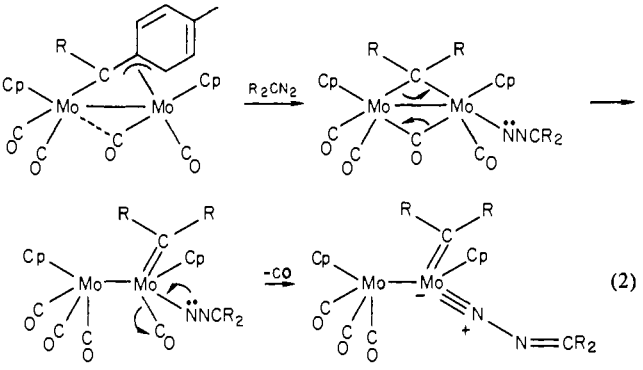
Key results of the molecular structure determination[11] (Figure 2) are (1) a Mo1—Mo2 single bond distance[12] of 3.052 (2) Å, (2) the presence of terminal alkylidene and N-terminal diazoalkane ligands on the same molybdenum, (3) a Mo2=C15 double bond length[13] of 1.98 (1) Å for the terminal alkylidene, (4) a Mo2—N1 bond length of 1.74 (1) Å, a N1—N2 bond length of 1.32 (1) Å, a Mo2—N1—N2 bond angle of 174.7 (9)°, and a N2—C16 bond length of 1.32 (1) Å consistent with a Mo2≡N1—N2=C16 grouping,[14] and (5) a shift of one carbonyl from Mo2 to Mo1 to give a $Mo(CO)_3$ group. Both molybdenums acquire 18-electron configurations, Mo1 by its array of ligands and Mo2 by the donation of the lone pair on N1 in a dative fashion to give a $Mo2^{-}\equiv N1^{+}$ polarized triple bond. Figure 3 shows a molecular core view approximately down the molybdenum–molybdenum bond; the angle between the alkylidene and diazoalkane ligands is 97.6 (5)°, and the three angles around the trigonal alkylidene carbon C15 total 360° within experimental error.

A plausible mechanism for this bridge → terminal alkylidene conversion is shown in reaction 2. N-Terminal coordination of



(2)

the diazoalkane to one molybdenum leads to an intermediate in which the semi-bridging carbonyl has assumed a bridging position; rearrangement yields an intermediate with terminal alkylidene and carbonyl ligands. The available terminal nitrogen lone pair is then donated to give carbon monoxide and the observed product.

It has been shown that the inherent coordination unsaturation of the Mo≡Mo triple bond in $Cp_2Mo_2(CO)_4$ affords a starting point for the synthesis of a variety of dinuclear complexes.[15,16] The residual unsaturation in μ-alkylidene complexes of the type $Cp_2Mo_2(CO)_4(CR_2)$[3] makes them especially attractive models[17] of surface-adsorbed alkylidenes since surface metal atoms are also coordinatively unsaturated.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Science Foundation (CHE-7907748), and the AMAX Foundation for support of this research.

Registry No. 1, 80398-83-0; **2**, 76114-00-6.

(11) Compound **2** crystallizes from a room temperature ether solution in the triclinic space group $P\bar{1}$ (No. 2) with lattice constants a = 12.247 (5) Å, b = 14.462 (7) Å, c = 11.486 (5) Å, α = 113.22 (3)°, β = 95.60 (3)°, γ = 90.32 (3)°, Z = 2, V = 1858 (1) cm^3, ρ_{calcd} = 1.47 g cm^{-3}, and ρ_{obsd} = 1.45 g cm^{-3} (flotation). The structure was refined to anisotropic convergence on 26 nonhydrogen atoms (isotropic on all others), after removal of calculated hydrogen atom structure factors from the data (2396 reflections with $I > 3\sigma(I)$). The final R value was 5.3 and the weighted R value was 5.4.

(12) (a) Adams, R. D.; Collins, D. M.; Cotton, F. A. *Inorg. Chem.* **1974**, *13*, 1086–1090. (b) Klingler, R. J.; Butler, W.; Curtis, M. D. *J. Am. Chem. Soc.* **1978**, *100*, 5034–5039.

(13) (a) The Mo=C double bond distance in **2**, 1.98 (1) Å, is appreciably longer than the Mo≡C triple bond distance of 1.83 (2) Å found in $(OC)_5ReMo(CPh)(CO)_4$[13b] but it is somewhat shorter than the Mo=C double bond distance of 2.06 (1) Å in $CpMo(CO)_2(GePh_3)[C(OEt)Ph]$.[13c] (b) Huttner, G.; Frank, A.; Fischer, E. O. *Isr. J. Chem.* **1977**, *15*, 133–142. (c) Chan, L. Y. Y.; Dean, W. K.; Graham, W. A. G. *Inorg. Chem.* **1977**, *16*, 1067–1071.

(14) (a) Formal molybdenum–nitrogen triple bond distances in organoimido complexes show little variation, being approximately 1.73 Å. See: Nugent, W. A.; Haymore, B. L. *Coord. Chem. Rev.* **1980**, *31*, 123–175. (b) The diazoalkane intraligand distances in **2** compare favorably with values observed in several mononuclear tungsten–diazoalkane complexes,[14c,d] which exhibit N—N bond distances of 1.31–1.34 Å and N=C bond distances of 1.28–1.30 Å. (c) Hidai, M.; Mizobe, Y.; Sato, M.; Kodama, T.; Uchida, Y. *J. Am. Chem. Soc.* **1978**, *100*, 5740–5748. (d) Ben-Shoshan, R.; Chatt, J.; Leigh, G. J.; Hussain, W. *J. Chem. Soc., Dalton Trans.* **1980**, 771–775 and references therein.

(15) Curtis, M. D.; Messerle, L.; Fotinos, N. F.; Gerlach, R. F. *Adv. Chem. Ser.* **1981**, *No. 155*, 221–257.

(16) Curtis, M. D.; Han, K. R.; Butler, W. M. *Inorg. Chem.* **1980**, *19*, 2096–2101 and references therein.

(17) (a) A molybdenum-containing Fischer–Tropsch catalyst with good selectivity for C_2–C_4 aliphatic hydrocarbons and superior sulfur tolerance was recently reported.[17b,c] (b) Murchison, C. B.; Murdick, D. A. (to Dow Chemical Company) U.S. Patent 4 151 190, 1979; *Chem. Abstr.* **1979**, *91*, 41855e. (c) Murchison, C. B.; Murdick, D. A. *Hydrocarbon Process.* **1981**, *60*, 159–164.

A Formal [1,3]-Sigmatropic Rearrangement of an Anionic Oxy-Cope System. A Consecutive Mechanism[1]

Tsutomu Miyashi, Atsuo Hazato, and Toshio Mukai*

Photochemical Research Laboratory and Department of Chemistry, Faculty of Science Tohoku University, Sendai 980, Japan

Received September 21, 1981

The thermal [1,3]-sigmatropic rearrangement of the oxy- and related Cope systems[2] such as anti A or syn A to C is regarded as one of the most useful two-carbon homologation reactions. The mechanism for this simple ring expansion reaction, however, is still ambiguous not only experimentally[3] but also theoretically.[4] One possible mechanism is the direct one[5] where the C_4 carbon of anti A or syn A directly migrates to the C_1 position to achieve a formal [1,3]-sigmatropic rearrangement of A to C. Alternatively, the indirect mechanism[6] involves successive [1,3]- and [3,3]-sigmatropic rearrangements where, in the case of anti A, the C_3 carbon initially migrates to the C_6 position either with inversion or with retention of configuration to regenerate isomeric Cope systems anti B and syn B, the former of which epimerizes to syn B through syn A by successive [1,3]-sigmatropic rearrangements, and then the ordinary Cope rearrangement of syn B gives C, achieving the indirect and consecutive mechanism (Figure 1). However, difficulties in isolation and detection of regenerated Cope systems such as anti B, syn A, and syn B which often equal anti A in thermal reactivity make the reaction pathway ambiguous and hence it is difficult to discriminate between the two mechanisms.

During our extended studies on the rearrangement[7] of anionic oxy-Cope systems, we succeeded in isolation of intermediates

(1) Organic Thermal Reaction, 52. No. 51: K. Sato, Y. Yamashita, and T. Mukai, *Tetrahedron Lett.*, 5303 (1981).

(2) The oxy- and related Cope system includes the oxy- (R = H), the methoxy- (R = CH_3), the siloxy- (R = $Si(CH_3)_3$), and anionic oxy- (R = Na, K, and Li) Cope systems. The discussion is restricted only for the rearrangement of A to C, in which the new bonding occurs between the C_1 and C_4 positions.

(3) See, for the oxy-Cope system, (a) J. A. Berson and M. Jones, Jr., *J. Am. Chem. Soc.*, **86**, 5017, 5019 (1964); for the methoxy-Cope system, (b) J. A. Berson and E. J. Walsh, Jr., *ibid.*, **90**, 4732 (1968); (c) J. A. Berson, T. Miyashi, and G. Jones, II., *ibid.*, **96**, 3468 (1974); for the siloxy-Cope system, (d) R. W. Thies, *ibid.*, **94**, 7074 (1972); (e) R. W. Thies and J. E. Billigmeier, *ibid.*, **96**, 200 (1974); for the anionic oxy-Cope system, (f) R. W. Thies and E. P. Seitz, *J. Chem. Soc., Chem. Commun.*, 846 (1976); (g) R. W. Theis and E. P. Seitz, *J. Org. Chem.*, **43**, 1050 (1978); see also ref 7.

(4) S. Inagaki, T. Minato, H. Fujimoto, and K. Fukui, *Chem. Lett.*, 89 (1976).

(5) The direct mechanism includes (i) a concerted direct C_4 carbon migration to the C_1 position of A via processes such as [1,3]-sigmatropic, with retention of configuration,[3c] and multicyclic interaction[4] pathways and (ii) a nonconcerted migration via processes such as diradical[3a] and ionic[3f] pathways.

(6) The indirect mechanism was tentatively proposed for anionic oxy-Cope systems.[7] See also ref 3d, e, g.

(7) T. Miyashi, A. Hazato, and T. Mukai, *J. Am. Chem. Soc.*, **100**, 1008 (1978).

0002-7863/82/1504-0891$01.25/0

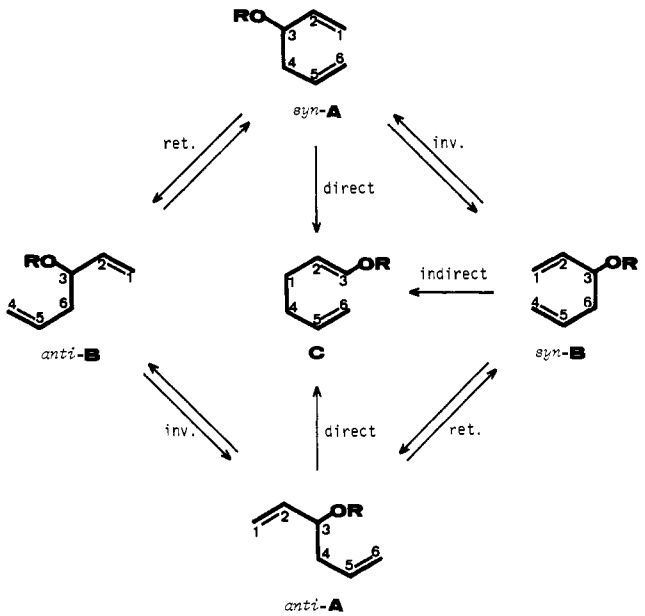
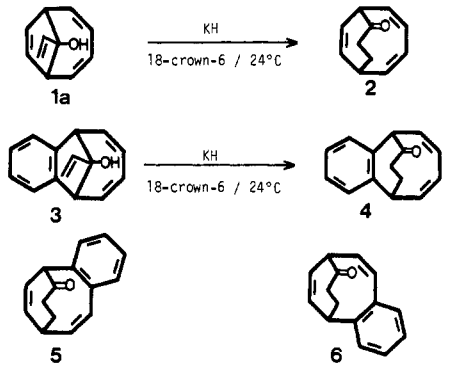


Figure 1. Direct and indirect [1,3]-sigmatropic rearrangements of A to C in the oxy- and related Cope systems.

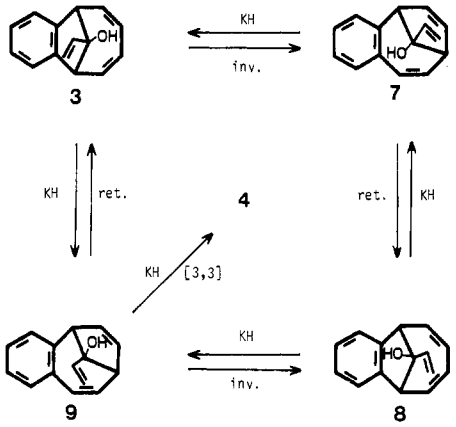
Scheme I



involved in the indirect mechanism. In this communication, we report our first observation of the indirect mechanism, including the hitherto unknown anionic [1,3]-sigmatropic rearrangement with retention of configuration and circumambulatory [1,3]-sigmatropic rearrangement with inversion of configuration in the anionic oxy-Cope systems incorporated in the bicyclo[4.2.1]nonatriene system.

The systems we chose are 8-*endo*-hydroxy-8-*exo*-vinyl-bicyclo[4.2.1]nona-2,4,6-triene (**1a**) and the benzo analogue **3**. When **1a** (mp 56.5 °C)[8] was treated with potassium hydride (KH) at 24 °C for 2 min in the presence of 18-crown-6[9] in dry tetrahydrofuran, ketone **2**[10] was obtained quantitatively. Similarly, **3** (mp 115 °C)[11] afforded a quantitative yield of **4** (mp 95 °C)[12]

Scheme II



under the same conditions. One intriguing feature is that the isomeric ketone **5** was not formed from **3**, indicating that successive [1,5]-, with retention of configuration, and [3,3]-sigmatropic rearrangements[7] to give **5** do not operate, but instead a formal [1,3]-sigmatropic rearrangement of A to C exclusively occurs in **3**. The low-temperature preparative scale experiment, however, gained insights into the sequence of this rearrangement. Thus, upon treating **3** with KH at 0°C for 5 min in the presence of 18-crown-6, three isomeric vinyl alcohols, **7** (mp 83.5 °C),[13] **8** (mp 134 °C),[13] and **9** (mp 174 °C),[13] were isolated in 20, 24, and 0.8% yields, respectively, together with ketone **4** (24%) and the recovered **3** (18%). Furthermore, the gas chromatographic analysis of this reaction revealed that at the initial stage the rapidly decreasing **3** equilibrated with the rapidly forming **7** within 1 min, **3** and **7** then gradually decreased in a state of equilibrium with a slow increase in the amounts of **4** and **8**, and at the final stage only the amount of **4** slowly increased with a slow decrease of the three-component equilibrium mixture of **3**, **7**, and **8**. That **7**, **8**, and **9** are intermediates in the formation of **4** from **3** was substantiated by independent treatment of these vinyl alcohols with KH under the same conditions. Similar to **3**, **7** rapidly rearranged to give a mixture of **3**, **7**, **8**, and **4**, while **8** rather slowly rearranged

(8) Satisfactory elemental analyses were obtained for all new compounds in this report. The vinyl alcohol **1a** was prepared from bicyclo[4.2.1]nona-2,4,6-trien-9-one and the stereochemical assignment to **1a** was derived from Eu(fod)$_3$ pseudocontact ^{1}H NMR spectra. **1a**: IR (KBr) 3350, 3050, 2950, 1410, 1340 cm^{-1}; *m/e* (rel intensity) 160 (M$^+$, 85%), 145 (100%); UV (cyclohexane) λ_{max} 220 (sh, log ϵ 3.57), 269 (3.50) nm; ^{1}H NMR (CCl_4, 100 MHz) δ 2.0 (s, 1 H, OH), 2.80 (dd, $J_{1,8} = J_{6,7} = 1.0$, $J_{1,2} = J_{6,5} = 8.0$ Hz, C_1-, C_6H), 5.70–6.30 (m, 5 H, C_2-, C_3-, C_4-, C_5-, C_{10}H), 5.35 (d, C_7-, C_8H), 4.90 (dd, $J_{vic} = 2.0$, $J_{10,11} = 11.0$ Hz, cis C_1H), 5.25 (dd, $J_{vic} = 2.0$, $J_{10,11} = 17.0$ Hz, trans C_{11}H).

(9) D. A. Evans and A. M. Golob, *J. Am. Chem. Soc.*, **97**, 4765 (1975).

(10) Compound **2**: IR (neat) 3050, 3000, 2850, 1695, 1600, 1450 cm^{-1}; *m/e* (rel intensity) 160 (M$^+$, 73%), 117 (100%); UV (cyclohexane) λ_{max} 248 (sh, log ϵ 2.83), 306 (sh, 2.84), 317 (sh, 2.77), 327 (sh, 2.60) nm; ^{1}H NMR (CD_2Cl_2, 200 MHz) δ 1.95 (m, 2 H, C_{11}H), 2.55 (dddd, $J_{vic} = 13.0$, $J_{1,10} = 1.5$, $J_{10,11} = 4.0$, 6.0 Hz, exo C_{10}H), 3.00 (ddd, $J_{10,11} = 6.0$, 11.0 Hz, endo C_{10}H), 3.10 (m, C_6H), 3.63 (ddd, $J_{1,2} = J_{1,8} = 9.0$ Hz, C_1H), 5.60 (ddd, $J_{7,8} = 11.0$, $J_{6,8} = 2.0$ Hz, C_8-H), 5.83 (dd, $J_{6,7} = 9.0$ Hz, C_7H), 5.8 (dd, $J_{2,3} = 10.0$ Hz, C_2H), 5.90–6.05 (m, 3 H, C_3-, C_4-, C_5H).

(11) The vinyl alcohol **3** was prepared from the corresponding ketone. The stereochemical assignment to **3** was derived from Eu(fod)$_3$ pseudocontact ^{1}H NMR spectra. **3**: IR (KBr) 3350, 1590, 1470, 1450, 1410, 1330 cm^{-1}; UV (cyclohexane) λ_{max} 232 (sh, log ϵ 3.62), 256 (sh, 3.45), 269 (3.59), 276 (3.61), 288 (sh, 3.30) nm; *m/e* (rel intensity) 210 (M$^+$, 38%), 154 (100%); ^{1}H NMR (CCl_4, 100 MHz) δ 3.05 (d, $J_{1,2} = J_{5,6} = 8.0$ Hz, C_1-, C_6H), 6.08 (ddd, $J_{2,3} = J_{4,5} = 12.0$, $J_{2,4} = 4.0$ Hz, C_2-, C_5H), 5.88 (dd, $J_{3,5} = 4.0$ Hz, C_3-, C_4H), 5.95 (dd, $J_{10,11} = 10.0$, 18.0 Hz, C_{10}H), 4.92 (dd, $J_{vic} = 2.0$, $J_{10,11} = 10.0$ Hz, trans C_{11}H), 5.35 (dd, $J_{10,11} = 18.0$ Hz, cis C_{11}H).

(12) Compound **4**: IR (KBr) 1710 1490, 1330, 1300 cm^{-1}; UV (cyclohexane) λ_{max} 248 (sh, log ϵ 3.51), 251 (3.65), 270 (3.63), 296 (sh, 2.60), 306 (2.60), 316 (sh, 2.5) nm; *m/e* (rel intensity) 210 (M$^+$, 9%) 154 (100%); ^{1}H NMR (CCl_4, 100 MHz) δ 4.24 (d, $J_{1,2} = 10.0$ Hz, C_1H), 5.80–6.0 (m, C_2-, C_3-, C_4-, C_5H), 3.82 (ddd, $J_{5,6} = 7.0$, $J_{6,11} = 4.0$ Hz, C_6H), 2.72 (m, 2 H, C_{10}H), 2.28 (m, $J_{vic} = 14.0$, $J_{6,11} = 4.0$, $J_{10,11} = 6.0$ Hz, exo C_{11}H), 2.10 (m, J_{vic} 14.0, $J_{6,11} = 4.0$ Hz, endo C_{11}H).

(13) The stereochemical assignments to **7**, **8**, and **9** were derived from Eu(fod)$_3$ pseudocontact ^{1}H NMR spectra. Compound **7**: IR (KBr) 3350, 1480, 1440, 1410 cm^{-1}; UV (cyclohexane) λ_{max} 230 (sh, log ϵ) 3.73), 256 (sh, 3.47), 268 (3.60), 276 (3.62), 286 (sh, 3.38) nm; *m/e* (rel intensity) 210 (M$^+$, 12%), 155 (100%); ^{1}H NMR (CCl_4, 100 MHz) δ 3.42 (d, $J_{1,8} = 3.0$ Hz, C_1H), 6.50 (d, $J_{4,5} = 12.0$ Hz, C_4H), 5.96 (dd, $J_{5,6} = 8.0$ Hz, C_5H), 2.88 (dd, $J_{6,7} = 3.0$ Hz, C_6H), 5.52 (dd, $J_{7,8} = 7.0$ Hz, C_7H), 5.40 (dd, C_8H), 6.20 (dd, $J_{10,11} = 10.0$, 18.0 Hz, C_{10}H), 4.98 (dd, $J_{vic} = 2.0$, $J_{10,11} = 10.0$ Hz, trans C_{11}H), 5.38 (dd, $J_{10,11} = 18.0$ Hz, cis C_{11}H). **8**: IR (KBr) 3350, 1590, 1470, 1420, 1310 cm^{-1}; UV (cyclohexane) λ_{max} 230 (sh, log ϵ 3.73), 256 (sh, 3.47), 268 (3.6), 276 (3.62), 286 (sh, 3.38) nm; *m/e* (rel intensity) 210 (M$^+$, 13%), 141 (100%); ^{1}H NMR (CCl_4, 100 MHz) δ 3.40 (d, $J_{1,2} = J_{5,6} = 8.0$ Hz, C_1-, C_6H), 6.00 (ddd, $J_{2,3} = J_{4,5} = 12.0$, $J_{2,4} = 4.0$ Hz, C_2-, C_5H), 5.62 (dd, $J_{3,5} = 4.0$ Hz, C_3-, C_4H), 6.34 (dd, $J_{10,11} = 10.0$, 18.0 Hz, C_{10}H), 5.12 (dd, $J_{vic} = 2.0$, $J_{10,11} = 10.0$ Hz, trans C_{11}H), 5.47 (dd, $J_{vic} = 2.0$, $J_{10,11} = 18.0$ Hz, cis C_{11}H). **9**: IR (KBr) 3350, 1480, 1350 cm^{-1}; UV (cyclohexane) λ_{max} 230 (sh, log ϵ 3.6), 254 (sh, 3.47), 268 (3.58), 275 (3.60), 286 (3.32) nm; *m/e* (rel intensity) 210 (M$^+$, 11%) 154 (100%); ^{1}H NMR (CCl_4, 100 MHz) δ 3.48 (d, $J_{1,8} = 3.0$ Hz, C_1H), 6.23 (d, $J_{4,5} = 12.0$ Hz, C_4H), 5.93 (dd, $J_{5,6} = 8.0$ Hz, C_5H), 2.90 (dd, $J_{67} = 3.0$ Hz, C_6H), 5.58 (dd, $J_{7,8} = 7.0$ Hz, C_7H), 5.36 (dd, C_8H), 5.85 (dd, $J_{10,11} = 10.0$, 18.0 Hz, C_{10}H), 4.93 (dd, $J_{vic} = 2.0$, $J_{10,11} = 10.0$ Hz, trans C_{11}H), 5.35 (dd, $J_{vic} = 2.0$, $J_{10,11} = 18.0$ Hz, cis C_{11}H).

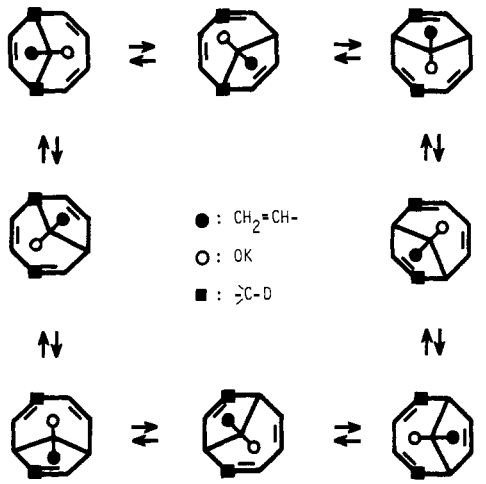
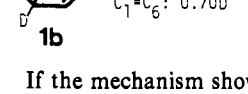


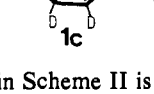
Figure 2. Circumambulatory [1,3]-sigmatropic rearrangement of **1b** with inversion of configuration in each step.

to a mixture composed of the same products. On the other hand, **9** afforded **4** as the major product along with a mixture of four vinyl alcohols as the minor products.

Although the formation of detectable amounts of **9** was not clearly observed except in the preparative scale experiments because of its very low accumulation, it is noteworthy that all vinyl alcohols afforded the same products. Moreover, evidence that neigher **5** nor **6**, direct [1,3]-sigmatropic rearranged ketones from **7** and **9**, was formed from any vinyl alcohols is rather surprising if ketone **4** were directly formed from **3** and **8**. Thus, a plausible mechanism for the formation of **4** from **3**, **7**, and **8** can be proposed as shown in Scheme II, where **4** is formed in the indirect mechanism through **9** which is in equilibrium with **3**, **7**, and **8** under the conditions employed. In order to gain further insight into the interrelation among vinyl alcohols, reactions and kinetic studies without 18-crown-6 were carried out, expecting suppression of high energy pathways of these four [1,3]-sigmatropic pathways. Below 49.5 °C, the rapid equilibrium between **3** and **7** was only observed. For instance, at 49.5 °C, both **3** and **7** equilibrated each other within 15 min, and the formation of the equilibrium mixture of **3**, **7**, and **8** required prolonged heating for more than 5 h, while the formation of **4** was suppressed even upon prolonged heating of a mixture of **3**, **7**, and **8** at 64.5 °C. This likely suggests that the addition of 18-crown-6[9] significantly accelerates high-energy pathways such as the more sterically unfavorable inversion pathway from **8** to **9** as compared with those between **3** and **7** and/or the energetically unfavorable retention pathway from **3** to **9** included in the indirect mechanism. Thus, the following activation parameters were obtained for the interconversions between **3** and **7** (20.2–49.5 °C) and between **7** and **8** (41.0–64.5 °C) without 18-crown-6, providing the first detection of the symmetry-forbidden anionic [1,3]-sigmatropic retention pathways[14] between **7** and **8** which compete with the inversion pathway from **7** to **3** in the rate ratio k_{ret}/k_{inv} = 1/82.2 at 49.5 °C; E_a = 19.9 kcal/mol (log A = 11.6) for **3** → **7**; E_a = 18.8 kcal/mol (log A = 10.7) for **7** → **3**; E_a = 20.6 kcal/mol (log A = 10.0) for **7** → **8**; E_a = 22.3 kcal/mol (log A = 11.2) for **8** → **7**.



1b C_1=C_6: 0.70D



1c

C_1=C_6: (0.26±0.02)D
C_2=C_5: (0.15±0.01)D
C_3=C_4: (0.13±0.02)D
C_7=C_8: (0.15±0.01)D

If the mechanism shown in Scheme II is correct, during the rearrangement of **1a** to **2** by successive [1,3]-, with retention of configuration, and [3,3]-sigmatropic rearrangements, the competitive [1,3]-sigmatropic rearrangement with inversion of configuration must involve the circumambulation of the C_9 carbon of **1a** which can be seen when **1b**[15] is used. The recovered vinyl alcohol **1c**[17] isolated after treating **1b** with KH at 20 °C for 11 min unequivocally indicated the occurrence of the circumambulatory [1,3]-sigmatropic rearrangement with inversion of configuration in each step as shown in Figure 2, supplementing the operation of a consecutive mechanism.

Registry No. 1a, 80434-45-3; **2**, 80434-46-4; **3**, 80434-47-5; **4**, 80434-48-6; **7**, 80434-49-7; **8**, 80482-66-2; **9**, 80447-41-2.

(14) The symmetry-forbidden [1,3]-sigmatropic rearrangement with retention of configuration has been detected in pyrolyses of several "neutral" systems and discussed in detail by Berson. See J. A. Berson, *Acc. Chem. Res.*, **5**, 406 (1972), and references cited therein.

(15) Compound **1b** was prepared according to the procedure[16] reported by Paquette. Bicyclo[4.3.0]nona-2,4-dien-8-one was deuteriated with $NaOCH_3/CH_3OD$. Successive bromination, dehydrobromination, and the addition of CH_2=CHLi gave **1b**.

(16) L. A. Paquette, R. H. Meisinger, and R. E. Wingard, Jr., *J. Am. Chem. Soc.*, **94**, 2155 (1972).

(17) The distribution of deuteriums in **1c** was obtained from Eu(fod)$_3$ pseudocontact ^{1}H NMR spectra.

Enzymic Reduction of an Epoxide to an Alcohol

Sharon R. Steckbeck, James A. Nelson, and Thomas A. Spencer*

Department of Chemistry, Dartmouth College Hanover, New Hampshire 03755

Received October 30, 1981

We wish to report the first example of direct enzymic reduction of an epoxide to an alcohol.[1,2] Incubation of 24(*R*),25-oxidolanosterol (**1**) with standard S_{10} rat liver homogenate (RLH)[3] results in formation of 24(*R*)-hydroxycholesterol (**2**). Evidence is presented below which indicates that this transformation does not occur via an intermediate 24-keto steroid.[2]

In connection with our previous demonstration[4] that squalene 2,3(*S*);22(*S*),23-dioxide is converted efficiently by RLH to 24(*S*),25-epoxycholesterol (**3**), we wished to establish that 24(*S*),25-oxidolanosterol (**4**) would also be converted by RLH to **3**. Preparation of [2-^{3}H]**4** required separation by preparative TLC[5] of a mixture of the known[6] acetates of [2-^{3}H]**4** and [2-^{3}H]**1**[7] followed by saponification. Incubation of the [2-^{3}H]**4** with RLH for 30 min afforded 18% of product with the TLC[5] R_f value of **3**, plus 45% of unreacted **4**. The identity of **3** was confirmed, as before,[4] by $LiAlH_4$ reduction to 25-hydroxycholesterol (**5**), isotopic

(1) Dixon and Webb (Dixon, M.; Webb, E. C. "Enzymes", 3rd ed.; Academic Press: New York, 1979) list no enzyme which effects this conversion.

(2) Siekmann, Disse, and Breuer (Siekmann, L.; Disse, B.; Breuer, H. *J. Steroid Biochem.* **1980**, *13*, 1181-1205) claim that incubation of 16α,17-epoxyprogesterone (i) with rat liver microsomes affords 5% of 16β-hydroxyprogesterone (ii) and suggest that this conversion proceeds via 16-oxoprogesterone; i → ii obviously cannot be a direct epoxide reduction.

(3) RLH was prepared according to Popjak (Popjak, G. *Methods Enzymol.* **1969**, *15*, 438-440). Incubations were conducted as follows. To 5.0 mL of S_{10} RLH, without addition of coenzymes, was added 25–55 μg of purified ^{3}H-labeled substrate (specific activity ca. 38 000 dpm/μg) dissolved in ca. 50 μL of an aqueous solution containing 70–100 mg per mL of Triton WR 1339 (Ruger Chemical, Irvington, NJ). The resulting mixture was incubated at 37 °C for 60 min unless a different length of time is specified in the text. All incubations were run at least in duplicate.

(4) Nelson, J. A.; Steckbeck, S. R.; Spencer, T. A. *J. Biol. Chem.* **1981**, *256*, 1067-1068.

(5) TLC analyses were performed on LK5D silica gel plates (Whatman, Inc., Clifton, NJ); preparative TLC plates were prepared with Silica Gel 60 PF 254 + 366 (EM Laboratories, Inc., Elmsford, NY). Various ratios of ether–hexane were employed as eluent, unless noted otherwise.

(6) Boar, R. B.; Lewis, D. A.; McGhie, J. F. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2231-2235.

(7) [2-^{3}H]Lanosterol, specific activity = 38 000 dpm/μg, prepared by treatment of the corresponding ketone with acidic tritium oxide in THF, by the method of Nadeau and Hanzlik (Nadeau, R. G.; Hanzlik, R. P. Reference 3, pp 346–349) was converted to the mixture of acetates of [2-^{3}H]**1** and [2-^{3}H]**4** by the procedure given in ref 6.

0002-7863/82/1504-0893$01.25/0