in the transannular cyclization of **10**.

***cis*- (8a) and *trans*-2-Thiabicyclo[4.4.0]decane 2-α-Oxide (9a).** Treatment of **7** in THF with 0.5 equiv of BuLi at −20 °C produced a mixture of the title compounds whose proportion changed during the course of the reaction from ~1:1 to ~100% of **9a**[20] when the mixture was allowed to equilibrate. Reduction of **9a** gave sulfide **9**,[21] while reduction of a **8a**/**9a** ≃ 1:3 mixture gave the expected mixture of *cis*- and *trans*-1-thiadecalin (**8** and **9**).[21] Inversion of the same **8a**/**9a** ≃ 1:3 mixture gave a sulfoxide product whose major component was the trans β-oxide **9b**,[20] while the minor component was the cis β-oxide **8b**.[22] Consequently **8a**, from which **8b** obtains by sulfur inversion, must be *cis*-2-thiabicyclo[4.4.0]decane 2-α-oxide: ^{13}C NMR δ 56.4 (C_1), 43.8 (C_3), 34.6, 31.9 (C_5, C_7, interchangeable), 25.6, 24.2 (C_8, C_9, interchangeable), 20.7 (C_{10}), 16.6 (C_4), 21.5 (C_7).

Attempted Cyclization of (*Z*)-Thiacycloalk-4-enes. The oxides of (*Z*)-thiacyclooct-4-ene[15] and (*Z*)-7,7-dimethylthiacyclono-4-ene[45] in THF were treated with BuLi (0.5 equiv) at room temperature. Quenching with H_2O after various lenghts of time (up to 2 h) failed to yield any product of transannular cyclization.

Registry No. (±)-**1**, 104808-85-7; (±)-**1a**, 104808-86-8; (±)-**2**, 72074-95-4; (±)-**2a**, 79760-34-2; (±)-**3**, 104872-74-4; (±)-**4**, 104808-82-4; (±)-**4a**, 104808-96-0; (±)-**4b**, 104872-88-0; (±)-**4c**, 104872-89-1; (±)-**5**, 104808-81-3; (±)-**5a**, 79760-35-3; (±)-**5b**, 104808-83-5; (±)-**5c**, 104872-77-7; (±)-**6**, 104872-75-5; (±)-**6a**, 79813-60-8; (±)-**6b**, 104872-90-4; (±)-**6c**, 104872-78-8; (±)-**7**, 104808-80-2; (±)-**8**, 104808-94-8; (±)-**8a**, 104872-83-5; (±)-**8b**, 104872-85-7; (±)-**9**, 87716-82-3; (±)-**9a**, 104872-84-6; (±)-**9b**, 104872-86-8; (±)-**10**, 104808-79-9; **10** (sulfide), 68013-79-6; (±)-**11**, 104808-84-6; (±)-**11a**, 104872-79-9; (±)-**11b**, 104872-81-3; (±)-**12**, 104808-89-1; (±)-**12a**, 104872-80-2; (±)-**12b**, 104872-82-4; $\overline{CH_2}$-$\overline{(CH_2)_2CH{=}C(CH_2)_3S(CH_2)_3CHCH{=}CHCH_2}CH_2$, 104808-93-7; (±)-*trans*-2-(2-hydroxyethyl)cyclopentanol, 104872-76-6; (±)-*cis*-2-(2-hydroxyethyl)cyclopentanol, 62324-21-4; (*E*)-thiacyclodec-4-ene, 68013-80-9; cyclopentanone (pyrrolidine enamine), 7148-07-4; ethyl bromoacetate, 105-36-2; (±)-ethyl (2-oxocyclopentyl)acetate, 104808-87-9; 2-(2-hydroxyethyl)cyclopentanol (dimesylate), 104808-88-0; ethyl acrylate, 140-88-5; (±)-*trans*-2-(3-hydroxypropyl)cyclopentanol, 104808-90-4; (±)-*cis*-2-(3-hydroxypropyl)cyclopentanol, 104808-91-5; bis(3-(cyclopent-1-enyl)prop-1-yl) sulfide, 104808-92-6; (±)-(*Z*)-thiacyclooct-4-ene oxide, 104872-87-9; (±)-(*Z*)-7,7-dimethylthiacyclonon-4-ene oxide, 104808-95-9; bis(3-(cyclopent-2-en-1-yl)prop-1-yl) sulfide, 104808-97-1.

A Stereospecific Tandem Wagner–Meerwein Rearrangement in the Solvolysis of 19-Mesyloxy Steroids

Pavel Kočovský*

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 16610 Prague 6, Czechoslovakia

František Tureček

The J. Heyrovský Institute of Physical Chemistry and Electrochemistry, Czechoslovak Academy of Sciences, 12138 Prague 2, Czechoslovakia

Vratislav Langer

Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences, 16206 Prague 6, Czechoslovakia

Jana Podlahová and Jaroslav Podlaha

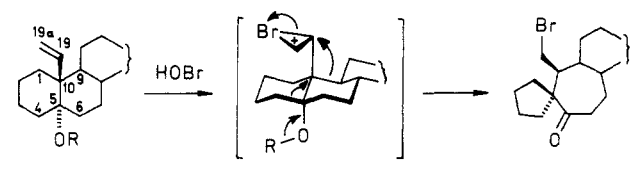
Department of Organic Chemistry, Charles University, 12840 Prague 2, Czechoslovakia

Received April 15, 1986

Acetolysis of 5α-cholestane-5,19-diol 19-methanesulfonate (**9**) smoothly leads to a new spirocyclic compound **11** as a result of tandem migrations of two antiparallel skeletal carbon–carbon bonds. This stereospecific, cascade rearrangement is found to be a general reaction of 5α-hydroxy and 5α-alkoxy steroids with an electron-deficient center at C(19) and may be viewed as a double pinacol rearrangement. The driving force for the rearrangement to occur is the eventual conversion of the hydroxyl or alkoxyl into the carbonyl group. The importance of the stereoelectronic control in the Wagner–Meerwein rearrangement is demonstrated. The structure of the spirocyclic compound **11** was determined by single-crystal X-ray analysis.

The course of the Wagner–Meerwein rearrangement[1] can be dramatically influenced by stereoelectronic effects (Figure 1). The importance of overlap between the carbocationic vacant orbital and the σ bond in the transition state was demonstrated by von Schleyer and co-workers.[1b,2]

Scheme I



1, R = H
2, R = CH_3
3, R = H
4, R = CH_3
5

Nickon and Weglein[3] pointed out that for a concerted Wagner–Meerwein rearrangement to occur the leaving and the migrating group should be antiperiplanar in an ideal case (sp^3 alignment factor). Accordingly, if two groups are

(1) For a review, see: (a) March, J. *Advanced Organic Chemistry*; 3rd ed.; Wiley-Interscience: New York, 1985. (b) Saunders, M.; Chandrasekhar, J.; Schleyer, P. v. R. In "Rearrangements of Carbocations" *Rearrangements in Ground and Excited States*; de Mayo, P., Ed; Academic: New York, 1980; Vol. 1, pp 24–34. (c) Kirk, D. N.; Hartshorn, M. P. *Steroid Reaction Mechanisms*; Elsevier: Amsterdam, 1968. (d) Sukh Dev *Fortschr. Chem. Org. Naturst.* **1981**, *40*, 49. (e) Cargill, R. L.; Jackson, T. E.; Pert, N. P.; Pond, D. M. *Acc. Chem. Res.* **1974**, *7*, 106.

(2) (a) Schleyer, P. v. R.; Lam, L. K. M.; Raber, D. J.; Fry, J. L.; McKervey, M. A.; Alford, J. R.; Cuddy, B. D.; Keizer, V. G.; Geluk, H. W.; Schaltmann, J. L. M. *J. Am. Chem. Soc.* **1970**, *92*, 5246. (b) Majerski, Z.; Schleyer, P. v. R.; Wolf, A. P. *J. Am. Chem. Soc.* **1970**, *92*, 5731. (c) see also: Tureček, F.; Hanuš, V.; Sedmera, P.; Antropiusová, H.; Mach, K. *Collect. Czech. Chem. Commun.* **1981**, *46*, 1474.

(3) Nickon, A.; Weglein, R. C. *J. Am. Chem. Soc.* **1975**, *97*, 1271.

0022-3263/86/1951-4888$01.50/0

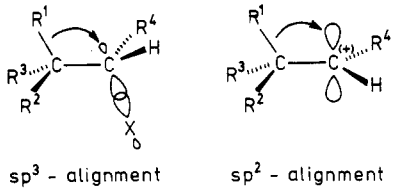
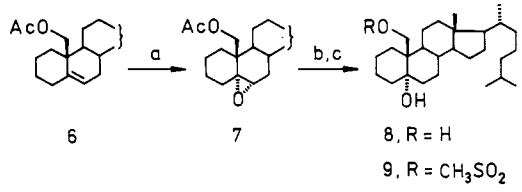


Figure 1.

Scheme II[a]



[a] (a) MCPBA, $CHCl_3$, room temperature; (b) $LiAlH_4$, Et_2O, room temperature; (c) CH_3SO_2Cl, C_5H_5N, 0 °C.

considered for migration, that which can attain a conformation closer to the ideal alignment will migrate preferentially.[3,4] The maximum allowable deviation from antiperiplanarity is believed to be about 30°.[1b] In a similar manner, in nonconcerted rearrangements with developing carbocation centers the migrating group and the receptor p orbital should be, ideally, in one plane[4] (sp^2 alignment factor).[5]

Rigid polycyclic skeletons of triterpenoids and steroids can undergo cascade Wagner–Meerwein 1,2-migrations of antiperiplanarly disposed groups,[6] either concerted or nonconcerted.[1-9] These "backbone" rearrangements[10-12] have been interpreted as a search of the system for the more stable structures[13] via stereoelectronically favored

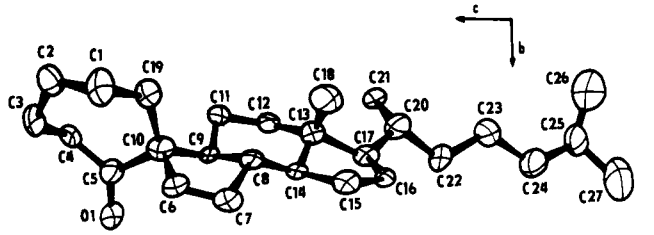
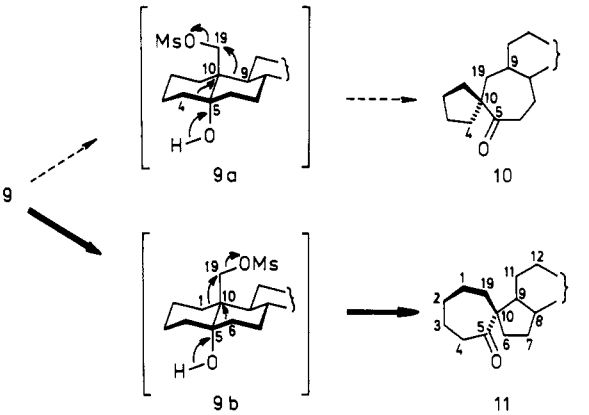


Figure 2.

Scheme III



pathways. A typical feature of these rearrangements is that only axially oriented hydrogen atoms or alkyl groups do migrate. Recently we have observed a novel tandem rearrangement of two *skeletal* (equatorial) carbon–carbon bonds on attempted hypobromous acid addition to steroidal olefins **1** and **2** (Scheme I).[14,15]

The rearrangement of **1** and **2** to **5** is triggered off by the formation of an electron-deficient center at C(19). It was therefore of interest to explore the behavior of a related species generated in a different way, e.g., by solvolysis of the corresponding 19-mesyloxy derivative. Solvolyses of steroidal 19-sulfonyloxy derivatives have been studied extensively for years, and rearrangements via migration of the C(1)–C(10),[16,17] C(9–C(10),[18] and C(5)–C(10)[19a] bonds have been reported. The 5,6-double bond[20] and 5β,6β-cyclopropane rings[19] can also participate at the C(19) cationic center.[21]

(4) (a) Smith, A. B., III; Wexler, B. A. *Tetrahedron Lett.* **1984**, *22*, 2317. (b) Smith, A. B., III; Wexler, B. A.; Tu, C.-Y.; Konopelski, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1308 and references therein.

(5) (a) Brouwer, D. M.; Hogeveen, H. *Recl. Trav. Chim. Pays-Bas* **1970**, *89*, 211. (b) Berson, J. A. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 79.

(6) (a) Dutler, H.; Jeger, O.; Ruzicka, L. *Helv. Chim. Acta* **1955**, *38*, 1268. (b) Brownlie, G.; Spring, F. S.; Stevenson, R.; Strachan, W. S. *J. Chem. Soc.* **1956**, 2419. (c) Corey, E. J.; Ursprung, J. J. *J. Am. Chem. Soc.* **1956**, *78*, 5041. (d) Turner, R. B.; Meador, W. R.; Winkler, R. E. *J. Am. Chem. Soc.* **1957**, *79*, 4122. (e) Berrier, C.; Jacquesy, J.-C.; Jacquesy, R. *Tetrahedron Lett.* **1971**, 4567. (f) Ambles, A.; Berrier, C.; Jacquesy, R. *Bull. Soc. Chim. Fr.* **1975**, 835.

(7) For concerted rearrangements, see: (a) Frappier, F.; Khuong-Huu, Q.; Jarreau, F. X. *Bull. Soc. Chim. Fr.* **1969**, 3265. (b) Jones, J. G. Ll.; Marples, B. A. *J. Chem. Soc. C* **1971**, 572. (c) Bathurst, E. T. J.; Coxon, J. M. *J. Chem. Soc., Chem. Commun.* **1974**, 131. (d) Bathurst, E. T. J.; Coxon, J. M.; Hartshorn, M. P. *Aust. J. Chem.* **1974**, *27*, 1505.

(8) For nonconcerted rearrangements, see: (a) Janot, M. M.; Frappier, F.; Thierry, J.; Lukacs, G.; Jarreau, F. X.; Goutarel, R. *Tetrahedron Lett.* **1972**, 3499. (b) Yakatani, Y.; Ponsinet, G.; Wolf, G.; Zundel, J. L.; Ourisson, G. *Tetrahedron* **1972**, *28*, 4249. (c) Jacquesy, J.-C.; Jacquesy, R.; Jolly, G. *Tetrahedron Lett.*, **1972**, 4739. (d) Jacquesy, J.-C.; Jacquesy, R.; Jolly, G. *Bull. Soc. Chim. Fr.* **1975**, 2281, 2289. (e) Jacquesy, J.-C.; Jacquesy, R.; Jolly, G. *Tetrahedron* **1975**, *31*, 2237. (f) Frappier, F.; Hull, W. E.; Lukacs, G. *J. Org. Chem.* **1981**, *46*, 4314.

(9) For comments on the concerted–nonconcerted dichotomy in backbone rearrangements, see: Thierry, J.-C.; Frappier, F.; Pais, M.; Jarreau, F.-X. *Tetrahedron Lett.* **1974**, 2149.

(10) Blunt, J. W.; Hartshorn, M. P.; Kirk, D. N. *Tetrahedron* **1966**, *22*, 3195.

(11) For review, see ref 1c and: Kočovský, P. *Chem. Listy* **1979**, *73*, 583.

(12) Jacquesy, J.-C.; Levisalles, J.; Wagnon, J. *Chem. Commun.* **1967**, 25.

(13) (a) Eliel, E. L.; Allinger, N. L.; Angyal, J. J.; Morrison, G. A. *Conformational Analysis*; Wiley-Interscience: New York, 1965; p 301. (b) Bascoul, J.; Cocton, B.; Crastes de Paulet, A. *Tetrahedron Lett.* **1969**, 2401. (c) Kirk, D. N.; Shaw, P. M. *Chem. Commun.* **1971**, 948. (d) Kirk, D. N.; Shaw, P. M. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2284. (e) Frappier, F.; Thierry, J.; Jarreau, F.-X. *Tetrahedron Lett.* **1971**, 1887. (f) Chavis, C.; Bascoul, J.; Crastes de Paulet, A. *Tetrahedron* **1977**, *33*, 1119. (g) Bascoul, J.; Noyer, E.; Crastes de Paulet, A. *Bull. Soc. Chim. Fr.* **1972**, 2744. (h) See, however (Frappier, F.; Bivin, J.; Jarreau, F.-X. *C. R. Seances Acad. Sci., Ser C* **1972**, *274*, 2190.

(14) (a) Kočovský, P.; Tureček, F. *Collect. Czech. Chem. Commun.* **1981**, *46*, 2877. (b) Kočovský, P.; Tureček, F. *Collect. Czech. Chem. Commun.* 2892. (c) For a preliminary communication, see: Kočovský, P.; Tureček, F. *Tetrahedron Lett.* **1981**, *22*, 2699.

(15) We have also shown that the corresponding 5-deoxy derivative does not react with electrophilic reagents due to severe steric hindrance. For a detailed discussioin of this topic, see: Kočovský, P.; Starý, I.; Tureček, F.; Hanuš, V. *Collect. Czech. Chem. Commun.* **1983**, *48*, 2994.

(16) Dauben, W. H.; Ben-Efraim, D. A. *J. Med. Chem.* **1968**, *11*, 287.

(17) Joska, J.; Fajkoš, J. *Zajíček, J. Collect. Czech. Chem. Commun.* **1985**, *50*, 1611.

(18) Kohen, F.; Van Bever, W.; Counsell, R. E. *J. Org. Chem.* **1970**, *35*, 2272.

(19) (a) Fajkoš, J.; Joska, J.; Tureček, F. *Collect. Czech. Chem. Commun.* **1980**, *45*, 584. (b) Isomeric 4β,5β-cyclopropano derivatives react analogously: Fajkoš, J.; Joska, J., personal communication.

(20) (a) Bonet, J. J.; Wehrli, H.; Schaffner, K. *Helv. Chim. Acta* **1962**, *45*, 2615. (b) Halpern, O.; Crabbé, P.; Cross, A. D.; Delfin, I.; Cervantes, L.; Bowers, A. *Steroids* **1964**, *4*, 1. (c) Tadanier, J. *J. Org. Chem.* **1966**, *31*, 2124. (d) Maeda, M.; Komatsu, H.; Yamamoto, Y.; Shimoirisa, H.; Yonetani, S.; Kojima, M. *J. Pharm. Soc. Jpn.* **1976**, *96*, 935.

(21) By contrast, 5,6-unsaturated 19-mesyloxy and tosyloxy steroids undergo rapid displacement with I^-, Br^-, and Cl^- to produce the corresponding unrearranged 19-halogenated compounds.[22] Treatment of the resulting 19-iodo derivatives with various nucleophiles in HMPA also leads to a clean substitution without rearrangement.[23] Furthemore, reduction of 5,6-saturated 19-mesyloxy derivatives by NaI–Zn method[24] in the presence of ^2H_2O or ^3H_2O gives high yields of 19-deuterated and/or tritiated products.[25] Analogous saturated decaline derivatives undergo simple substitution at the angular methyl group when treated with NaCN in HMPA.[26]

Results

The synthesis of the model 19-mesyloxy derivative **9** (Scheme II) started with *m*-chloroperoxybenzoic acid epoxidation of the known 19-acetoxy-5-cholestene[27] (**6**) to 5α,6α-epoxide **7**,[27] which was reduced with $LiAlH_4$ to diol **8**. The latter compound was converted to mesylate **9** in conventional manner.

Acetolysis of **9** (Scheme III) was smooth and afforded essentially one product in high yield. Evaporation of the mother liquor obtained after crystallization of the main product gave a mixture of the latter compound (80%) and its isomer (20%). According to the mass balance, the selectivity of the acetolysis is about 20:1. For the main product two isomeric structures could be suggested (**10** or **11**) which were consistent with the spectral data. The mass spectrum afforded formula $C_{27}H_{46}O$ for the molecular ion and further showed fragment ions due to losses of C_3H_5, C_3H_7, C_2H_3O, C_4H_8, and (C_4H_8 + CH_3), while the loss of C_5H_8, typical for **5** and its derivatives, was not observed. The infrared spectrum revealed the presence of a ketone carbonyl group (ν_{CO} = 1697 cm^{-1}). The presence of a $CCOCH_2$ subunit was deduced from the ^1H NMR spectrum, consistent with exchange of two protons upon treatment with $^2H_2O/NaO^2H$. The ^{13}C NMR spectrum showed the signal of a ketone carbonyl bearing two substituents in α position (δ 218.50) and a new quaternary sp^3 carbon (δ 59.77), while signals due to a double bond were absent. Hence the compound is a tetracyclic ketone with spiro arrangement of rings A and B. Nevertheless, the spectral methods could not decide between structures **10** and **11**, which was finally achieved by single-crystal X-ray analysis in favor of **11**. The molecular structure of **11** is depicted in Figure 2. The bond lengths and angles in **11** are unexceptional and do not deviate significantly from the standard values. The A ring is very close to the ideal chair conformation: the mean planes defined by C(4)–C(5)–C(10)–C(19) and C(3)–C(4)–C(1)–C(19) bisect at the dihedral angle of 121.5° and the ring dihedral angles correspond to theoretical values[28] within ±6°, except for those in the environment of C(5) which are affected by coplanarity of C(1), C(5), C(4) and C(10). The conformations of the B, C, and D rings are analogous to those of the majority of other steroid structures.[29] The B ring is intermediate between C_2 (half-chair) and C_s (envelope with the mirror plane through C(8) and ring-puckering parameter[30] of φ_m = 44.3°, Δ = 12.6°). Ring C is nearly ideal chair, while ring D is similar to B except that its geometry is closer to C_2, as documented by its φ_m = 46.5° and Δ = 5.6°. The cholestane side chain adopts a nearly fully extended conformation with the C(17)–C(25) distance of 6.36 Å and the torsional angles within the chain of 180 (9)° and 63 (4)°, alternatively. Owing to an extensive thermal motion of the side chain, the distances and angles involving C(20) through C(27) are not very reliable.

The structure of the minor product from the solvolysis of **9** was not elucidated in detail. Based on the close similarity of its ^{13}C NMR spectrum with that of **11**, the structure of the minor product can tentatively be assigned as **10**.

Scheme IV

Discussion

The experiments presented here and in the previous papers[14] demonstrate the importance of the stereoelectronic control in the Wagner–Meerwein rearrangements.[31] The driving force for the rearrangement to occur is apparently the eventual conversion of the tertiary 5α-OH in **1** and **9** (or 5α-OCH_3 in **2**) to the carbonyl group of the final product. This sequence of two stereospecific 1,2-shifts of antiperiplanarly oriented equatorial carbon-carbon bonds can be viewed as a double pinacol rearrangement (Scheme IV). In similar conformationally locked systems it might find synthetic applications in the stereospecific approach to spirocycles.[32] Furthermore, it might set the mechanistic basis for interpretation of the biogenesis of certain spirocyclic isoprenoids.

The preference for the particular reaction course, i.e., the initial migration of the C(1)–C(10) bond in **9** vs. the C(9)–C(10) bond in **1** and **2**, is difficult to account for. The reaction course in **1** and **2** can tentatively be explained by steric repulsion between 19a-H and 4β-H and 11β-H which prevents the vinyl group to be oriented perpendicularly to the C(1)–C(10) bond, whereas a favorable orientation of the vinyl with respect to the C(9)–C(10) bond meets no steric congestion of 19a-H. On the other hand, the reaction course in **9** may be affected by subtle conformational and other effects that cannot be assessed safely from mechanistic speculation or Dreiding models.[33] As known from the previous studies[14,16–19] seemingly minor distorsions of the ring geometry probably cause deviations from the ideal antiperiplanarity of the crucial bonds in the transition state and thus may be of importance for the choice of the reaction pathway. The rotational barrier about the C(10)–C(19) bond may be another factor.

Experimental Section

Materials and Equipment. Melting points (uncorrected) were obtained on a Kofler block. Optical rotations were measured in $CHCl_3$ with an error of ±3°. The infrared spectra were obtained on a Perkin-Elmer 621 instrument in CCl_4. ^1H NMR spectra were measured on Varian XL-200 (200.058 MHz, FT mode) and Tesla BS 476 (60 MHz) instrument in $CDCl_3$ at 25 °C. Chemical shifts are given in δ values (ppm) relative to the signal of tetramethylsilane (δ = 0.00). Apparent coupling constants were obtained from first-order analysis. ^{13}C NMR spectra were measured on a Varian XL-200 instrument (50.309 MHz, FT mode) in $CDCl_3$ and with tetramethylsilane as an internal reference. The degrees of carbon protonation was determined from the "attached proton test" phases.[34] The mass spectra were measured on a Jeol D-100 double focusing spectrometer (75 eV, 3 kV). The samples were introduced by using a direct inlet probe at lowest temperature enabling evaporation. The elemental composition of ions was

(22) (a) Halpern, O.; Villote, R.; Bowers, A. *Chem. Ind. (London)* **1963**, 116. (b) Djerassi, C.; Kielczewski, M. A. *Steroids* **1963**, *2*, 125.
(23) Wright, J. N.; Calder, M. R.; Akhtar, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1733.
(24) Kočovský, P.; Černý, V. *Collect. Czech. Chem. Commun.* **1979**, *44*, 246.
(25) Tureček, F.; Vereš, K.; Kočovský, P.; Pouzar, V.; Fajkoš, J. *J. Org. Chem.* **1983**, *48*, 2233.
(26) Gula, M. J.; Spencer, T. A. *J. Org. Chem.* **1980**, *45*, 805.
(27) Kočovský, P. *Collect. Czech. Chem. Commun.* **1980**, *45*, 3008.
(28) Hendrickson, J. B. *J. Am. Chem. Soc.* **1967**, *89*, 7036.
(29) Cambridge Crystallographic Database of Organic Compounds (1985 release).
(30) Altona, C.; Geise, H. J.; Romers, C. *Tetrahedron* **1968**, *24*, 13.
(31) For other recent examples see ref 4.
(32) For other approaches to spirocycles, see: Kočovský, P.; Tureček, F.; Hájíček, J. *Synthesis of Natural Products: Problems of Stereoselectivity*; CRC: Boca Raton, FL, 1986; Vol. I.
(33) Even the knowledge of the exact geometry of the starting compound (in crystal and in solution) may lead to a wrong prediction of the reaction pathway.[4]
(34) Lecocq, C.; Lallemand, J. Y. *J. Chem. Soc., Chem. Commun.* **1981**, 150.

determined by accurate mass measurements. Standard workup of an ethereal solution means washing with 5% HCl (aqueous), water, and 5% $KHCO_3$ (aqueous), drying with Na_2SO_4, and evaporation of the solvent in vacuo. Crystal data: $P2_1$, a = 12.962 (3) Å, (b = 6.260 (1) Å c = 15.711 (3) Å, β = 102.20 (2)°, Z = 2; $C_{27}H_{46}O$, M_r = 386.67, ρ_{calcd} = 1.03 g·cm^3, ρ_{obsd} = 1.023 (3) g·cm^{-3} (flotation in aqueous $ZnBr_2$), platelike crystal, 0.35 × 0.25 × 0.06 mm^3. Data collection:[35] Syntex $P2_1$, Cu Kα radiation (λ = 1.54178 Å), 2752 unique reflections in the $0 < 2\theta \leq 158°$ range, 1304 of them observed with $I > 1.96\sigma(I)$, room temperature, no absorption correction (μ = 4.13 cm^{-1}). Structure solution: direct methods and weighted Fourier syntheses, refinement by full-matrix least-squares to R = 0.089, R_w = 0.097 using MAGEX 80[36] and SHELX programs. Positions and anisotropic thermal parameters of non-H atoms together with positions and isotropic thermal parameters of H atoms refined in two blocks; average thermal parameters for hydrogens of CH_3, CH_2, and CH groups respectively were employed, methyl groups being treated as rigid bodies. No features greater than +0.17 and −0.20 e Å^{-3} were found in the final difference map. The atomic coordinates, anisotropic thermal parameters, and bond lengths and angles are available as supplementary material.

5α-Cholestane-5,19-diol (8). To a stirred solution of epoxide **7** (1.5 g) in ether (100 mL) was added lithium aluminum hydride (100 mg), the mixture was stirred at room temperature overnight and then quenched with saturated aqueous ammonium chloride. The organic layer was worked up as usual. The product was dissolved in benzene and filtered through a pad of aluminum oxide, and the solvent was evaporated in vacuo to yield diol **8** (1.1 g): $[\alpha]_D$ +18° (c 2.3); ^{1}H NMR 0.67 (s, 3 H), 3.78 (d, J = 12 Hz, 1 H), 4.07 (d, J = 12 Hz, 1 H).

Anal. Calcd for $C_{27}H_{48}O_2$: C, 80.14; 14; H, 11.96. Found: C, 80.03; H, 12.19.

5α-Cholestane-5,19-diol 19-Methanesulfonate (9). Diol **8** (1.0 g) was dissolved in pyridine (5 mL) and treated with methanesulfonyl chloride (0.5 mL) at 0 °C for 2 h. The mixture was then poured into ice, and the product was extracted with ether. Standard workup gave pure mesylate (**9** (1.05 g) as a colorless oil: $[\alpha]_D$ +24° (c 1.8); ^{1}H NMR 0.67 (s, 3 H), 2.98 (s, 3 H), 4.32 (d, J = 10 Hz, 1 H), 4.57 (d, J = 10 Hz, 1 H).

Anal. Calcd for $C_{28}H_{50}O_4S$: C, 69.66; H, 10.44; S, 6.64. Found: C, 69.52; H, 10.64; S, 6.89.

Acetolysis of 9. Mesylate **9** (500 mg) was refluxed with anhydrous sodium acetate (500 mg) in acetic acid (7 mL) and acetic anhydride (0.7 mL) for 30 min. The reaction mixture was cooled and diluted with water and the product taken up into ether. After standard workup the residue was crystallized from aqueous acetone[37] to afford pure ketone **11** (261 mg): mp 97–98 °C; $[\alpha]_D$ + 35° (c 1.6); IR 1697 cm^{-1}; ^{1}H NMR 0.66 (s, 3 H), 2.13 (ddd, J = 13.3, 10.0, and 2.0 Hz, 1 H), 2.55 (m, 2 H); ^{13}C NMR 12.15 (q), 18.70 (q), 22.53 (q), 22.60 (t), 22.80 (q), 23.87 (t), 24.67 (t), 25.44 (t), 26.57 (t), 27.98 (d), 28.45 (t), 29.40 (t), 30.78 (t), 33.72 (t), 35.68 (d), 36.20 (t), 36.45 (t), 39.50 (t, 2 C), 42.29 (d), 42.72 (s), 43.33 (t), 54.72 (d), 55.69 (d), 56.04 (d), 59.77 (s), 218.50 (s).

Anal. Calcd for $C_{27}H_{46}O$: C, 80.87; H, 11.99. Found: C, 80.65; H, 12.07.

^{1}H NMR spectrum of **10**: 0.71 (s, 3 H), 2.36 (m, 1 H), 2.85 (dd, J = 12.0 and 12.0 Hz, 1 H). ^{13}C NMR spectrum of **10**: 11.91 (q), 18.58 (q), 22.53 (q), 22.85 (q), 23.81 (t), 24.46 (t), 25.35 (t), 26.07 (t), 28.16 (t), 29.47 (t), 32.11 (t), 32.90 (t), 33.50 (t), 35.74 (d), 36.07 (t), 39.58 (t), 39.95 (t), 40.38 (t), 41.84 (d), 42.64 (s), 45.98 (t), 54.78 (d), 55.76 (d), 56.17 (d), 58.34 (s), 217.68 (s). The spectra were taken in a mixture with **11**.

Acknowledgment. We thank Dr. S. Vašíčková for measurement of IR spectra, J. Jelínková for measurement of 60-MHz ^{1}H NMR spectra, and the staff of the Analytical Laboratory of this Institute (Head Dr. J. Horáček) for elemental analyses.

Supplementary Material Available: Tables of atomic coordinates, anisotropic thermal parameters, and bond lengths and angles (5 pages). Ordering information is given on any current masthead page.

(35) Langer, V.; Humel, K. *Acta Crystallogr. Sect. C.: Cryst. Struct. Commun.*, in press.
(36) Hull, S. E.; Viterbo, D.; Woolfson, M. M.; Zhang, Z.-H. *Acta Crystallogr., Sect. A.: Found. Crystallogr.* **1981**, *A37*, 566.

(37) This single crystallization afforded material sufficient for the X-ray analysis.

Crown Ether Mediated Transport of Guanidinium Thiocyanate through a Bulk Liquid Membrane and the Correlation with the Complex Stability Constants

Theodorus B. Stolwijk,† Peter D. J. Grootenhuis,† Peter D. van der Wal,† Ernst J. R. Sudhölter,† David N. Reinhoudt,*† Sybolt Harkema,‡ Jos W. H. M. Uiterwijk,‡ and Laminus Kruise‡

Laboratories of Organic Chemistry and Chemical Physics, Twente University of Technology, 7500 AE Enschede, The Netherlands

Received March 18, 1986

A series of crown ethers with a ring varying between 18 and 33 ring atoms and possessing subunits of catechol and 1,3-xyleno have been synthesized. X-ray analysis of the 1:1 complex of guanidinium perchlorate and [2,8]dibenzo-30-crown-10 revealed complete encapsulation of the guanidinium cation by the crown ether. Association constants of guanidinium chloride and the synthesized crown ethers have been determined in methanol. Rates of transport of guanidinium thiocyanate through bulk liquid membranes of chloroform have been monitored by using the crown ethers as the carrier. The observed rates of transport could be correlated well to the determined association constants by the relation $J = (66.7 \times 10^{-8})(\alpha k K(CH_3OH)/[1 + \alpha k K(CH_3OH)])$ in which $\alpha = K(CHCl_3)/K(CH_3OH)$. The highest flux ($J(CHCl_3)$ = 38.9 × 10^{-8} mol cm^{-2} h^{-1}) was observed for benzo-30-crown-10, as carrier, which also showed the highest association constant in CH_3OH (K = 68 M^{-1}). It is concluded that the diffusion of the crown ether guanidinium thiocyanate complex is the rate-determining step in the overall transport process.

Introduction

Bulk liquid membranes are often used to investigate the complexation and transport properties of synthetic and natural ionophores with salts. The relation between the transport rate and the association constant was investigated initially by Reusch and Cussler[1] followed by Lamb et al.[2a] and Behr et al.[2b] The latter showed that with

†Laboratory of Organic Chemistry.
‡Laboratory of Chemical Physics.

(1) Reusch, C. F.; Cussler, E. L. *AIChE J.* **1973**, *19*, 736.

0022-3263/86/1951-4891$01.50/0