MgBr is prepared by the addition of anhydrous $MgBr_2$ to M = Li and stirring for 15 min at −65 °C. Additional metal ions are introduced as needed. [c] Following isolation by flash chromatography.[9] [d] Ratios determined by NMR integration of the benzylic protons on the corresponding isopropylidene derivatives.[10] [e] Reaction run in THF solvent at −78 °C.

comes more pronounced as the steric demand of the nucleophile increases (compare entries B, I, and M). The enantiofacial bias of the carbanion is also influenced by the nature of the oxygen substituent, as exemplified by entries C–G. When oxygen is simply methylated (entry C), stereorandom condensation of the organolithium compound is observed. However, incorporation of an acetal oxygen noticeably enhances the syn selectivity of the carbanion (entries D and E), while further oxygen sub-

(5) Syn and anti descriptors used in the manner of: Masamune, S.; Choy, W.; Kerdesky, F. A. J.; Imperiali, B. *J. Am. Chem. Soc.* **1981**, *103*, 1566. All compounds are racemic with only one enantiomer depicted for clarity.

(6) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201; see also: Rondan, N. G.; Houk, K. N.; Beak, P.; Zajdel, W. J.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Org. Chem.* **1981**, *46*, 4108.

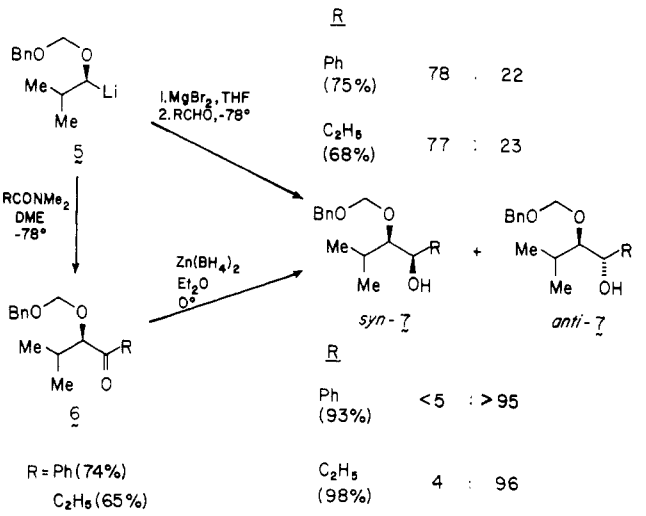
(7) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

(8) Satisfactory spectral and analytical data was obtained for all compounds.

(9) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2972.

(10) The syn isomer was identified by independent synthesis (Still, W. C.; McDonald, J. H., III *Tetrahedron Lett.* **1980**, 1031).

Scheme II



stitution shows no improvement (entries F and G). The nature of the metal is also an important factor. In every case examined, syn selection increases with the replacement of the organolithium compound with the corresponding organomagnesium derivative. Addition of catalytic amounts of copper salts gives modest improvement (entry K), while attempts to further enhance diastereoselectivity through other organometallic species was, unfortunately, precluded by their unreactive nature.[11]

This data lends itself to a rational of kinetic stereoselection as presented in Scheme I. Diastereotopic transition states **4a** and **4b** seem reasonable through extrapolation of the mechanism proposed for the addition of simple organolithium and organomagnesium reagents to carbonyl compounds.[12] Enantiofacial discrimination results from the unfavorable R_1/R_2 interaction present in **4b** (minor) but absent in **4a** (major). The stereoregulating effect of the metal center is still unclear, though adjustment in the ground-state energy of **1** and geometrical preference in transition states **4a**/**4b** remain as possibilities.[13] In all cases, internal coordination of the type **3** apparently imparts a directing effect upon the interaction of the reaction partners.

Along more practical lines, these asymmetric carbanions should allow convenient, stereoselective access to 1,2-diol derivatives. The utility of these intermediates is illustrated in Scheme II.[14,15] Direct condensation of organomagnesium derivative **5** with either benzaldehyde or propionaldehyde leads to an approximately 3.5:1 mixture of diol derivatives **7** favoring the syn isomer. Alternatively, these carbanions may be acylated to give carbonyl compounds **6**,[16] which are cleanly reduced to the anti isomers **7** with zinc borohydride.[17] It is noteworthy that this scheme allows convergent synthesis of diols of either stereochemical series through formation of the same carbon–carbon bond.

In conclusion, these studies demonstrate the enantiofacial discrimination of some asymmetric carbanions in their condensation with prochiral carbonyl compounds. While this preliminary work already offers a synthetically useful, convergent approach to some 1,2-diols, improved syn selection can now be expected on the basis of the emergence of a model for the transition state in these condensations. Furthermore, these results underscore the importance in considering the reaction parameters described at the outset in the design of stereoselective transformations. Finally, the present observations may shed light on the factors governing the stereoselectivity exhibited by related asymmetric carbanionic species.[18] Further refinement of the stereoregulating features, as well as exploitation of the synthetic potential of these condensations, will be reported in due course.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (AI 17595-02) for support of this work.

Registry No. **1A**, 83879-83-9; **1B**, 83876-84-0; **1C**, 83876-85-1; **1D**, 83876-86-2; **1E**, 83876-87-3; **1F**, 83876-88-4; **1G**, 83876-89-5; **1H**, 83876-90-8; **1I**, 83876-91-9; **1J**, 83876-92-0; **1L**, 83876-93-1; **1M**, 83897-16-9; *anti*-**2A**, 83876-94-2; *syn*-2A, 83877-00-3; *anti*-**2C**, 83876-95-3; *syn*-**2C**, 83877-01-4; *anti*-**2D**, 83876-96-4; *syn*-**2D**, 83877-02-5; **2E**, 83877-03-6; *anti*-**2F**, 83876-97-5; *syn*-**2F**, 83877-04-7; *anti*-**2G**, 83876-98-6; *syn*-**2G**, 83877-05-8; *anti*-**2L**, 83876-99-7; *syn*-**2L**, 83877-06-9; **6** (R = Ph), 83877-07-0; **6** (R = C_2H_5), 83877-08-1; *anti*-**7**(R = C_2H_5), 83897-17-0; *syn*-**7** (R = C_2H_5), 83877-09-1; benzaldehyde, 100-52-7; propanal, 123-38-6; *trans*-4-ethyl-2,2-dimethyl-5-phenyl-1,3-dioxolane, 83877-10-5; *cis*-4-ethyl-2,2-dimethyl-5-phenyl-1,3-dioxolane, 83877-11-6; *trans*-4-isopropyl-2,2-dimethyl-5-phenyl-1,3-dioxolane, 83877-12-7; *cis*-4-isopropyl-2,2-dimethyl-5-phenyl-1,3-dioxolane, 83877-13-8; *trans*-4-*tert*-butyl-2,2-dimethyl-5-phenyl-1,3-dioxolane, 83877-14-9; *cis*-4-*tert*-butyl-2,2-dimethyl-5-phenyl-1,3-dioxolane, 83877-15-0.

Supplementary Material Available: A listing of the NMR data for the cyclic derivatives used for stereochemical analysis is available (2 pages). Ordering information is given on any current masthead page.

(11) No reaction was observed when the organolithium species was treated with boron, aluminum, and zinc compounds as well as stoichiometric quantities of copper salts, prior to condensation with the aldehyde.

(12) (a) Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* **1975**, *75*, 521. (b) Ashby, E. C. *Pure Appl. Chem.* **1980**, *52*, 545.

(13) For an example of steric preferences exhibited by different metals, see: Still, W. C.; Schneider, J. A. *Tetrahedron Lett* **1980**, 1035.

(14) All yields (in parentheses) reported after flash chromatography.[9]

(15) The analysis of the stereoisomeric mixture was carried by gas chromatographic resolution of the dimethyl acetals corresponding to *syn*-**7**/*anti*-**7** (prepared from *syn*-**7**/*anti*-**7** by (i) H_2, Pd–C, MeOH, (ii) $Me_2C(OMe)_2$, Me_2CO, TsOH). The isomer corresponding to *syn*-**7** eluted first on a 10-ft column of 5% SE-30 on Chromosorb W with a carrier gas flow rate of 30 mL/min.

(16) Further information on this useful transformation will be reported shortly.

(17) (a) Nakata, T.; Tanaka, T.; Oishi, T. *Tetrahedron Lett.* **1981**, 4723. (b) *Ibid.* **1980**, 1641.

(18) These results are consistent with the erythro selectivity shown by α-metallo carbonyl compounds.[3b]

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HI-Induced Reductive Coupling of Carbon Monoxide and Homologation of a Carboxylic Acid

Summary: Carbon monoxide reacts with aqueous HI to give acetic acid. Acetic acid reacts with carbon monoxide and aqueous HI to give propionic acid.

Sir: We report that HI can effect the remarkable transformations

$$CO \xrightarrow{HI,\ H_2O} CH_3CO_2H, \qquad (1)$$

and

$$CH_3CO_2H + CO \xrightarrow{HI,\ H_2O} CH_3CH_2CO_2H \qquad (2)$$

0022-3263/82/1947-5422$01.25/0