tional Science Foundation (CHE-8312691) and the University of Cincinnati for the award of a fellowship to A. H. is gratefully acknowledged. In addition we thank the National Science Foundation for grants used to purchase the NMR (CHE-8102974) and mass spectrometry (PCM-8219912) facilities used in this research.

Registry No. 6, 107798-93-6; 7, 107798-94-7; 8, 103865-84-5; 9, 103865-85-6; 10, 107798-95-8; 12, 5257-24-9; 16, 103865-88-9; 18, 103865-91-4; 19, 103865-92-5; 20, 103865-90-3; 21, 103865-89-0; 22, 7600-00-2; 23, 6626-84-2; 24, 107798-96-9; 25, 107798-97-0; 26, 107798-98-1; 27, 107798-99-2; 28, 107799-00-8; 29, 107799-01-9; PTAD, 4233-33-4; $MeO_2CCH_2CO_2Me$, 108-59-8; BuSH, 109-79-5; $PhCH_2Br$, 100-39-0; Me_3SiCN, 7677-24-9; 4-phenylurazole, 15988-11-1; 2,3-dimethylindole, 91-55-4; 2-methylindole, 95-20-5; Meldrum's acid, 2033-24-1; dimedone, 126-81-8; (1-cyclohexen-1-yloxy)trimethylsilane, 6651-36-1; pyrrole, 109-97-7; cyclopentadiene, 542-92-7.

Stereocontrolled Route to 2,3,5-Trisubstituted Tetrahydrofurans. Intermediates for the Total Synthesis of Polyether Antibiotics†

Herbert Frauenrath* and Jan Runsink

Institut für Organische Chemie der Technischen Hochschule Aachen, Professor-Pirlet-Str. 1, D 5100 Aachen, FRG

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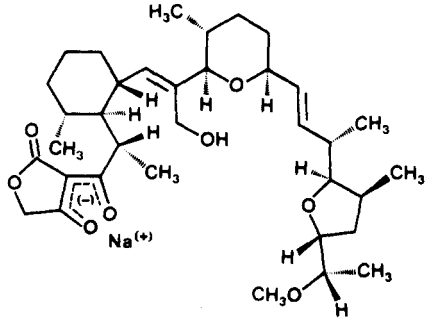
The stereoselective synthesis of diastereomers of 2,3,5-trisubstituted tetrahydrofurans has been accomplished by Lewis acid catalyzed vinyl acetal rearrangement. The reaction sequence starts with 4,7-dihydro-1,3-dioxepins **4**, which are isomerized to 4,5-dihydro-1,3-dioxepins **6**. The key step of the procedure is the stereocontrolled rearrangement of these mixed alkyl vinyl acetals **6**, followed by reduction. 2,3,5-Trisubstituted tetrahydrofurans are of general interest for the synthesis of polyether antibiotics.

Several naturally occurring compounds, especially a wide variety of important polyether antibiotics, contain tetrahydrofuran rings with a diversity of substitution patterns and stereochemistry.[1] Tetrahydrofuran rings with 2,3-cis and 2,5-trans relationship are common features in this class of compounds, as demonstrated with polyether antibiotic ICI 139603 produced by streptomyces longisporoflavus (**1**).[1,2]



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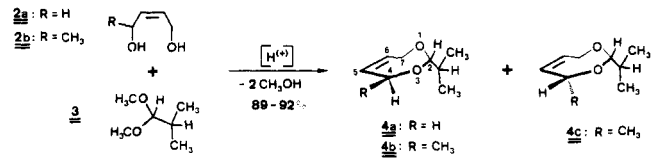
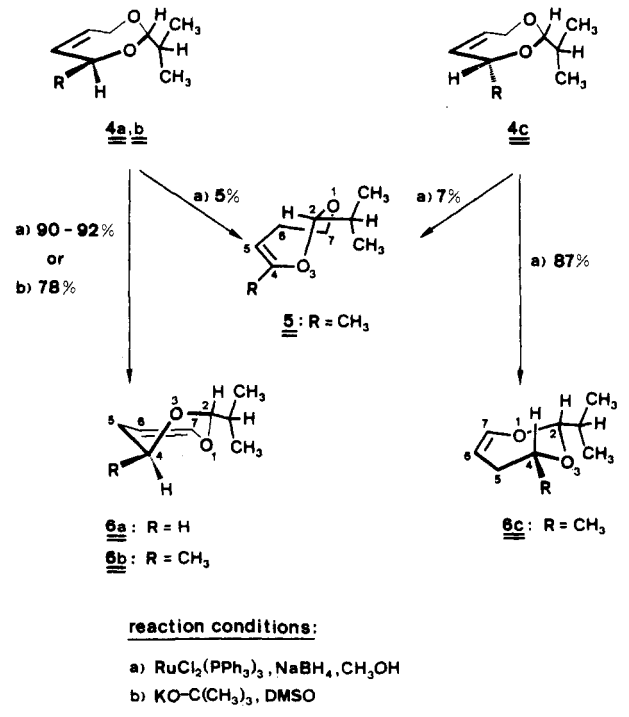
Although there are many routes to substituted tetrahydrofurans, only few proceed with high stereoselectivity.[3] Recently, we devised a new stereoselective preparation of 2,3-substituted tetrahydrofurans and 3,4-substituted 4-butanolides.[4] In this paper we now report the stereocontrolled synthesis of 2,3,5-substituted tetrahydrofurans starting with 2,4-substituted 4,7-dihydro-1,3-dioxepins. We used diastereomers of 2-isopropyl-4-methyl-4,7-dihydro-1,3-dioxepins **4b,c** as model compounds (Scheme I).[5] 2-Isopropyl-4,7-dihydro-1,3-dioxepin (**4a**) was used as starting material and transformed by the same reaction sequence for comparison and determination of the structures and conformations of the products.

Scheme I



Scheme II

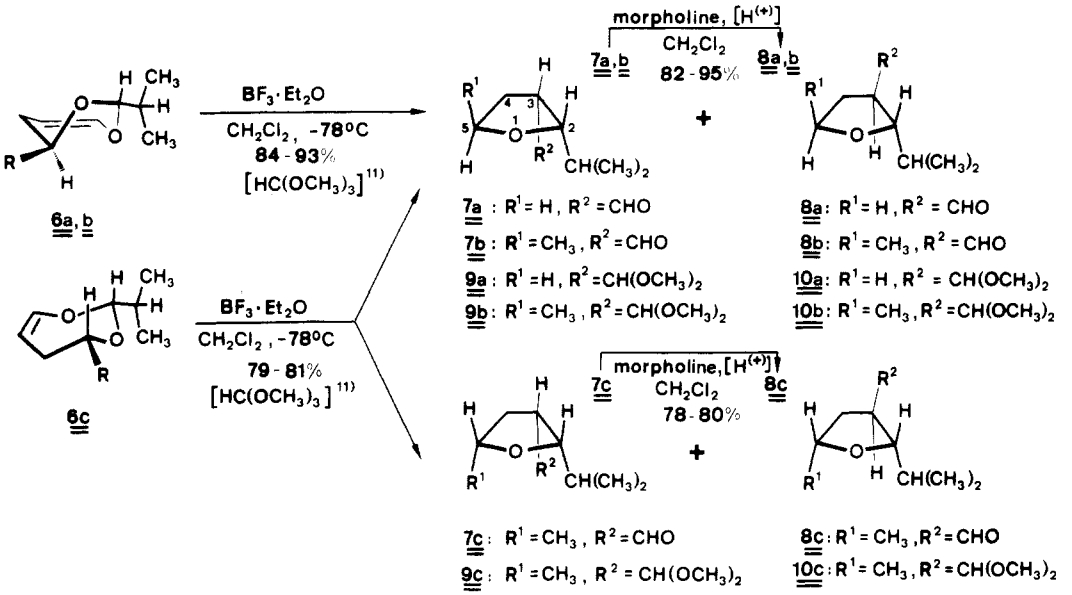


4a,b **4c** **5**: R = CH_3 **6a**: R = H **6b**: R = CH_3 **6c**: R = CH_3

† Presented in part at the VI International Conference on Organic Synthesis, Moscow, USSR, August 10-15, 1986, as a poster.

0022-3263/87/1952-2707$01.50/0

Scheme III



Results

Diastereomers **4b,c** are readily prepared as a 60:40 mixture by acid-catalyzed alcohol exchange of isobutyraldehyde dimethyl acetal (**3**) and *cis*-pent-2-ene-1,4-diol (**2b**) (Scheme I).[6] These diastereomers may be separated by distillation,[7] but a more convenient method to prepare the pure diastereomers **6b** or **6c** is effected by smooth isomerization of **4b,c** with $KOC(CH_3)_3$ at ambient temperatures (Scheme II).[8] The stereochemistry of **4b** and **4c** is deduced from their following transformations.

Double-bond isomerization of the 4,7-dihydro-1,3-dioxepins **4** is carried out in high yields (≥87%) with catalytic amounts of $RuCl_2(PPh_3)_3$ in CH_3OH activated in situ with $NaBH_4$ to give the catalytically more active hydridic complex (Scheme II).[9] Following this procedure, isomer **5** resulting from regioisomeric double-bond migration is only formed in low yield (≤7%) along with traces of hydrogenation products.

This isomerization is also effected by $KOC(CH_3)_3$, but in somewhat lower yield (78%). If this base-induced isomerization is performed with a mixture of **4b** and **4c** at ambient temperatures using equimolar amounts of base relative to **4b**, only **4b** is isomerized. By this method **4c** can be separated more easily from the excess isomer **4b**, since **4c** and **6b** or the following products of **6b** have more significant differences in their physical and chemical behavior.

Investigations on the conformation of **4b** show equatorial–equatorial positions for the substituents and the same boat conformation, as we already have found for 2-monosubstituted 4,5-dihydro-1,3-dioxepins.[10] So the substituents must have the trans configuration in **6b**. In **6c** the substituents have a cis relationship, and now the conformation changes over to a chair conformation, likewise having the substituents in equatorial positions (Scheme II).

Lewis acid catalyzed rearrangement of **6b** and **6c** at −78 °C affords 2,3,5-trisubstituted tetrahydrofurans with a 2,3-cis relationship[10] in high yields (**6a**, 93%; **6b**, 84%; **6c**, 79%) (Scheme III). Whereas ring contraction of **6b** leads to tetrahydrofurans **7b** and **8b** in a 89:11 ratio, the diastereoselectivity of the rearrangement of **6c** is lower, possibly due to more steric hindrance in the transition state or changed conformation. Surprisingly, the rearrangement of **6c** affords not only **7c** and **8c** but also **7b** and **8b**; e.g., when the rearrangement of **6c** is effected by $BF_3{\cdot}Et_2O$ at −78 °C, a **7c**:**8c**:**7b**:**8b** = 54:19:24:3 mixture is found. At 30 °C using CF_3CO_2D/CD_3CO_2D as catalyst (NMR experiment), the ratio is **7c**:**8c**:**7b**:**8b** = 33:24:32:11. These results indicate an inversion of configuration at center 4 in the rearrangement of **6c** (see also Discussion).[5] Since the 2,3,5-trisubstituted tetrahydrofurans also slowly change their relative configurations in the 2- and 3-positions due to epimerization, they are best trapped as the corresponding acetals **9** and **10** with trimethyl orthoformate and CH_3OH (Scheme III)[11] if they are not reduced immediately. The aldehydes **7** are epimerized nearly stereospecifically (98:2) to aldehydes **8** with a 2,3-trans relationship

(1) (a) Hamill, R. L.; Crandall, L. W. In *Antibiotics: Isolation, Separation, Purification*; J. Chromatography Library; Weinstein, M. J., Wagman, G. H., Eds.; Elsevier: Amsterdam, 1978; Vol. 15, pp 479–520. (b) Wierenga, W. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley-Interscience: New York, 1981; Vol. 4, pp 287–294, 299–325. (c) Westley, J. W., Ed. *Polyether Antibiotics: Naturally Occurring Acid Ionophores*; Marcel Dekker: New York, 1982; 2 Vols. (d) Paterson, J.; Mansuri, M. M. *Tetrahedron* **1985**, *41*, 3569.

(2) (a) Davies, D. H.; Snape, E. W.; Suter, P. J.; King, T. J.; Falshaw, C. P. *J. Chem. Soc., Chem. Commun.* **1981**, 1073. (b) Grandjean, J.; Laszlo, P. *Tetrahedron Lett.* **1983**, *24*, 3319. (c) Bulsing, J. M.; Laue, E. D.; Leeper, F. J.; Staunton, J.; Davies, D. H.; Ritchie, G. A. F.; Davies, A.; Davies, A. B.; Mabelis, R. P. *J. Chem. Soc., Chem. Commun.* **1984**, 1301.

(3) For example, see: (a) Bartlett, P. A. In *Selectivity–a Goal for Synthetic Efficiency*; Bartmann, W., Trost, B. M., Eds.; Verlag Chemie: Weinheim, 1984; Workshop Conferences Hoechst/Vol. 14, pp 1–19. (b) Michael, J. P.; Ting, P. C.; Bartlett, P. A. *J. Org. Chem.* **1985**, *50*, 2416. (c) Terlinden, R.; Boland, W.; Jaenicke, L. *Helv. Chim. Acta* **1983**, *66*, 466. (d) Batmangherlich, S.; Davidson, A. H. *Tetrahedron Lett.* **1983**, *24*, 2889. (e) Kula, J.; Gõra, J. *Liebigs Ann. Chem.* **1984**, 1860.

(4) Frauenrath, H.; Philipps, T. *Liebigs Ann. Chem.* **1985**, 1951.

(5) All products described in this work are racemic. For a better demonstration only one absolute configuration is depicted in the schemes.

(6) Azeotropic removal of water from the reaction mixture of isobutyraldehyde and **2b** in the presence of *p*-toluenesulfonic acid affords nearly the same ratio of diastereomers, but in lower yield. So the method of alcohol exchange of **3** and **2b** was preferred in this work.

(7) We used a spinning band column for rectification.

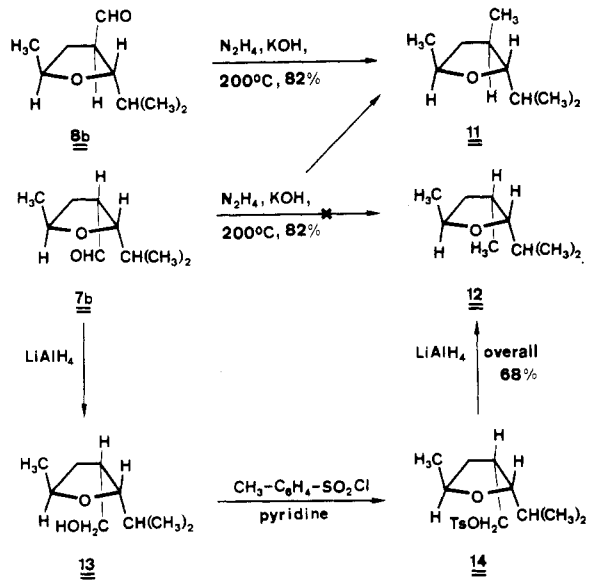
(8) Possibly the method of Noyori et al.[8b] may lead to one diastereomer with high selectivity. (b) Tsunoda, T; Suzuki, M; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.

(9) Frauenrath, H.; Philipps, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 274.

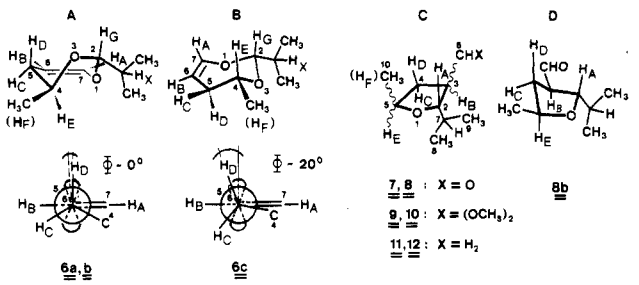
(10) Frauenrath, H.; Runsink, J.; Scharf, H.-D. *Chem. Ber.* **1982**, *115*, 2728.

(11) For the synthesis of acetals **9** the aldehydes **7** were trapped with trimethyl orthoformate and CH_3OH at −78 °C. Acetals **10** were synthesized by usual methods (compare also Experimental Section).

Scheme IV



Scheme V



by refluxing in CH_2Cl_2 in the presence of morpholine[4] without effecting the 2,5 stereochemical relationship (Scheme III).

Aldehydes **7** and **8** are reduced to the corresponding methyl derivatives by the Wolff–Kishner procedure.[12] Due to the strong basic conditions of this reaction, 2,3-cis configurated aldehydes like **7b** give 2,5-substituted 3-methyltetrahydrofurans **11**, likewise having a 2,3-trans relationship (Scheme IV). To achieve the synthesis of 2,5-substituted 3-methyltetrahydrofurans **12** with a 2,3-cis relationship, a three-step procedure is necessary involving $LiAlH_4$ reductions.[4] This procedure also proceeds with high stereoselectivity and high overall yields (Scheme IV). In principle also 2,5-substituted 3-methyltetrahydrofurans with a 2,5-cis relationship may be synthesized by the same procedures. But, since these structural features are not found in naturally occurring polyether antibiotics, these reductions were not performed in this work.

NMR data can only prove the relative configurations of 2,3,5-trisubstituted tetrahydrofurans, when the conformations of the 4,5-dihydro-1,3-dioxepins **6** are known.[10] ^{13}C NMR data reveal that in contrast to **6c**, **6a** and **6b** have a boat conformation with equatorial-like positions of the substituents (figure A, Scheme V). Then both the ^{13}C resonance of the methyl-bearing carbon and of the neighboring carbon atom are deshielded about 5–9 ppm in **4b** and **6b** with respect to **4a** and **6a**, whereas the signals of the remaining carbon atoms reveal only moderate shifts. These observations parallel those of cyclohexane[13] and 1,3-dioxane[14] derivatives.

The shielding of several signals in the ^{13}C NMR spectra of **4c** and **6c** with respect to those of **4b** and **6b** (up to 8 ppm) manifests considerable steric strain (γ effects of an axial-like methyl group and/or conformational distortion of the ring). Likewise there is no significant difference in ^1H chemical shifts and coupling constants for **6a** and **6b**. The large coupling constant J_{DE} = 10.4 Hz (Scheme V) shows an anti arrangement for these protons and thus an equatorial-like position for the methyl group (trans) in **6b**. The conformation of **6c** is a chair conformation again with both substituents in equatorial-like positions (cis) (figure B, Scheme V). Typical values in the ^1H NMR spectrum of compounds **6** are (i) the vicinal coupling constant J_{DE} = 10.4 Hz, (ii) the allylic coupling constants J_{AD} change from −2.9 Hz for **6b** to −2.2 Hz for **6c** and J_{AC} from approximately 0 Hz for **6b** to 0.9 Hz for **6c**, (iii) the geminal coupling constant J_{CD} changes from −16.4 Hz for **6b** to −17.1 Hz for **6c**, and (iv) the chemical shifts of the resonances of H_E and H_G are deshielded 1.03 and 0.90 ppm, respectively, in **6c** with respect to **6b**.

Thus H_D and H_E have positions anti to each other in **6b** as well as in **6c**, and the torsion angle Φ between the C_6–H_D bond (Scheme V) and the π orbital on C_5 changes from 0° for **6b**[10] to about 20° for **6c**,[15] which is only possible in the chair conformation. The deshielding of the H_E and H_G resonances in **6c** (Scheme V) must be attributed to van der Waals repulsion, since these protons come very close to each other in the chair conformation.

Since epimerization of 2,3-cis aldehydes **7b,c** leads to the 2,3-trans aldehydes **8b,c**,[4] only a proof of the 2,5 stereochemical relationship of one compound of **7b,c** or **8b,c** is necessary. The ^1H NMR spectroscopic data of **8b** reveal vicinal coupling constant values of $J_{B,C}$ = 4.0 Hz, $J_{B,D}$ = 10.3 Hz, $J_{C,E}$ = 5.9 Hz, and $J_{D,E}$ = 9.0 Hz. Therefore the protons B and D as well as the protons D and E (Scheme V, figure C) have an anti relationship in **8b**. Also the chemical shift of the resonance of proton D is shielded with respect to the corresponding value for **8a** due to the cis methyl group. Generally in this type of ring system the coupling constants do not reveal much information about the stereochemistry because of the conformational mobility of the five-membered ring. However, for **8b** the coupling constants are in accordance with a preferential envelope conformation (Scheme V, figure D), which has minimal steric repulsion between the substituents. The structural assignment of the acetals **9a–c** and **10a–c** follows from their chemical conversion. For **10b** the same reasoning with respect to the structures holds as that for **8b**.

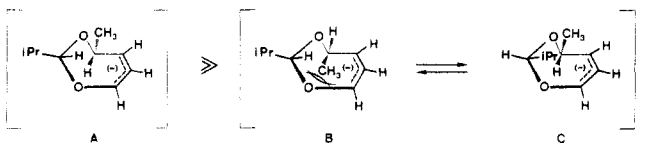
Discussion

The preparative results clearly show that 2,3,5-trisubstituted tetrahydrofurans with a 2,5-trans relationship are easily prepared by this method with the desired relative configuration at centers 2 and 3. On the other hand the synthesis of 2,3,5-trisubstituted tetrahydrofurans with a 2,5-cis relationship is also possible but more difficult due to a strong steric demand in the transition state of the rearrangement. But, since these tetrahydrofurans have not yet been found as structural features in naturally occurring polyether antibiotics, the presented method provides a convenient synthesis of subunits of kwown natural compounds.

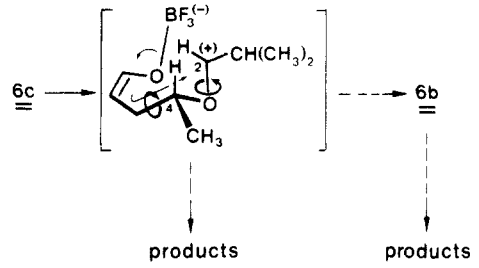
The fact that 2-isopropyl-4-methyl-4,7-dihydro-1,3-dioxepin (**4b**) with a trans relationship of the substituents is preferentially isomerized with respect to **4c** by use of a base can be explained by the formation of an allyl anion,

(12) Minlon, H. *J. Am. Chem. Soc.* **1949**, *71*, 3301.
(13) Christl, M.; Reich, H. J.; Roberts, J. D. *J. Am. Chem. Soc.* **1971**, 93, 3463.
(14) Kellie, G. M.; Ridell, F. G. *J. Chem. Soc. B* **1971**, 1030.
(15) Sternhell, S. *Q. Rev., Chem. Soc.* **1969**, *23*, 236.

Scheme VI



Scheme VII



which is believed to be an intermediate in the reaction mechanism. Proton abstraction and formation of the allyl anion forces centers 5, 6, 7, and 1 into a plane (Scheme VI), which is strongly disfavored for **4c** (Scheme VI, figure B) due to van der Waals repulsion of the cis configurated CH_3 group. The alternative conformation of the allyl anion (Scheme VI, figure C[16]) also disfavors the allyl anion intermediate because of van der Waals repulsion of an axial standing isopropyl group in this case.

The unexpected change of the 2,5-relationship in the rearrangement of **6c** might be explained by two mechanisms: (a) **6c** is transformed in an equilibrium to **6b** by rotation of center 2 of the zwitterionic intermediate, followed by conformational relaxation (Scheme VII, compare also ref 10) and (b) since **6c** has a chair conformation, there is no preference for a *lk* or *ul* coupling[17] of the zwitterionic intermediate in contrast to **6b**. In this case the isomer ratio of products 7 and 8 follows from simple rotation of both centers 2 and 4, respectively, in the transition state of the rearrangement of **6c**.

Experimental Section[18]

General Procedure for Alcohol Exchange of Isobutyraldehyde Dimethyl Acetal (3) and *cis*-But-2-ene-1,4-diol (2a) or *cis*-Pent-2-ene-1,4-diol (2b). Isobutyraldehyde dimethyl acetal (**3**) (71 g, 1.2 molar equiv) and 0.5 mol of **2a** or **2b** were stirred in vacuo (15 Torr) in the presence of *p*-toluenesulfonic acid at ambient temperatures for 24 h. Then the reaction mixture was diluted with 100 mL of ether and neutralized by washing twice with saturated aqueous K_2CO_3 solution. After drying (K_2CO_3) the solvent and excess **3** were removed by distillation. The crude products were purified by vacuum distillation through a 20-cm Vigreux column.

2-Isopropyl-4,7-dihydro-1,3-dioxepin (4a; 65.4 g, 92%) was obtained as a colorless liquid: bp 53–55 °C/12 Torr; IR 3030, 2980, 2960, 2930, 2910, 2880, 1470, 1445, 1390, 1375, 1365, 1260, 1205, 1120 cm^{-1}; ^1H NMR (CS_2) δ 5.59 (2, m, C=CH), 4.25, 4.00 (4, 2 m, OCH_2), 4.19 (1, d, J = 7.0 Hz, OCHO), 1.77 (1, m, isopropyl CH), 0.86 (6, d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (C_6D_6) (Scheme I) δ 130.0 ($C_{5/6}$), 108.99 (C_2), 65.60 ($C_{4/7}$), 32.00 (isopropyl CH), 18.18 (isopropyl CH_3). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.60; H, 9.90.

2-Isopropyl-4-methyl-4,7-dihydro-1,3-dioxepin (4b, 4c, 69.5 g, 89%) was obtained as a colorless liquid, consisting of a 60:40 mixture of **4b** and **4c** (GC): bp 63–66 °C/15 Torr. **(2*S**,4*S**)-2-Isopropyl-4-methyl-4,7-dihydro-1,3-dioxepin (4b)**: colorless liquid; bp 85–86.5 °C/100 Torr (spinning band column); IR 3010, 2995, 2985, 2970, 2955, 2940, 1475, 1465, 1450, 1400, 1375, 1370, 1130, 1070 cm^{-1}; ^1H NMR (CS_2) δ 5.49 (2, m, C=CH), 4.27 (1, m, CHO), 4.27, 3.92 (2, 2 m, CH_2O), 4.23 (1, d, J = 6.3 Hz, OCHO), 1.75 (1, m, isopropyl CH), 1.22 (3, d, J = 6.8 Hz, CH_3), 0.88, 0.84 (6, 2 d, J = 6.7 Hz, 2 isopropyl CH_3); ^{13}C NMR (C_6D_6) δ 135.13 (C_5), 129.18 (C_6), 108.21 (C_2), 74.43 (C_4), 63.94 (C_7), 32.46 (isopropyl CH), 21.89 (CH_3), 18.14, 18.02 (2 isopropyl CH_3). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.14; H, 10.35. **(2*S**,4*R**)-2-Isopropyl-4-methyl-4,7-dihydro-1,3-dioxepin (4c)**: colorless liquid; bp 87–88 °C/100 Torr (spinning band column); IR 3070, 3040, 2995, 2985, 2970, 2910, 2895, 2860, 2730, 1475, 1465, 1450, 1395, 1380, 1300, 1270, 1140, 1125, 1110 cm^{-1}; ^1H NMR (CS_2) δ 5.44 (2, m, C=CH), 4.50 (1, m, CHO), 4.24 (1, d, J = 7.5 Hz, OCHO), 4.14 (2, m, CH_2O), 1.80 (1, m, isopropyl CH), 1.17 (3, d, J = 6.9 Hz, CH_3), 0.88, 0.85 (6, 2d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (C_6D_6) δ 135.11 (C_5), 129.22 (C_6), 107.04 (C_2), 67.55 (C_7), 66.41 (C_4), 31.51 (isopropyl CH), 21.56 (CH_3), 18.72, 18.64 (2 isopropyl CH_3). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.23; H, 10.35.

General Procedure for the Double-Bond Isomerization of 4,7-Dihydro-1,3-dioxepins 4 with $RuCl_2(PPh_3)_3$. To a solution of 0.2 mol of 4,7-dihydro-1,3-dioxepin (**4**) in 50 mL of CH_3OH was added 0.2 mol % of $RuCl_2(PPh_3)_3$ under N_2 atmosphere. When treated with $NaBH_4$ (0.4 g), the temperature of the reaction mixture rose to about 50 °C. Then the solution was refluxed for 3 h. For workup the solvent was evaporated, and the crude products were purified by distillation under reduced pressure.

2-Isopropyl-4,5-dihydro-1,3-dioxepin (6a, 26.2 g, 92%) was obtained as a colorless liquid: bp 47–49 °C/14 Torr; IR 3045, 2960, 2930, 2880, 1655, 1645, 1475, 1460, 1425, 1385, 1370, 1350, 1290, 1275, 1265, 1225, 1190, 1120 cm^{-1}; ^1H NMR ABCDEFGXY$_6$ spectrum (Scheme V) (CS_2) δ_A 6.23, δ_B 4.68, δ_C 2.04, δ_D 2.38, δ_E 3.14, δ_F 4.03 δ_G 4.10, δ_X 1.77, δ_Y 0.91 (J_{AB} = 7.2, J_{AD} = −2.19, J_{AG} = 0.3, J_{BC} = 7.4, J_{BD} = 2.9, J_{BE} = −0.3, J_{BF} = 0.8, J_{CD} = −16.4, J_{CE} = 2.8, J_{CF} = 2.7, J_{DE} = 11.9, J_{DF} = 4.9, J_{EF} = −11.4, J_{EG} = 0.3, J_{GX} = 4.6, J_{XY} = 6.7 Hz); (C_6D_6) δ_A 6.32, δ_B 4.62, δ_C 1.76, δ_D 2.28, δ_E 2.99, δ_F 3.90, δ_G 4.13, δ_X 1.98, δ_Y 1.01; ^{13}C NMR (C_6D_6) δ 146.51 (C_7), 110.64 (C_2), 106.82 (C_6), 69.41 (C_4), 33.92 (isopropyl CH), 30.34 (C_5), 17.47, 17.29 (2 isopropyl CH_3) (Scheme V). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.63; H, 9.89.

(2*R,4*S**)-2-Isopropyl-4-methyl-4,5-dihydro-1,3-dioxepin (6b)** was obtained as a colorless liquid, containing 94% **6b** and 5% **5** (assigned by NMR). Redistillation (spinning band column) gave pure **6b** (28.1 g, 90%): bp 59–60 °C/15 Torr; IR 3055, 2980, 2940, 2890, 1610, 1605, 1475, 1465, 1450, 1405, 1390, 1380, 1370, 1345, 1305, 1285, 1235, 1195, 1120 cm^{-1}; ^1H NMR ABCDEF$_3$GXY$_6$ spectrum (Scheme V) (CS_2) δ_A 6.19, δ_B 4.56, δ_C 2.11, δ_D 2.11, δ_E 3.33, δ_F 1.21, δ_G 4.16, δ_X 1.81, δ_Y 0.90; (C_6D_6) δ_A 6.36, δ_B 4.50, δ_C 1.76, δ_D 2.12, δ_E 3.17, δ_F 1.08, δ_G 4.22, δ_X 2.01, δ_Y 1.04 (J_{AB} = 7.2, J_{AD} = −2.9, J_{AG} = 0.3, J_{BC} = 7.5, J_{BD} = 2.9, J_{BE} = −0.3, J_{CD} = −16.4, J_{CE} = 2.7, J_{DE} = 10.4, J_{EG} = 0.4, J_{EF} = 6.1, J_{GX} = 4.5, J_{XY} = 6.9 Hz); ^{13}C NMR (C_6D_6) δ 146.55 (C_7), 109.66 (C_2), 105.79 (C_6), 76.33 (C_4), 37.59 (C_5), 33.97 (isopropyl CH), 21.72 (CH_3), 17.66, 17.40 (2 isopropyl CH_3) (Scheme V). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.12; H, 10.27.

(2*R,4*R**)-2-Isopropyl-4-methyl-4,5-dihydro-1,3-dioxepin (6c).** A colorless liquid was obtained, consisting of 92% **6c** and 7% **5** (GC). Redistillation (spinning band column) gave pure **6c** (27.2 g, 87%): bp 62–63 °C/15 Torr; IR 3065, 2980, 2940, 2920, 2890, 1660, 1655, 1625, 1480, 1465, 1455, 1395, 1375, 1350, 1320, 1300, 1280, 1265, 1235, 1195, 1120 cm^{-1}; ^1H NMR ABCDEF$_3$GXY$_6$ spectrum (Scheme V) (CS_2) δ_A 6.13, δ_B 4.54, δ_C 1.94, δ_D 2.48, δ_E 4.36, δ_F 1.14, δ_G 5.06, δ_X 1.72, δ_Y 0.88 (J_{AB} = 6.7, J_{AD} = −2.2, J_{AG} = 0.4, J_{AC} = 0.9, J_{BC} = 7.5, J_{BD} = 3.0, J_{CD} = −17.1, J_{CE} = 3.0, J_{DE} = 10.4, J_{EF} = 6.4, J_{GX} = 4.7, J_{XY} = 6.6 Hz); (C_6D_6) δ_A 6.24; δ_B 4.43, δ_C 1.66, δ_D 2.27, δ_E 4.41, δ_F 1.01, δ_G 5.16, δ_X 1.92, δ_Y 1.01; ^{13}C NMR (C_6D_6) δ 147.49 (C_7), 103.84 (C_6), 103.84 (C_2), 74.02 (C_4), 33.44

(16) Figure C, Scheme VI, is the mirror image of the ring conformer of figure B.

(17) Seebach, D.; Prelog, V. *Angew. Chem.* **1982**, *94*, 696.

(18) General procedures: IR spectra were recorded on a Perkin-Elmer Model 377 instrument. Spectra were measured on neat liquids as thin films. ^1H NMR spectra were recorded on a Varian EM 390 instrument. Me_4Si was used as internal standard. ^{13}C NMR spectra were recorded on a Varian CFT 20 instrument. Preparative HPLC purifications were performed on an Abimed Gilson Model 303 instrument using 7μ Lichrosorb Si 60, 2.2 × 26 cm prep. cartridges from Bischoff. Gas–space chromatography (GC) was performed on a Carlo Erba Model Fractovap 301 instrument equipped with a 5-m 5% Apiezon L on Gaschrom Q 80–100-mesh column. Solvents were purified by usual methods prior to use.

(isopropyl CH), 32.77 (C_5), 22.10 (CH_3), 17.32 (2 isopropyl CH_3) (Scheme V). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.12; H, 10.36.

Selective Isomerization of 4b with $KOC(CH_3)_3$. A 60:40 mixture of **4b** and **4c** (78 g, 0.5 mol) was dissolved in 100 mL of Me_2SO. After addition of 33.6 g of $KOC(CH_3)_3$ (1 molar equiv with respect to **4b**), the reaction mixture was stirred at ambient temperatures for 8 h. For workup the solution was poured into 200 mL of H_2O, and the aqueous phase was extracted three times with 100 mL of ether. The ethereal solution was washed with brine and dried (K_2CO_3). After filtration and evaporation of the solvent the crude product was purified by vacuum distillation. A colorless liquid (66 g) was obtained, consisting of unreacted **4c** and **6b** along with traces of **6c**. Redistillation (spinning band column) afforded **6b** (36.5 g, 78% with respect to $KOC(CH_3)_3$ and **4c** (21.9 g, 70%).

General Procedure for the Rearrangement of 4,5-Dihydro-1,3-dioxepins 6. **6** (0.1 mol) was dissolved in 100 mL of CH_2Cl_2 and cooled to −78 °C; 3 mL of BF_3·Et_2O were added, and the reaction mixture was stirred for another 3 h at −78 °C. Then the reaction mixture was poured into 100 mL of cold, saturated K_2CO_3 solution. After separation of the phases, the organic layer was washed again twice with saturated K_2CO_3 solution. The washings were extracted three times with 50 mL of CH_2Cl_2, and the combined organic layers were dried with $MgSO_4$. After filtration the solvent was evaporated at 20 °C, affording substituted tetrahydrofuran-3-carbaldehydes with a 2,3-cis relationship without further purification (when these products were distilled, a nearly 1:1 mixture of isomers **7** and **8** was found).

Rearrangement of 2-Isopropyl-4,5-dihydro-1,3-dioxepin (6a). The general procedure was followed. A 92:8 mixture (13.2 g, 93%) of **7a** and **8a** was obtained as a colorless liquid. **(2*S**,3*S**)-2-Isopropyltetrahydrofuran-3-carbaldehyde (7a).** An analytically pure sample was provided by HPLC: IR 2980, 2880, 2730, 1720, 1470, 1450, 1390, 1370, 1355, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) (Scheme V) δ 9.70 (1, d, J = 4.5 Hz, CHO), 4.11 (1, m, H_E), 3.77 (1, m, H_F), 3.47 (1, dd, J = 9.8, 5.5 Hz, H_A), 2.93 (1, m, H_B), 2.2 (2, m, $H_{C,D}$), 1.82 (1, m, isopropyl CH), 1.05, 0.96 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 88.13 (C_2), 52.40 (C_3), 26.76 (C_4), 66.68 (C_5), 200.52 (C_6), 29.30 (C_7), 20.73, 18.89 ($C_{8,9}$). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.50; H, 9.97.

Rearrangement of (2*R,4*S**)-2-Isopropyl-4-methyl-4,5-dihydro-1,3-dioxepin (6b).** The general method was followed. A 89:11 mixture (13.1 g, 84%) of **7b** and **8b** was obtained as a colorless liquid. **(2*S**,3*S**,5*S**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde (7b).** An analytically pure sample was provided by HPLC: IR ($CHCl_3$) 2970, 2930, 2870, 2720, 1725, 1470, 1450, 1385, 1095, 1025, 980, 915 cm^{-1}; ^1H NMR (CCl_4) (Scheme V) δ 9.57 (1, d, J = 4.8 Hz, CHO), 3.91 (1, ddq, J = 7.5, 7.2, 6.0 Hz, H_E), 3.40 (1, dd, J = 9.8, 6.0 Hz, H_A), 2.79 (1, dddd, J = 8.6, 6.0, 4.8, 3.9 Hz, H_B), 2.18 (1, ddd, J = 13.0, 8.6, 7.2 Hz, H_C), 1.87 (1, m, isopropyl CH), 1.68 (1, ddd, J = 13.0, 7.5, 3.9 Hz, H_D), 1.30 (3, d, J = 6.0 Hz, CH_3), 1.00, 0.92 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 87.99 (C_2), 53.27 (C_3), 34.02 (C_4), 74.46 (C_5), 200.60 (C_6), 29.08 (C_7), 20.86, 20.72, 18.73 (C_8, C_9, C_{10}). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.24; H, 10.35.

Rearrangement of (2*R,4*R**)-2-Isopropyl-4-methyl-4,5-dihydro-1,3-dioxepin (6c).** The general method was followed. A 54:19:24:3 mixture (12.3 g, 79%) of **7c**, **8c**, **7b**, and **8b** was obtained, which was not stable under purification conditions. The NMR data were obtained from this mixture. **(2*S**,3*S**,5*R**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde (7c):** ^1H NMR (CCl_4) δ 9.67 (1, d, J = 4.0 Hz, CHO), other signals superimposed by resonances of the other isomers; ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 86.04 (C_2), 53.86 (C_3), 35.20 (C_4), 73.72 (C_5), 200.60 (C_6), 29.78 (C_7), 18.92 (C_8, C_9), 22.13 (C_{10}).

General Method for Epimerization of Aldehydes 7. Aldehyde **7** (0.1 mol), obtained by the general method for the rearrangement of **6**, was dissolved in 50 mL of CH_2Cl_2. After addition of 10 mol % morpholine and 1 mol % *p*-toluenesulfonic acid, the solution was refluxed for 24 h. Workup was performed by washing with dilute acid and drying ($MgSO_4$). After evaporation of the solvent the crude products were purified by distillation.

(2*S,3*R**)-2-Isopropyltetrahydrofuran-3-carbaldehyde (8a).** The general procedure for epimerization was followed. A colorless liquid (13.5 g, 95%) was obtained, consisting of a 98:2 mixture of **8a** and **7a**: IR 2980, 2880, 2720, 1720, 1470, 1450, 1390, 1370, 1290, 1245, 1180, 1075, 985, 935, 920 cm^{-1}; ^1H NMR (Scheme V) δ 9.64 (1, d, J = 3.0 Hz, CHO), 3.8 (3, m, H_A, H_E, H_F), 2.80 (1, m, H_B), 2.2 (2, m, H_C, H_D), 1.80 (1, m, isopropyl CH), 0.97, 0.91 (6, 2d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) δ 84.10 (C_2), 54.63 (C_3), 27.84 (C_4), 67.26 (C_5), 199.61 (C_6), 32.50 (C_7), 18.65, 18.47 (C_8, C_9). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.51; H, 9.98.

(2*S,3*R**,5*S**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde (8b).** The general method for epimerization was follwed. A colorless liquid was obtained (14.1 g, 90%), consisting of a 98:2 mixture of **8b** and **7b**; IR ($CHCl_3$) 2980, 2940, 2880, 2735, 1725, 1475, 1455, 1390, 1290, 1265, 1205, 1100, 1030 cm^{-1}; ^1H NMR (CCl_4) (Scheme V) δ 9.59 (1, d, J = 2.5 Hz, CHO), 3.85 (1, ddq, J = 9.0, 5.9, 6.0 Hz, H_E), 3.67 (1, dd, J = 6.4, 6.2 Hz, H_A), 2.71 (1, dddd, J = 10.3, 6.4, 4.0, 2.5 Hz, H_B), 2.25 (1, ddd, J = −12.6, 5.9, 4.0 Hz, H_C), 1.53 (1, ddd, J = −12.6, 10.3, 9.0 Hz, H_D), 1.78 (1, m, isopropyl CH), 1.21 (3, d, J = 6.0 Hz, CH_3), 0.96, 0.91 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 83.86 (C_2), 54.71 (C_3), 34.86 (C_4), 74.62 (C_5), 199.51 (C_6), 32.72 (C_7), 18.53, 18.42 (C_8, C_9), 20.40 (C_{10}). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.25; H, 10.24.

(2*S,3*R**,5*R**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde (8c).** The general procedure for epimerization was followed. A colorless liquid (12.2 g, 78%) was obtained, consisting of a 77:17:2 mixture of **8c**, **8b**, and **7b**: ^1H NMR (CS_2) (Scheme V) δ 9.49 (1, d, J = 3.2 Hz, CHO), 4.03 (1, ddq, J = 8.5, 5.4, 6.0 Hz, H_E), 3.76 (1, dd, J = 7.3, 6.7 Hz, H_A), 2.70 (1, dddd, J = 9.0, 8.4, 6.7, 3.2 Hz, H_B), 2.10 (1, ddd, J = −12.4, 8.4, 5.4 Hz, H_D), 1.68 (1, m, isopropyl CH), 1.67 (1, ddd, J = −12.4, 9.0, 8.5 Hz, H_C), 1.18 (3, d, J = 6.0 Hz, CH_3), 0.91, 0.83 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 83.47 (C_2), 56.03 (C_3), 35.68 (C_4), 74.62 (C_5), 199.18 (C_6), 32.81 (C_7), 18.79, 18.20 (C_8, C_9), 20.67 (C_{10}).

General Procedure for the Formation of Acetals 9 with 2,3-Cis Relationship. **6** (0.1 mol) was dissolved in 100 mL of CH_2Cl_2 and cooled with stirring to −78 °C. After addition of 3 mL of BF_3·Et_2O, the mixture was stirred for another 2 h at −78 °C. Then 3 molar equiv of trimethyl orthoformate and 50 mL of CH_3OH were added at the same temperature, and after stirring for another 1 h, the solution was allowed to come to room temperature. The CH_2Cl_2 solution was washed twice with saturated K_2CO_3 solution and dried (K_2CO_3). After filtration and evaporation of the solvent the crude products were purified by distillation.

(2*S,3*S**)-2-Isopropyltetrahydrofuran-3-carbaldehyde dimethyl acetal (9a)** was obtained as a colorless liquid (16 g, 85 %), consisting of a 92:8 mixture of **9a** and **10a**. bp 83–85 °C/14 Torr; IR 2990, 2960, 2875, 2830, 1470, 1450, 1390, 1365, 1295, 1275, 1220, 1190, 1120, 1105, 1075, 1060, 985, 970 cm^{-1}; ^1H NMR (CS_2) (Scheme V) δ 4.23 (1, d, J = 7.8 Hz, OCHO), 3.6 (2, m, H_E, H_F), 3.20 (1, dd, J = 8.3, 5.4 Hz, H_A), 3.23, 3.17 (6, 2s, OCH_3); 2.30 (1, m, H_B), 1.80 (2, m, H_C, H_D), 1.69 (1, m, isopropyl CH), 0.87, 0.85 (6, 2d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (C_6/D_6) (Scheme V) δ 86.82 (C_2), 43.29 (C_3), 28.16 (C_4), 66.23 (C_5), 103.27 (C_6), 53.65, 50.75, (2 OCH_3), 29.24 (C_7), 20.67, 20.62 (C_8, C_9). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71. Found: C, 63.84; H, 10.65.

(2*S,3*S**,5*S**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde dimethyl acetal (9b)** was obtained as a colorless liquid (17.0 g, 84%), consisting of a 89:11 mixture of **9b** and **10b**: bp 96–98 °C/16 Torr; IR 2960, 2935, 2880, 2820, 1465, 1445, 1380, 1240, 1195, 1120, 1105, 1060 cm^{-1}; ^1H NMR (CCl_4) (Scheme V) δ 4.29 (1, d, J = 8.1 Hz, OCHO), 3.81 (1, tq, J = 7.2, 6.1 Hz, H_E), 3.28 (1 dd, J = 7.8, 5.5 Hz, H_A), 3.26, 3.17 (6, 2s, OCH_3), 2.37 (1, tt, J = 8.1, 5.5 Hz, H_B), 1.93 (1, ddd, J = −12.6, 8.1, 7.2 Hz, H_C), 1.75 (1, m, isopropyl CH), 1.49 (1, ddd, J = −12.6, 7.2, 5.5 Hz, H_D), 1.17 (3, d, J = 6.1 Hz, CH_3), 0.92, 0.89 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 86.27 (C_2), 43.47 (C_3), 35.17 (C_4), 73.21 (C_5), 103.15 (C_6), 53.25, 49.94 (2 OCH_3), 28.60 (C_7), 20.63, 20.26 (C_8, C_9), 21.38 (C_{10}). Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.37; H, 11.00.

(2*S,3*S**,5*R**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde dimethyl acetal (9c)** was obtained as a colorless

liquid (16.4 g, 81%), consisting of a 60:17:10:10 mixture of **9c**, **10c**, **9b**, and **10b**: ^{1}H NMR (CCl_4) (Scheme V) δ 4.28 (1, d, J = 7.6 Hz, OCHO), 4.06 (1, m, H_E), 3.40 (1, dd, J = 8.4, 4.8 Hz, H_A), 3.27, 3.20 (6, 2 s, 2 OCH_3), 2.36 (1, m, H_B), 2.10 (1, ddd, J = -12.6, 7.0, 3.6 Hz, H_D), 1.73 (1, m, isopropyl CH), 1.42 (dt, J = -12.6, 7.5 Hz, H_C), 1.12 (3, d, J = 6.1 Hz, CH_3), 0.91, 0.86 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 85.18 (C_2), 43.62 (C_3), 36.12 (C_4), 72.53 (C_5), 102.36 (C_6), 53.33, 50.20 (2 OCH_3), 28.93 (C_7), 20.45, 20.20 (C_8, C_9), 22.64 (C_{10}).

General Procedure for the Formation of Acetals 10 with 2,3-Trans Relationship. 8 (0.1 mol), prepared by the general method for epimerization of aldehydes 7 to 8, was dissolved in 100 mL of CH_3OH. Then 0.3 mol of trimethyl orthoformate and 0.3 g of *p*-toluenesulfonic acid were added, and the mixture was refluxed for 5 h. After being cooled to room temperature, the solution was washed twice with saturated K_2CO_3 solution and dried (K_2CO_3). After filtration and evaporation of the solvent and excess trimethyl orthoformate the crude products were purified by distillation.

(2*S,3*R**)-2-Isopropyltetrahydrofuran-3-carbaldehyde dimethyl acetal (10a)** was obtained as a colorless liquid (17.1 g, 91%): bp 84-86 °C/16 Torr; IR 2960, 2940, 2880, 2830, 1465, 1450, 1390, 1365, 1260, 1215, 1190, 1120, 1075, 1060, 990, 900 cm^{-1}; ^{1}H NMR (CS_2) (Scheme V) δ 4.10 (1, d, J = 7.2 Hz, OCHO), 3.60 (2, m, H_E, H_F), 3.38 (1, t, J = 5.0 Hz, H_A), 3.25, 3.22 (6, 2 s, 2 OCH_3), 2.17 (1, m, H_B), 1.81 (2, t, J = 6.6 Hz, H_C, H_D), 1.64 (1, m, isopropyl CH), 0.88, 0.84 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (C_6D_6) (Scheme V) δ 85.75 (C_2), 44.53 (C_3), 28.71 (C_4), 67.16 (C_5), 106.66 (C_6) 54.23, 52.14 (2 OCH_3), 32.24 (C_7), 20.09, 17.60 (C_8, C_9). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71. Found: C, 63.74; H, 10.77.

(2*S,3*R**,5*S**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde dimethyl acetal (10b)** was obtained as a colorless liquid (16.6 g, 82%): bp 96-98 °C/16 Torr; IR 2960, 2930, 2880, 2830, 1465, 1450, 1390, 1385, 1365, 1190, 1120, 1105, 1080, 1065, 980, 910 cm^{-1}; ^{1}H NMR (CCl_4) (Scheme V) δ 4.15 (1, d, J = 7.2 Hz, OCHO), 3.82 (1, ddq, J = 9.6, 5.4, 6.0 Hz, H_E), 3.43 (1, dd, J = 5.0, 4.6 Hz, H_A), 3.27, 3.23 (6, 2s, 2 OCH_3), 2.18 (1, dddd, J = 9.6, 7.2, 5.0, 2.5 Hz, H_B), 1.90 (1, ddd, J = -12.5, 5.4, 2.5 Hz, H_C), 1.68 (1, m, isopropyl CH), 1.32 (1, ddd, J = -12.5, 9.6Hz, H_D), 1.14 (3, d, J = 6.0 Hz, CH_3), 0.90, 0.86 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 85.38 (C_2), 44.46 (C_3), 36.08 (C_4), 73.82 (C_5), 106.07 (C_6), 54.12, 51.77 (2 OCH_3), 32.25 (C_7), 19.77, 17.17 (C_8, C_9), 20.77 (C_{10}). Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.25; H, 10.92.

(2*S,3*R**,5*R**)-2-Isopropyl-5-methyltetrahydrofuran-3-carbaldehyde dimethyl acetal (10c)** was obtained as a colorless liquid (16.2 g, 80%), consisting of a 77:17:2 mixture of **10c**, **10b**, and **9b**: bp 96-100 °C/16 Torr; ^{1}H NMR (CCl_4) (Scheme V) δ 4.13 (1, d, J = 7.5 Hz, OCHO), 3.90 (1, m, H_E), 3.46 (1, t, J = 5.4 Hz, H_A), 3.26, 3.23 (6, 2 s, 2 OCH_3), 1.14 (3, d, J = 6.0 Hz, CH_3), 0.89, 0.86 (3, 2 d, J = 6.6 Hz, 2 isopropyl CH_3), other signals superimposed; ^{13}C NMR (CCl_4/C_6D_6) (Scheme V) δ 85.42 (C_2), 45.10 (C_3), 36.58 (C_4), 73.79 (C_5), 106.78 (C_6), 53.70, 51.41 (2 OCH_3), 31.66 (C_7), 20.14, 17.34 (C_8, C_9), 21.32 (C_{10}).

Wolff-Kishner Reduction of Aldehydes 7b and 8b. 7b or **8b**, 7.8 g (0.05 mol), 5 mL of $N_2H_4 \cdot H_2O$, and 5 g of KOH were dissolved in 25 mL of diethylene glycol and heated to 200 °C. When the N_2 evolution was completed, the mixture was cooled to room temperature and poured into cold water. The aqueous phase was extracted three times with ether, and the ethereal solution was washed with dilute HCl and saturated Na_2CO_3 solution and dried ($MgSO_4$). After filtration the solvent was distilled, and the crude products were purified by vacuum distillation.

(2*S,3*R**,5*S**)-2-Isopropyl-3,5-dimethyltetrahydrofuran (11)** was obtained as a colorless liquid (5.8 g, 82%): bp 34-35 °C/10 Torr; ^{1}H NMR ($CDCl_3$) (Scheme V) δ 4.02 (1, sextett, J = 6.0 Hz, H_E), 3.16 (1, t, J = 6.0 Hz, H_A), 2.3-1.5 (3, m, H_B, H_C, H_D), 1.18 (3, d, J = 6.0 Hz, CH_3), 1.02 (3, d, J = 6.0 Hz, CH_3), 0.95 (6, 2 d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR ($CDCl_3$) (Scheme V) δ 91.78 (C_2), 35.46 (C_3), 42.50 (C_4), 73.46 (C_5), 32.11 (C_7), 19.07, 18.25 (C_8, C_9), 21.17, 19.85 (C_6, C_{10}). Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.76. Found: C, 75.93; H, 12.71.

$LiAlH_4$ Reduction of Aldehyde 7b. Crude **7b**, 15.6 g (0.1 mol), obtained following the general method for the rearrangement of **6b**, was dissolved in 100 mL of anhydrous ether. Treatment with 0.1 mol of $LiAlH_4$ at -78 °C and usual workup gave the corresponding alcohol. Without isolation the crude product was dissolved in ether and treated with *p*-toluenesulfonic acid chloride in the presence of pyridine. After workup the reaction product was dissolved in ether and treated again with 0.1 mol of $LiAlH_4$. Workup gave **(2*S**,3*S**,5*S**)-2-isopropyl-3,5-dimethyltetrahydrofuran (12,** 9.6 g, 68%): bp 146-148 °C (spinning band column); ^{1}H NMR ($CDCl_3$) (Scheme V) δ 3.9 (1, m, H_E), 3.28 (1, dd, J = 6.0, 7.0 Hz, H_A), 2.3-1.5 (3, m, H_B, H_C, H_D), 1.20 (3, d, J = 6.0 Hz, CH_3), 1.02 (3, d, J = 6.0 Hz, CH_3), 0.95 (6, d, J = 6.6 Hz, 2 isopropyl CH_3); ^{13}C NMR ($CDCl_3$) (Scheme V) δ 90.51 (C_2), 37.53 (C_3), 44.33 (C_4), 74.35 (C_5), 32.11 (C_7), 18.97, 18.15 (C_8, C_9), 21.33, 19.35 (C_6, C_{10}). Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.76. Found: C, 75.94; H, 12.82.

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Registry No. **2a**, 6117-80-2; **2b**, 6117-82-4; **3**, 41632-89-7; **4a**, 5417-35-6; **4b**, 108008-25-9; **4c**, 108008-26-0; **5**, 108008-24-8; **6a**, 35174-08-4; **6b**, 108008-27-1; **6c**, 108008-28-2; **7a**, 108008-29-3; **7b**, 108034-74-8; **7b** (alcohol), 108008-39-5; **7b** (tosyl ether), 108008-40-8; **7c**, 108008-31-7; **8a**, 77734-06-6; **8b**, 108008-30-6; **8c**, 108008-32-8; **9a**, 108034-75-9; **9b**, 108008-35-1; **9c**, 108008-37-3; **10a**, 108008-34-0; **10b**, 108008-36-2; **10c**, 108008-33-9; **11**, 108008-38-4; **12**, 108034-56-6; $CH(OCH_3)_3$, 149-73-5; 4-$H_3CSO_2C_6H_4COCl$, 98-59-9.

Polycyclic Amines via Novel [2 + 2] Cycloaddition of Imine[1]

B. Kh. Rammash, J. L. Atwood,[2] J. A. Weeks,[2] and J. L. Wong*

Department of Chemistry, University of Louisville, Louisville, Kentucky 40292

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2,3,4,5,5-Pentachloro-1-azacyclopentadiene (1) has been shown to react differently with enes and dienes to form some unusual [4 + 2] cycloadducts. A [2 + 2] adduct is now isolated from a reaction of 1 with norbornadiene in acetonitrile. In addition to the previously reported azaaldrin (2) and isoazaaldrin (3) as products, a urazole-type adduct was identified by spectroscopic and X-ray diffraction studies to be **2b**. The mechanism of this new adduct formation via a novel [2 + 2] ene-imine reaction is discussed.

The construction of polycyclic compounds containing nitrogen via [4 + 2] cycloaddition of monoazadienes has made great strides in recent years. The 2-aza dienes have proved to be versatile addends in forming tetrahydro-

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