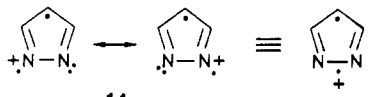
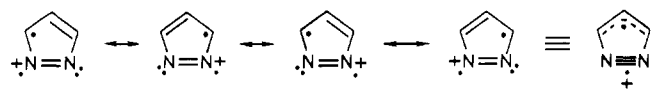
than the $4\pi$S-$CSb_1$ cation; however, only qualitative comparisons can be made.

In the $5\pi$T-$OSb_1$ cation the maximum $\pi$-spin density resides on C4. The slightly longer N–N distance than a normal N=N distance is accommodated by the resonance-contributing structures shown as **14** which is



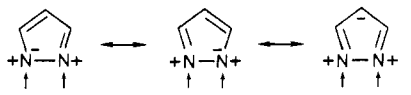
**14** **15**

equivalent to the MO description in **15** in which the (n + n) MO is doubly occupied in the (n − n) MO is singly occupied. In the $5\pi$T-$OSa_2$ cation the $\pi$-electron spin density resides predominantly on C3 and C5. The N–N distance is intermediate between that of N=N and N≡N. This cation is best represented by the resonance-contributing structures shown as **16**, of the MO description shown in **17**.



**16** **17**

**Six $\pi$-Electron, Open-Shell Cations.** Calculations have also been carried on the six $\pi$-electron, $\sigma$-triplet, and singlet open-shell cationic systems. The total energies are given in Table III, and the $\pi$ and nonbonded MO energies are given in Table IV. The 3-21G optimized structural parameters, $\pi$ and total charge densities, and spin densities are given in the structure in Figure 2. The 6-31G optimized structural parameters are given in Table 2 of the supplementary material. The structure and $\pi$ charge distribution of the $6\pi$T-OS cation suggest that the structure is best represented by the resonance structures shown as **18**. The



**18**

structure of the $6\pi$S-OS cation is quite similar to that of the triplet structure except for a slightly longer N–N distance. Its overall electronic structure is similar to that shown as the hybrid **18**. Both the triplet and singlet structures are slightly higher in energy that the $4\pi$S-$CSb_1$ cation.

## Summary

Of the closed-shell singlet cationic structures, the $4\pi$S-$OBb_1$ cation is the lowest in energy. The electronic properties predicted from the calculations correspond to those observed experimentally. The calculations indicate that several other singlet and triplet electronic configurations lie close in energy. The highest lying configuration appear to be the aromatic six $\pi$-electron closed-shell system.

**Acknowledgment.** We thank the Computing Center of the University of Notre Dame and Professor John Dow or the Department of Physics for computing time; the latter facility is supported by the Office of Naval Research (Contract No. ONR N0014-84-K-0352).

**Registry No.** **1**, 61355-01-9; **2**, 109391-18-6; **3**, 53283-24-2; **4**, 109391-19-7; **5**, 24100-66-1; **6**, 5363-19-9; **7**, 109391-21-1; **12**, 109391-20-0.

**Supplementary Material Available:** Tables of calculated structural parameters for the pyrazole cations studied (7 pages). Ordering information is given on any current masthead page.

# Stereoselective Intramolecular Iodoetherification of 4-Pentene-1,3-diols: Synthesis of *cis*-2-(Iodomethyl)-3-hydroxytetrahydrofurans

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Intramolecular iodoetherification of 4-pentene-1,3-diol and its monosubstituted derivatives, irrespective of the substitution pattern, provides *cis*-2-(iodomethyl)-3-hydroxytetrahydrofurans in high yields. The cis selectivity generally exceeds 95%. Some of the disubstituted 4-pentene-1,3-diols similarly undergo the selective cyclization; however, the others show anomalies on regio- and/or stereoselectivities, providing either tetrahydropyrans or *trans*-2-(iodomethyl)-3-hydroxytetrahydrofurans as main products. A mechanism that may reconcile all of these results is proposed.

The control of stereochemistry in an acyclic system is an important consideration in the synthesis of many complex molecules.[1] However, despite the great advances that have been made in cyclic systems, the control of stereochemistry in acyclic systems remains a challenge. The hydroxy group of allylic alcohols often provides a moderate to strong stereo-directing effect during addition to double bonds (epoxidation,[2] glycolation,[3] halogenation,[4] etc.[5]). Katzenellenbogen,[6] Chamberlin,[7] and we[8] have demonstrated that the hydroxyl group of 3-hydroxy-4-penten-

(1) (a) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2. (b) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, Chapters 5 and 6.

(2) (a) Sharpless, K. B. *Aldrichimica Acta* **1979**, *12*, 63. (b) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1979**, 4733. (c) Chautemps, P.; Pierre, J.-L. *Tetrahedron* **1976**, *32*, 549 (d) Adams, C. E.; Walker, F. J.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 420.

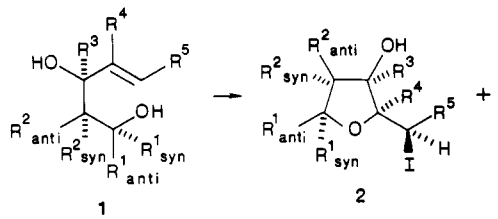
(3) (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3943, 3947; *Tetrahedron* **1984**, *40*, 2247. (b) Stork, G.; Kahn, M. *Ibid.* **1983**, *24*, 3951. (c) Danishefsky, S. J.; Larson, E.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1274. (d) Vedejs, E.; McClure, C. K. *Ibid.* **1986**, *108*, 1094.

(4) (a) Santelli, M.; Viala, J. *Tetrahedron Lett.* **1977**, 4397. (b) Midland, M. M.; Halterman, R. L. *J. Org. Chem.* **1981**, *46*, 1227.

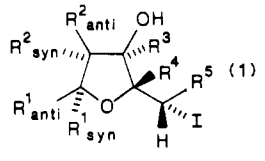
0022-3263/87/1952-4062$01.50/0 

amides and 3-hydroxy-4-pentenoic acid plays an important role to effect the selective cyclization and provides *cis*-3-hydroxy-4-(halomethyl)-γ-butyrolactones. The cis-directed cyclization by the allylic hydroxyl group is general, and wide application is found for the cyclization of 4-pentene-1,3-diols[9] and 3-hydroxy-4-pentenylamines[10] by combination with a variety of electrophiles (e.g., halogens, *m*-chloroperbenzoic acid, Pd(II), Hg(II), etc.).

In this paper, we describe the full account of the systematic investigation on the intramolecular iodoetherification of 4-pentene-1,3-diols, reported previously as a preliminary communication (eq 1).[11] These reactions



1 2



3 (1)

generally proceed diastereoselectively in a synthetically valuable level in a predictable way and provide *cis*-2-(iodomethyl)-3-hydroxytetrahydrofurans **2**, important intermediates for the synthesis of polyether antibiotics.[9e,12] There are some striking anomalies underscoring the mechanistic subtleties of the reaction.

## Results and Discussion

**Iodoetherification of 4-Pentene-1,3-diols.** Intramolecular iodoetherification of 4-pentene-1,3-diols was done under three different conditions. The substrate diol (1 mmol) dissolved in $Et_2O$–$H_2O$ (5 mL–2 mL/mmol of substrate) was treated with $I_2$ (1.2 mmol) at 0 °C or at 20–25 °C in the presence of $NaHCO_3$ (2 mmol) (condition A). Iodoetherification with *N*-iodosuccinimide (1.2 equiv) in dichloromethane (condition B) or with iodonium dicollidine perchlorate (1.5 equiv) in chloroform was also examined (condition C). The results of the iodoetherification of the parent 4-pentene-1,3-diol (**1a**) and its monosubstituted derivatives (**1b**–**1o**) are summarized in Table I.[13]

**Table I. Iodoetherification of Monosubstituted 4-Pentene-1,3-diols 1[a]**

| entry | 1: R[b] | reactn condn:[c] temp (°C), time (h) | 2:3 ratio[d] (isol yield, %) |
|---|---|---|---|
| 1 | **a**: R = H | A: 0, 3 | 95:5 (87) |
| 2 | **a**: R = H | B: −78, 2 | 92:8 (89) |
| 3 | **b**: $R^4$ = Me | A: 0, 3 | 91:9 (94) |
| 4 | **c**: $R^4$ = *i*-Pr | A: 0, 6 | >95:<5 (73) |
| 5 | **d**: $R^2$ = $(CH_2)_5$ | A: 0, 2 | >95:<5 (98) |
| 6 | **d**: $R^2$ = $(CH_2)_5$ | B: −78, 3 | >95:<5 (93) |
| 7 | **d**: $R^2$ = $(CH_2)_5$ | C: 0, 1 | 85:15 (99) |
| 8 | **e**: $R^1_{syn}$ = Ph[h] | A: 0, 12 | >95:<5 (98) |
| 9 | **f**: $R^1_{anti}$ = Ph | A: 20, 24 | 94:6 (81) |
| 10 | **g**: $R^1_{syn}$ = *t*-Bu[h] | A: 0, 18 | >95:<5 (85) |
| 11 | **h**: $R^1_{anti}$ = *t*-Bu | A: 25, 60 | >95:<5 (83)[e] |
| 12 | **i**: $R^1_{syn}$ = $CH_2CO_2Et$[h] | A: 0, 4 | >95:<5 (78) |
| 13 | **j**: $R^1_{anti}$ = $CH_2CO_2Et$ | A: 25, 30 | 90:10 (68) |
| 14 | **k**: $R^2_{syn}$ = Ph | A: 0, 6 | >95:<5 (96)[f] |
| 15 | **l**: $R^2_{anti}$ = Ph | A: 0, 5 | 90:10 (99) |
| 16 | **m**: $R^2_{syn}$ = *t*-Bu[h] | A: 0, 70 min | >95:<5 (90)[g] |
| 17 | **n**: $R^2_{anti}$ = *t*-Bu[h] | A: 0, 70 min | >95:<5 (93) |
| 18 | **o**: $R^2$ = $(CH_2)_5$, $R^5$ = Me | B: −78, 2 | 93:7 (93) |

[a] For the structures of **1**–**3**, see eq 1. [b] Unless otherwise specified, R should be H. [c] Key: A, $I_2$ (1.5 mmol), $NaHCO_3$ (2 mmol) in ether–$H_2O$ (5 mL–2 mL/mmol of **1**); B, *N*-iodosuccinimide (1.2 mmol) in dichloromethane; C, iodonium dicollidine perchlorate (1.5 mmol) in chloroform. [d] Generally, a diastereomeric pair of **2** and **3** could not be separated by column chromatography, and the ratio of **2** to **3** was determined by means of $^{13}C$ NMR, $^1H$ NMR, HPLC, or a combination of these methods for the sample purified by flash chromatography. The ratio of **21** to **31** was obtained from the isolated yield. Yield refers to the combined yields of **2** and **3**. Unless otherwise noted, conversion is 100%. [e] Conversion is 70%. [f] Conversion is 75%. [g] Conversion is 76%. [h] A diastereomeric mixture of diols were used as a starting material: **1e**:**1f** = 55:45; **1g**:**1h** = 58:42; **1i**:**1j** = 71:29; **1m**:**1n** = 55:45.

Generally, the reaction was clean, and only one spot ascribable to the product mixture (**2** and **3**) was observed on silica gel TLC (benzene–ethyl acetate or hexane–ethyl acetate). The yields are meant to refer to the product mixture isolated by means of flash column chromatography over silica gel. The product ratio was determined by means of $^1H$ NMR, $^{13}C$ NMR, HPLC, or a combination of these methods. Irrespective of the reaction conditions (A–C), the yields are almost the same and equally satisfactory, but the selectivities of **2** to **3** differ slightly depending on the reaction conditions. Generally, condition A showed better selectivity than conditions B and C (cf. entries 1 and 2 and entries 5–7). As is apparent from Table I concerning the parent and monosubstituted 4-pentene-1,3-diols, irrespective of the substitution pattern, the reaction shows the high cis selectivity without exception, and in most cases the selectivity exceeds 95%.

As for the reactivity, $R^2$-substituted derivatives (**1k**–**1n**) are by far the most reactive, and among them the $R^2_{anti}$ derivatives (**1l** and **1n**) react slightly faster than the corresponding $R^2_{syn}$ derivatives (**1k** and **1m**, respectively),

(5) Cyclopropanation: (a) Ratier, M.; Castaing, M.; Godet, J.-Y.; Pereyre, M. *J. Chem. Res., Synop.* **1978**, 179. Nitrile oxide cycloadditions: (b) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jäger, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880. (c) Jäger, V.; Schohe, R.; Paulus, E. F. *Tetrahedron Lett.* **1983**, *24*, 5501. (d) Houk, K. N.; Duh, H.-Y.; Wu, Y.-D.; Moses, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754.

(6) Rollinson, S. W.; Amos, R. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4114.

(7) (a) Chamberlin, A. R.; Dezube, M.; Dussault, P.; McMills, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 5819. See also: (b) Ohfune, Y.; Kurokawa, N. *Tetrahedron Lett.* **1985**, *26*, 5307.

(8) (a) Tamaru, Y.; Mizutani, M.; Furukawa, Y.; Kawamura, S.; Yoshida, Z.; Yanagi, K.; Minobe, M. *J. Am. Chem. Soc.* **1984**, *106*, 1079. (b) Tamaru, Y.; Higashimura, H.; Naka, K.; Hojo, M.; Yoshida, Z. *Angew. Chem.* **1985**, *97*, 1070.

(9) (a) Semmelhack, M. F.; Bodurow, C.; Maum, M. *Tetrahedron Lett.* **1984**, *25*, 3171. (b) Freeman, F.; Robarge, K. D. *Ibid.* **1985**, *26*, 1943. (c) Tamaru, Y.; Kobayashi, T.; Kawamura, S.; Ochiai, H.; Hojo, M.; Yoshida, Z. *Ibid.* **1985**, *26*, 3207. (d) Reitz, A. B.; Nortey, S. O.; Maryanoff, B. E. *Ibid.* **1985**, *26*, 3915. (e) Williams, D. R.; White, F. H. *Tetrahedron Lett.* **1985**, *26*, 2529; **1986**, *27*, 2195. The homoallylic hydroxyl group of 4-pentene-1,2-diols does not show such a directing ability: (f) Williams, D. R.; Grote, J.; Harigaya, Y. *Tetrahedron Lett.* **1984**, *25*, 5231.

(10) (a) Tamaru, Y.; Kawamura, S.; Tanaka, K.; Yoshida, Z. *Tetrahedron Lett.* **1984**, *25*, 1063. (b) Tamaru, Y.; Kobayashi, T.; Kawamura, S.; Ochiai, H.; Yoshida, Z. *Ibid.* **1985**, *26*, 4479. The ether oxygen of 4-(benzyloxy)-5-pentenylamine, on the Hg(II)-assisted cyclization, does not exhibit any directing effect: (c) Bernotas, R. C.; Ganem, B. *Ibid.* **1985**, *26*, 1123, 4981.

(11) Tamaru, Y.; Kawamura, S.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 2885.

(12) Wierenga, W. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1981; Vol. 4.

(13) Although diols **1d** and **1o** are apparently multisubstituted, these diols were summarized in Table I for simplicity, because the pentamethylene substituent at $C_2$ does not effect the product selectivities and yields.

judging from the conversions under the same conditions (entries 14–17).[14] On the other hand, each of the three pairs of $R^1$ diastereomers (**1e** and **1f**, **1g** and **1h**, **1i** and **1j**) showed a fascinating difference in reactivity. $R^1_{syn}$ isomers (**1e**, **1g**, and **1i**) react as usual and attain completion at 0 °C within 18 h, while the $R^1_{anti}$ isomers were completely unreactive under the same conditions. Although separation of the mixture of these $R^1$ diastereomers of diols **1** was very difficult by means of column chromatography, we could separately conduct the reaction of each diastereomer using a mixture of these (**1e**:**1f** = 55:45; **1g**:**1h** = 58:42; **1i**:**1j** = 71:29) by virtue of the large differences in reactivity. For example, when a mixture of **1e** and **1f** was reacted with $I_2$ (1.5 equiv to the mixture of diols, under condition A) at 0 °C for 12 h, *cis,trans*-2-(iodomethyl)-3-hydroxy-5-phenyltetrahydrofuran (**2e**) was obtained as a sole product and no other products (such as **3e**, **2f**, and **3f**) were detected (entry 8). The unreacted **1f** was quantitatively recovered in a stereochemically homogeneous state. The anti diols, on the other hand, undergo iodoetherification at the elevated temperatures (20–25 °C) and furnished the cis cyclization products (**2**) in similarly high selectivity. The anti isomer **1h** ($R^1$ = *t*-Bu) was most reluctant, and even after 60 h at 25 °C, the reaction attained only 70% conversion (entry 11).

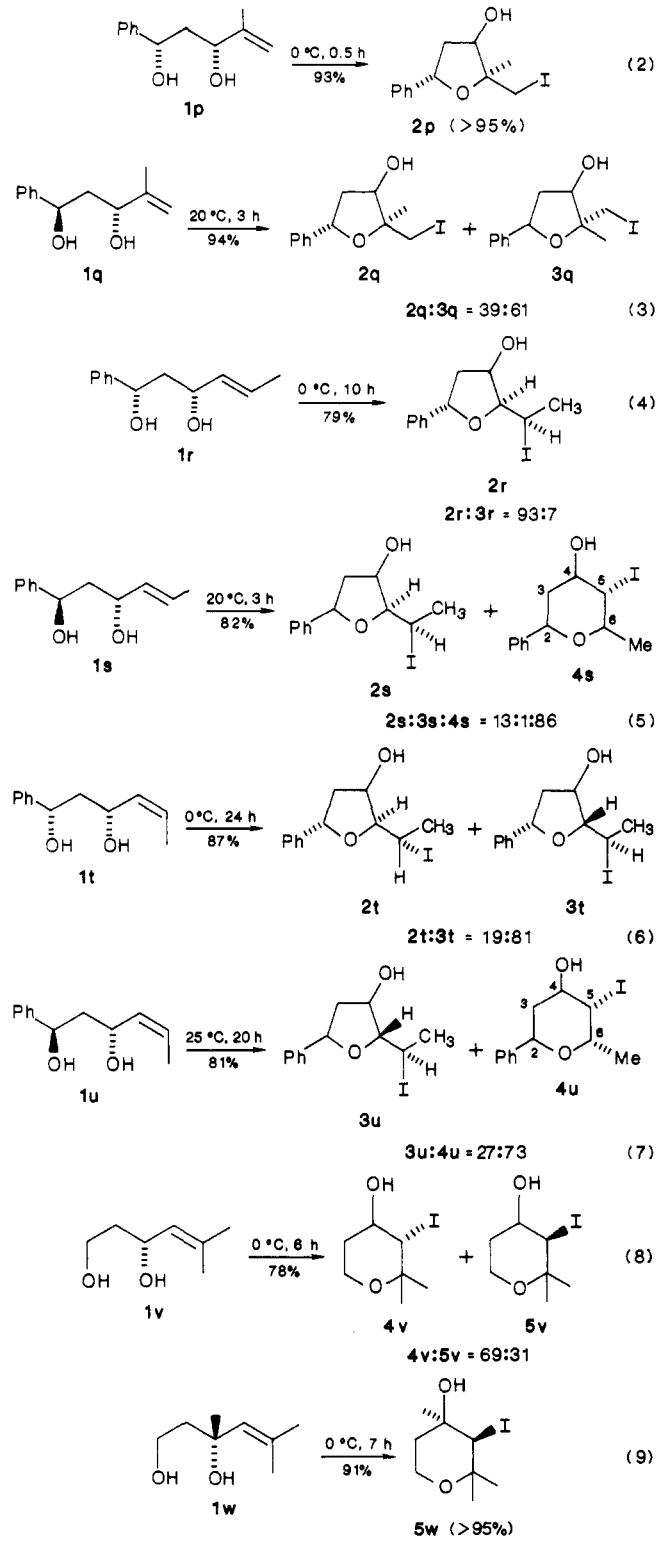
In order to further pursue the origin of the unexpectedly large differences in reactivity caused by the $C_1$ diastereomerism of diols, we examined the diols with an additional substituent on the $C_4$ and $C_5$ carbons and found that some of these exhibited anomolous behavior on stereoselectivity. The results are shown in Scheme I.

As for reactivity, as expected from the results mentioned above, only the syn diastereomers **1p** and **1r** were selectively consumed, and the corresponding anti diastereomers **1q** and **1s** were quantitatively recovered, respectively, when the mixtures of diols (**1p**:**1q** = 55:45, **1r**:**1s** = 57:43) were subjected to the reaction under condition A. In marked contrast to this, the pair of diastereomers **1t** and **1u**, characterized by a cis geometry of the double bond, did not show such a large difference in reactivity. When a mixture of **1t** and **1u** (66:34) was reacted at 0 °C for 24 h under condition A, **1u** attained 10% conversion, while 7% of **1t** was still remaining (93% conversion).

As for the stereo- and regioselectivity, the syn isomers **1p** and **1r** provided the expected cis tetrahydrofurans (**2p** and **2r**, respectively), while all the other isomers showed striking anomalies. Despite the close structural similarity to **1b**, **1c**, and **1p**, **1q** preferentially provided the trans cyclization product **3q** (**2q**:**3q** = 39:61). More drastic reversal of stereoselectivity was observed for **1t** and **1u**, where trans tetrahydrofurans were obtained either selectively (**3t**:**2t** = 81:19) or exclusively (**3u**:**2u** = >95:<5). Recently, a similar trans selective cyclization was reported by Williams[9e] on the iodoetherification of *cis*-1-(benzyloxy)-3-hydroxy-4-hexenes. Another anomaly is concerned with the regioselectivity. Both the anti diastereomers **1s** and **1u** provided tetrahydropyrans **4s** and **4u**, respectively, as major products together with tetrahydrofurans **2s** and **3u** as minor products. Tetrahydropyrans were also obtained by the iodoetherification of terminally disubstituted diols **1v** and **1w**.

The stereochemistry of tetrahydrofurans was determined by the higher field resonances of the iodomethyl carbons of the cis isomers relative to those of the corresponding trans isomers (by ca. $\delta$ 5) in their $^{13}C$ NMR spectra and also by the larger downfield shifts of the iodomethyl protons in the cis isomers compared with those of the corresponding trans isomers, as observed in doping experiments with $Eu(fod)_3$ in their $^1H$ NMR spectra.[16] Furthermore, by the cyclization reaction with phenyl isothiocyanate, the

**Scheme I. Iodoetherification of Di- and Trisubstituted 4-Pentene-1,3-diols (Condition A)**

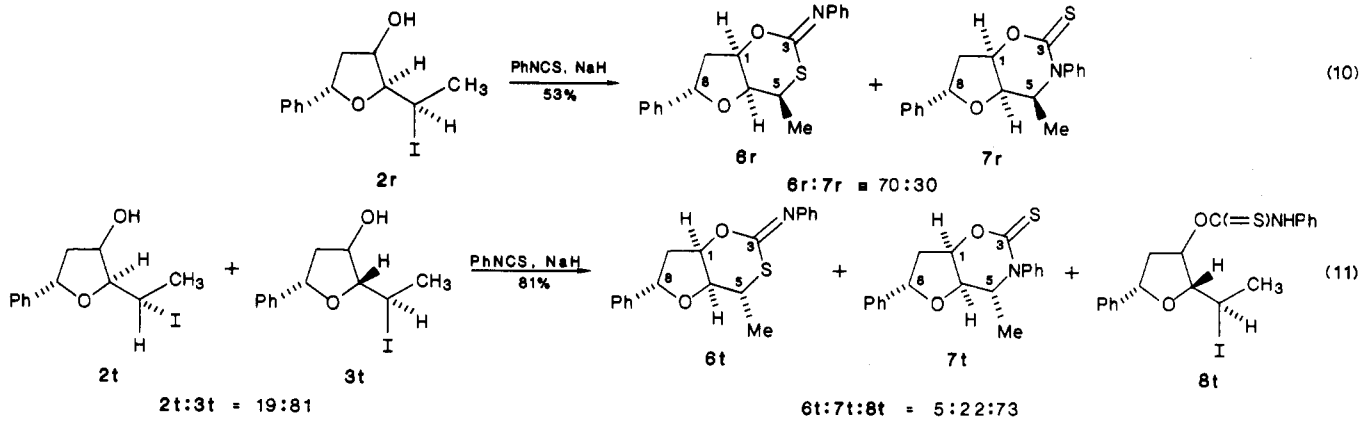



(14) Although the kinetics of iodoetherification is rather complex,[15] the reactivity ratio of **1n** to **1m** is roughly estimated to be 8 on the basis of a competition reaction at −20 °C under condition A, supposing the cyclization follows first-order kinetics to the 1,3-diols.

(15) Bernett, R. G.; Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1985**, *50*, 2048.

(16) (a) Gaudemer, A. In *Stereochemistry*; Kagan, H. B., Ed.; George Thieme Verlag: Stuttgart, 1977. (b) Levy, G. C.; Lichter, R. L.; Nelson, G. L. *Carbon-13 NMR Spectroscopy*, 2nd ed.; Wiley: New York, 1980.

**Scheme II**




cis stereochemistry was confirmed by the formation of a bicyclic [4.3.0] system. The trans isomer did not undergo the cyclization (Scheme II, vide infra).

The authentic trans isomers were prepared either by an inversion of the corresponding cis isomers according to the Mitsunobu method[17] (e.g., benzoate of **3a** from **2a** in 95% yield; diethyl azodicarboxylate, triphenylphosphine in THF at 0 °C) or by an oxidation–reduction sequence (**2c**:**3c** = 1:2.5 from **2c**; $CrO_3(py)_2$ in dichloromethane and then $NaBH_4$ in THF-methanol).

The structures of **2r** and **2t**, which rely on the assumption that iodine and oxygen add to the double bond in a trans fashion, were determined unequivocally by converting them to bicyclic compounds by treatment with NaH and phenyl isothiocyanate in THF (Scheme II). In these reactions, two types of cyclization products, thiocarbonimidate **6** and thiocarbamate **7**, were produced. From **2r**, bicyclic monothiocarbonimidate **6r** was obtained as a major product, while from **2t** bicyclic thiocarbamate **7t** was produced as a major product. **3t** did not undergo the cyclization, only providing **8t**. This is probably owing to a steric prohibition of cyclization to form the trans-fushed bicyclo[4.3.0]nonane system under the conditions. The monothiocarbonimidate **6** was discriminated from thiocarbamate **7** on the basis of its characteristic strong absorption of the C=N bond (ca. 1640 $cm^{-1}$) in the IR spectrum and a high-field resonance of the $C_5$-H proton in the $^1H$ NMR spectrum (ca. $\delta$ 3.4 for **6** and ca. $\delta$ 4.1 for **7**). The coupling constants $J^3_{H_5H_6}$ (5.5 Hz for **6r** and 9.5 Hz for **6t**) clearly indicate the axial–equatorial and axial–axial arrangements of these protons in **6r** and **6t**, respectively. No such clear-cut standard for the structural determination of **7r** and **7t** was obtained from the coupling constants in the $^1H$ NMR spectra of these isomers ($J^3_{H_5H_6}$ = 2.7 Hz for **7r** and 2.5 Hz for **7t**). This is probably owing to a deformation from a chair conformation of the six-membered ring in **7t** forced by a repulsion between the equatorial methyl group and the phenyl group attached to the planar ($sp^2$-like) nitrogen atom.[18]

The structure of tetrahydropyran derivative **4** was determined by the coupling pattern of the ring protons characteristic to cyclohexane structure in the $^1H$ NMR spectra. The all-equatorial structure of **4s** follows from $H_2$ (dd, $J$ = 2.2, 11.4 Hz), $H_5$ (t, $J$ = 10.3 Hz), and $H_6$ (dq, $J$ = 10.3, 7.2 Hz). The axial methyl of **4u** is apparent from the coupling pattern of $H_5$ (dd, $J$ = 4.9, 10.0 Hz) and $H_6$ (dq, $J$ = 4.9, 6.8 Hz). Furthermore, the tetrahydropyran structure is signified by the lower field resonances of the carbons bearing iodine compared with those of the corresponding carbons of tetrahydrofurans (e.g., $\delta$ 46.8 for CHI of **4s** and $\delta$ 23.5 for CHI of **2s**). The structure of **5w** was proven by X-ray crystallography (supplementary material).

In conclusion, the reaction described in this paper constitutes a general route to *cis*-3-hydroxy-2-(iodomethyl)-tetrahydrofuran, the structure being frequently observed in naturally occurring polyether antibiotics. Stereoselective synthesis of **2i** (entry 12 in Table I and Scheme III) is one example, which might be used as a synthetic intermediate of palytoxin $C_{110}$–$C_{115}$ segment.[19]

The selectivity of cis (**2**) to trans (**3**) is generally high, and the ratio does not change during a long exposure of the products to the reaction conditions. Taking this observation into consideration and also that cis isomers, in general, are thermodynamically less stable than trans isomers, the reaction seems to proceed under a kinetic control. The whole feature of the reactions may be summarized as follows:

(1) The parent 4-pentene-1,3-diol (**1a**) and its monosubstituted derivatives (**1b**–**1o**), irrespective of the substitution pattern ($R^1$, $R^2$, $R^4$, $R^5$),[20] provide the *cis*-2-(iodomethyl)-3-hydroxytetrahydrofurans **2** in high selectivity (Table I). The cis selectivity generally exceeds 95%. The reactivity order is $R^2_{anti} > R^2_{syn}$, $R^1_{syn} > R^1_{anti}$.

(2) Among the disubstituted diols, the $R^1_{syn}$ isomers **1p** and **1r** react as usual and provide the cis isomers **2** in high selectivity, while the reactions of the $R^1_{anti}$ isomers **1q** and **1s** are very sluggish and show anomalies in the stereo- and regioselectivity (scheme I).

(3) $R^5_{cis}$ substituent dramatically alters the stereoselectivity; the *trans*-2-(iodomethyl)-3-hydroxytetrahydrofurans **3** become the main products (eq 6 and 7).

The reasons for the stereo- and regioselectivities and relative reactivities summarized above are not completely understood, but all the observations might be rationalized by assuming a transition state **9** characterized by (i) an intramolecular hydrogen bonding forming a six-membered ring, (ii) a nearly eclipsed (or slightly clockwise-rotated) conformation of the $C_3$ hydroxyl group in the $C_4$–$C_5$ double-bond plane, and (iii) a more or less concerted iodoetherification, which proceeds in a trans fashion.[21] The

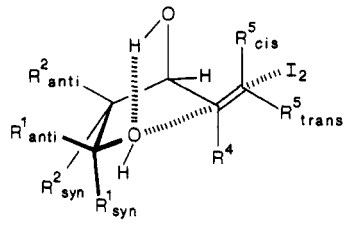
(17) Mitsunobu, O. *Synthesis* **1981**, 1.

(18) (a) Johnson, F. *Chem. Rev.* **1968**, *68*, 375. (b) Overman, L. E.; Yokomatsu, T. *J. Org. Chem.* **1980**, *45*, 5229. (c) Wilson, S. R.; Misra, R. N. *Ibid.* **1980**, *45*, 5079. (d) Hart, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 397. (e) Hart, D. J.; Kanai, K. *J. Org. Chem.* **1982**, *47*, 1555.

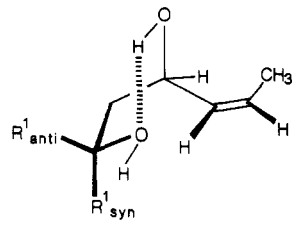
(19) Ko, S. S.; Klein, L. L.; Pfaff, K.-P.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 4415.

(20) Although not examined, judging from the reactions of **1t** and **1u**, $R^5$ cis monosubstituted diols also might provide trans cyclization products **3**[9e] predominantly.

(21) (a) do Amaral, L.; Melo, S. C. *J. Org. Chem.* **1973**, *38*, 800. (b) Cambie, R. C.; Hayward, R. C.; Roberts, J. L.; Rutledge, P. S. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1864.

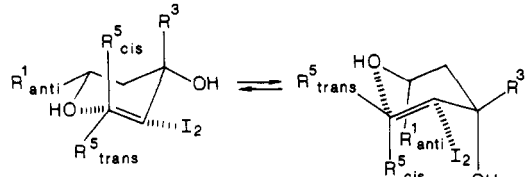


9



10

hydrogen bonding is invoked to rationalize the reactivity order $R^2_{anti} > R^2_{syn}$, $R^1_{syn} > R^1_{anti}$ and the anomalies in regioselectivity encountered for the disubstituted diols. Among the $R^1_{syn}$, $R^1_{anti}$, $R^2_{syn}$, and $R^2_{anti}$ substituted derivatives, the $R^1_{syn}$ derivatives are energetically most unfavorable to form a bicyclic structure in the transition state **9** owing to an increase of nonbonding interactions and, hence, show the low reactivity as observed for **1f**, **1h**, **1j**, **1q**, **1s**, and **1u**. Under such a situation, **1s** ($R^1_{anti} = R^5_{trans}$ = Me, $R^3 = R^5_{cis}$ = H) might preferentially follow a six-membered transition state **11** to give **4s**, because this



11



12

transition state seems to be particularly favorable for **1s**, not only because all the substituents are equatorial but also because an incipient carbonium ion generated at the $C_5$ carbon is more stable than the one generated at the $C_4$ carbon, provided that the allylic hydroxyl group only exerts an inductive effect. The case seems similar for the reaction of **1u**, which also provides tetrahydropyran **4u** as a main product. From the viewpoint of the carbonium ion stability, the tetrahydropyran formation from terminally disubstituted diols (**1v**, **1w**) is quite reasonable: **1w** specifically reacts through a transition state **12** ($R^3 = R^5_{cis} = R^5_{trans}$ = Me, $R^1_{anti}$ = H).[22] **1v** preferentially reacts through a transition state **11** ($R^5_{cis} = R^5_{trans}$ = Me, $R^1_{anti} = R^3$ = H), owing to a minimization of a 1,3-diaxial repulsion.

Both the $R^2_{syn}$ and $R^2_{anti}$ substituents suffer from a gauche interaction in **9**; however, $R^2_{anti}$ does so to a lesser extent because the $C_3$ hydroxyl group might be estimated to be sterically smaller than the olefinic part ($C_4$–$C_5$). This may be reflected by the slightly higher reactivity of the diastereomers with the $R^2_{anti}$ substituent than the diastereomers with the $R^2_{syn}$ substituent as observed for the pairs **1l** and **1k** and **1n** and **1m**.

The importance of intramolecular hydrogen bonding in the transition state **9** may be further supported by the following observation. When a mixture of 3-acetyl-protected derivatives of **1e** and **1f** (72:28) was reacted under condition A at 0 °C for 36 h, a mixture of the acetyl derivatives of **2e** and **2f** was obtained in a 93:7 ratio (63%), together with the recovered starting materials [3-acetoxy derivatives of **1e** and **1f**, 20:80 (26%)]. By comparison with entry 8 in Table I, this result indicates that protection of the 3-hydroxyl group with the acetyl group, and hence presumable prohibition of an intramolecular hydrogen bonding, reduces the relative reactivity between the syn and anti diastereomeric diols (**1e** and **1f**).

(22) If the conformational stabilities of **11** and **12** are almost the same, as in the case of **1w**, the reaction will selectively proceed via **12**, in which the $C_3$ hydroxyl group eclipses the double-bond plane (vide infra).[23]

According to theoretical[23] and experimental[24] analyses of 3-buten-2-ol, the most stable conformer is the one in which the allylic C–H linkage eclipses the C–C double-bond plane (like the $C_3$–$C_5$ moiety in **10**). Slightly higher in energy is the conformer with the C–O bond eclipsing the C–C double-bond plane (as in **9**). Accordingly, the conformer in a transition state **9** is not the most stable one, but the responsibility of transition state **9** for the cis-selective cyclization may be attributed to an enhanced reactivity of the olefin toward electrophilic reagents, because the HOMO of the double bond might be raised by a mixing with the lone-pair electrons of the oxygen atom (homoallyl anion).[23] The conformation around the allylic alcohol moiety of transition state **12** is in a situation similar to that of **9**, and provided that the thermodynamic stabilities of **11** and **12** are almost the same, the cyclization would preferentially proceed via **12**. The specific formation of **5w** from **1w** seems to be just the case.

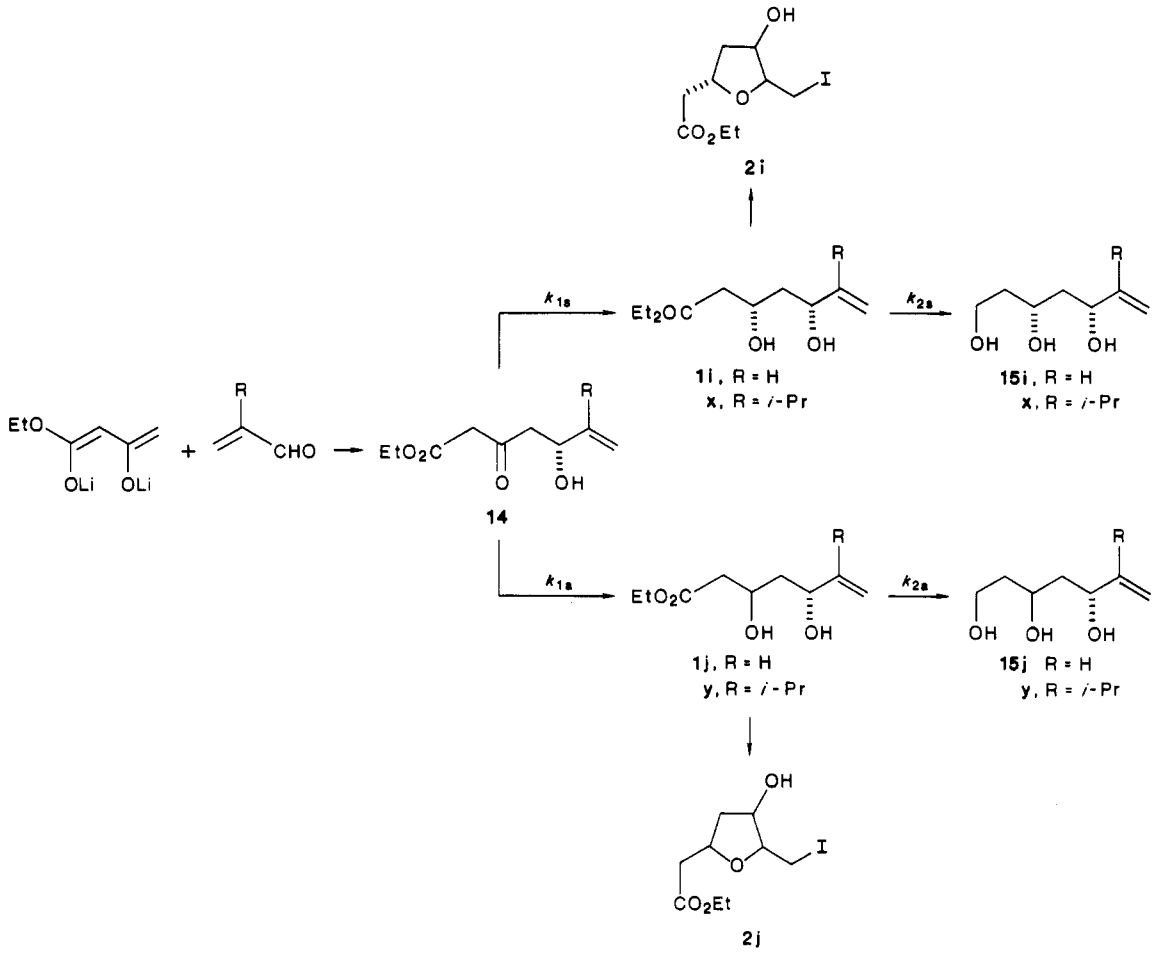
Many examples have been reported on the diastereoselective addition reaction of 3-penten-2-ols. Generally, the *cis*- and *trans*-3-penten-2-ols show the same diastereoface selection, the cis isomer showing the higher selectivity.[25] In marked contrast to this, the cis diols **1t** and **1u** showed an opposite selectivity to the trans isomers **1r** and **1s**, respectively, giving rise to the *trans*-2-(iodomethyl)-3-hydroxytetrahydrofurans **3**, selectivel. For **1t** and **1u**, the repulsion between the 3-hydroxyl and $R^5_{cis}$ = Me groups in **9** is such that **10** becomes by far the most stable conformer, where the allylic C–H linkage eclipses the olefin plane. For the *cis*-3-penten-2-ols, electrophiles are presumed to approach the olefin from the opposite side of the allylic hydroxyl group in a conformer like **10**.[3a,9e,25] However, for **1t** and **1u**, we believe that iodide approaches from the same side of the $C_3$ hydroxyl group in **10**, because this side is apparently sterically less crowded than the other side. The similar reversal of diastereoselectivity was observed for the iodolactonization[7a] and iodoetherification[9e] of *cis*-3-hydroxy-4-hexenoic acids and *cis*-1-(benzyloxy)-3-hydroxy-4-hexenes, respectively.

The mechanism involving hypoiodite of $C_1$-OH or $C_3$-OH may be ruled out judging from the trans iodoetherification of the double bond as observed for the formation of **2r**, **2s**, **2t**, etc., and the usual cis selective cyclization as observed for 3-acetyl derivatives of **1e** and **1f**, respectively (vide supra).

**Preparation and Structure of 4-Pentene-1,3-diols.** All of the starting 4-pentene-1,3-diols were prepared by aldol condensation of unsaturated aldehydes and lithium enolates of esters or ketones, followed by reduction with $LiAlH_4$ or $NaBH_4$. Typical examples are shown in Scheme III. The diastereomeric pairs of diols are generally inseparable by means of column chromatography. Some stereochemically pure 1,3-diols (**1k** and **1l**, **1t** and **1u**) could be obtained by the separation of diastereomers of their precursors (see the Experimental Section). Diols, however, were separated as their acetonide derivatives (**13**) by flash column chromatography. The structural determination of diols is based on the characteristic coupling patterns of the ring protons of the acetonide six-membered chairlike conformation in the $^1H$ NMR spectra. A few examples are shown in Figure 1.

(23) Kahn, S. D.; Hehre, W. J. *Tetrahedron Lett.* **1985**, *26*, 3647.
(24) (a) Smith, Z.; Carballo, N.; Wilson, E. B.; Marstokk, K.-M.; Mollendal, H. *J. Am. Chem. Soc.* **1985**, *107*, 1951. See also: (b) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jäger, V.; Schohe, R.; Fronczek, F. R. *Ibid.* **1984**, *106*, 3880. (c) Gonnela, N. C.; Nakanishi, K.; Martin, V. S.; Sharpless, K. B. *Ibid.* **1982**, *104*, 3775.
(25) Williams, D. R.; White, F. H. *Tetrahedron Lett.* **1986**, *27*, 2195. See also ref 3a and 9e.

**Scheme III**



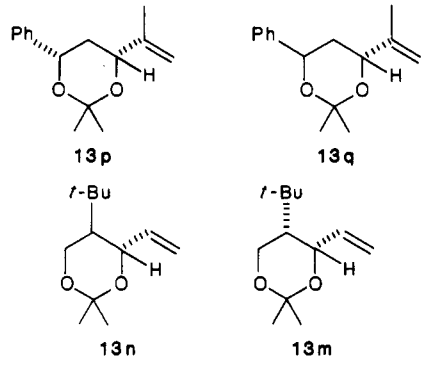
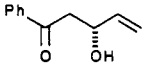
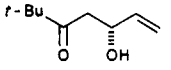
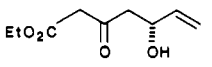
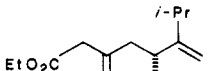


**Figure 1.** Structure determination of diols. $^1$H NMR coupling pattern of the methyne proton indicated: **13p**, dd, $J$ = 3.4, 10.3 Hz; **13q**, t, $J$ = 7.8 Hz; **13n**, dd, $J$ = 7.6, 9.5 Hz; **13m**, dd, $J$ = 3.7, 6.8 Hz.

Generally, reduction of 3-hydroxy ketones with $NaBH_4$[26] or $LiAlH_4$ shows only a slight preference of syn to anti, and temperature dependence of the selectivity is very small (entries 1–4, Table II). The diastereoselectivity for the reduction of ethyl 3-oxo-5-hydroxy-6-heptenoate (**14**, R = H) and its derivative (**14**, R = isopropyl) showed an interesting dependence on the reaction conditions (entries 5–8 in Table II and Scheme III). When the reduction with $NaBH_4$ was conducted at the higher temperatures and/or for the longer times, the proportion of syn diols to anti diols became higher at the expense of the combined yield of syn and anti diols. This quite unusual behavior could be rationalized by close examination of the reaction mixture (entry 8). In this experiment, in addition to diols (**1x**:**1y** = 100:0 in 45% yield), triols (**15x**:**15y** = 29:71 in 46% yield) were obtained. Judging from these data, supposing that the reduction of ketone is much faster than the reduction of ester and also that the reaction obeys first-order kinetics with respect to substrate,[27] we can

**Table II. Reduction of 2-Hydroxy Ketones**

| entry | substrate | reactn cond:[a] reductant, temp (°C), time (min) | yield, % (ratio) |
|---|---|---|---|
| 1 |  | $LiAlH_4$, 0, 30 | 95 (**1e**:**1f** = 55:45) |
| 2 | | $NaBH_4$, 0, 45 | 100 (**1e**:**1f** = 51:49) |
| 3 |  | $NaBH_4$, 0, 45 | 97 (**1g**:**1h** = 58:42) |
| 4 | | $NaBH_4$, 50, 30 | 99 (**1g**:**1h** = 61:39) |
| 5 |  | $NaBH_4$, 0, 90 | 80 (**1i**:**1j** = 71:29) |
| 6 | **14**, R = H | $NaBH_4$, 40, 30 | 70 (**1i**:**1j** = 87:13) |
| 7 |  | $NaBH_4$, 50, 2 | 78 (**1x**:**1y** = 82:18) |
| 8 | **14**, R = *i*-Pr | $NaBH_4$, 50, 10 | 45 (**1x**:**1y** = 100:0)[b] |

[a] $LiAlH_4$ (1 equiv) in dry ether or $NaBH_4$ (2 equiv) in ethanol was used. [b] In addition to **1x** was obtained a mixture of triols (**15x**:**15y** = 29:71) in 46% yield; see Scheme III.

(26) For a selective reduction of 3-hydroxy ketones with trialkylborane–$NaBH_4$, see: (a) Narasaka, K.; Pai, F.-C. *Tetrahedron* **1984**, *40*, 2233. See also: (b) Oishi, T.; Nakata, T. *Acc. Chem. Res.* **1984**, *17*, 338.

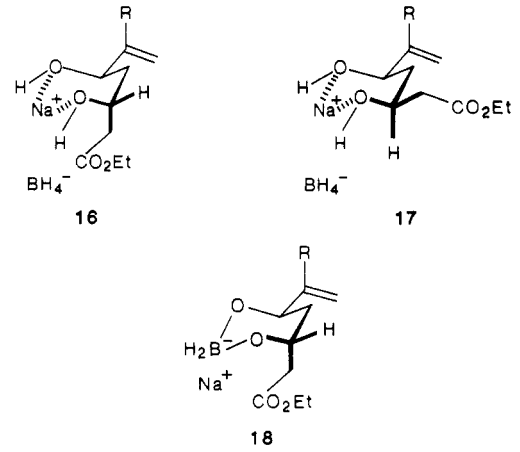



**Figure 2.**

roughly estimate that the reduction of **14** (R = isopropyl) to **1x** proceeds 1.8 times faster than the reduction to **1y** ($k_{1s}/k_{1a}$ = 1.8), and a further reduction of **1x** to **15x** is 20 times slower than the reduction of **1y** to **15y** ($k_{2s}/k_{2a}$ = $^1/_{20}$; Scheme III). That is, the selectivity for the syn diols is doubly enhanced: one is the usual syn selective reduction of 3-hydroxy ketones; the other is the highly selective reduction of the ester group of *anti*-3,5-dihydroxy esters (**1j**, **1y**), with remaining *syn*-3,5-dihydroxy esters (**1i**, **1x**) enriched.

One plausible rationale for the latter process is shown in Figure 2. In an intermediate **16**, which is formed by coordination of sodium to *anti*-3,5-dihydroxy ester **1j** or **1y**, the axial ester group is exposed to the vicinity of $BH_4$ and should be reduced much faster than the ester group in an intermediate **17** (formed from **1i** or **1x**), in which the ester group is located apart from $BH_4^-$. A borate intermediate (**18**) is also likely.[28]

## Experimental Section

Melting points were determined in capillary tubes with a Büchi apparatus and were not corrected. Unless otherwise specified, short-path (bult-to-bulb) distillations were carried out in a Kugelrohr apparatus. Microanalyses were performed by the Microanalysis Center of Kyoto University. Analyses agreed with the calculated values within ±0.3%. Infrared spectra were measured with a Hitachi Model EPI-G3 grating spectrophotometer. Proton magnetic resonance spectra were determined either at 60 MHz on a JEOL JNM-PMX60 instrument or at 90 MHz on a JEOL FX90Q instrument with tetramethylsilane as an internal standard. $^{13}C$ NMR spectra were determined at 22.4 MHz on a JEOL FX90Q instrument with tetramethylsilane as an internal standard. Mass spectra were measured either on a Hitachi Model RMU6C or on a JEOL D-300 instrument (high-resolution mass spectrophotometer).

**Solvents and Reagents.** Tetrahydrofuran was dried and distilled from benzophenone and sodium immediately prior to use under argon atmosphere. Dichloromethane, methyl acetate, methyl cyclohexanecarboxylate, and acetophenone were distilled over $P_2O_5$. Acrolein, methacrolein, croton aldehyde, and mesityl oxide were distilled over calcium chloride and kept under argon.

**General Procedure for Preparation of 4-Pentene-1,3-diols (1).** The reaction was carried out under argon, and all reagents were transferred via a syringe through a septum cap under argon atmosphere. Into a solution of diisopropylamine (1.1 equiv) in anhydrous THF (0.5 M solution) was added *n*-butyllithium (1.1 equiv in hexane solution) at −78 °C, and the mixture was stirred for 5 min at the same temperature. To the mixture was added an ester or ketone at −78 °C, and the mixture was stirred for 2 h at the same temperature. To the mixture was added quickly an unsaturated aldehyde (1.5 equiv). After being stirred at −78 °C for 3 min, the reaction mixture was quenched by addition of 1 N HCl at −78 °C and extracted with ether. After being washed with saturated NaCl and then with aqueous $NaHCO_3$, the extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent gave an aldol product as an oil. Into a suspension of lithium aluminum hydride (1–1.5 equiv) in ether was added the crude aldol product with stirring and cooling in an ice bath. After completion of the addition, the mixture was refluxed for 1 h, and then 15% aqueous NaOH[29] was added dropwise into the reaction mixture with stirring and cooling in an ice bath. After filtration of a dry granular precipitate, the filtrate was condensed to leave a colorless oil, which was purified either by distillation under reduced pressure or by column chromatography over silica gel to give an expected diol in 75–90% overall yield. **1e/1f**: 55:45 inseparable mixture ($LiAlH_4$ reduction). **1g/1h**: 58:42 inseparable mixture ($NaBH_4$ reduction). **1i/1j**: inseparable mixture, ratio dependent on the reduction conditions (Table II). **1k/1l**: inseparable mixture, corresponding diastereomeric mixture of aldols is separable (syn aldol, $R_f$ 0.47, anti aldol, $R_f$ 0.38; benzene–ethyl acetate, 10:1). **1m/1n**: 55:45 inseparable mixture ($NaBH_4$ reduction). **1p/1q**: 55:45 inseparable mixture ($LiAlH_4$ reduction). **1r/1s**: 57:43 inseparable mixture ($LiAlH_4$ reduction). **1t/1u**: 50:50 inseparable mixture ($NaBH_4$ reduction).

**Ethyl *syn*-3,5-dihydroxy-6-heptenoate (1i)**: obtained selectively in 50% yield by the reduction of ethyl 3-oxo-5-hydroxy-6-heptenoate (**14**, R = H) with $NaBH_4$ (2 equiv in ethanol at 40 °C for 50 min); IR (neat film) 3380 (s), 2950 (m), 1720 (s), 1640 (w), 1165 (m), 1060 (m), 1020 (m), 990 (m), 920 (m), 850 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.28 (t, $J$ = 7.1 Hz, 3 H), 1.68 (m, 2 H), 2.50 (d, $J$ = 6.3 Hz, 2 H), 4.08 (q, $J$ = 7.1 Hz, 2 H), 4.37 (m, 2 H), 5.0–5.4 (m, 2 H), 5.89 (ddd, $J$ = 5.6, 10.0, 17.1 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.8, 41.7, 42.3, 60.4, 67.7, 72.1, 114.3, 140.1, 172.0.

**Ethyl *anti*-3,5-dihydroxy-6-heptenoate (1j)**: obtained in a pure state as the residue of the iodoetherification of a mixture of **1i** and **1j** (Table I, entry 12); IR (neat film) 3400 (s), 1720 (s), 1245 (m), 1165 (m), 1060 (m), 990 (w), 925 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.27 (t, $J$ = 7.08 Hz, 3 H), 1.72 (m, 2 H), 2.50 (d, $J$ = 5.86 Hz, 2 H), 4.17 (q, $J$ = 7.08 Hz, 2 H), 4.42 (m, 2 H), 5.04–5.41 (m, 2 H), 5.93 (ddd, $J$ = 5.6, 10.0, 17.3 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 14.1, 41.4, 41.8, 60.6, 65.4, 69.2, 114.3, 140.5, 172.5.

**3,5-*syn*-1,3,5-Trihydroxy-6-isopropyl-6-heptene (15x)**: oil; IR (neat film) 3320 (s), 2950 (s), 1620 (w), 1100 (m), 1060 (s), 900 (m), 850 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.06 (d, $J$ = 6.6 Hz, 6 H), 1.47–1.84 (m, 4 H), 2.27 (sep, $J$ = 7.1 Hz, 1 H), 3.68–3.93 (m, 2 H), 3.93–4.51 (m, 2 H), 4.90 (s, 1 H), 5.09 (s, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 22.45, 23.05, 30.17, 38.91, 42.80, 60.52, 71.77, 74.70, 107.03, 158.62.

**3,5-*anti*-1,3,5-Trihydroxy-6-isopropyl-6-heptene (15y)**: oil; IR (neat film) 3350 (s), 2980 (s), 1650 (m), 1100 (m), 1070 (s), 905 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.05 (d, $J$ = 6.6 Hz, 6 H), 1.52–1.87 (m, 4 H), 2.21 (sep, $J$ = 7.1 Hz, 1 H), 3.65–3.93 (m, 2 H), 3.93–4.29 (m, 1 H), 4.29–4.54 (m, 1 H), 4.94 (s, 1 H), 5.12 (s, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 22.27, 23.05, 30.23, 38.67, 42.26, 60.34, 67.64, 70.69, 106.43, 158.51.

***cis*-1-Phenyl-4-hexene-1,3-diol (1t, 1u).** Crude 2-butynaldehyde, prepared by treatment of 2-butyn-1-ol (50 mmol) with activated $MnO_2$ (44.8 g, Aldrich)[30] in 60 mL of dry dichloromethane at an ambient temperature for 2 h under argon followed by filtration of inorganics and distillation of the solvent under argon in the presence of a small amount of hydroquinone monomethyl ether, was reacted with the lithium enolate of acetophenone as described above to give 1-phenyl-1-oxo-3-hydroxy-4-hexyne ($R_f$ 0.4, benzene–ethyl acetate, 8:1) in 20% yield. A diastereomeric pair of diols (*anti*- and *syn*-1-phenyl-4-hexyne-1,3-diols: 1:1 mixture; $R_f$ 0.38 and 0.30, benzene–ethyl acetate, 2:1), obtained quantitatively by the reduction of 1-phenyl-1-

(27) Apparently this is not the case. This assumption is made just to demonstrate to what extent the second reduction contributes to the selective formation of *syn*-1,3-diols.

(28) (a) Baker, R.; Ravenscroft, P. D.; Swain, C. J. *J. Chem. Soc., Chem. Commun.* **1984**, 74. (b) Ibuka, T.; Chu, G. N. *Chem. Pharm. Bull.* **1986**, *34*, 2380.

(29) Mičović, V. M.; Mihailović, M. L. J. *J. Org. Chem.* **1953**, *18*, 1190.

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oxo-3-hydroxy-4-hexyne with $NaBH_4$ (1 equiv) in ethanol at an ambient temperature for 2 h, was hydrogenated separately over Lindler catalyst (0.36 g/g of substrate)[31] in ethanol (room temperature, 1 atm $H_2$ for ca. 20 min) to give **1t** or **1u** in a quantitative yield. **1t**: IR (neat film) 3300 (s), 3000 (w), 1650 (w), 1600 (w), 1490 (m), 1055 (s), 910 (m), 845 (m), 750 (m), 725 (w), 690 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.66 (d, $J$ = 5.4 Hz, 3 H), 1.7–2.2 (m, 2 H), 4.6–5.1 (m, 2 H), 5.40 (m, 2 H), 7.32 (s, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.0 (Me), 45.3 ($C_2$), 67.5 ($C_3$), 74.0 ($C_1$), 125.5, 125.6, 127.1, 128.1, 132.8, 144.3. **1u**: IR (neat film) 3300 (s), 3000 (w), 1650 (w), 1600 (w), 1490 (m), 1040 (s), 950 (m), 920 (m), 860 (m), 795 (w), 755 (m), 730 (w), 695 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.58 (d, $J$ = 5.1 Hz, 3 H), 1.93 (t, $J$ = 5.9 Hz, 2 H), 4.71 (q, $J$ = 5.9 Hz, 1 H), 5.02 (t, $J$ = 5.9 Hz, 1 H), 5.54 (m, 2 H), 7.33 (s, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 12.9 (Me), 44.7 ($C_2$), 64.8 ($C_3$), 71.1 ($C_1$), 125.4, 125.5, 126.9, 128.1, 132.7, 144.3; mass spectrum, $m/z$ (relative intensity) 192 (M, 0.3), 174 (7.1), 159 (7.8), 149 (8.9), 107 (48), 105 (48), 104 (100), 58 (69).

**General Procedure for Iodoetherification. Method A.** To a stirred mixture of 4-pentene-1,3-diol (**1**) and $NaHCO_3$ (2 equiv) in $Et_2O$–$H_2O$ (5 mL–2 mL/mmol of the substrate) was added iodine (1.2 equiv) at 0 °C. The mixture was stirred for the period of time indicated in Table I and Scheme I. To the resultant solution was added aqueous $Na_2SO_3$, and the solution was extracted with ethyl ether (20 mL × 2). The extracts were washed with 2 N HCl and then with saturated $NaHCO_3$. After the extracts were dried over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was subjected to preparative TLC or flash column chromatography over silica gel.

**Method B.** To a stirred solution of **1** in dichloromethane (5 mL/mmol of **1**) was added NIS (1.2 equiv) at −78 °C, and the mixture was stirred at the same temperature for the period of time indicated in Table I. To the resultant solution was added aqueous $Na_2SO_3$, and the solution was extracted with ethyl acetate (2×). The extracts were washed with 2 N HCl and then with saturated $NaHCO_3$.

**Method C.** To a stirred solution of **1d** in chloroform (5 mL/mmol of **1d**) was added iodonium dicollidine perchlorate (1.5 equiv)[32] at 0 °C, and the solution was stirred for 1 h at 0 °C. After the mixture was washed with aqueous $Na_2SO_3$ and $NaHCO_3$ and dried over $MgSO_4$, the solvent was evaporated, and the colorless residue was purified by flash column chromatography over silica gel to give a mixture of **2d** and **3d** (85:15) in 99% yield.

***cis*-2-(Iodomethyl)-3-hydroxytetrahydrofuran (2a)**: mp 44.5–45.5 °C (benzene–hexane); IR (KBr disk) 3400 (s), 2850 (m), 1410 (w), 1195 (w), 1130 (m), 1165 (m), 1040 (s), 1020 (s), 980 (m), 920 (m), 900 (w), 880 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.77–2.44 (m, 3 H), 3.29 (d, $J$ = 7.1 Hz, 2 H), 3.83–4.27 (m, 3 H), 4.52 (m, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 1.8 ($CH_2I$), 35.5 ($C_4$), 67.2 ($C_5$), 71.7 ($C_3$), 83.0 ($C_2$); mass spectrum, $m/z$ (relative intensity) 228 (M, 1), 101 (100), 58 (62), 57 (90). Anal. Calcd for $C_5H_9O_2I$: C, 26.33; H, 3.98; O, 14.03. Found: C, 26.25; H, 4.03; O, 13.98.

***cis*-2-Methyl-2-(iodomethyl)-3-hydroxytetrahydrofuran (2b)**: mp 47.5–48.5 °C (benzene–hexane); IR (KBr disk) 3350 (s), 2950 (m), 1440 (m), 1370 (m), 1280 (m), 1190 (s), 1110 (s), 1040 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.39 (s, 3 H), 1.77–2.53 (m, 2 H), 3.29 (d, $J$ = 12.7 Hz, 1 H), 3.40 (d, $J$ = 12.7 Hz, 1 H), 3.80–4.27 (m, 3 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 11.5 ($CH_2I$), 24.5 (Me), 34.5 ($C_4$), 65.9 ($C_5$), 76.3 ($C_3$), 83.4 ($C_2$); mass spectrum, $m/z$ (relative intensity) 242 (M, 1), 185 (45), 115 (100), 101 (49), 58 (73), 57 (64). Anal. Calcd for $C_6H_{11}O_2I$: C, 29.77; H, 4.58; O, 13.22. Found: C, 29.74; H, 4.62; O, 13.33.

***cis*-2-(Iodomethyl)-2-isopropyl-3-hydroxytetrahydrofuran (2c)**: mp 84.5–85.0 °C (benzene–hexane); IR (KBr disk) 3370 (s), 2950 (m), 1460 (w), 1430 (m), 1300 (m), 1200 (s), 1135 (m), 1110 (s), 1070 (m), 1035 (s), 975 (m), 905 (m), 805 (m), 780 (m); $^1H$ NMR ($CDCl_3$) $\delta$ 0.92 (d, $J$ = 6.9 Hz, 3 H), 0.94 (d, $J$ = 6.9 Hz, 3 H), 1.87–2.45 (m, 3 H), 3.46 (s, 2 H), 3.68–4.13 (m, 2 H, coalescing to two kinds of d, $J$ = 8.3 Hz and $J$ = 8.3 Hz, by irradiation at 2.16), 4.38 (dt, $J$ = 5.6 and 6.8 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 11.9 ($CH_2I$), 16.4 (Me), 17.2 ($CH_3$), 34.3, 36.0 ($C_4$, $CHMe_2$), 65.0 ($C_5$), 73.5 ($C_3$), 85.1 ($C_2$). Anal. Calcd for $C_8H_{15}O_2I$: C, 35.57; H, 5.60; O, 11.85. Found: C, 35.40; H, 5.63; O, 11.59.

***cis*-3-(Iodomethyl)-4-hydroxy-2-oxaspiro[4.5]decane (2d)**: mp 73–73.5 °C (benzene–hexane); IR (KBr disk) 3400 (s), 2900 (s), 2830 (m), 1450 (m), 1115 (m), 1010 (s), 915 (s), 820 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.26–1.7 (m, 10 H), 1.82 (d, 1 H, $J$ = 5.4 Hz, 1 H), 3.31 (m, 2 H), 3.77 (s, 2 H), 4.03 (dd, $J$ = 5.4, 3.4 Hz, 1 H, coalescing to a d, $J$ = 3.4 Hz, by irradiation at 1.82), 4.32 (ddd, $J$ = 3.4, 6.6, 8.1 Hz, 1 H, coalescing to a d, $J$ = 3.4 Hz, by irradiation at 3.31); $^{13}C$ NMR ($CDCl_3$) $\delta$ 2.6 ($CH_2I$), 22.7, 23.6, 26.0, 29.3, 33.9 ($C_6$–$C_{10}$), 47.9 ($C_5$), 77.2, 82.0 ($C_1$, $C_3$, $C_4$); mass spectrum, $m/z$ (relative intensity) 296 (M, 0.04), 169 (33), 125 (74), 97 (100). Anal. Calcd for $C_{10}H_{17}O_2I$: C, 40.55; H, 5.79; O, 10.81. Found: C, 40.27; H, 5.89; O, 10.64.

***cis,trans*-2-(Iodomethyl)-3-hydroxy-5-phenyltetrahydrofuran (2e)**: mp 57.0–58.0 °C (benzene–hexane); IR (KBr disk) 3350 (s), 2900 (m), 1300 (m), 1010 (s), 950 (s), 880 (s), 760 (s), 695 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, $D_2O$ added) $\delta$ 2.10 (ddd, $J$ = 3.9, 10.5, 13.1 Hz, 1 H, coalescing to a dd, $J$ = 3.9, 13.1 Hz, by irradiation at 5.34), 2.46 (dd, $J$ = 5.8, 13.1 Hz, 1 H, coalescing to a d, $J$ = 13.1 Hz, by irradiation at 5.34), 3.34 (d, $J$ = 7.6 Hz, 2 H), 4.44 (dd, $J$ = 3.2, 7.6 Hz, 1 H, coalescing to a d, $J$ = 3.2 Hz, by irradiation at 3.34), 4.66 (m, 1 H), 5.34 (dd, $J$ = 5.9, and 10.5 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 2.2 ($CH_2I$), 44.4 ($C_4$), 72.6 ($C_3$), 80.5 ($C_5$), 83.4 ($C_2$), 125.4, 127.5, 128.4, 142.2 (Ph); mass spectrum, $m/z$ (relative intensity) 304 (M, 3), 177 (7), 134 (100), 133 (42), 105 (47), 92 (69). Anal. Calcd for $C_{11}H_{13}O_2I$: C, 43.44; H, 4.31; O, 10.52. Found: C, 43.49; H, 4.39; O, 10.35.

***cis,cis*-2-(Iodomethyl)-3-hydroxy-5-phenyltetrahydrofuran (2f)**: mp 58.5–59.0 °C (benzene–hexane); IR (KBr disk), 3400 (s), 2920 (w), 2850 (w), 1495 (m), 1450 (m), 1415 (w), 1165 (m), 1110 (s), 1040 (s), 760 (s), 700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.95 (ddd, $J$ = 2.7, 6.6, 13.9 Hz, 1 H), 2.0 (m, 1 H), 2.66 (ddd, $J$ = 6.6, 8.4, 13.9 Hz, 1 H), 3.36 (d, $J$ = 7.1 Hz, 1 H), 4.07 (dd, $J$ = 3.7, 7.1 Hz, 1 H), 4.45 (m, 1 H, coalescing to a dd, $J$ = 3.7, 6.6 Hz, by irradiation at 1.95), 4.93 (dd, $J$ = 6.6, 8.4 Hz, 1 H, coalescing to a d, $J$ = 8.4 Hz, by irradiation at 1.95), 7.32 (m, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 1.1 ($CH_2I$), 43.4 ($C_4$), 72.3 ($C_3$), 79.9 ($C_5$), 83.1 ($C_2$), 125.7, 127.4, 128.2, 142.0 (Ph). Anal. Calcd for $C_{11}H_{13}O_2I$: C, 43.44; H, 4.31; O, 10.52. Found: C, 43.40; H, 4.32; O, 10.23.

***cis,trans*-2-(Iodomethyl)-3-hydroxy-5-*tert*-butyltetrahydrofuran (2g)**: IR (neat film) 3420 (br s) 2950 (s), 1190 (w), 1120 (m), 1100 (m), 1055 (s), 980 (w), 955 (m), 875 (m), 820 (w), 760 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.88 (s, 9 H), 1.51–1.95 (m, 3 H, incl OH), 3.26 (m, 2 H), 3.84–4.20 (m, 2 H), 4.51 (m, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 2.3 ($CH_2I$), 25.3 (Me), 33.9 ($CMe_3$), 36.0 ($C_4$), 72.7 ($C_3$), 82.9 ($C_2$), 86.9 ($C_5$).

***cis,cis*-2-(Iodomethyl)-3-hydroxy-5-*tert*-butyltetrahydrofuran (2h)**: mp 56.0–56.2 °C (hexane); IR (KBr disk) 3400 (br s), 2950 (s), 1170 (m), 1100 (m), 1040 (s), 960 (m), 930 (w), 875 (m), 840 (m), 800 (w), 755 (w) $cm^{-1}$; $^1H$ NMR ($C_6D_6$) $\delta$ 0.92 (s, 9 H), 1.07 (d, $J$ = 6.1 Hz, 1 H), 1.42 (ddd, $J$ = 3.0, 8.4, 13.9 Hz, 1 H), 1.77 (ddd, $J$ = 6.8, 7.7, 13.9 Hz, 1 H), 2.99–3.24 (m, 2 H), 3.30 (dd, $J$ = 7.7, 8.4 Hz, 1 H), 3.63 (dt, $J$ = 4.0, 7.3 Hz, 1 H), 4.01 (m, 1 H, coalescing to a ddd, $J$ = 3.0, 4.0, 6.8 Hz, by irradiation at 1.07); $^{13}C$ NMR ($CDCl_3$) $\delta$ 1.4 ($CH_2I$), 25.5 (Me), 33.1 ($CMe_3$), 36.3 ($C_4$), 72.1 ($C_3$), 82.0 ($C_2$), 86.1 ($C_5$). Anal. Calcd for $C_9H_{17}O_2I$: C, 38.04; H, 6.03; O, 11.26. Found: C, 37.84; H, 6.03; O, 11.27.

***cis,trans*-2-(Iodomethyl)-3-hydroxy-5-[(ethoxycarbonyl)methyl]tetrahydrofuran (2i)**: oil; IR (neat film) 3450 (s), 2950 (m), 1720 (s), 1180 (m), 1160 (m), 1090 (w), 1050 (m), 1025 (m), 970 (w), 950 (w), 920 (w), 875 (m), 850 (m), 815 (w), 720 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.26 (t, $J$ = 7.1 Hz, 3 H), 1.7–2.4 (m, 2 H), 2.5–2.8 (m, 2 H), 3.25 (m, 2 H), 4.15 (q, $J$ = 7.1 Hz, 2 H), 4.23 (m, 1 H), 4.58 (m, 1 H), 4.73 (m, 1 H, coalescing to a dd, $J$ = 3.7, 8.8 Hz, by irradiation at 2.65); $^{13}C$ NMR ($CDCl_3$) $\delta$ 1.7 ($CH_2I$), 14.1 (Me), 40.6 ($CH_2$-$C_5$), 41.1 ($C_4$), 60.5 ($CH_2CH_3$), 72.3, 75.1 ($C_3$, $C_5$), 82.5 ($C_2$).

***cis,cis*-2-(Iodomethyl)-3-hydroxy-5-[(ethoxycarbonyl)methyl]tetrahydrofuran (2j)**: oil; IR (neat film) 3430 (s), 2950 (m), 1720 (s), 1180 (s), 1100 (m), 1025 (s), 940 (w), 880 (m), 830 (w), 755 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.25 (t, $J$ = 7.1 Hz, 3 H), 1.92 (dd, $J$ = 5.6, 15.0 Hz, 1 H), 2.47 (ddd, $J$ = 6.3, 9.0, 15.0 Hz, 1 H), 2.72 (m, 2 H), 3.29 (m, 2 H), 3.93 (dd, $J$ = 2.9, 6.8 Hz, 1 H), 4.15 (q, $J$ = 7.1 Hz, 2 H), 4.1–4.5 (m, 2 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 1.2 ($CH_2I$), 14.0 (Me), 39.8 ($C_4$), 60.5 ($CH_2CH_3$), 72.0, 74.2 ($C_3$, $C_5$), 83.5 ($C_2$); high-resolution mass spectrum, calcd for M –

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$CH_2CO_2Et$ 226.9570, found $m/z$ (relative intensity) 296 (0.8), 269 (4.1), 251 (2.4), 226.9560 (27), 183 (17), 169 (21), 143 (75), 97 (100), 81 (50).

***cis,trans*-2-(Iodomethyl)-3-hydroxy-4-phenyltetrahydrofuran (2k)**: mp 100.0–100.5 °C (benzene–hexane); IR (KBr disk) 3440 (s), 1280 (m), 1185 (m), 1110 (m), 1080 (m), 1040 (s), 985 (m), 900 (m), 820 (m), 760 (s), 700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.20 (d, $J$ = 5.0 Hz, 1 H), 3.34 (m, 2 H), 3.44 (m, 1 H), 4.01 (dd, $J$ = 5.4, 9.0 Hz, 1 H), 4.15–4.52 (m, 4 H), 7.3 (s 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 1.8 ($CH_2I$), 54.4 ($C_4$), 72.3, 79.0 ($C_3$, $C_5$), 81.4 ($C_2$), 126.9, 127.2, 128.7, 139.6. Anal. Calcd for $C_{11}H_{13}O_2I$: C, 43.44; H, 4.31; O, 10.52. Found: C, 43.19; H, 4.22; O, 10.67.

***cis,cis*-2-(Iodomethyl)-3-hydroxy-4-phenyltetrahydrofuran (2l)**: mp 103.5–104.0 °C (benzene–hexane); IR (KBr disk) 3400 (s), 2900 (m), 1600 (w), 1490 (m), 1470 (m), 1180 (m), 1110 (m), 1045 (m), 1025 (s), 990 (w), 940 (m), 900 (m), 870 (m), 805 (m), 760 (w), 710 (m), 700 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 3.12–3.75 (m, 3 H), 4.29–4.52 (m, 4 H), 7.31 (s, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 2.0 ($CH_2I$), 50.8 ($C_4$), 70.8, 73.3 ($C_3$, $C_5$), 83.7 ($C_2$), 127.3, 128.5, 128.6, 135.3. Anal. Calcd for $C_{11}H_{13}O_2I$: C, 43.44; H, 4.31; O, 10.52. Found: C, 43.23; H, 4.06; O, 10.69.

***cis,trans*-2-(Iodomethyl)-3-hydroxy-4-*tert*-butyltetrahydrofuran (2m)**: oil; IR (neat film) 3300 (s), 2900 (s), 1175 (w), 1090 (w), 1030 (s), 990 (s), 915 (s), 820 (w), 780 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.94 (s, 9 H), 1.73 (d, $J$ = 5.5 Hz, 1 H), 2.05 (dt, $J$ = 3.2, 8.6 Hz, 1 H), 3.22–3.56 (m, 2 H), 3.61 (t, $J$ = 8.6 Hz, 1 H), 3.82 (dt, $J$ = 4.6, 6.9 Hz, 1 H), 4.10 (t, $J$ = 8.6 Hz, 1 H), 4.23 (m, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 1.2 ($CH_2I$), 27.6 (Me), 31.0 ($CMe_3$), 60.2 ($C_4$), 68.2 ($C_5$), 74.2 ($C_3$), 83.1 ($C_2$); high-resolution mass spectrum, calcd for M – I 157.1227, found $m/z$ (relative intensity) 157.1219 (8.3), 113 (7.5), 101 (14), 85 (9.5), 69 (13), 57 (100).

***cis,cis*-2-(Iodomethyl)-3-hydroxy-4-*tert*-butyltetrahydrofuran (2n)**: oil; IR (neat film) 3450 (s), 2940 (s), 1170 (w), 1120 (m), 1050 (m), 1020 (m), 990 (m), 925 (m), 875 (w), 830 (m), 780 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.04 (s, 9 H), 1.60 (d, $J$ = 6.4 Hz, 1 H), 2.05 (dt, $J$ = 3.8, 10.0 Hz, 1 H), 3.15–3.38 (m, 2 H), 3.96–4.23 (m, 3 H), 4.40 (ddd, $J$ = 2.9, 3.8, 6.4 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 2.0 ($CH_2I$), 29.2 (Me), 31.0 ($CMe_3$), 54.6 ($C_4$), 68.9 ($C_5$), 73.4 ($C_3$), 83.4 ($C_2$).

***cis*-3-(1′-Iodoethyl)-4-hydroxy-2-oxaspiro[4.5]decane (2o)**: mp 64.0–65.0 °C (benzene–hexane); IR (KBr disk) 3450 (s), 2900 (s), 2830 (s), 1445 (m), 1435 (m), 1160 (w), 1120 (s), 1040 (s), 1020 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.34–1.67 (m, 10 H), 1.90 (s, 1 H), 2.01 (d, $J$ = 6.1 Hz, 3 H), 3.75 (d, $J$ = 8.0 Hz, 1 H), 3.85 (d, $J$ = 8.0 Hz, 1 H), 4.08–4.16 (m, 3 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 25.5 (CHI), 26.0 (Me), 22.5, 23.5, 29.1, 33.8 ($C_6$–$C_{10}$), 47.5 ($C_5$), 77.5 ($C_1$), 78.5 ($C_3$), 86.9 ($C_4$); mass spectrum, $m/z$ (relative intensity) 310 (M, 0.04), 183 (49), 155 (70), 57 (100). Anal. Calcd for $C_{11}H_{19}O_2I$: C, 42.59; H, 6.17; O, 10.32. Found: C, 42.47; H, 6.22; O, 10.17.

***cis,trans*-2-(Iodomethyl)-2-methyl-3-hydroxy-5-phenyltetrahydrofuran (2p)**: mp 77.5–78.5 °C (benzene–hexane); IR (KBr disk) 3400 (m), 3300 (m), 2950 (m), 1440 (m), 1080 (s), 1040 (s), 750 (s), 700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.56 (s, 3 H), 1.97–2.50 (m, 3 H), 3.30 (d, $J$ = 9.5 Hz, 1 H), 3.56 (d, $J$ = 9.5 Hz, 1 H), 4.34 (m, 1 H), 5.34 (dd, $J$ = 5.9, 10.0 Hz, 1 H), 7.32 (m, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 11.6 ($CH_2I$), 25.7 (Me), 43.1 ($C_4$), 80.1, 84.6 ($C_2$, $C_3$, $C_5$), 125.5, 127.3, 128.1, 141.8 (Ph); mass spectrum, $m/z$ (relative intensity) 318 (M, 0.6), 177 (m), 134 (100), 92 (43). Anal. Calcd for $C_{12}H_{15}O_2I$: C, 45.30; H, 4.75; O, 10.06. Found: C, 45.23; H, 4.74; O, 10.31.

***cis,cis*- and *cis,trans*-2-(Iodomethyl)-2-methyl-3-hydroxy-5-phenyltetrahydrofuran (mixture of 2q and 3q)**: oil; IR (neat film) 3400 (s), 2950 (m), 1600 (w), 1490 (m), 1450 (m), 1415 (m), 1375 (m), 1180 (m), 1090 (m), 1040 (s), 920 (m), 760 (s), 700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.46 (s, 3 H), 1.50 (s, 3 H), 1.84–2.17 (m, 1 H), 3.31–3.59 (m, 2 H), 3.99–4.59 (m, 1 H), 4.89–5.14 (m, 1 H), 7.33 (m, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 12.1 ($CH_2I$ for 2 q), 15.7 ($CH_2I$ for 3 q), 21.1 (Me for 3 q), 23.9 (Me for 2 q); mass spectrum, calcd for $C_{12}H_{15}O_2I$ 318.01351, found $m/z$ (relative intensity) 318.013 69 (M, 2), 177 (25), 134 (95), 105 (61), 92 (100).

***rel*-(1′*R*,2*S*,3*R*,5*S*)-2-(1′-Iodoethyl)-3-hydroxy-5-phenyltetrahydrofuran (2r)**: mp 118.0–118.5 °C (benzene–hexane); IR (KBr disk) 3400 (m), 2900 (m), 1490 (m), 1450 (m), 1360 (m), 1215 (m), 1115 (m), 1000 (m), 760 (s), 700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.88–2.21 (m, 1 H), 2.09 (d, $J$ = 6.6 Hz, 3 H), 2.46 (dd, $J$ = 5.6, 12.7 Hz, 1 H), 4.19–4.35 (m, 2 H), 4.67 (t, $J$ = 4.5 Hz, 1 H), 5.35 (dd, $J$ = 5.9, 10.3 Hz, 1 H), 7.29 (s, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 25.1 ($CH_2I$), 25.8 (Me), 44.0 ($C_3$), 74.1 ($C_3$), 78.4 ($C_5$), 80.6 ($C_2$), 125.2, 127.2, 128.2, 142.6 (Ph). Anal. Calcd for $C_{12}H_{14}O_2I$: C, 45.30; H, 4.75; O, 10.06. Found: C, 45.46; H, 4.69; O, 9.82.

***rel*-(1′*R*,2*S*,3*R*,5*R*)-2-(1′-Iodoethyl)-3-hydroxy-5-phenyltetrahydrofuran (2s)**: mp 103.0–103.5 °C (benzene–hexane); IR (KBr disk) 3450 (m), 2960 (m), 2910 (m), 2850 (m), 1600 (w), 1495 (m), 1370 (m), 1160 (m), 1090 (m), 1075 (m), 1050 (s), 1000 (m), 910 (m), 800 (w), 760 (m), 730 (m), 700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.85 (d, $J$ = 5.3 Hz, 1 H), 2.05 (m, 1 H), 2.08 (d, $J$ = 6.6 Hz, 3 H), 2.62 (ddd, $J$ = 6.3, 8.6, 15.2 Hz, 1 H), 3.96 (dd, $J$ = 3.2, 10.0 Hz, 1 H), 4.35 (dq, $J$ = 6.6, 10.0 Hz, 1 H, coalescing to a d, $J$ = 10.0 Hz, by irradiation at 2.08), 4.50 (m, 1 H), 4.98 (dd, $J$ = 6.1, 8.6 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 23.5 (CHI), 25.9 (Me), 43.1 ($C_4$), 73.9 ($C_3$), 80.3 ($C_5$), 88.7 ($C_2$), 125.8, 127.4, 128.3, 142.6 (Ph). Anal. Calcd for $C_{12}H_{14}O_2I$: C, 45.30; H, 4.75; O, 10.06. Found: C, 45.21; H, 4.71; O, 10.11.

***rel*-(2*R*,4*R*,5*R*,6*R*)-2-Phenyl-4-hydroxy-5-iodo-6-methyltetrahydropyran (4s)**: mp 78.8–80.4 °C (benzene–hexane); IR (KBr disk) 3400 (m), 2850 (m), 1500 (m), 1450 (m), 1380 (m), 1180 (w), 1130 (s), 1090 (s), 1070 (s), 1020 (m), 910 (m), 870 (m), 760 (m), 730 (m), 700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.55 (d, $J$ = 5.4 Hz, 3 H), 1.78 (dd, $J$ = 11.2, 13.2 Hz, 1 H), 2.31 (ddd, $J$ = 2.2, 4.6, 13.2 Hz, 1 H), 2.58 (d, $J$ = 2.7 Hz, 1 H), 3.59–4.02 (m, 3 H, by addition of $Eu(fod)_3$, these absorptions were separated and two of them were coalesced to a d, $J$ = 10.3 Hz, 1 H, and a t, $J$ = 10.3 Hz, 1 H, by irradiation at 1.55), 4.47 (dd, $J$ = 2.2, 11.2 Hz, 1 H), 7.32 (m, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 21.9 (Me), 42.4 ($C_3$), 46.8 ($C_5$), 74.6, 77.3 ($C_4$, $C_6$), 77.6 ($C_2$), 125.9, 128.2, 128.4, 140.7 (Ph).

***rel*-(1′*S*,2*S*,3*R*,5*S*)-2-(1′-Iodoethyl)-3-hydroxy-5-phenyltetrahydrofuran (2t as a 19:81 mixture with 3t)**: $^{13}C$ NMR ($CDCl_3$) $\delta$ 24.4 (Me), 24.8 (CHI), 45.4 ($C_4$), 71.4 ($C_3$), 77.9 ($C_5$), 88.5 ($C_2$).

***rel*-(1′*R*,2*R*,3*R*,5*S*)-2-(1′-Iodoethyl)-3-hydroxy-5-phenyltetrahydrofuran (3t as a 81:19 mixture with 2t)**: oil; IR (neat film) 3400 (s), 2900 (m), 1490 (m), 1450 (m), 1090 (m), 1050 (m), 1020 (m), 960 (m), 930 (w), 840 (w), 755 (m), 695 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.97 (d, $J$ = 7.08 Hz, 3 H), 2.13 (m, 2 H), 3.68 (dd, $J$ = 2.93, 3.42 Hz, 1 H), 4.2–4.5 (m, 2 H), 5.15 (dd, $J$ = 6.35, 9.52 Hz, 1 H), 7.35 (m, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 24.4 (Me), 29.2 (CHI), 44.2 ($C_4$), 76.0 ($C_3$), 80.2 ($C_5$), 90.5 ($C_2$), 125.9, 127.5, 128.2, 140.6 (Ph).

***rel*-(1′*R*,2*R*,3*R*,5*R*)-2-(1′-Iodoethyl)-3-hydroxy-5-phenyltetrahydrofuran (3u)**: oil; IR (neat film) 3350 (s), 1485 (m), 1435 (m), 1055 (s), 1015 (m), 980 (w), 950 (w), 900 (w), 805 (w), 750 (m), 690 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.78 (d, $J$ = 4.9 Hz, 1 H), 2.00 (d, $J$ = 7.08 Hz, 3 H), 2.0–2.24 (m, 1 H), 2.74 (td, $J$ = 6.6, 13.2 Hz, 1 H), 3.68 (dd, $J$ = 4.15, 5.60 Hz, 1 H), 4.42 (dq, $J$ = 4.15, 7.08 Hz, 1 H), 4.50 (m, 1 H), 5.77 (dd, $J$ = 6.6, 8.8 Hz, 1 H), 7.33 (m, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 24.6 (Me), 30.1 (CHI), 43.5 ($C_4$), 76.1 ($C_3$), 79.8 ($C_5$), 88.4 ($C_2$), 125.5, 127.4, 128.3, 142.1.

***rel*-(2*R*,4*R*,5*R*,6*S*)-2-Phenyl-4-hydroxy-5-iodo-6-methyltetrahydropyran (4u)**: mp 128.5–129.0 °C (benzene–hexane); IR (KBr disk) 3300 (s), 1450 (m), 1150 (m), 1130 (w), 1120 (m), 1070 (s), 1060 (m), 1040 (m), 1010 (m), 960 (m), 900 (w), 855 (m), 815 (w), 745 (s), 690 (s) $cm^{-1}$; $^1H$ NMR ($C_6D_6$) $\delta$ 1.50 (d, $J$ = 6.8 Hz, 3 H), 1.67 (m, 1 H), 2.18 (ddd, $J$ = 2.7, 4.4, 12.9 Hz, 1 H), 3.78 (m, 1 H), 4.07 (dd, $J$ = 4.9, 10.0 Hz, 1 H), 4.36 (dq, $J$ = 4.9, 6.8 Hz, 1 H), 4.62 (dd, $J$ = 2.7, 11.0 Hz, 1 H), 7.3 (s, 5 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 15.6 (Me), 41.7 ($C_5$), 42.6 ($C_3$), 68.7, 70.6, 73.6, 125.9, 127.7, 128.4, 140.9. Anal. Calcd for $C_{12}H_{15}O_2I$: C, 45.30; H, 4.75; O, 10.06. Found: C, 45.30; H, 4.70; O, 9.97.

***cis*-2,2-Dimethyl-3-iodo-4-hydroxytetrahydropyran (5v)**: oil; IR (neat film) 3400 (s), 2950 (s), 1455 (m), 1435 (m), 1380 (m), 1360 (m), 1220 (m), 1200 (m), 1180 (m), 1115 (s), 1075 (s), 950 (m), 900 (m), 760 (m), 675 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.39 (s, 3 H), 1.55 (s, 3 H), 1.77–2.01 (m, 2 H), 2.16 (d, $J$ = 5.3 Hz, 1 H), 3.6 (ddd, $J$ = 5.0, 5.0, 12.0 Hz, 1 H), 3.70 (m, 1 H), 4.0 (ddd, $J$ = 4.9, 6.8, 12.0 Hz, 1 H), 4.45 (d, $J$ = 3.1 Hz, 1 H); $^{13}C$ NR ($CDCl_3$) $\delta$ 27.2 (Me), 27.9 (Me), 32.9 ($C_5$), 52.7 ($C_3$), 57.9 ($C_6$), 68.3 ($C_4$), 74.4 ($C_2$).

***trans*-2,2-Dimethyl-3-iodo-4-hydroxytetrahydropyran (4v)**: IR (KBr disk) 3380 (s), 2950 (s), 2920 (m), 1360 (m), 1015 (s), 1075 (s), 760 (m), 665 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.28 (s, 3 H), 1.40 (s, 3 H), 1.37–1.66 (m, 2 H), 2.24 (br s, 1 H), 3.03–3.50 (m, 2 H,

coalescing to a d, $J$ = 12.5 Hz, by irradiation at 1.5), 3.57 (m, 1 H, coalescing to a d, $J$ = 10.5 Hz, by irradiation at 1.5), 3.40 (d, $J$ = 10.5 Hz, 1 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.9 (Me), 32.1 (Me), 37.1 ($C_5$), 52.5 ($C_3$), 60.1 ($C_6$), 70.7 ($C_4$), 76.9 ($C_2$).

***rel*-(3*S*,4*R*)-2,2-Dimethyl-3-iodo-4-hydroxy-4-methyltetrahydropyran (5w)**: mp 100–101 °C (benzene–hexane); IR (KBr disk) 3300 (s), 2940 (m), 1375 (m), 1360 (s), 1260 (m), 1220 (m), 1115 (s), 1060 (s), 1020 (w), 940 (w), 750 (s) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.31 (s, 3 H), 1.38 (s, 3 H), 1.64 (s, 3 H), 1.89 (m, 2 H), 3.8 (m, 1 H, coalescing to a d, $J$ = 11.7 Hz, by irradiation at 1.89), 4.0 (m, 1 H, coalescing to a d, $J$ = 11.7 Hz, by irradiation at 1.89), 4.16 (s, 3 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.1 (Me), 32.4 (Me), 35.4 (Me), 38.0 ($C_5$), 57.5 ($C_6$), 57.9 ($C_3$), 70.2, 75.5 ($C_2$, $C_4$); mass spectrum, $m/z$ (relative intensity) 270 (M, 0.2), 212 (25), 143 (20), 89 (82), 59 (100). Anal. Calcd for $C_8H_{15}O_2I$: C, 35.57; H, 5.60; O, 11.85. Found: C, 35.49; H, 5.63; O, 11.96.

**Preparation of the Trans-Enriched Mixture of *cis*- and *trans*-2-(Iodomethyl)-2-isopropyl-3-hydroxytetrahydrofurans 2s and 3s.** Into a stirred solution of pyridine (12 mmol) in dichloromethane (15 mL) was added chromium trioxide (6 mmol) dropwise at 0 °C under argon, and then the mixture was allowed to warm slowly to an ambient temperature. A mixture of **2s** and **3s** (93:7) dissolved in 2 mL of dichloromethane was added rapidly to the mixture at an ambient temperature, and the resultant mixture was stirred until TLC monitoring showed the complete disappearance of the starting material (ca. 70 min). To the resultant solution was added 2 N HCl, and the solution was extracted with ethyl ether (30 mL × 2). The ether extracts were washed with saturated $NaHCO_3$. After the mixture was dried over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was purified by column chromatography (silica gel, benzene) to give *rel*-(1′*R*,2*S*,5*R*)-2-(1′-iodoethyl)-3-oxo-5-phenyltetrahydrofuran as a single isomer in a quantitative yield. Into a stirred solution of sodium borohydride (0.6 mmol) in methyl alcohol (5 mL) was added a THF solution of the ketone obtained above at room temperature. After being stirred for 2 h, the resultant solution was diluted with water (10 mL) and extracted with ethyl ether (30 mL × 2). The ether extracts were dried over anhydrous magnesium sulfate, and the solvent was evaporated to give an oil, which was purified by flash column chromatography to give an inseparable mixture of **2s** and **3s** in a ratio of 1:2.5.

**Preparation of *cis*-2-(Iodomethyl)-3-benzoxytetrahydrofuran (Benzoate of 2a).** Into a stirred solution of **2a**, triethylamine (3 equiv), and 4-(dimethylamino)pyridine (0.1 equiv) in dry THF was added benzoic anhydride (1.5 equiv) at room temperature, and the mixture was stirred overnight. To the resultant solution was added 1 N HCl, and the solution was extracted twice with ethyl ether. The ether extracts were washed with saturated $NaHCO_3$ and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by flash column chromatography (silica gel, benzene) to give the benzoate of **2a** in a quantitative yield: oil; IR (neat film) 2970 (w), 2860 (w), 1720 (vs), 1600 (w), 1580 (w), 1445 (m), 1310 (m), 1270 (vs), 1175 (m), 1050 (s), 1020 (m), 895 (w), 800 (w), 710 (s) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.03–2.65 (m, 2 H), 3.30–3.38 (m, 2 H), 3.88–4.36 (m, 4 H), 5.66 (m, 1 H, coalescing to a d, $J$ = 3.9 Hz, by irradiation at 2.3), 7.27–8.10 (m, 5 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 0.5 ($CH_2I$), 33.9 ($C_4$), 67.1 ($C_5$), 74.7 ($C_3$), 81.9 ($C_2$), 128.5, 129.6, 133.3 (Ph), 165.6 (C=O).

**Preparation of *trans*-2-(Iodomethyl)-3-benzoxytetrahydrofuran (Benzoate of 3a).** The reaction was carried out under argon, and all reagents were transferred via a syringe through a septum cap under argon atmosphere. Into a solution of **2a**, $Ph_3P$ (1.1 equiv), and PhCOOH (1.1 equiv) in dry THF (0.1 M solution) was added slowly diethyl azodicarboxylate (DEAD; 1.1 equiv) at 0 °C. The mixture was stirred for 3 h at 0 °C and diluted with 1 N HCl, and the solution was extracted twice with ethyl ether. The ether extracts were washed with saturated $NaHCO_3$ and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by flash column chromatography (silica gel, benzene) to give the benzoate of **3a** quantitatively: oil; IR (neat film) 2950 (w), 2850 (w), 1715 (vs), 1600 (m), 1445 (m), 1365 (w), 1310 (m), 1270 (vs), 1210 (m), 1170 (m), 1150 (m), 1095 (m), 950 (w), 710 (m) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.01–2.61 (m, 2 H), 3.40 (d, $J$ = 5.4 Hz, 2 H), 3.85–4.28 (m, 3 H), 5.29 (m, 1 H, coalescing to a d, $J$ = 2.0 Hz, by irradiation at 2.3); $^{13}$C NMR ($CDCl_3$) $\delta$ 6.9 ($CH_2I$), 32.9 ($C_4$), 67.7 ($C_5$), 79.0, 83.3 ($C_2$, $C_3$), 128.4, 129.6, 133.3 (Ph), 166.0 (C=O).

**General Procedure for the Preparation of Acetonides 13 of Diastereomeric Mixtures of Diols 1.** A mixture of a diastereomeric mixture of diols, 2,2-dimethoxypropane (a large excess), and *p*-toluenesulfonic acid (a catalytic amount) was stirred at an ambient temperature for 2 days. Extraction with ether ether, washing with $NaHCO_3$, drying the extracts over anhydrous magnesium sulfate, and evaporation of the solvent provided a colorless oil. Two isomers were separated by flash column chromatography over silica gel (hexane–benzene gradient).

***cis*-2,2-Dimethyl-4-phenyl-6-isopropenyl-1,3-dioxacyclohexane (13p)**: mp 54–55 °C (hexane); IR (KBr disk) 2970 (m), 1650 (w), 1500 (w), 1380 (s), 1250 (s), 1200 (s), 1160 (s), 1070 (s), 1015 (m), 960 (s), 870 (s), 760 (s), 700 (s) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.54 (s, 3 H), 1.58 (s, 3 H), 1.58 (m, 2 H), 1.74 (s, 3 H), 4.40 (dd, $J$ = 3.4, 10.3 Hz, 1 H), 4.80–5.08 (m, 3 H), 7.33 (m, 5 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.2, 19.6, 30.2, 37.9, 71.4, 72.3, 98.9, 110.8, 125.7, 127.4, 128.2, 142.2, 144.9. Anal. Calcd for $C_{15}H_{21}O_2$: C, 77.55; H, 8.68. Found: C, 77.27; H, 8.70.

***trans*-2,2-Dimethyl-4-phenyl-6-isopropenyl-1,3-dioxacyclohexane (13q)**: IR (neat film) 2960 (m), 1650 (m), 1450 (w), 1375 (m), 1220 (s), 1160 (m), 1100 (m), 1070 (m), 700 (m) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.48 (s, 6 H), 1.79 (s, 3 H), 1.97–2.19 (m, 2 H), 4.30 (t, $J$ = 7.8 Hz, 1 H), 4.80–5.07 (m, 3 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.4, 24.7, 38.4, 68.5, 69.6, 100.7, 110.2, 125.8, 128.3, 127.2, 142.5, 145.0.

***cis*-2,2-Dimethyl-4-phenyl-6-vinyl-1,3-dioxacyclohexane (13e)**: IR (neat film) 2980 (m), 1500 (w), 1380 (s), 1255 (s), 1200 (s), 1165 (s), 1100 (m), 870 (m), 755 (m), 700 (s) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.54 (s, 3 H), 1.59 (s, 3 H), 1.54–1.79 (m, 2 H), 4.50 (m, 1 H, coalescing to a dd, $J$ = 3.2, 10.7 Hz, by irradiation at 5.99), 4.93 (dd, $J$ = 3.4, 11.0 Hz, 1 H), 5.04–5.40 (m, 2 H), 5.98 (ddd, $J$ = 5.4, 10.5, 17.3 Hz, 1 H), 7.34 (m, 5 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.6, 30.2, 38.9, 70.1, 71.1, 98.9, 115.1, 125.7, 127.4, 128.2, 138.4, 142.1.

***trans*-2,2-Dimethyl-4-phenyl-6-vinyl-1,3-dioxacyclohexane (13f)**: IR (neat film) 2980 (m), 1500 (w), 1450 (m), 1380 (s), 1220 (s), 1170 (m), 1065 (m), 750 (s), 700 (s) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.48 (s, 6 H), 2.07 (t, $J$ = 7.6 Hz, 2 H), 4.5 (q, $J$ = 7.3 Hz, 1 H), 4.93 (t, $J$ = 7.8, 1 H), 5.07–5.38 (m, 2 H), 5.98 (ddd, $J$ = 5.4, 10.3, 17.3 Hz, 1 H), 7.3 (m, 5 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 25.0, 25.5, 38.9, 67.9, 68.2, 100.6, 114.8, 125.8, 127.2, 128.3, 138.6, 142.4.

***trans*-2,2-Dimethyl-4-vinyl-5-*tert*-butyl-1,3-dioxacyclohexane (13n)**: oil; 2880 (s), 1640 (w), 1210 (m), 1170 (m), 1090 (m), 1020 (m), 925 (m), 880 (m) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 0.93 (s, 9 H), 1.38 (s, 3 H), 1.43 (s, 3 H), 1.59 (m, 1 H), 3.80 (m, 2 H), 4.22 (dd, $J$ = 7.6, 9.5 Hz, 1 H), 5.12–5.42 (m, 2 H), 5.92 (ddd, $J$ = 7.6, 9.8, 17.3 Hz, 1 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.0 (Me), 28.0 (Me), 28.4 (Me), 31.6 ($CMe_3$), 48.7 ($C_5$), 60.2 ($C_6$), 72.3 ($C_4$), 98.1 ($C_2$), 117.3, 140.4.

***cis*-2,2-Dimethyl-4-vinyl-5-*tert*-butyl-1,3-dioxacyclohexane (13m)**: oil; 2880 (s), 1640 (w), 1200 (m), 1140 (m), 1080 (m), 1010 (m), 920 (m), 880 (w), 860 (w), 820 nw) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.02 (s, 9 H), 1.41 (s, 6 H), 1.58 (m, 1 H, coalescing to a d, $J$ = 3.7 Hz, by irradiation at 3.97), 3.97 (m, 2 H), 4.58 (m, 1 H), 5.04–5.41 (m, 2 H), 6.19 (ddd, $J$ = 6.6, 10.0, 16.9 Hz, 1 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.6 (Me), 27.8 (Me), 29.6 (Me), 32.7 ($CMe_3$) 47.5 ($C_5$), 61.5 ($C_6$), 74.5 ($C_4$), 98.8 ($C_2$), 114.7, 138.8.

**Preparation of *rel*-(1*R*,5*S*,6*S*,8*S*)-3-(*N*-Phenylimino)-8-phenyl-5-methyl-2,7-dioxa-4-thiabicyclo[4.3.0]nonane (6r) and *rel*-(1*R*,5*S*,6*S*,8*S*)-3-Thioxo-4,8-diphenyl-5-methyl-2,7-dioxa-4-azabicyclo[4.3.0]nonane (7r).** Into a suspension of NaH (1.2 equiv) in dry THF was added a solution of **2r** and phenyl isothiocyanate (1.2 equiv) in dry THF at 0 °C under argon. The mixture was stirred at 0 °C for 4 h and then at an ambient temperature overnight. After addition of saturated NaCl, the mixture was extracted with ether (2×), and the extracts were dried over $MgSO_4$ and then condensed to give a yellow oil. Flash chromatography over silica gel ($R_f$ 0.45 (**2r**), 0.50 (**6r**), 0.25 (**7r**); benzene-ethyl acetate, 8:1) gave **6r** and **7r** in 37 and 16% yields, respectively.

***rel*-(1*R*,5*R*,6*S*,8*S*)-3-(*N*-Phenylimino)-8-phenyl-5-methyl-2,7-dioxa-4-thiabicyclo[4.3.0]nonane (6t), *rel*-(1*R*,5*R*,6*S*,8*S*)-3-thioxo-4,8-diphenyl-5-methyl-2,7-dioxa-4-azabicyclo[4.3.0]nonane (7t), and the isothiocyanate adduct**

**of 2t (8t) (5:22:73)** were obtained and isolated by the similar treatment of a mixture of **2t** and **3t** (19:81) in 81% yield. **6r**: mp 90.8–91.3 °C (hexane); IR (KBr disk) 1630 (s), 1590 (m), 1485 (m), 1440 (m), 1130 (s), 1090 (m), 1050 (m), 1010 (m), 975 (w), 950 (w), 920 (w), 910 (m), 850 (w), 840 (w), 810 (w), 780 (w), 765 (m), 745 (m), 695 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.50 (d, $J$ = 7.1 Hz, 3 H), 2.01–2.44 (m, 1 H, coalescing to a dd, $J$ = 5.7, 14.0 Hz, by irradiation at 5.36), 2.62–2.95 (m, 1 H, coalescing to a d, $J$ = 14.0 Hz, by irradiation at 5.36), 3.46 (dq, $J$ = 5.5, 7.1 Hz, 1 H), 4.71 (t, $J$ = 5.5 Hz, 1 H), 5.10 (t, $J$ = 6.0 Hz, 1 H), 5.36 (dd, $J$ = 5.9, 9.3 Hz, 1 H), 6.83–7.41 (m, 10 H). Anal. Calcd for $C_{19}H_{19}NO_2S$: C, 70.13; H, 5.88; N, 4.30; O, 9.83. Found: C, 70.13; H, 5.90; N, 4.60; O, 10.06. **7r**: mp 219.0–219.5 °C (benzene–hexane); IR (KBr disk) 1490 (m), 1460 (m), 1440 (s), 1200 (s), 1150 (m), 1050 (m), 950 (w), 935 (w), 865 (w), 830 (w), 780 (m), 765 (m), 750 (m), 700 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.17 (d, $J$ = 6.8 Hz, 3 H), 2.22 (ddd, $J$ = 4.4, 10.0, 13.9 Hz, 1 H), 2.94 (dd, $J$ = 5.6, 13.9 Hz, 1 H), 4.11 (dq, $J$ = 2.7, 6.8 Hz, 1 H), 4.68 (dd, $J$ = 2.7, 4.4 Hz, 1 H), 5.21 (t, $J$ = 4.4 Hz, 1 H), 5.42 (dd, $J$ = 5.6, 10.0 Hz, 1 H), 7.36 (m, 10 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 17.1 (Me), 42.9 ($C_9$), 55.0 ($C_5$), 78.8, 80.6, 82.1, 125.5, 127.9, 128.2, 128.3, 125.5, 141.0, 141.8, 188.5. Anal. Calcd for $C_{19}H_{19}NO_2S$: C, 70.13; H, 5.88; N, 4.30; O, 9.83. Found: C, 70.24; H, 5.83; N, 4.40; O, 9.97. **6t**: mp 116.0–117.0 °C (hexane); IR (KBr disk) 1640 (s), 1590 (m), 1120 (s), 1050 (m), 1015 (m), 970 (m), 905 (m), 750 (s), 690 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.40 (d, $J$ = 6.8 Hz, 3 H), 2.20 (ddd, $J$ = 5.9, 10.5, 13.9 Hz, 1 H), 2.76 (dd, $J$ = 4.6, 13.9 Hz, 1 H), 3.39 (dq, $J$ = 6.8, 9.5 Hz, 1 H), 4.45 (dd, $J$ = 5.1, 9.5 Hz, 1 H), 5.00 (dd, $J$ = 5.1, 5.9 Hz, 1 H), 5.22 (dd, $J$ = 4.6, 10.5 Hz, 1 H), 6.82–7.4 (m, 10 H); mass spectrum, $m/z$ (relative intensity) 325 (M, 70), 173 (48), 146 (43), 145 (46), 135 (43), 119 (66), 117 (77), 105 (100), 104 (95), 93 (67), 91 (52). **7t**: mp 201–202 °C (benzene–hexane); IR (KBr disk) 1490 (m), 1460 (m), 1195 (s), 1160 (m), 1070 (m), 765 (m), 750 (m), 700 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.42 (d, $J$ = 7.0 Hz, 3 H), 2.21 (ddd, $J$ = 3.9, 10.3, 14.2 Hz, 1 H), 2.96 (dd, $J$ = 5.6, 14.2 Hz, 1 H), 4.00 (dq, $J$ = 2.5, 7.0 Hz, 1 H), 4.60 (dd, $J$ = 2.5, 4.2 Hz, 1 H), 5.28 (dd, $J$ = 3.9, 4.2 Hz, 1 H), 5.45 (dd, $J$ = 5.6, 10.3 Hz, 1 H), 7.35 (s, 10 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 16.4 (M), 43.2 ($C_9$), 58.5 ($C_5$), 78.7, 80.5, 80.9, 125.4, 127.3, 127.8, 128.0, 128.5, 129.4, 140.8, 144.5, 186.0; high-resolution mass spectrum, calcd for $C_{19}H_{19}NO_2S$ 325.1136, found $m/z$ (relative intensity) 325.1120 (M, 39), 302 (71), 244 (18), 220 (60), 173 (30), 146 (31), 135 (22), 119 (23), 117 (28), 105 (100). **8t**: mp 126.0–127.0 °C (benzene–hexane); IR (KBr disk) 3200 (m), 1595 (m), 1550 (s), 1490 (m), 1200 (s), 1170 (m), 1115 (m), 1080 (m), 1040 (m), 1010 (m), 740 (s), 695 (m), 680 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.01 (d, $J$ = 7.1 Hz, 3 H), 2.41 (m, 2 H), 3.75 (dd, $J$ = 2.2, 2.9 Hz, 1 H), 4.08 (dq, $J$ = 2.9, 7.1 Hz, 1 H), 5.09 (t, $J$ = 8.1 Hz, 1 H), 5.75 (m, 1 H, coalescing to a dd, $J$ = 2.7, 3.4 Hz, by irradiation at 3.75), 7.35 (m, 10 H), 8.5 (s, 1 H). Anal. Calcd for $C_{19}H_{20}INO_2S$: C, 50.34; H, 4.45; N, 3.09; O, 7.06. Found: C, 50.49; H, 4.34; N, 2.79; O, 7.00.

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**Supplementary Material Available:** X-ray data for **5w**, including stereoscopic view and tables of non-hydrogen atom coordinates, non-hydrogen thermal parameters, and bond distances and angles (2 pages). Ordering information is given on any current masthead page.

# Consecutive Ring Closure and Neophyl Rearrangement of Some Alkenylaryl Radicals

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The endo cyclization products **4a**, **18a**, **18b**, **25b**, and **25c** obtained from the reaction of tributylstannane with the bromoarenes **1a**, **12a**, **12b**, **22b**, and **22c**, respectively, are formed, at least in part, by exo cyclization of the corresponding substituted aryl radicals followed by neophyl rearrangement of the initial products. Kinetic data show that the rearrangement is more rapid for the radicals **15a** and **15b** containing the naphthalene nucleus than it is for the benzenoid radicals **24b** and **24c** and is facilitated by the presence of the electron-attracting substituent in **3a**.

Interest in the ring closure of suitably constituted *o*-alkenylaryl or *o*-(alkenyloxy)aryl radicals has increased dramatically during recent years. The main thrust of these investigations has been twofold. On the one hand, they have been directed toward the determination of the rates and regiochemistry of such cyclizations and the factors which affect them.[1-5] On the other, there has been some attention given to the utility of aryl radical cyclization for the construction of bi- and polycyclic systems, many of which are related to important naturally occurring compounds.[6-13]

Results obtained in these laboratories[1-7,12,13] and elsewhere[8-11] indicate that most suitably constituted alkenylaryl or (alkenyloxy)aryl radicals, like their alkenyl radical counterparts,[14] undergo ring closure exclusively or pre-

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