THE JOURNAL OF Organic Chemistry

VOLUME 48, NUMBER 17

AUGUST 26, 1983

Reaction of Enol Ethers with Formaldehyde and Organoaluminum Compounds

Barry B. Snider* and Gary B. Phillips

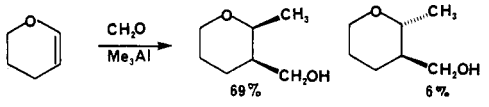
Department of Chemistry, Brandeis University, Waltham, Massachusetts 02254

Received October 26, 1982

Reaction of formaldehyde and trimethylaluminum with an enol ether derived from an aldehyde gives the adduct resulting from addition of hydroxymethyl and methyl groups to the enol ether double bond. The threo isomer is formed selectively (90–95%) from either isomer of the starting enol ether. The mechanism of this reaction is discussed. Reaction of formaldehyde and trimethylaluminum with an enol ether derived from a ketone gives the ene adduct, which should allow selective sequential reaction at the α and α' positions of ketones.

The acid-catalyzed addition of aldehydes to alkenes, the Prins reaction, has been extensively investigated as a carbon–carbon bond forming reaction.[1] More recently, Lewis acid catalyzed reactions of aldehydes with silyl enol ethers have been developed as an attractive variant of the crossed aldol reaction.[2] We have found that Me_2AlCl, which is a proton scavenger as well as a Lewis acid, is a useful catalyst for the Prins reaction.[3] With use of Me_2AlCl, ene adducts can now be obtained in good yield from aliphatic and aromatic aldehydes and reactive alkenes and from formaldehyde with all alkenes.

Recently, we reported that $CH_2O{\cdot}Me_3Al$ reacts with electron-rich alkenes to give a zwitterion that reacts further to give homoallylic alcohols (ene adducts), allylic alcohols, and the product of cis addition of hydroxymethyl and methyl groups to the double bond.[4] For instance, dihydropyran reacts with $CH_2O{\cdot}Me_3Al$ to give a 75% yield of a 92:8 cis–trans mixture of 3-(hydroxymethyl)-2-methyltetrahydropyran (eq 1). Since 1,3-dihydroxy com-

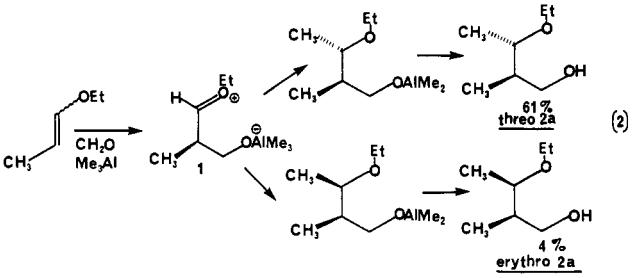


(1)

pounds are of synthetic utility, we decided to explore the reactions of acyclic enol ethers with formaldehyde–alkylaluminum complexes.

Results

Reaction of ethyl propenyl ether, as a 78:22 cis–trans mixture, with 2 equiv of paraformaldehyde and 2 equiv of Me_3Al at 0 °C in CH_2Cl_2 (Table I, run 1) gives a 65% yield of an 18:1 mixture of *threo*- and *erythro*-3-ethoxy-2-methyl-1-butanol (**2a**)[5] (see eq 2). The relative stereo-



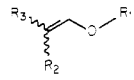
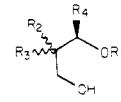
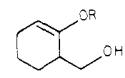
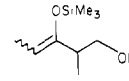
(2)

chemistry of the isomers of **2a** was proven by unambiguous synthesis of both isomers by sodium borohydride reduction of 3-ethoxy-2-methylbutanal.[6] Stereochemical assignment was based on comparison of chromatographic and spectroscopic properties of the two isomers. The threo isomer is more strongly intramolecularly hydrogen bonded as determined by measurement of its IR spectrum in dilute solution ($\epsilon_{3510}/\epsilon_{3620}$)[7] and is therefore less polar (GC and TLC). In addition, the 2-methyl group and C-2 and C-3 of the threo isomer absorb further downfield than those

(1) Adams, D. R.; Bhatnagar, S. P. *Synthesis* **1977**, 661.
(2) (a) Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 818. (b) Fleming, I. *Chimia* **1980**, *34*, 265.
(3) Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, *104*, 555.
(4) (a) Snider, B. B.; Cordova, R.; Price, R. T. *J. Org. Chem.* **1982**, *47*, 3643. (b) Snider, B. B.; Rodini, D. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, 3927.
(5) Threo and erythro are defined as is now standard for β-hydroxycarbonyl compounds.
(6) Nazarov, I. N.; Makin, S. M.; Kruptsov, B. K. *J. Gen. Chem. USSR* **1959**, *29*, 3641.
(7) (a) Aaron, H. S. In "Topics in Stereochemistry"; Eliel, E. L., Allinger, N. L., Eds; Wiley: New York, 1979; Vol. 11, pp 1–53. (b) Tichý, M. In "Advances in Organic Chemistry"; Raphael, R. A., Taylor, E. C., Wynberg, H., Eds.; Wiley-Interscience: New York, 1965; Vol. 5, p 115. (c) Maskens, K.; Polgar, N. *J. Chem. Soc., Perkin Trans. 1* **1973**, 109.

0022-3263/83/1948-2789$01.50/0

Table I. Reaction of Enol Ethers with Formaldehyde and Organoaluminum Compounds

run	enol ether	Al compd	product (% yield, *threo/erythro*)
			 **2**
1	R_1 = Et, R_2 = Me, R_3 = H	Me_3Al	a, R_4 = Me (65%, 18:1)
2	R_1 = Et, R_2 = Me, R_3 = H	Et_3Al	b, R_4 = Et (30%, 19:1)
3	R_1 = Et, R_2 = Me, R_3 = H	Et_2AlCN	c, R_4 = CN (8%, 1.33:1)
4	R_1 = Et, R_2 = Me, R_3 = H	$Me_2AlC{\equiv}CC_6H_{13}$	d, R_4 = $C{\equiv}CC_6H_{13}$ (6%, 1:1.2)
5	R_1 = Et, R_2 = Me, R_3 = H	$EtClAlC{\equiv}CC_6H_{13}$	d, R_4 = $C{\equiv}CC_6H_{13}$ (68%, 1.25:1)
6	R_1 = $SiMe_3$, R_2 = Me, R_3 = H	Me_3Al	e, R_4 = Me (84%, >10:1)
7	R_1 = Me, R_2 = Me, R_3 = H	Me_3Al	f, R_4 = Me (33%, 16:1)
8	R_1 = Et, R_2 = R_3 = H	Me_3Al	g, R_4 = Me (62%)
9	R_1 = $SiMe_3$, R_2 = R_3 = Me	Me_3Al	h, R_4 = Me (51%)
			 **3**
10	R = Me	Me_3Al	a (87%)
11	R = $SiMe_3$	Me_3Al	b (82%)
12	R = $SiMe_2$-*t*-Bu	Me_3Al	c (81%)
13		Me_3Al	 (72%) **4**

of the erythro isomer in the ^{13}C NMR spectrum.[8]

Trimethylsilyl propenyl ether reacts with $CH_2O{\cdot}Me_3Al$ selectively to give *threo*-**2e** (run 6), which can easily be converted to the threo diol that was characterized as its bis(*p*-nitrobenzoate) derivative. Other enol ethers react similarly (runs 7–9). $CH_2O{\cdot}Et_3Al$ reacts with ethyl propenyl ether to give predominantly *threo*-**2b**.

Aluminum cyanides and acetylides were investigated in an attempt to introduce more complex functionality. $CH_2O{\cdot}Et_2AlCN$ reacts with enol ethers to give the expected protected cyanohydrins **2c**. Unfortunately the yield is poor and a 60:40 mixture of diastereomers is formed (run 3). The major product, glycolonitrile, results from direct addition of cyanide to formaldehyde. $CH_2O{\cdot}EtClAlC{\equiv}CC_6H_{13}$ reacts with ethyl propenyl ether to give a 68% yield of **2d** as a 1.25:1 mixture of diastereomers (run 5). When $Me_2AlC{\equiv}CC_6H_{13}$ is used (run 4) the major product is 2-nonyn-1-ol, since the acetylide of this reagent is more nucleophilic.

Enol ethers derived from ketones do not react analogously with $CH_2O{\cdot}Me_3Al$ but instead give ene type adducts **3** and **4** resulting from proton abstraction by the oxygen via a six-membered ring transition state (runs 10–13). Only aldol products can be isolated if typical Lewis acids, e.g., $TiCl_4$, are used instead of Me_3Al.[2a] The ability to isolate the enol ether should allow selective sequential reaction at the α and α' position of ketones.

Me_2AlCl is more acidic than Me_3Al with a less nucleophilic alkyl group. Reaction of $CH_2O{\cdot}Me_2AlCl$ with ethyl propenyl ether gives **2a** as a 5:1 mixture of threo–erythro isomers in lower yield. Reaction of $CH_2O{\cdot}Me_2AlCl$ with enol ethers derived from ketones gives aldol products rather than enol ethers **3** or **4**.

Attempted extension of these reactions to acetaldehyde was unsuccessful. Only 2-propanol was obtained from reactions of enol ethers with $CH_3CHO{\cdot}Me_3Al$. Adducts analogous to **2** could not be obtained from $CH_2O{\cdot}Al(i\text{-}Bu)_3$ or $CH_2O{\cdot}AlH(i\text{-}Bu)_2$.

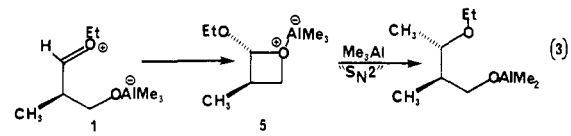
(8) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *J. Org. Chem.* **1979**, *44*, 4294.

Mechanism

The stereoselective formation of *threo*-**2a** was not anticipated from our earlier studies with $CH_2O{\cdot}Me_3Al$.[4a] Both (*E*)- and (*Z*)-propenyl ethyl ether give an identical 18:1 mixture of *threo*- and *erythro*-**2a**, establishing that the reaction proceeds through a common intermediate. Reaction of $CH_2O{\cdot}Me_3Al$ with excess (*E*)- or (*Z*)-1-methoxy-1-nonene leads to the recovery of geometrically pure enol ether, indicating that the enol ether double bond is not isomerized under the reaction conditions.

These results are consistent with the formation of the zwitterionic intermediate **1** shown in eq 2. Selective formation of the threo isomer directly from **1** implies a preferred geometry for **1**. Although chelation is not possible, electrostatic interactions could lead to a preferred geometry that would lead to the selective formation of *threo*-**2a**. This result cannot be rationalized, even a posteriori, from examination of models.

An alternative explanation, which is supported by circumstantial evidence, involves the reversible cyclization of **1** to give the more stable trans-substituted oxetane **5** followed by ring opening of the acetal with inversion by an S_N2 mechanism (see eq 3). Formation of oxetanes has



(3)

been observed in the $ZnCl_2$-catalyzed reactions of ketene acetals and aldehydes.[9,10] The proposed opening has precedent in the cleavage of 2-alkoxyoxetanes, prepared from photolysis of aldehydes and enol ethers, with Grignard reagents.[11] This mechanism is consistent with the

(9) Aluminum acetylides and cyanides are more nucleophilic than simple aluminum alkyls as evinced by the selective transfer of these groups from dialkylalkynylaluminum and dialkylaluminum cyanides.

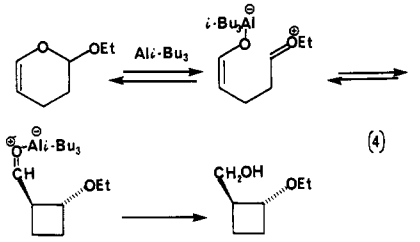
(10) Scheerin, H. W.; Aben, R. W. M.; Ooms, P. H. J.; Nivard, R. J. F. *J. Org. Chem.* **1977**, *42*, 3128.

(11) (a) Schroeter, S. H.; Orlando, C. M., Jr. *J. Org. Chem.* **1969**, *34*, 1181. (b) Schroeter, S. H. *J. Org. Chem.* **1969**, *34*, 1188.

lack of stereoselectivity in the formation of **2c** and **2d**. The more nucleophilic cyanide and acetylide groups may add to the zwitterion faster than it closes to the oxetane.

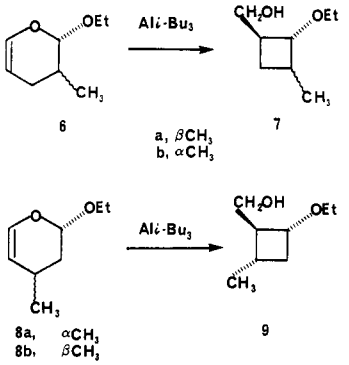
2-Alkoxycyclobutanemethanols

The formation of cyclobutanes from zwitterions vinylogous to **1** has been extensively studied. Reaction of 2-alkoxy-3,4-dihydro-2*H*-pyrans with Grignard reagents[12] or trialkylaluminum compounds[13] results in reversible ring opening to the zwitterion, which closes reversibly to the *trans*-2-alkoxycyclobutanecarboxaldehyde, which is trapped by addition of an alkyl group or, in the case of Al(*i*-Bu)$_3$, a hydride group (eq 4). This is analogous to the proposed selective formation of *trans*-oxetane **5**.



(4)

We have explored the stereochemical consequences of methyl substitution on the pyran ring. Reaction of a 60:40 mixture of **8a** and **8b** with Al(*i*-Bu)$_3$ in hexane at 67 °C for 2 days gives an 84% yield of cyclobutanemethanol **9** as a single stereoisomer. Similarly, trans-isomer **6a** gives a 90:10 mixture of **7a** and **7b**, while *cis*-isomer **6b** gives a 30:70 mixture of **7a** and **7b**.



There is thus a strong preference for the formation of the most stable trans,trans isomer, although the zwitterions do not fully equilibrate. The trans stereochemistry of the hydroxymethyl and ethoxy groups of **7** is established by the absence of an absorption due to intramolecular hydrogen bonding in the IR spectrum.[12c,13] The stereochemistry of the methyl substituent is assigned by analysis of the ^{13}C NMR spectrum, using the reported spectrum of *trans*-2-ethoxycyclobutanemethanol[13] and substituent parameters for methylcyclobutanes.[14]

Conclusion

The reaction of CH_2O·Me_3Al with enol ethers derived from aldehydes provides a general, stereoselective route to derivatives of threo 1,3-diols. Further studies will be required to establish the mechanism of this unusual reaction.

(12) (a) Quelet, R.; d'Angelo, J. *Bull. Soc. Chim. Fr.* **1967**, 3390. (b) Quelet, R.; d'Angelo, J. *C. R. Acad. Sci.* **1967**, *264*, 216. (c) d'Angelo, J. *Bull. Soc. Chim. Fr.* **1969**, 381.

(13) Menicagli, R.; Malanga, C.; Lardicci, L. *J. Org. Chem.* **1982**, *47*, 2288.

(14) Eliel, E. L.; Pietrusiewicz, K. M. *Org. Magn. Reson.* **1980**, *13*, 193. Note especially vic$_{1,2}$ parameters in Table II.

Experimental Section

NMR spectra were obtained on Varian EM-390, Perkin-Elmer R32, or Bruker WH90 NMR spectrometers. IR spectra were obtained on a Perkin-Elmer 683 spectrometer. GC analyses were carried out on the following $^1/_4$ in. columns on 60/80 Chromosorb WNAW at a flow rate of 35 mL/min: A (10 ft, 10% Carbowax 20 M) or B (12 ft, 8% UCON LB-550X). Analyses were performed by Galbraith Laboratories.

CH_2Cl_2 was distilled from CaH_2. Me_3Al and Me_2AlCl in heptane solution were obtained from Texas Alkyls Inc. Et_3Al, Al(*i*-Bu)$_3$, and $EtAlCl_2$ in hexane solution and Et_2AlCN in toluene solution (which was diluted with CH_2Cl_2 to give a less viscous solution) were obtained from Alfa Products. Ethyl propenyl ether was obtained from Tridom Chemical, Inc. Trimethylsilyl propenyl ether,[15] methyl propenyl ether,[16] trimethylsilyl isobutenyl ether,[17] trimethylsilyl 1-cyclohexenyl ether,[18] *tert*-butyldimethylsilyl 1-cyclohexenyl ether,[19] methyl 1-cyclohexenyl ether,[20] and (*Z*)-3-[(trimethylsilyl)oxy]-2-pentene[21] were prepared by literature procedures. A 64:36 mixture of *cis*- and *trans*-2-ethoxy-3-methyl-3,4-dihydro-2*H*-pyran (**6b** and **6a**) was prepared by heating acrolein and ethyl propenyl ether at 167 °C for 1 day in a pressure bottle.[22] The isomers were separated by preparative GC (B, 120 °C) and characterized.[23] A 60:40 mixture of isomers of 2-ethoxy-4-methyl-3,4-dihydro-2*H*-pyran (**8a** and **8b**) was prepared by heating crotonaldehyde and ethyl vinyl ether for 2 days at 180 °C in a pressure bottle.[23,24]

General Procedures. A flask containing paraformaldehyde was flame-dried in vacuo and flushed with nitrogen. The enol ether and dry CH_2Cl_2 were added. The solution, containing suspended paraformaldehyde, was cooled to 0 °C and treated with the Lewis acid solution. After reaction was complete, the reaction was quenched by dilution with ether followed by slow addition of water until gas evolution ceased. Silyl ethers were quenched with sodium bicarbonate solution and separated from precipitated alumina by suction through Celite. Other reactions were treated with 1 M hydrochloric acid to dissolve the precipitated alumina. The organic layer was separated and the aqueous layer was washed twice with ether. The combined organic layers were washed with brine, dried ($MgSO_4$ or K_2CO_3 for silyl ethers), and evaporated in vacuo.

***threo*-3-Ethoxy-2-methyl-1-butanol (*threo*-2a; Run 1).** Ethyl propenyl ether (78:22 *Z*–*E* mixture, 430 mg, 5 mmol), paraformaldehyde (306 mg, 10 mmol), and Me_3Al (6.8 mL of 1.48 M solution in heptane, 10 mmol) in 15 mL of CH_2Cl_2 for 10 min at 0 °C reacted to give 473 mg (71%) of crude product. Evaporative distillation (67 °C, 2.1 torr) of 280 mg gave 254 mg (65%) of an 18:1 mixture of *threo*-**2a** and *erythro*-**2a**.

The data for *threo*-**2a** follow: NMR ($CDCl_3$) δ 3.87 (s, 1, OH), 3.69 (dq, 1, *J* = 9.4, 7 Hz, C*H*HCH$_3$), 3.7–3.5 (m, 2), 3.5–3.2 (m, 2), 1.7 (m, 1), 1.21 (t, 3, *J* = 7.5 Hz), 1.18 (d, 3, *J* = 6 Hz), 0.88 (d, 3, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 79.6 (C-3), 66.3 (C-1), 63.7 (O*C*H$_2$CH$_3$), 40.6 (C-2), 16.8 (C-4), 15.2 (OCH$_2$*C*H$_3$), 13.1 (C-2 *C*H$_3$); IR (CCl_4) 3630, 3510, 2970, 2930, 2900, 2890, 1375, 1110, 1085 cm^{-1}; $\epsilon_{3510}/\epsilon_{3630}$ = 3.7; GC (A, 100 °C) t_R 24.6 min. Anal. Calcd for $C_7H_{16}O_2$: C, 63.60; H, 12.20. Found: C, 63.56; H, 12.16.

***erythro*- and *threo*-3-Ethoxy-2-methyl-1-butanol (2a).** 3-Ethoxy-2-methylbutanal[6] (363 mg, 2.8 mmol, mixture of isomers) was reduced with $NaBH_4$ in ethanol to give a 60:40 mixture of threo and erythro alcohols. Preparative GC gave pure *threo*-**2a**

(15) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(16) Newman, M. S.; Vander Zwan, M. C. *J. Org. Chem.* **1973**, *38*, 2910.

(17) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503.

(18) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. O. *J. Org. Chem.* **1969**, *34*, 2324.

(19) Clark, R. D.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 1396.

(20) Wohl, R. *Synthesis*, **1974**, 38.

(21) Cazeau, P.; Moulines, F.; Laporte, O.; Duboudin, F. *J. Organomet. Chem.* **1980**, *201*, C9.

(22) Ansell, M. F.; Gadsby, B. *J. Chem. Soc.* **1958**, 3388.

(23) Dauben, W. G.; Krabbenhoft, H. O. *J. Org. Chem.* **1977**, *42*, 282. Descotes, G.; Martin, J.-C.; Mathicolonis, N. *Bull. Soc. Chim. Fr.* **1972**, 1077.

(24) Longley, R. I., Jr.; Emerson, W. S. *J. Am. Chem. Soc.* **1950**, *72*, 3079.

and *erythro*-**2a**. The data for *threo*-**2a** are identical with those described above. The data for *erythro*-**2a** follow: NMR ($CDCl_3$) δ 3.4–3.7 (m, 4), 3.45 (dq, 1, J = 9.2, 7.1 Hz), 3.3 (br, 1, OH), 1.9 (m, 1), 1.20 (t, 3, J = 7 Hz), 1.16 (d, 3, J = 6.5 Hz), 0.88 (d, 3, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 77.2 (C-3), 64.8 (C-1), 63.7 (OCH_2CH_3), 39.4 (C-2), 15.2, 15.1, and 11.5 (C-2 CH_3); IR (CCl_4) 3630, 3510, 2970, 1120 cm^{-1}; $\epsilon_{3510}/\epsilon_{3630}$ = 2.5; GC (A, 100 °C) t_R 26.3 min.

***threo*-3-[(Trimethylsilyl)oxy]-2-methyl-1-butanol (*threo*-2e; Run 6).** Trimethylsilyl propenyl ether (106 mg, 0.81 mmol), paraformaldehyde (494 mg, 1.6 mmol), and Me_3Al (1.1 mL of 1.48 M solution in heptane, 1.6 mmol) in 3 mL of CH_2Cl_2 for 15 min at 0 °C reacted to give 120.3 mg (84%) of *threo*-**2e** containing <10% of the erythro isomer: NMR (CCl_4) δ 3.74 (dq, 1, J = 6, 6 Hz), 3.49 (m, 2), 1.58 (m, 1), 1.3 (br, 1, OH), 1.16 (d, 3, J = 6 Hz), 0.90 (d, 3, J = 6 Hz), 0.13 (s, 9); ^{13}C NMR ($CDCl_3$) δ 72.4, 65.4, 42.0, 21.2, 13.4, –0.1; IR (CCl_4) 3640, 3530, 2960, 1250, 1070, 1050, 850 cm^{-1}.

If precautions were not taken to keep the workup alkaline, the adduct **2e** slowly decomposed to *threo*-2-methyl-1,3-butanediol, which was characterized as the bis(*p*-nitrobenzoate): mp 127–128 °C (lit.[25] mp 128 °C for threo isomer and 113 °C for erythro isomer); NMR ($CDCl_3$) δ 8.28 (d, 4, J = 9 Hz), 8.16 (d, 4, J = 9 Hz), 5.30 (dq, 1, J = 6,6 Hz), 4.49 (dd, 1, J = 5,11 Hz), 4.32 (dd, 1, J = 6, 11 Hz), 2.41 (m, 1), 1.44 (d, 3, J = 6 Hz), 1.17 (d, 3, J = 7 Hz).

***threo*-3-Methoxy-2-methyl-1-butanol (*threo*-2f; Run 7).** Methyl propenyl ether (148 mg, 2.0 mmol), paraformaldehyde (124 mg, 4.1 mmol), and Me_3Al (2.7 mL of 1.48 M solution in heptane, 4.0 mmol) in 6 mL of CH_2Cl_2 at 0 °C for 30 min reacted to give 80 mg (33%) of a 16:1 mixture of *threo*-**2f** and *erythro*-**2f**: NMR ($CDCl_3$) δ 3.57 (d, 2, J = 6 Hz), 3.36 (s, 3), 3.30 (dq, 1, J = 6, 6 Hz), 3.0 (br, 1, OH), 1.73 (dtq, 1, J = 6, 6, 6 Hz), 1.17 (d, 3, J = 6 Hz), 0.90 (d, 3, J = 6 Hz); NMR (C_6D_6) δ 3.51 (d, 2, J = 6 Hz), 3.09 (s, 3), 2.9–3.2 (m, 1), 2.8 (br, 1, OH), 1.69 (m, 1), 0.96 (d, 3, J = 6 Hz), 0.79 (d, 3, J = 7 Hz) (this spectrum is different than that reported for the erythro isomer in the same solvent[26]); ^{13}C NMR ($CDCl_3$) δ 81.8, 66.7, 56.1, 40.6, 16.2, 13.3; the erythro isomer absorbed at δ 79.2, 64.8, and 38.8; IR (CCl_4) 3640, 3530, 2980, 2960, 1100 cm^{-1}; GC (A, 100 °C) t_R 28.3 (threo) and 30.3 min (erythro).

2-Ethoxy-3-methylcyclobutanemethanols (7a and 7b). $Al(i\text{-}Bu)_3$ (17 mL of 0.87 M in hexane, 15 mmol) was placed in a flame-dried flask under nitrogen equipped with a condenser. A 64:36 mixture of dihydropyrans **6b** and **6a** (1.04 g, 7.3 mmol) was added and the solution heated at 67 °C for 22 h. Normal workup gave 898 mg (85%) of a 54:46 mixture of **7a** and **7b**. Evaporative distillation of 770 mg (66 °C, 1.85 torr) gave 690 mg (76%) of pure product. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.38; H, 11.22. Pure samples of **7a** and **7b** were obtained by preparative GC.

The data for **7a** follow: NMR ($CDCl_3$) δ 3.7–3.5 (m, 2), 3.48 (q, 2, J = 7 Hz), 3.5–3.2 (m, 1), 2.5–2.1 (m, 3), 1.6 (m, 2), 1.18 (t, 3, J = 7 Hz), 1.10 (d, 3, J = 6.2 Hz); ^{13}C NMR ($CDCl_3$) (determined from mixture) δ 81.8, 63.6, 63.4, 42.8, 34.9, 23.0, 14.8, 14.6; IR (CCl_4) 3640, 2980, 2960, 2880, 1130 cm^{-1}; GC (B, 150 °C) t_R 11.7 min.

The data for **7b** follow: NMR ($CDCl_3$) δ 3.8–3.5 (m, 1), 3.66 (br d, 2, J = 6 Hz), 3.40 (q, 2, J = 7 Hz), 2.7–2.3 (m, 1), 1.6–1.3 (m, 4), 1.18 (t, 3, J = 7Hz), 1.09 (d, 3, J = 7 Hz); ^{13}C NMR ($CDCl_3$; determined from mixture) δ 75.0, 63.6, 63.4, 42.2, 30.7, 19.0, 14.8, 13.8; IR (CCl_4) 3640, 2980, 2940, 2880, 1140 cm^{-1}; GC (B, 150 °C) t_R 12.8 min.

Reaction of pure *cis*-**6b** gave a 30:70 mixture of **7a** and **7b** as determined by GC analysis. Reaction of pure *trans*-**6a** gave a 90:10 mixture of **7a** and **7b** as determined by GC analysis.

***trans,trans*-2-Ethoxy-4-methylcyclobutanemethanol (9).** Reaction of a 60:40 mixture of pyrans **8a** and **8b** (66 mg, 0.47 mmol) and $Al(i\text{-}Bu)_3$ (1.1 mL of 0.87 M in hexane, 1.3 mmol) as described above gave 64 mg (94%) of crude **9**. Evaporative distillation (70 °C, 2.9 torr) gave 57 mg (84%) of pure **9**: NMR (CCl_4) δ 3.56 (d, 2, J = 6 Hz), 3.38 (q, 2, J = 6 Hz), 3.6–3.0 (m, 2), 2.30 (ddd, 1, J = 10, 6, 6 Hz), 2.0–1.2 (m, 3), 1.17 (t, 3, J = 6 Hz), 1.13 (d, 3, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 72.2, 63.3, 63.1, 53.4, 35.0, 23.6, 20.5, 15.0; IR (CCl_4) 3640, 2980, 2940, 2880, 1150 cm^{-1}; GC (A, 150 °C) t_R 13.9 min. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 64.08; H, 11.08.

Acknowledgment. We thank the National Institutes of Health for financial support. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the partial support of this research.

Registry No. **2a** (isomer 1), 86335-63-9; **2a** (isomer 2), 86335-64-0; *threo*-**2b**, 86335-65-1; **2d** (isomer 1), 86335-66-2; **2d** (isomer 2), 86335-67-3; *threo*-**2e**, 86335-68-4; **2f** (isomer 1), 86335-69-5; **2f** (isomer 2), 86335-70-8; **2g**, 82655-81-0; **2h**, 86335-71-9; **3a**, 39781-72-1; **3b**, 86335-72-0; **3c**, 86335-73-1; **4**, 86335-74-2; **6a**, 60582-03-8; **6b**, 60582-02-7; **7a**, 86335-75-3; **7b**, 86363-10-2; **8a**, 17322-76-8; **8b**, 17322-77-9; **9**, 86335-76-4; CH_2O, 50-00-0; Me_3Al, 75-24-1; Et_3Al, 97-93-8; Et_2AlCN, 5804-85-3; $Me_2AlC{\equiv}CC_6H_{13}$, 68113-74-6; $EtClAlC{\equiv}CC_6H_{13}$, 86335-77-5; $Al(i\text{-}Bu)_3$, 100-99-2; ethyl (*E*)-propenyl ether, 4696-26-8; ethyl (*Z*)-propenyl ether, 4696-25-7; trimethylsilyl propenyl ether, 19879-97-1; methyl propenyl ether, 7319-16-6; ethyl vinyl ether, 109-92-2; trimethylsilyl isobutenyl ether, 6651-34-9; methyl 1-cyclohexenyl ether, 931-57-7; trimethylsilyl 1-cyclohexenyl ether, 6651-36-1; *tert*-butyldimethylsilyl 1-cyclohexenyl ether, 62791-22-4; (*Z*)-3-[(trimethylsilyl)oxy]-2-pentene, 51425-54-8; *threo*-2-methyl-1,3-butanediol bis(*p*-nitrobenzoate), 19903-09-4; acrolein, 107-02-8; crotonaldehyde, 4170-30-3; 3-ethoxy-2-methylbutanal (isomer 1), 80060-41-9; 3-ethoxy-2-methylbutanal (isomer 2), 80060-40-8.

Supplementary Material Available: Experimental data for runs 2, 3, 5 and 8–13 in Table I (4 pages). Ordering information is given on any current masthead page.

(25) Fremnaux, B.; Davidson, M.; Hellios, M.; Coussemant, F. *Bull. Soc. Chim. Fr.* **1967**, 4243.

(26) Maskens, K.; Polgar, N. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1117.

Palladium-Catalyzed Cyclizations of Bromo Dienes

C. K. Narula, K. T. Mak, and R. F. Heck*

Department of Chemistry and the Center for Catalytic Science and Technology, University of Delaware, Newark, Delaware 19711

Received November 15, 1982

1-Bromo 1,5-dienes, 2-bromo 1,6-dienes, and 2-bromo 1,7-dienes have been found to undergo palladium–triarylphosphine catalyzed cyclizations in the presence of piperidine to form five- or six-membered ring products in good yields. The major or only cyclic products formed are piperidino- or (piperidinomethyl)cyclopentenes and -cyclohexenes. The five-membered ring products are preferred over the six when there is a choice.

Palladium-catalyzed ring closures involving formation of carbon–nitrogen or carbon–oxygen bonds are well-known. Ring closures by forming carbon–carbon bonds have received much less attention. Palladium enolates obtained by exchange of palladium acetate with trimethylsilyl ethers will cyclize if a double bond is present

0022-3263/83/1948-2792$01.50/0