δ 0.95 (s, 3 H), 1.07 (s, 3 H), 1.14 (s, 3 H), 1.40 (s, 3 H), 2.33 (d, J_{AB} = 14.7 Hz, 1 H), 2.89 (d, J_{AB} = 14.1 H), 2.92 (d, J_{AB} = 14.1 Hz, 1 H), 3.78 (d, J_{AB} = 14.7 Hz, 1 H); IR (KBr) 1062 cm^{-1} (s); MS, *m/e* 192 (M^+). Anal. Calcd for $C_8H_{16}OS_2$: C, 49.96; H, 8.38. Found: C, 50.25; H, 8.40.

3,3,4,4-Tetramethylthiolane (14). Sodium (0.152 g, 6.6 mmol), thioacetic acid (0.334 g, 4.4 mmol, 0.313 mL), and HMPA (20 mL) were placed in a 50-mL round-bottom flask and stirred at room temperature for 12 h before the addition of 1 g (2.2 mmol) of ditosylate **8**. The reaction mixture was heated to 100 °C for 12 h, poured over ice and water (ca. 100 mL), and extracted with three 60-mL portions of Et_2O. The ethereal extracts were washed with water (5 × 50 mL), dried over anhydrous Na_2SO_4, and concentrated in a rotary evaporator to furnish a reddish solid (0.267 g, 100% yield), which was decolorized by distillation in a Kugelrohr apparatus, (40–44 °C/0.5 mmHg) to afford 0.238 g (89.2% yield) of the pure product **14**: ^1H NMR (90 MHz, $CDCl_3$) δ 0.98 (s, 12 H), 2.70 (s, 4 H).

3,3,4,4-Tetramethylthiolane 1-Oxide (15). Thiolane **14** (679 mg, 4.72 mmol) was oxidized following the same procedure used in the preparation of sulfoxide **6** (vide supra). The crude product was purified by flash chromatography[33] with AcOEt/hexane (1:1) as the eluant. Pure **15** (479 mg, 63.5% yield) was obtained as white, very hygroscopic crystals, whose melting point could not be reliably measured: ^1H NMR (90 MHz, $CDCl_3$) δ 0.95 (s, 6 H), 1.25 (s, 6 H), 2.67 (d, J_{AB} = 14.1 Hz, 2 H), 3.21 (d, J_{AB} = 14.1 Hz, 2 H); IR (KBr) 1487 (m), 1463 (m), 1412 (w), 1393 (m), 1381 (m), 1370 (w), 1197 (w), 1102 (m), 1030 (s), 1003 (m); MS, *m/e* 160 (M^+).[38]

Thioacetic Anhydride ($CH_3COSCOCH_3$). Thioacetic acid (7.45 g, 97.5 mmol, 6.99 mL) was placed in a 250-mL round-bottom flask provided with addition funnel and a Dewar condenser containing dry ice. Acyl chloride (13.86 mL, 195 mmol) was added dropwise and the reaction mixture was allowed to warm up to room temperature and then to gentle reflux for 4 h. Distillation afforded in a first fraction the unreacted acyl chloride (21–22 °C/5 mmHg) and in the second fraction the desired product [55 °C/5 mmHg (lit.[39] bp 155–158 °C); 17.3 g, 75% yield]: ^1H NMR (90 MHz, $CDCl_3$) δ 2.54 (s).

Acknowledgment. We are grateful to Guillermo Uribe for recording the FT NMR spectra, to Humberto Bojórquez and Luis Velasco for recording the mass spectra, to Prof. Richard S. Glass for several useful comments, and to CONACYT as well as Avon Cosmetics, S.A., for partial financial support.

Registry No. **6**, 114763-95-0; **7**, 114763-96-1; **8**, 70178-81-3; **9**, 33367-54-3; **10**, 97-62-1; **12**, 31469-16-6; **13**, 10519-69-4; **14**, 114763-97-2; **15**, 114763-98-3; **18**, 114763-99-4; **19**, 114764-00-0; Me_3SiCl, 75-77-4; TsCl, 98-59-9; AcS^-R^+, 10387-40-3; $CH_3COSCOCH_3$, 3232-39-1; thioacetic acid, 507-09-5.

(38) The mass data can be compared with those for the 1,1,4,4-tetramethyl analogue: La Londe, R. T.; Wong, C. F.; Tsai, I. M.; Wróbel, J. T.; Ruszkowska, J.; Kabzinska, K.; Martin, T. I.; McLean, D. B. *Can. J. Chem.* **1976**, *54*, 3860–3868.

(39) Bonner, W. A. *J. Am. Chem. Soc.* **1950**, *72*, 4270–4271.

A New and Stereospecific Synthesis of Cyclitols: (1,2,4/3)-, (1,2/3,4)-, and (1,3/2,4)-Cyclohexanetetrols

Nihat Akbulut and Metin Balci*

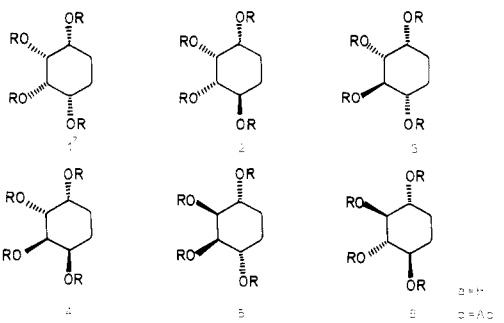
Department of Chemistry, Faculty of Science, Atatürk University, Erzurum, Turkey

Received July 20, 1987

A new and stereospecific synthesis of (1,2,4/3)-, (1,2/3,4)-, and (1,3/2,4)-cyclohexanetetrols **3a**, **4a**, and **6a** is described. Syn and anti epoxy endoperoxides **9** and **10** were synthesized by epoxidation of endoperoxide **8** with *m*-chloroperbenzoic acid. Catalytic reduction of **9** and **10** gave the corresponding diols **13** and **15**. Triethylamine-catalyzed rearrangement afforded isomeric epoxy hydroxy ketones **17** and **18**. Reduction of the carbonyl group in **17** and **18** with $NaBH_4$ gave isomeric mixtures (**13** + **20**) and (**15** + **20**), respectively. All three possible epoxy diols (**13**, **15**, **20**) were converted to the corresponding epoxy diacetates and characterized by means of analytical methods. Epoxide opening was carried out in acidified water. Opening of **13** and **15** produced only one tetrol **3a**. Reaction of **21** with acidified water followed by acetylation gave a mixture of **4b** and **6b**.

Introduction

Zelinskii et al.[1] reported that 1,3-cyclohexadiene is converted into a tetrol by oxidation with permanganate. Nearly 20 years later Posternak and Friedli[2] proved that the product was DL-(1,2,3/4)-cyclohexanetetrol (**2a**). Reinvestigation by Sable et al.[3] confirmed this finding; they isolated in addition to **2a** small amounts of the isomeric (1,2,4/3) tetrol (**3a**) and the (1,2/3,4) tetrol (**4a**). Direct hydroxylation of 1,3-cyclohexadiene with monoperoxysuccinic acid gives a mixture of 3-cyclohexene-1,2-diol and (1,4/2,3)-cyclohexanetetrol (**5a**).[4] (1,3/2,4) tetrol (**6a**) has been synthesized by reduction of conduritol B[5a] and also by bromination of *vibo*-quercitol[5b] followed by catalytic reduction.



Studies of the reaction mechanism of hydroxylation of cyclic conjugated dienes[3,6] by permanganate have revealed

(1) Zelinskii, N. D.; Denisenko, I. Ya.; Eventona, M. S. *Dokl. Akad. Nauk. SSSR* **1935**, *1*, 313.

(2) Posternak, T.; Friedli, H. *Helv. Chim. Acta* **1953**, *36*, 251.

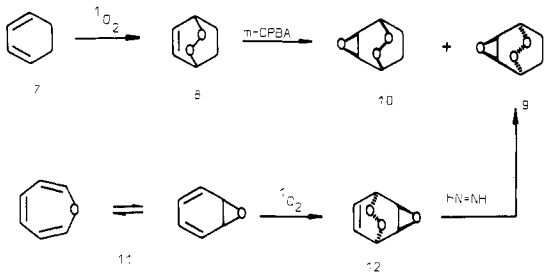
(3) Sable, H. Z.; Powel, K. A.; Katchian, H.; Niewoehner, C. B.; Kadlec, S. B. *Tetrahedron* **1970**, *26*, 1509.

(4) Yanov, N. P.; Laopatic, D. V. *Org. Katal.* **1970**, *15*. For the synthesis of **5a**, see also ref 6.

(5) (a) McCasland, G. E.; Horswill, E. C. *J. Am. Chem. Soc.* **1953**, *75*, 4020. (b) Suami, T.; Ogawa, S.; Yabe, K.; Uchida, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2804.

0022-3263/88/1953-3338$01.50/0

Scheme I

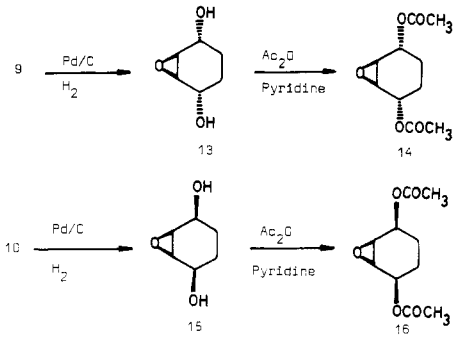


that products are formed from two competing reactions: normal hydroxylation gives the cycloalkene-1,2-diols and (1,2/3,4) tetrol while abnormal hydroxylation leads to the other products like **2a** and **3a**. On this basis, direct hydroxylation of bicyclic dienes by permangante is not a suitable method for the synthesis of the corresponding tetrols. Therefore, we describe a new and stereocontrolled method for the synthesis of **3a**, **4a**, and **6a**.[7] Our synthetic sequence is based on introduction of the two oxygen functionalities by photooxygenation of 1,3-cyclohexadiene. The other oxygen functionalities are introduced through the classical peracid epoxidation reactions. Suitable ring-opening reactions give the desired tetrols stereospecifically. The successful synthesis of these tetrols will be of considerable utility in the synthesis of natural products. Because of the array of functionalities available in **9** and **10**, they may serve as useful entries to the synthesis of the more complicated polyoxygenated systems, conduritols[8] and aminocyclitols.[9,10]

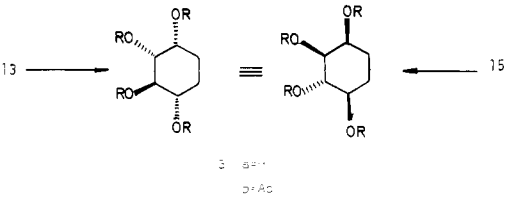
Results and Discussion

Formation of Epoxy Endoperoxides 9 and 10. Oxidation of endoperoxide 8,[11] obtained by photooxygenation of 1,3-cyclohexadiene, with *m*-chloroperbenzoic acid (*m*-CPBA) gives two isomeric epoxy endoperoxides in a 55:45 ratio. These isomers were separated by column chromatography on silica gel ($CHCl_3$/*n*-pentane, 1:1). The ^1H NMR spectra of these epoxy endoperoxides are consistent with the symmetry of their structures. However, we were not able to distinguish between the two isomers **9** and **10** on the basis of spectral data. The configurational assignment of syn and anti to the two isomeric epoxy endoperoxides is easily made by chemical means (Scheme I). We synthesized the anti isomer **9** by an independent route from oxepine–benzene oxide (**11**).[12] Foster and Berchtold reported that reaction of oxepine–benzene oxide with singlet oxygen afforded the unsaturated anti epoxy endoperoxides **12**.[13] We synthesized **12** in the same way as described in the literature. Reduction of the double bond in **12** with diimide occurs without reduction of the peroxide bond to give anti epoxy endoperoxide **9** quantitatively, identical with the major product obtained by photooxygenation and epoxidation of 1,3-cyclohexadiene.

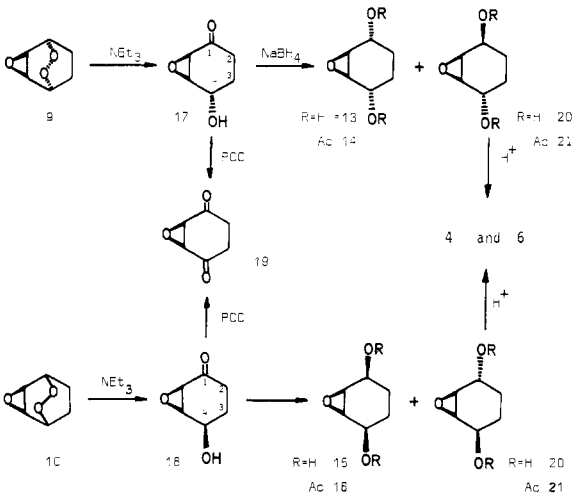
Scheme II



Scheme III



Scheme IV



Catalytic Hydrogenation of 9 and 10. Bicyclic endoperoxides can be readily reduced by hydrogen to the corresponding cis diols. Catalytic hydrogenation of **9** and **10** gave epoxy diols **13** and **15**, respectively. Since only the oxygen–oxygen bond breaks in this reaction, the configuration at all four carbon atoms must be the same as in the starting materials. Furthermore, the ^1H NMR spectra of the epoxy diols prove symmetrical structures in which a plane of symmetry bisects the methylene groups and oxirane ring and is therefore consistent only with structures **13** and **15**. The epoxy diols **13** and **15** were converted to the corresponding diacetates **14** and **16** with acetic anhydride in pyridine (Scheme II). The ^1H NMR spectra of these diacetates consist of four groups of signals which are assigned to methylene, methyl, epoxide and OC–H protons, respectively. Due to the zero coupling of the oxirane protons of compound **14** with the adjacent OC–H protons, their signal is sharper than those of the epoxide protons of the isomer **16**.

Epoxide Opening of 13 and 15. The stereoselective rupture of the C–O bonds of an epoxide by nucleophilic reagents has been stated to be governed by conformational

(6) (a) Franks, J. A., Jr.; Tolbert, B.; Steyn, R.; Sable, H. Z. *J. Org. Chem.* **1965**, *30*, 1440. (b) Steyn, R.; Sable, H. Z. *Tetrahedron* **1969**, *25*, 3579.

(7) The graphical representations used in this paper depict only one enantiomer of a racemic mixture.

(8) Aleksejczyk, R. A.; Berchtold, G. A. *J. Am. Chem. Soc.* **1985**, *107*, 2554.

(9) Suami, T.; Yabe, K. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1931. See also ref 5b.

(10) van Tamelen, E. E.; Dewey, R. S.; Timmons, R. J. *J. Am. Chem. Soc.* **1961**, *83*, 3725.

(11) (a) Murray, R. W.; Kaplan, M. L. *J. Am. Chem. Soc.* **1969**, *91*, 5358. (b) Kanoko, C.; Sugimoto, A.; Tanaka, S. *Synthesis* **1974**, 876.

(12) Vogel, E.; Günther, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 385.

(13) (a) Foster, C. H.; Berchtold, G. A. *J. Am. Chem. Soc.* **1972**, *94*, 7939. (b) Foster, C. H.; Berchtold, G. A. *J. Org. Chem.* **1975**, *40*, 3743.

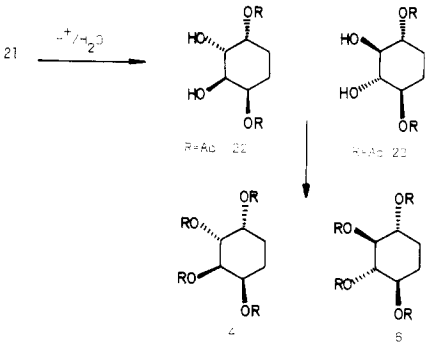
factors,[14] electronic effects,[15] and steric effects.[16] In the trans epoxide ring opening by addition of water in a classic S_N2 mechanism, both epoxides **13** and **15** should give simple product **3a**. Since the new hydroxyl group is cis (trans) to the preexisting hydroxyl groups which are present in **13** (**15**), three hydroxyl groups in the tetrol **3a** must be on the same side of cyclohexane ring as shown in **3a** (Scheme III). Although some cases are known where of configuration is retained during ring opening,[17] all these examples are of severely hindered epoxides formed from noncyclic olefines opened with nucleophiles or in nonpolar solvents. All analytical methods indicate the presence of only one tetrol from both **13** and **15**. Furthermore, the melting point (138.5–140.0 °C) of **3a** is in agreement with those reported in the literature (142.0 °C,[2] 139.5–140.0 °C[3]). Acetylation of the latter gave tetraacetate **3b** whose ^1H NMR spectrum shows the presence of one axial and three equatorial acetoxy groups.

NEt_3-Catalyzed Rearrangement of 9 and 10. After completing the synthesis of **3** we were interested in the synthesis of the asymmetrical diol **20** which opens entry to tetrols **4a** and **6a**. Therefore, we studied the NEt_3-catalyzed rearrangement of **9** and **10** (Scheme IV).

Base-catalyzed reaction of bicyclic endoperoxides results generally in the formation of hydroxy ketons.[18] Treatment of **9** or **10** with triethylamine in CH_2Cl_2 at 0 °C led within a few hours to the expected epoxy ketols **17** and **18** in yields of 90% and 93%, respectively. The ^1H NMR spectra of these isomers are fully in agreement with the proposed structures. The epoxide protons give rise to a well-resolved AB system. The B part (low field) of AB system is further split by the adjacent OC–H protons. The coupling constants are J_{34} = 0.8 Hz, J_{23} = 4.0 Hz in **17** and J_{34} = 2.7 Hz, J_{23} = 3.8 Hz in **18**. Inspection of Dreiding models indicates that the dihedral angle between H_3 and H_4 is 70–80° in **17** and 30–40° in **18**. The configurational assignment was made on the basis of these data and the known configuration of the starting materials **9** and **10**. **17** and **18** were subjected to oxidation to prove the structures chemically. The reaction of **17** and **18** with pyridine chlorochromate[19] (PCC) was complete in 2 h at room temperature and gave in both cases epoxy diketone **19** as the sole product. The ^1H NMR spectrum of **19** is highly characteristic and consists of a singlet at 3.6 ppm (epoxide protons) and an AA'BB' system at 2.3–3.3 ppm.

With the ketons **17** and **18** in hand, reduction of the ketone moiety could now be attempted. While catalytic hydrogenation of **9** and **10** affords only symmetrical epoxy diols **13** and **15**, reduction of **17** and **18** with $NaBH_4$ in CH_3OH provides a mixture of diols in both cases. The attempted separation of the above-mentioned diol mixtures failed. We, therefore, converted the diol mixtures to the corresponding diacetates. The mixture of **16** and **21** could be easily separated by column chromatography on silica gel and subsequent thin-layer chromatography. However, the mixture of **14** and **21** required repeated thin layer chromatography. Comparison of the spectral data of the isolated symmetrical diacetates with those obtained from catalytic hydrogenation of **9** and **10** showed complete agreement. The ^1H NMR spectrum of **21** is markedly different from those of **14** and **16**. Due to the lack of symmetry of the molecule, resonances of the methyl protons and epoxide protons are separated.

Scheme V



Since the mixture of **16** + **21** was readily separated, reduction of **18** with $NaBH_4$ provided a good synthetic method for preparing **21**, which was needed for the acid-catalyzed epoxide opening in the next step. Ring opening of **13** and **15** by nucleophilic attack leads to single pair of enantiomers **3a**. Such is not the case with **20**, from which a pair of diastereoisomers is expected, and, indeed, ring opening of **21** with acidified water produced a mixture of **22** and **23** (Scheme V). For separation and structure determination, this mixture was converted to the tetraacetate derivatives **4b** and **6b** which were separated by column chromatography (**6b**, 380 mg, 30%; **4b**, 620 mg, 48%). Analytical samples were obtained by TLC separation. The substance with the larger R_f value was identified as **6b**, mp 137–138 °C (lit.[3] mp 138.5–139.0 °C), and the substance with the smaller R_f value was **4b**, mp 108–109 °C (lit.[5b] 104–110 °C). The ^1H NMR spectra of **4b** and **6b** were also in full agreement with those reported in the literature. The compounds **4a** and **6a** were isolated by hydrolysis of **4b** and **6b**. All physical and spectroscopic properties compared well with those of the previously reported tetrols.[3,5b]

In summary, with relatively little synthetic effort but extensive chromatography, we achieved the stereospecific synthesis of three cyclohexanetetrols **3a**, **4a**, and **6a**, all starting from readily available 1,3-cyclohexadiene.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Solvents were concentrated at reduced pressure. Infrared spectra were obtained from films on NaCl plates for liquids or from solution in 0.1-mm cells or KBr pellets for solids on a Perkin-Elmer 337 infrared recording spectrophotometer. The ^1H NMR spectra were recorded on an EM 360 Varian spectrometer and are reported in δ units with Me_4Si as internal standard. All column chromatography was performed on silica gel 60 (Merck). TLC was carried out on Merck 0.2-mm silica gel 60 F_{254} analytical aluminum plates.

***syn*- and *anti*-3,6,7-Trioxatricyclo[3.2.2.$0^{2,4}$]nonane (9 and 10).** To a solution of endoperoxide **8** (5.6 g, 0.05 mol), prepared by singlet oxygenation of 1,3-cyclohexadiene[11] in 25 mL of CH_2Cl_2, was added *m*-chloroperbenzoic acid (13.0 g, 0.075 mmol) during 8 h, and the mixture was stirred for 3 days at room temperature. The precipitate (*m*-chloroperbenzoic acid) was removed by filtration. Concentration at 25 °C and chromatography (70 g) at 0 °C, eluting with $CHCl_3$/petroleum ether (2:3), gave first *m*-chloroperbenzoic acid and second the anti endoperoxide **9** isolated in 38% yield (2.4 g), recrystallized from CH_2Cl_2/*n*-pentane: colorless crystals, mp 141–142 °C; IR (KBr, cm^{-1}) 2540, 1600, 1450,

(14) (a) Nokajima, M.; Tomida, I.; Kurihara, N.; Takei, S. *Chem. Ber.* **1959**, *92*, 173. (b) Posternak, T. In *Les Cyclitols*; Hermann: Paris, 1962; p 38.

(15) Lemieux, R. U.; Kullnig, R. K.; Moir, R. Y. *J. Am. Chem. Soc.* **1958**, *80*, 2237.

(16) Sable, H. Z.; Adamson, T.; Tolbert, B.; Posternak, T. *Helv. Chim. Acta* **1963**, *46*, 1157.

(17) (a) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill Book Co. Inc.: New York, 1962. (b) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737. (c) Wasserman, H. H.; Aubrey, N. E. *J. Am. Chem. Soc.* **1956**, *78*, 1726.

(18) (a) Balci, M. *Chem. Rev.* **1981**, *81*, 91. (b) Kornblum, N.; de La Mare, H. E. *J. Am. Chem. Soc.* **1951**, *73*, 880.

(19) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

1350, 1057, 898, 862, 640; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.5–2.2 (m, 4 H), 3.6–3.8 (m, 2 H), 4.3–4.55 (m, 2 H). Anal. Calcd for $C_6H_8O_3$: C, 56.25; H, 6.25. Found: C, 55.83; H, 6.37.

Eluting with chloroform gave as a third fraction the endoperoxide **10** in a yield of 29% (1.9 g), recrystallized from CCl_4: colorless crystals, mp 109–110.5 °C; IR (KBr, cm^{-1}) 2935, 1400, 1340, 1250, 1060, 880, 800; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.6–2.6 (AA'BB' system, 4 H), 3.42–3.5 (br s, 2 H), 4.3–4.5 (m, 2 H). Anal. Calcd for $C_6H_8O_3$: C, 56.25; H, 6.25. Found: C, 56.02; H, 6.14.

***anti*-3,6,7-Trioxatricyclo[3.2.2.0^{2,4}]nonane (9) via Diimide Reduction of *anti*-3,6,7-Trioxatricyclo[3.2.2.0^{2,4}]non-8-ene.** A 100-mL flask was charged with potassium azodicarboxylate[20] (7.84 g, 40 mmol) in 40 mL of dry CH_2Cl_2. The slurry was cooled to 0 °C and a solution of **12** (500 mg, 4 mmol) in 20 mL of CH_2Cl_2 was added. While cooling and stirring, a solution of HOAc (2.4 g, 40 mmol) in 10 mL of CH_2Cl_2 was added dropwise within 30 min and stirred until complete discharge of the characteristic yellow azodicarboxylate color. Subsequently 50 mL of H_2O was added slowly and the organic layer was extracted with saturated, aqueous $NaHCO_3$ and washed with water. After drying and concentration, the residue was filtered through a short column, eluting with $CHCl_3$/*n*-pentane (1:1). Evaporation of solvent gave **9** (230 mg, 45%) as colorless crystals. The compound was identical in its physical and spectral properties with those obtained as the first fraction by the epoxidation reaction of compound **8**.

Catalytic Reduction of 9 and 10: *t*-2,*c*-3-Epoxy-*c*-4-hydroxy-*r*-1-cyclohexanol (13) and *c*-2,*t*-3-Epoxy-*c*-4-hydroxy-*r*-1-cyclohexanol (15). Into a 50-mL flask were placed Pd/C (10 mg, 5%) and **9** (256 mg, 2 mmol) in 10 mL of methanol. The reaction mixture was hydrogenated for 1 h at room temperature and normal pressure. The catalyst was removed by filtration. Concentration gave **13** (234 mg, 90%) as colorless crystals from $CHCl_3$: mp 76–77.5 °C; IR (KBr, cm^{-1}) 3440–3240, 2950, 1650, 1440, 1200, 1050, 980; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.4–1.7 (m, 4 H), 1.9–2.1 (br s, 2 H), 3.2 (s, 2 H), 3.9–4.25 (m, 2 H). Anal. Calcd for $C_6H_{10}O_3$: C, 55.38; H, 7.69; Found: C, 55.13; H, 7.55.

Compound **16** was synthesized from peroxide **10** as described above for the synthesis of the diol **13**. Diol **15** was obtained in 83% yield as colorless needles from ether: mp 71–71.5 °C; IR (KBr, cm^{-1}) 3300–3450, 2950, 1420, 1250, 1060, 990, 930, 895; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.4–1.6 (m, 4 H), 2.4–2.9 (br s, 2 H), 3.45 (br s, 2 H), 3.8–4.1 (m, 2 H). Anal. Calcd for $C_6H_{10}O_3$: C, 55.38; H, 7.69. Found: C, 55.07; H, 7.52.

14 and 16. To a stirred solution of **13** (390 mg, 30 mmol) in 10 mL of pyridine was added acetic anhydride (765 mg, 75 mmol). The reaction mixture was stirred at room temperature for 4 h. Water (40 mL) was added to the reaction mixture, and the solution was extracted with $CHCl_3$. The combined organic extracts were washed with water, dried, and removed under reduced pressure. The residue was filtered through a short column (10 g), eluting with CH_2Cl_2. Concentration gave **14** (417 mg, 65%): IR (CCl_4, cm^{-1}) 2850, 1740, 1370, 1240, 1030, 905; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.5–1.7 (m, 4 H), 2.1 (s, 6 H), 3.1 (br s, 2 H), 4.9–5.1 (m, 2 H). Anal. Calcd $C_{10}H_{14}O_5$: C, 56.07; H, 6.54. Found: C, 57.02; H, 6.23.

16 was synthesized as described above: mp 147–149 °C (recrystallized from ether/*n*-pentane); IR (CCl_4, cm^{-1}) 2960, 2940, 1730, 1240, 1030, 905; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.45–1.7 (m, 4 H), 2.0 (s, 6 H), 3.32 (br s, 2 H), 4.8–5.1 (m, 2 H). Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.54. Found: C, 55.93; H, 6.33.

***trans*-2,3-Epoxy-4-hydroxycyclohexan-1-one (17) and *cis*-2,3-Epoxy-4-hydroxycyclohexan-1-one (18).** To a solution of **9** (512 mg, 4 mmol) in 20 mL of CH_2Cl_2 was added a solution of triethylamine (200 mg, 8 mmol) in 10 mL of CH_2Cl_2 at 0 °C. The reaction mixture was stirred at 0 °C for 1 h. Concentration and chromatography (10 g), eluting with $CHCl_3$/*n*-petroleum ether (1:1), gave **17** (476 mg, 93%); mp 39–40 °C (colorless prisms, recrystallized from ether/*n*-pentane at 0 °C); IR ($CHCl_3$, cm^{-1}) 3590, 3500–3400, 2940, 1710, 1380, 1060, 900; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.8–2.6 (m, 4 H), 2.85–3.1 (br s, 1 H), 3.25 (d, B part of AB system, J = 3.8 Hz, 1 H), 3.5 (dd, A part of AB system, J = 3.8 Hz, 2.7 Hz, 1 H), 4.3–4.6 (m, 1 H). Anal. Calcd $C_6H_8O_3$: C, 56.25; H, 6.25. Found: C, 55.84; H, 6.13.

18. The same procedure was employed as described above for the synthesis of **17** from the peroxide **9**. **18**: wax; yield 90%; IR (film, cm^{-1}) 3500, 3300, 2945, 1715, 1410, 1330, 1260, 1060; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.8–2.6 (m, 5 H), 3.34 (d, B part of AB system, J = 4.0 Hz, 1 H), 3.6 (dd, A part of AB system, J = 4.0 Hz, 0.8 Hz, 1 H), 4.0–4.3 (m, 1 H). Anal. Calcd for $C_6H_8O_3$: C, 56.25; H, 6.25. Found: C, 56.87; H, 6.41.

2,3-Epoxy-1,4-cyclohexanedione (19). To a solution of **17** (128 mg, 1 mmol) in 10 mL of CH_2Cl_2 was added pyridine chlorochromate (300 mg, 1.2 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h and was filtered through a short column (10 g), eluting with CH_2Cl_2. Concentration gave pure **19** (44 mg, 35%): IR (CCl_4, cm^{-1}) 2920, 1730, 1425, 1273, 1195, 1020, 955, 862; ^{1}H NMR (60 MHz, $CDCl_3$) δ 2.2–3.25 (AA'BB' system, 4 H), 3.6 (s, 2 H). Anal. Calcd for $C_6H_6O_3$: C, 57.14; H, 4.76. Found: C, 57.40; H, 4.52.

The same procedure was employed also to **18** to give **19** in a yield of 44%.

$NaBH_4$ Reduction of 18. **18** (1092 mg, 9 mmol) was dissolved in 50 mL of absolute THF. $NaBH_4$ (6 g, 0.16 mol) was added in portions during 15 min. The reaction mixture was allowed to stir for 4 h at room temperature. The reaction mixture was filtered through a column (10 g), eluting with $CHCl_3$. Concentration gave a diol mixture of **15** and **20**. Chromatography of this mixture on silica gel (30 g), eluting with $CHCl_3$/MeOH (97:3), gave a pure diol mixture (900 mg, 81%). This mixture could not be separated. Therefore, the mixture was acetylated as described for the synthesis of **14** and **16**. After a short column chromatography (10 g), a mixture of **16** and **21** (1152 mg, 70%) was obtained. The ratio of these isomers was determined by ^{1}H NMR spectroscopy to be 45:55 (16:21). The acetate mixture was separated on a column (60 g), eluting with ether/*n*-petroleum ether (1:4). As the first fraction, **21** was isolated (280 mg). The other fractions which contain **21** and **16** were submitted again to column chromatography. An analytical sample of **21** was obtained by TLC followed by crystallization from ether/petroleum ether. **21**: mp 98–99 °C (colorless prisms); IR (KBr, cm^{-1}) 2990, 2940, 1740, 1440, 1250, 1050, 860, 810, 795; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.3–1.8 (m, 4 H), 2.05 (s, 3 H), 2.07 (s, 3 H), 3.2–3.5 (AB system, 2 H), 4.8–5.3 (m, 2 H). Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.54. Found: C, 56.38; H, 6.68. As the last fraction, **16** (330 mg) was isolated. Comparison of the spectral data of this compound with those isolated by catalytic hydrogenation of **10** followed by acetylation indicated their identity. $NaBH_4$ reduction of compound **17** under the conditions employed for the reduction of compound **18** gave a mixture of the diols **13** and **20**. This mixture was acetylated as described for the formation of **14** from diol **13**. No efficient separation of the resulting mixture could be achieved.

(1,2,4/3)-Cyclohexanetetrol 3a. **13** (520 mg, 4 mmol) was dissolved in 15 mL of 0.02 N H_2SO_4 and the resulting solution was heated at 105 °C for 1 h. After cooling to room temperature, the acid was neutralized with $BaCO_3$. After filtration of the precipitate, the solvent was removed. The residue was filtered through a short column (5 g), eluting with ether/MeOH (4:1). After removal of the solvent, the residue was recrystallized from MeOH/ether (373 mg, 63%). For the spectroscopic studies **3** was converted into the corresponding tetraacetate **3b** as described by for synthesis of **14** and **16**. **3b**: yield 58%; IR (CCl_4, cm^{-1}) 2960, 1740, 1445, 1370, 1250, 1050; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.7–1.9 (m, 4 H), 2.0 (s, 9 H), 2.1 (s, 3 H), 4.67–5.60 (m, 4 H).

(1,2/3,4)- and (1,3/2,4)-Tetraacetoxycyclohexane (4b and 6b). **20** or **21** (520 mg, 4 mmol) was dissolved in 15 mL of 0.02 N H_2SO_4, and the resulting solution was heated at 105 °C for 3 h. After cooling to room temperature, the acid was neutralized with $BaCO_3$. After filtration of the precipitate and concentration, the residue was filtered through a short column (5 g), eluting with ether/MeOH (6:1). After concentration the residue was dissolved in 20 mL of pyridine. To the stirred solution was added acetic anhydride (1530 mg, 15 mmol). The reaction mixture was stirred at room temperature for 4 h. Water (50 mL) was added to the reaction mixture, and the solution was extracted with ether. The combined organic extracts were washed with dilute HCl and water and concentrated. The ratio of the these isomers was determined by ^{1}H NMR spectroscopy to be 60:40 (**4b**:**6b**). The tetraacetate

(20) (a) Bedos, P.; Ruyer, A. *C. R. Hebd Seances Akad Sci.* **1933**, *106*, 625. (b) McCasland, G. E.; Horswill, E. C. *J. Am. Chem. Soc.* **1953**, *75*, 4020.

mixture was separated on a column (50 g), eluting with petroleum ether/ether (7:3). As the first fraction **6b** (380 mg, 30%) and as the second fraction **4b** (620 mg, 48%) were isolated. Pure analytical samples were obtained by TLC separation. Comparison of the physical data of **4b** and **6b** with those reported in the literature[3,5b] was in full agreement.

(1,2/3,4)- and (1,3/2,4)-Cyclohexanetetrol (4a and 6a). A mixture of **4b** or **6b** (316 mg, 1 mmol) and 4 N hydrochloric acid (10 mL) was heated at 90 °C for 5 h. Then the solution was concentrated to give an oily product, which crystallized upon addition of ethanol to afford colorless crystals. Recrystallization from methanol gave pure samples whose melting points did not change. **4a**: 117 mg (77%), mp 215–217 °C (lit.[2] mp 216 °C, lit.[3] mp 209–211 °C). **6a**: 103 mg (70%), mp 185–185.5 °C (lit.[2,5b] mp 187–188 °C). All physical data were in full agreement with those reported in the literature.

Acknowledgment. We thank Atatürk University for the Financial support (Grant 1986/5) of this work. We also express our thanks to the Department of Chemistry and the firm TÜRK HENKEL (in İstanbul) for partial support and to Mr. Sahmettin Yildiz for technical assistance.

Kinetics of Ionization of Nitromethane and Phenylnitromethane by Amines and Carboxylate Ions in Me_2SO–Water Mixtures. Evidence of Ammonium Ion–Nitronate Ion Hydrogen Bonded Complex Formation in Me_2SO-Rich Solvent Mixtures

Claude F. Bernasconi,* Dahv A. V. Kliner, Amy S. Mullin, and Jiu Xiang Ni

Thimann Laboratories of the University of California, Santa Cruz, California 95064

Received March 15, 1988

Rate constants of ionization of phenylnitromethane in seven amine buffers and six carboxylate buffers and of nitromethane in five amine buffers were determined in 90% Me_2SO–10% water. Similar experiments with a smaller selection of buffers were performed in water, 50% Me_2SO–50% water, and 70% Me_2SO–30% water. Buffer plots with amine buffers in 70% and 90% Me_2SO, but not with carboxylic acid buffers, showed downward curvature, which was attributed to a hydrogen-bonded association complex between the nitronate ion and the protonated amine. Association equilibrium constants for these complexes were determined, and τ values for hydrogen bonding were calculated on the basis of the Hine equation. These τ values ranging from 0.024 to 0.039 are much higher than those for the association between protonated amines and phenoxide ions in water (τ = 0.013, Stahl and Jencks, *J. Am. Chem. Soc.* **1986**, *108*, 4196), presumably because of reduced hydrogen-bonding stabilization of the nitronate ions by the solvent. Absence of downward curvature in the buffer plots with carboxylic acids is believed to be a consequence of somewhat lower association constants and, more importantly, of competing nitronic acid formation at the low pH values required to study the carboxylic acids. The possibility that the association complex might represent Bordwell's intermediate in the deprotonation of nitroalkanes ($BH^+\cdots\bar{C}H(R)NO_2$) is discussed and rejected. The *intrinsic* rate constants for proton transfer ($k_0 = k_1^B/q = k_{-1}^{BH}/p$ at $\Delta pK + \log p/q = 0$) increase strongly with increasing Me_2SO content of the solvent, but more so when the ionizing base is a carboxylate ion than when it is an amine. This increase is mainly due to a transition state in which solvation of the developing nitronate ion lags behind proton transfer. When the ionizing base is a carboxylate ion, early desolvation of the base adds to the solvent effect on k_0, but when the ionizing base is an amine, the late solvation of the developing ammonium ion attenuates the solvent effect on k_0. The Brønsted β values show the familiar increase with increasing Me_2SO content of the solvent, irrespective of buffer type.

The kinetic study of the ionization of nitroalkanes has played a central role in the development of current mechanistic notions about proton transfer at carbon in general.[1-5] This is because many features that are typical of proton transfer to or from carbon in general manifest themselves more dramatically with nitroalkanes than with other carbon acids.[6] The most notable characteristics that distinguish most proton transfers at carbon from such transfers between normal acids and bases are their high intrinsic barriers and the disparity of their Brønsted coefficients ("imbalances"), with α_{CH} (variation of deprotonation rate with pK_a of carbon acid) being larger than β_B (variation of deprotonation rate with pK_a of base).[1,2,4,7,8] According to current views,[9] these two features are in large measure related and actually just different manifestations of the same underlying phenomenon, namely, the fact that the development of resonance and solvation of the carbanion lags behind the proton transfer at the transition state.[1-3,7-10]

New mechanistic insights have come from the quantitative study of solvent effects on rates and equilibria of

(1) Fukuyama, M.; Flanagan, P. W. K.; Williams, F. T.; Frainer, L.; Miller, S. A.; Schechter, H. *J. Am. Chem. Soc.* **1970**, *92*, 4689.
(2) (a) Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 3907. (b) Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3107.
(3) Kresge, A. J. *Can. J. Chem.* **1975**, *52*, 1897.
(4) Keeffe, J. R.; Morey, J.; Palmer, C. A.; Lee, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1295.
(5) Cox, B. G.; Gibson, A. *J. Chem. Soc., Chem. Commun.* **1974**, 638.
(6) For reviews, see: (a) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1. (b) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University: Ithaca, NY, 1973. (c) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475. (d) Crooks, J. E. In *Proton Transfer Reactions*; Caldin, E., Gold, V., Eds.; Wiley: New York, 1975; p 153. (e) Hibbert, F. *Compr. Chem. Kinet.* **1977**, *8*, 97. (f) Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335.
(7) Bell, R. P.; Grainger, S. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1367.
(8) Terrier, F.; Farrell, P. G.; Lelièvre, J.; Chatrousse, A. P. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1479.
(9) (a) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301.
(10) Pross, A.; Shaik, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1129.

0022-3263/88/1953-3342$01.50/0