Synthesis and Chemistry of Some Orthoesters of Bicyclo[2.2.1]heptanediols

Ronald R. Sauers* and Paul A. Odorisio

The New Brunswick Department of Chemistry, Rutgers University, New Brunswick, New Jersey 08903

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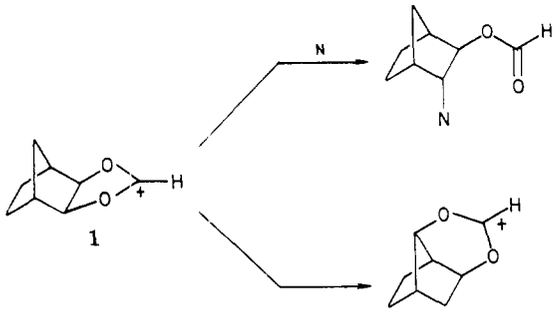
Orthoesters have been prepared from *cis,exo*-2,3-bornanediol, *cis,exo*-2,3-norbornanediol, and *cis,endo*-2,3-norbornanediol. Under a variety of conditions, dioxolenium ions were generated therefrom, e.g. hot trifluoracetic acid, acetyl chloride in acetone, hot phenyl isocyanate. The ions did not rearrange under any of the conditions tried, but acetone and cyclohexanone were alkylated by them. Further, the formation of bornylene or norbornene was the result of heating the orthoesters in phenyl isocyanate.

This study was initiated with the objective of investigating the chemistry of norbornyldioxolenium ions symbolized by formula **1**. On the one hand, there are potentially useful synthetic transformations of **1** involving nucleophilic ring opening (eq 1).[1-5] Of additional interest



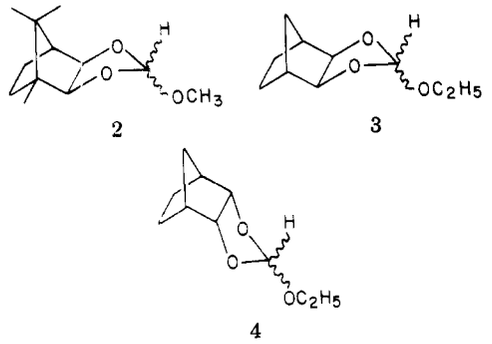
(1)

(2)

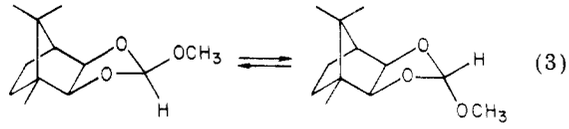
were the intramolecular rearrangements symbolized by eq 2. This kind of rearrangement could be highly synchronized or involve discrete ions formed by heterolysis of a C–O bond.[6,7] Recently, some examples of reactions involving carbon skeletal rearrangements of dioxolenium ions have been reported.[8,9]

Results and Discussion

Syntheses and Structure. The dioxolenium ions were prepared from orthoesters **2**, **3**, and **4** which in turn were prepared from the corresponding glycols by acid-catalyzed reactions with trimethyl or triethyl orthoformate. In all cases mixtures of esters were produced as evidenced by their NMR spectra. For example, the formyl protons of compound **3** appeared as singlets at δ 5.58 and 5.50 in an area ratio of 9:1. In a different preparation of **3** the ratio of these two-proton peaks was 4:1, an indication that product formation is partly formed under kinetically controlled conditions. The behavior of **2** was more extreme in that area ratios of the formyl protons at δ 5.6 and 5.5 varied from 2:3 to 16:1. There was no obvious change in the experimental procedures, and it is clear that minor changes in reaction conditions, workup, and/or NMR solvent purity affected the results. Most likely, the contact time with acids determines the epimeric content of the product. We found that on long standing or in some samples of $CDCl_3$ the epimeric content changed with time. For example, a sample which initially contained a 1:2 mixture was transformed to a 40:1 mixture in $CDCl_3$; further standing did not alter the ratio.



We interpret these data in terms of equilibration of the epimeric species **2a** and **2b** via dioxolenium ions (eq 3).



(3)

2a **2b**

By analogy with the work of Plĕnat et al.,[11] we assign structure **2a** to the thermodynamically more stable isomer and **2b** to the kinetically favored isomer. From an examination of molecular models it appears that the planar ion **1** can be more readily attacked from the endo face to form **2b**.

Reactions of Orthoformate with Electrophiles. Treatment of **3** with *p*-toluenesulfonic acid in acetic acid–acetic anhydride[12] (3 h, 25 °C) gave a product which was an acetoxy formate. Base-catalyzed hydrolysis of this product led to essentially pure *cis,exo*-2,3-norbornanediol. Under more vigorous conditions, trifluoroacetic acid at 75 °C for 2 h, there was obtained the bis(trifluoroacetate) **5** of the unrearranged system (eq 4). Under the same conditions, the endo orthoester **4** gave the (unrearranged) bis(trifluoroacetate) of *cis,endo*-2,3-norbornanediol.

The low tendency of these systems to undergo rearrangements and/or elimination[6] suggested that the dioxolenium ions are relatively stable toward heterolysis.

(1) Perst, H. "Oxonium Ions in Organic Chemistry"; Verlag Chemie: Weinheim, 1971.
(2) Meerwein, H. *Methoden Org. Chem.* (*Houben Weyl*) **1965**, *4*, 299.
(3) DeWolfe, R. H. "Carboxylic Ortho Acid Derivatives"; Academic Press: New York, 1970; Chapter 2.
(4) Newman, M. S.; Chen, C. H. *J. Am. Chem. Soc.* **1973**, *95*, 278.
(5) (a) Hartmann, W.; Heine, H.-G.; Wendisch, D. *Tetrahedron Lett.* **1977**, 2263. (b) Owen, G. R.; Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1976**, *41*, 3010. (c) Robbins, M. J.; Mengel, R.; Jones, R. A.; *J. Am. Chem. Soc.* **1973**, *95*, 4074. (d) An example of reaction 1 was reported subsequent to completion of this manuscript: Bazbouz, A.; Coste, J.; Christol, H.; and Plĕnat, F. *Tetrahedron Lett.* **1979**, 11.
(6) Related studies by Lambert, J. B.; Mark, H. W. *J. Amn. Chem. Soc.* **1978**, *100*, 2501, have revealed extensive rearrangement and elimination of an acetoxynorbornyl cation.
(7) Paulsen, H.; Brauer, O. *Chem. Ber.* **1977**, *110*, 331.
(8) Kelly, R. C.; Van Rheenen, V. *Tetrahedron Lett.* **1976**, 1067.
(9) Trost, B. M.; Latimer, L. H. *J. Org. Chem.* **1978**, *43*, 1031.
(10) Burgstahler, A. W.; Boger, D. L.; Naik, N. C. *Tetrahedron* **1976**, *32*, 309. These workers prepared the ethyl analogue but did not observe two isomers.
(11) Bazbouz, A.; Christol, H.; Coste, J.; Plĕnat, F. *Bull. Soc. Chim. Fr.* **1978**, 305.
(12) Winstein, S.; Buckles, R. E. *J. Am. Chem. Soc.* **1943**, *65*, 613.

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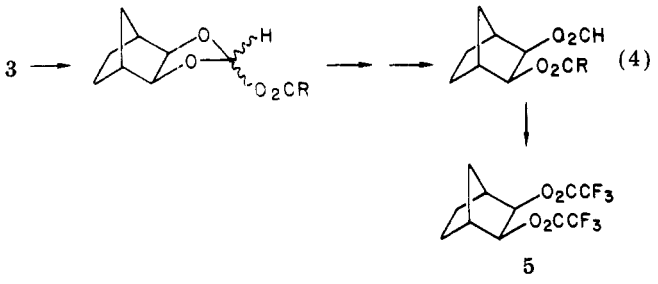
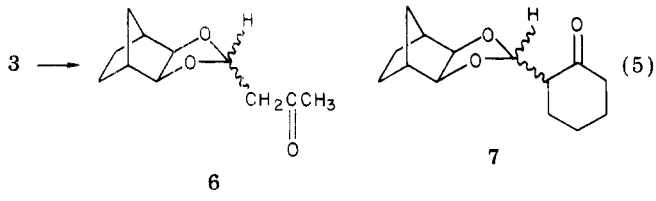


Instead, it is likely that they react via a more energetically favorable pathway which involves the formation and rearrangement of acyloxy dioxolanes.[12]

In an effort to promote nucleophilic reactions of the type shown in eq 1, we investigated the reaction of **3** and **4** with acetyl chloride.[5] Intractable mixtures of chloroformates were obtained using acetonitrile as solvent, but the reaction in acetone proved to be relatively clean.[13] A product with the molecular formula $C_{11}H_{16}O_3$ was obtained in 54% yield from the reaction between **3** and acetyl chloride. From an analysis of the spectral data it was deduced that the structure of this product corresponded to a mixture of the epimers of **6** (eq 5). A reasonable mechanism for the

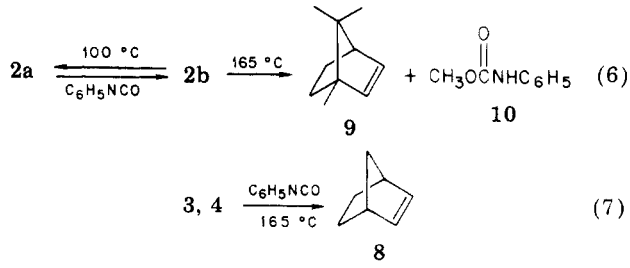


formation of **6** involves attack of **1** on the enol form of acetone followed by proton loss.[14]

In order to expand the synthetic utility of this transformation, we subjected cyclohexanone to the same reaction conditions and obtained a 30% yield of a substance to which we assign structure **7**. These reactions may be synthetically useful in view of the mildness of the reaction conditions and the possibility that simpler orthoesters may suffice.[15] It is clear that the success of the alkylation reactions depends on the failure of the nucleophilic substitution step (eq 1), a failure which we view as a manifestation of the general inertness of *exo*-norbornyl systems in S_N2 reactions.[16]

Finally, a series of reactions were run in which orthoesters **2**, **3**, and **4** were heated in phenyl isocyanate. Hoffmann and co-workers[17] have shown that this reagent effects dealkoxylation of orthoesters via a cationic intermediate and proposed Scheme I to rationalize their findings.

In agreement with Scheme I, we found that compound **2** underwent epimerization on heating to 100 °C in phenyl isocyanate. Under more forcing conditions bornylene and methyl phenylcarbamate were formed (eq 6). Under



similar conditions **3** and **4**[18] produced norbornene (eq 7). The formation of olefins in this reaction is most simply rationalized in terms of decarboxylation of the carbenes formed via proton loss from the intermediate dioxolenium ions (Scheme I).[19] This option was not available to the system studied by Hoffmann, and the generality of the decarboxylation step is yet to be demonstrated.

Summary and Conclusions

The chemistry of the dioxolenium ions examined in this study is clearly dominated by the bicycloheptyl framework. Nucleophilic attack is inhibited by steric and structural factors, but it is less clear why no carbon skeletal rearrangements could be induced. Despite this, some new facets of orthoester chemistry were observed including the alkylation of ketones and the formation of olefins on treatment with phenyl isocyanate.

Experimental Section

Infrared spectra were determined on a Perkin-Elmer Model 137 spectrometer. Nuclear magnetic resonance spectra were obtained from a Varian Model T-60 spectrometer. Chemical shifts are based on internal tetramethylsilane as a standard. Integration data is accurate to ±10%. Gas chromatographic data was obtained from an Aerograph Model A-90-P. Mass spectra were determined at 70 eV on a Hitachi RMU 7 instrument.

***cis,exo*-2,3-Norbornanediol.** A modification of the procedure given by Wiberg and Saegebarth[20] was used. A 5-L flask containing 1800 mL of *tert*-butyl alcohol, 400 mL of water, 900 g of crushed ice, and 19.2 g (0.204 mol) of norbornylene was cooled to 0 °C. A solution of 46.0 g (0.291 mol) of $KMnO_4$ and 10.0 g (0.25 mol) of NaOH in 1600 mL of water was added dropwise to the above solution over a 20-min period with stirring. After the addition was complete the reaction was quenched with excess sodium bisulfite to reduce any excess $KMnO_4$ and MnO_2. The resulting white precipitate was filtered and the filtrate was concentrated on a rotating evaporator to 1500 mL. The concentrated aqueous solution was extracted with four 1500-mL portions of CH_2Cl_2. The combined CH_2Cl_2 extracts were dried over anhydrous $MgSO_4$ and evaporated to give 13.51 g (52%) of crude diol, mp 131–135 °C. A 2.00-g portion of the crude diol was recrystallized from toluene and 1.64 g (82%) of white plates were collected, mp 139–140 °C (lit.[20] 139.5–140.5 °C).

Ethyl Orthoformate Ester of *cis,exo*-2,3-Norbornanediol (3). In a round-bottom flask connected to an apparatus for distilling, a mixture of 6.09 g (0.0475 mol) of *cis,exo*-2,3-norbornanediol, 8.45 g (0.0570 mol) of triethyl orthoformate, and 0.11 g (0.90 mmol) of benzoic acid was stirred and heated at 120–140 °C. The reaction was completed after 4.17 g (0.0905 mol, 95% of the theoretical 2 equiv) of ethanol was collected (approximately 2 h). The remaining reaction mixture was diluted to 50 mL with diethyl ether and washed with two 50-mL portions of 5% Na_2CO_3 solution and one 50-mL portion of distilled water. The ether layer was dried over anhydrous $MgSO_4$ and the ether was evaporated

(13) Preliminary experiments under more forcing conditions (neat acetyl chloride, 6 h at 85 °C) led to a four component product mixture which was not investigated further.

(14) A mechanism involving carbene formation followed by insertion on acetone C–H bonds was ruled out by the results of an experiment which utilized acetone-d_6 as solvent. The product isolated still contained a proton on the dioxolane ring (unpublished observation of P. A. O.): see Köll, P.; Deyhim, S. *Chem. Ber.* **1978**, *111*, 2913, for a possible analogy.

(15) Similar alkylations have been carried out on trimethylsilyl enol ethers using $TiCl_4$ (Mukaiyama, T.; Hayashi, M. *Tetrahedron Lett.* **1974**, 15) and directly on ketones using BF_3 (Mock, W. L.; Tsou, H-R.; Abstracts, 175th National Meeting of the American Chemical Society, Anaheim, Calif., March 13–17, 1978, No. ORGN-78.

(16) Schaefer, J. P.; Weinberg, D. S. *J. Org. Chem.* **1965**, *30*, 2639. Schaefer, J. P.; Dagani, M. J.; Weinberg, D. S. *J. Am. Chem. Soc.* **1967**, *89*, 6938.

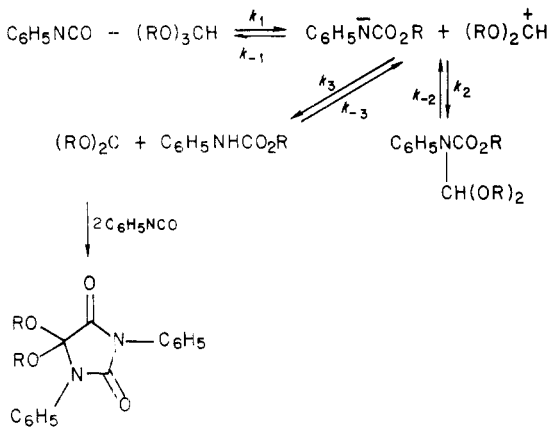
(17) Hoffmann, R. W.; Reiffen, M.; *Chem. Ber.* **1977**, *110*, 49.

(18) Pyrolysis of **4** lead to partial decarboxylation, but the starting material was decomposed under our conditions. More extensive studies are planned.

(19) For related studies on the pyrolysis of orthoesters, see: Crank, G.; Eastwood, F. W. *Aust. J. Chem.* **1964**, *17*, 1392.

(20) Wiberg, K. B.; Saegebarth, K. A. *J. Am. Chem. Soc.* **1957**, *79*, 2822.

Scheme I



on a rotating evaporator. The residue was distilled to give 6.6 g (76% yield) of **3**: bp 47–52 °C (0.025–0.050 mm); NMR (CCl_3D) δ 5.58 (s, 0.9 H), 5.50 (s, 0.1 H), 4.02 (d, 1.8 H, J = 1 Hz), 3.88 (d, 0.2 H, J = 1 Hz), 3.50 (q, 2 H, J = 7 Hz), 2.28 (d, 2 H, J = 2 Hz), 1.30 (m, 6 H), 1.17 (t, 3 H, J = 7 Hz); IR (liquid film) 3.40, 3.50, 8.70, 8.95, 9.35, 9.95 μm.

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.04; H, 8.71.

Reaction of Orthoformate 3 with Anhydrous Acetic Acid Containing 1 Molar Equivalent of *p*-Toluenesulfonic Acid. A mixture of 1.17 g (0.0062 mol) of *p*-toluenesulfonic acid monohydrate, 1.2 mL of acetic anhydride, and 5.5 mL of glacial acetic acid was refluxed for 3 h and then allowed to stand overnight with the exclusion of moisture. While stirring, 0.92 g (0.0050 mol) of orthoformate **3** was added to the above mixture at 20 °C. After 3 h at 20–29 °C, the mixture was extracted with three 50-mL portions of diethyl ether and the collected ether layers were washed with an equal volume of a 10% solution of K_2CO_3 and then dried over K_2CO_3. Evaporation of the ether on a rotating evaporator yielded 1.29 g of a viscous oil: NMR (CCl_3D) δ 8.16 (s, 2.0), 8.02 (s, 1.0), 4.80 (br s, 2.3), 4.65 (br s, 1.3), 4.30 (br s, 4.7), 3.92 (d, 2.0, J = 1 Hz), 3.80 (d, 1.0, J = 1.5 Hz), 3.65 (d, 1.3, J = 2 Hz), 2.25 (br, 8.7), 2.06 (s, 6.0), 1.25 (m, 24); IR (liquid film) 2.90, 3.38, 3.49, 5.79, 7.30, 8.04, 8.50, 9.50 μm. The mass spectrum had m/e values of 155, 153, 152, 139, 138, 127.

The oil was saponified in refluxing 10% NaOH/aqueous methanol. Most of the methanol was evaporated and the resulting aqueous solution was extracted with four 25-mL portions of ether. The collected ether layers were dried over anhydrous $MgSO_4$ and evaporation of the ether yielded 0.58 g (91%) of crude *cis,exo*-2,3-norbornanediol. Sublimation of this crude semisolid gave 0.44 g (69%), mp 138–140 °C, of white plates. The NMR and IR spectra were comparable to those of a sample produced by oxidation of norbornene.

Reaction of Orthoformate 3 with Trifluoroacetic Acid. A solution of 0.30 g (0.0016 mol) of orthoformate **3** in 2 mL of trifluoroacetic acid was placed in an NMR tube, cooled in a dry ice/acetone bath, and sealed with a flame. The tube was placed in an oil bath at 75 °C for 3 h during which time reaction was followed by NMR. After 3 h, the disappearance of singlet at δ 5.6 and appearance of a doublet at δ 5.0 (J = 2 Hz) was taken as evidence for the completion of the reaction. The tube was cooled in a dry-ice/acetone bath and opened with a flame. The excess trifluoroacetic acid was evaporated and the resulting residue was distilled in a Kugelrohr giving a fraction, 0.46 g (90% yield), at air jacket temperature of 50–70 °C (0.1 mm): NMR (CCl_3D) δ 4.98 (d, 2 H, J = 2 Hz), 2.51 (br s, 2 H), 1.2–2.2 (m, 6 H); IR (liquid film) 3.36, 3.48, 5.56, 7.24, 7.42, 8.20, 8.61, 11.13, 12.91, 13.82 μm; mass spectrum m/e 200, 178, 153, 109.

Preparation of *cis,exo*-2,3-Norbornyl Bis(trifluoroacetate) (5). In a flask at room temperature was mixed 5 mL of trifluoroacetic anhydride (prepared by dehydration of trifluoroacetic acid with P_2O_5) and 0.5 g of exo diol. The reaction mixture was allowed to stand overnight in a stoppered flask. The excess anhydride was evaporated and the residue was distilled at 0.1 mm Hg. One fraction was collected using a Kugelrohr with an air jacket temperature at 50–70 °C; yield 0.64 g (57%). The NMR and IR spectra were identical with those of the product isolated from reaction of orthoformate **3** and trifluoroacetic acid.

Anal. Calcd for $C_{11}H_{10}O_4F_6$: C, 41.26; H, 3.15; F, 35.60. Found: C, 40.96; H, 3.15; F, 35.32.

Reaction of Orthoformate 3 with Acetyl Chloride in Anhydrous Acetone. In a round-bottom flask was mixed 1.63 g (0.0089 mol) of orthoformate **3** and 3.2 mL of spectral grade acetone which had been dried over molecular sieve type 4A. Into the above solution with stirring at 30 °C was added 0.70 mL of acetyl chloride. The progress of the reaction was followed by TLC (silica gel plates eluted in chloroform containing benzene). After 15 min the formation of product was indicated by TLC but considerable starting material still remained. After 45 min TLC showed no starting material but the reaction mixture had two components. After evaporation of the excess acetone and low-boiling side products, the product mixture was distilled at 0.05 mm. The first fraction (0.12 g, 10% yield) had bp 24–52 °C and NMR and IR data were consistent with *cis,exo*-2,3-norbornanediol acetone ketal. The second fraction, 52–59 °C, weighed 0.23 g and was shown to be starting material by comparative NMR spectra.

Compound **6** was obtained as the third fraction (0.8 g, 54% yield): bp 60–64 °C; NMR (CCl_3D) δ 5.05 (t, 0.9 H, J = 5 Hz), 5.62 (t, 0.1 H, J = 5 Hz), 4.08 (d, 0.2 H, J = 2 Hz), 3.92 (d, 1.84 H, J = 1.5 Hz), 2.80 (d, 1.8 H, J = 5 Hz), 2.47 (d, 2 H, J = 5 Hz), 2.25 (br s, 2 H), 2.20 (s, 3 H), 0.18–1.8 (m, 6 H); IR (liquid film) 3.36, 5.79, 7.05, 7.40, 8.79, 9.38, 9.53, 9.79 μm; mass spectrum m/e 196 (molecular ion), 181, 169, 139, 127, 110.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.35; H, 8.16. Found: C, 67.24; H, 7.94.

Reaction of Orthoformate 3 with Acetyl Chloride in Cyclohexanone. To a mixture of 0.98 g (0.0053 mol) of orthoformate **3** and 2.25 g of cyclohexanone at room temperture was added 0.40 mL of acetyl chloride. After 15 min an aliquot of reaction mixture was withdrawn and placed in a NMR tube. The NMR spectrum showed the disappearance of the sharp singlet at δ 5.6 and appearance of two doublets at δ 5.6 and 5.0 (J = 5 Hz) after 30 min. The reaction was cooled to −78 °C and diluted with dry ether to 15 mL. An equal volume of 5% aqueous solution of $NaHCO_3$ was added to the ether layer to neutralize the hydrogen chloride generated during the reaction and also to quench unreacted acetyl chloride. The two layers were separated and the ether layer was washed with 5% $NaHCO_3$ and water and then dried over Na_2SO_4. After evaporation of the ether, 0.79 g of crude reaction mixture was isolated. Separation of the mixture was accomplished by gas chromatography on a 5 ft column of 20% SE30 at 168 °C. The peak of retention time 8 min was tentatively identified as the *cis,exo*-2,3-norbornane diol ketal of cyclohexanone. The peak of retention time 35 min (30% yield, using heptadecane internal standard) was identified as a stereoisomeric mixture of norbornanediol acetal-2-cyclohexanone (**7**): NMR δ 5.57 (d, 0.2 H, J = 5 Hz), 4.98 (d, 0.8 H, J = 5 Hz), 4.00 (d, 0.4 H, J = 2 Hz), 3.88 (d, 1.6 H, J = 2 Hz), 0.8–2.8 (br m, 17 H); IR (melt) 3.43, 5.86, 6.94, 8.71, 9.23, 9.59 μm; mass spectrum m/e 236, 219, 206, 203 (meta stable), 194, 179.

Anal. Calcd for $C_{14}H_{26}O_3$: C, 71.19; H, 8.47. Found: C, 71.03; H, 8.38.

Ethyl Orthoformate Ester of *cis,endo*-2,3-Norbornanediol (4).[21] This ester was prepared from 3.2 g of endo diol[21] and 9.3 g of triethyl orthoformate: yield 3.03 g (66%); bp 43–44 °C (0.3 mm); NMR (CCl_4) δ 5.80, 5.73 (s, 1 H), 4.38, 4.23 (t, 2 H), 3.67 (q, 2 H), 2.30 (br s, 2 H), 2–1.1 (m, 9 H).

Anal. Found: C, 64.97; H, 8.60.

An NMR tube was charged with 0.22 g of **4** and 1.5 g of trifluoroacetic acid and heated at 50 °C for 12 h. Upon evaporative distillation there was obtained an oil which displayed NMR peaks at δ 5.1 (t, 2 H), 2.7 (br s, 2 H), 2.1–1.3 (m, 6 H).

An authentic sample of the diester was prepared by treating 0.35 g of endo diol[21] with 2 mL of trifluoroacetic anhydride followed by distillation. The NMR spectra of the two samples were identical.

Anal. Found: C, 41.36; H, 3.10.

Methyl Orthoformate Ester of *cis,exo*-2,3-Bornanediol (2).[10] This compound was prepared from bornanediol[10] and

(21) Kwart, H.; Vosburgh, W. G. *J. Am. Chem. Soc.* **1954**, *76*, 5400.

trimethyl orthoformate using the above procedure. The product was obtained in 50–60% yields as an oil: bp 77.5–79 °C (0.05 mm); NMR (neat) δ 5.67 (s, 0.44 H), 5.57 (s, 0.56 H), 4.3–3.8 (m, 2 H), 3.56 (s, 0.56 H), 3.30 (s, 0.44 H), 2.1–0.67 (m, 14 H).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 68.00; H, 9.27.

Thermolysis of 2 in Phenyl Isocyanate. A solution of ca. 60 mg of **2** in 0.5 mL of phenyl isocyanate was prepared and examined immediately by NMR spectroscopy. The spectrum showed separate resonances for the epimeric methoxyl protons at δ 3.30 and 3.15 (area ratio 3.0:2.1) and methine protons at δ 5.55 and 5.45 (area ratio 0.64:1.0). The sample was sealed and kept at 25 °C for 4 days whereupon the ratio of the methoxyl proton areas changed to 1:8. The sample was heated at 100 °C for 40 h after which time the area ratio of the methoxy protons was 1:12.5. The tube was heated at 155 °C for 17 h whereupon all peaks attributed to **2** disappeared and new peaks appeared which were assigned to bornylene (**9**) and methyl phenylcarbamate (**10**). Bornylene resonances appeared at δ 5.83 (m, 2 H), 2.25 (t, 1 H) 2.0–1.1 (m, 4 H), 0.98 (s, 3 H), 0.85 (s, 3 H), and 0.73 (s, 3 H).

The other component of the reaction mixture showed two singlets at δ 3.60 and 3.47 (relative area 2:1). An authentic sample of **10** prepared from methanol and phenyl isocyanate showed only the peak at δ 3.60 in phenyl isocyanate at room temperature. After heating for 2 h at 160 °C the other peak appeared with relative area 3:1. Further heating led to a 1.8:1 mixture after 7 h at 165 °C.

Thermolysis of 3 in Phenyl Isocyanate. A solution of ca. 0.050 g of **3** in 0.5 mL of phenyl isocyanate was heated at 110 °C for 1 h. No significant changes were observed in the NMR spectrum. The sample was heated at 165 °C and periodically monitored by NMR. After 1 h there was observed peaks attributable to norbornene (**8**) and it was estimated that the reaction was ca. 50% complete using the solvent peaks as an internal standard. After 4 h the reaction was ca. 70% completed. Heating for 22 h led to complete destruction of **3** and to ca. quantitative formation of norbornene. The latter was identified by comparison of the NMR spectrum with that of an authentic sample in phenyl isocyanate [e.g. δ 6.0 (t) and 2.8 (m)]. The only significant extra peaks in the spectrum were those attributable to phenylethylurethane; δ 4.10 (q, J = 7 Hz) and 1.12 (t, J = 7 Hz).

Acknowledgment. We thank Ms. Yiang I for a sample of compound **2**.

Registry No. 2a, 70644-36-9; **2b**, 70701-40-5; **3** isomer 1, 70644-37-0; **3** isomer 2, 70701-41-6; **4** isomer 1, 70701-42-7; **4** isomer 2, 70701-43-8; **5**, 70644-38-1; **6** isomer 1, 70644-39-2; **6** isomer 2, 70701-44-9; **7** isomer 1, 70644-40-5; **7** isomer 2, 70701-45-0; **8**, 498-66-8; **9**, 464-17-5; **10**, 2603-10-3; *cis,exo*-2,3-norbornanediol, 16329-23-0; triethyl orthoformate, 122-51-0; *exo,exo*-2-(acetyloxy)-3-(formyloxy)norbornane, 70644-41-6; *cis,exo*-2,3-norbornanediol acetone ketal, 16329-26-3; cyclohexanone, 108-94-1; *cis,endo*-2,3-norbornanediol, 21462-06-6; *cis,exo*-2,3-bornanediol, 56614-57-4; trimethyl orthoformate, 149-73-5; phenyl isocyanate, 103-71-9.

Base-Catalyzed Oxygenation of *tert*-Butylated Phenols. 3.[1] Base-Catalyzed Reaction of Peroxyquinols Derived from Oxygenation of 2,6-Di-*tert*-butylphenols and Mechanism of Regioselective Formation of Epoxy-*o*-quinol from 2,4,6-Tri-*tert*-butylphenol

Akira Nishinaga,* Tadashi Shimizu, and Teruo Matsuura

Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto, Japan

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The chemical reactivities of peroxy anions of two types of hydroperoxides, 4-hydroperoxy-2,5-cyclohexadienones (**2**) and 6-hydroperoxy-2,4-cyclohexadienones (**3**) regioselectively derived from the oxygenation of 2,6-di-*tert*-butylphenols (**1**), toward bases with three countercations (K^+, Na^+, Li^+) are systematically investigated. In *N,N*-dimethylformamide with *tert*-butoxides, hydroperoxides **2** liberate predominantly molecular oxygen, whereas **3** are significantly decomposed leading to 4,5-epoxy-6-hydroxy-2-cyclohexenones (**5**). In *t*-BuOH or tetrahydrofuran (THF) with *t*-BuOK or *t*-BuONa, hydroperoxides **2** are converted to **3** which then undergo decomposition to **5** exclusively. With *t*-BuOLi, a reductive cleavage of the peroxy bond is a significant reaction pathway. In ethanol containing alkali, oxygen liberation and the reaction path depend on the nature of the substituent at the 4 position of the hydroperoxides. With 4-*t*-Bu substitution, an equilibrium between **2** and **3** is established. With a 4-Me group, a reductive cleavage of the peroxy bond takes place. 4-(4-MeOPh) substitution on **3** gives predominantly the product of type **5**. These results are principally interpreted in terms of solvation of the peroxy anions and the countercations. It is found that the ortho regioselective hydroperoxylation of 2,4,6-tri-*tert*-butylphenol with molecular oxygen in *t*-BuOK/*t*-BuOH involves the formation of hydroperoxide of type **2** in the first step followed by the exclusive conversion of **2** to that of type **3** via a π-complex intermediate.

In previous papers,[1,2] we reported base-catalyzed regioselective dioxygen incorporation into 2,6-di-*tert*-butylphenols (**1**). The dioxygen incorporation depends on the nature of the para substituent in **1** and the solvent used. In aprotic solvents such as *N,N*-dimethylformamide (DMF), dimethyl sulfoxide (Me_2SO), and hexamethylphosphoric triamide (HMPT) with *t*-BuOK, **1a,b** gave exclusively epoxy-*p*-quinols **4**, whereas in *tert*-butyl alcohol with *t*-BuOK, **1a,c** gave predominantly epoxy-*o*-quinols **5**. The reaction involves intramolecular decomposition of peroxy anions **2′** and **3′** regioselectively formed (Scheme I).[1,2] On the other hand, oxygenation of **1** (R = alkyl) in ethanol with KOH at 0 °C gives *p*-hydroperoxides **2** and in a mixture of *tert*-butyl alcohol and pentane with *t*-BuOK at 0 °C **1** (R = *t*-Bu, substituted phenyl) gives *o*-hydroperoxides **3**.[1,2]

With a view to obtaining insight into the mechanism of the oxygenation of **1** in more detail, we have investigated systematically the influence of solvents and countercations on the base-catalyzed reaction of hydroperoxides **2** and **3**. *tert*-Butoxides (*t*-BuOK, *t*-BuONa, *t*-BuOLi) have been

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