Proximity Effects. XL. Reactions of Lead Tetraacetate with Cyclic Alcohols and Cyclic Olefins[1,2]

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Reaction of lead tetraacetate with cyclooctanol gave 1,4-epoxycyclooctane among other products; cycloheptanol gave 1,4-epoxycycloheptane. 1-Methylcyclooctanol on treatment with lead tetraacetate gave a mixture of 1,4- and 1,5-epoxy-1-methylcyclooctane. Cyclooctene and cycloheptene also gave products formed by transannular reactions.

Since the earliest report[3] of the formation of a five-membered cyclic ether on treatment of a steroidal alcohol with lead tetraacetate numerous examples of this type have been reported for steroidal systems.[4] More recently the formation of cyclic ethers has been extended to saturated acyclic,[5] unsaturated acyclic,[6] unsaturated bicyclic,[7] and saturated bicyclic[8] alcohol systems. The cyclic ethers formed usually have been five membered rather than six membered, although in some cases[5,6] mixtures of the two have been obtained.

Treatment of cyclooctanol with lead tetraacetate in boiling benzene gave a mixture composed of 1,4-epoxycyclooctane (26%), cyclooctyl acetate (45%), cyclooctanone (5%), and unchanged cyclooctanol (24%). The yield of 1,4-epoxycyclooctane was somewhat higher when the reaction was carried out in cyclohexane. No detectable amount of the 1,5-isomer was found in the product. Study of molecular models shows that a hydrogen atom in the 5-position is just as close to the oxygen atom as one in the 4-position. Despite the statistical factor (twice as many hydrogens in the 4-position) the complete absence of 1,5-epoxycyclooctane is not readily explicable. Under similar conditions, 1-methylcyclooctanol gave a 1:3 mixture of 1,4- and 1,5-epoxy-1-methylcyclooctane.[9] Thus introduction of a methyl group must alter the geometry of the cyclooctane ring, whether in the ground state or a transition state, so as to favor the formation of 1,5- over 1,4-epoxide.

Cycloheptanol on treatment with lead tetraacetate afforded a mixture which contained the expected cycloheptyl acetate, cycloheptanone, cycloheptanol, and an epoxide, $C_7H_{12}O$. Conversion of the latter to *trans*-1,4-cycloheptanediol diacetate on treatment with
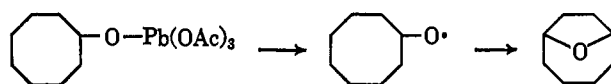
boron trifluoride in acetic anhydride established its structure as 1,4-epoxycycloheptane.

1-Methylcycloheptanol on treatment with lead tetraacetate gave in low yield an epoxide believed to be 1-methyl-1,4-epoxycycloheptane. Its structure has not been proved conclusively.

Cyclohexanol on treatment with lead tetraacetate produced cyclohexyl acetate; no 1,4-epoxycyclohexane was detected.
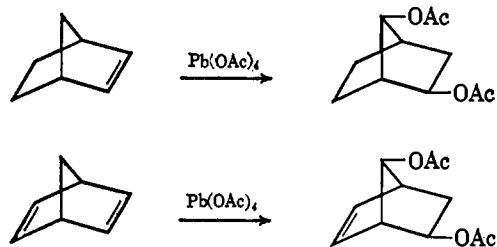
The selectivity of cyclic ether formation in the case of cyclooctanol is of synthetic utility for the preparation of 1,4-epoxycyclooctane since other available methods either involve multistep syntheses[10] or give a mixture of isomers.[11]

A free-radical mechanism[12] has been postulated for the formation of cyclic ethers in this reaction. The first intermediate seems to be the lead ester depicted below. The intermediate free radical can attack the hydrogen in the 4-position to give 1,4-epoxycyclooctane. In view of the result of treatment of 1-methyl-

cyclooctanol with lead tetraacetate, it is interesting to note that the free radical generated by photolysis of 1-methylcyclooctyl hypochlorite also produced both 1-methyl-1,4-epoxycyclooctane and 1-methyl-1,5-epoxycyclooctane among other products.[9]

The reaction of lead tetraacetate with an olefin to give a glycol acetate and allylic acetate was originally investigated by Criegee[13] and subsequently by others.[14] A mechanism with a cationic intermediate[14a,d,f] has been suggested for this reaction. The implication of a cationic intermediate is strengthened by the fact

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(2) Paper XXXIX: A. C. Cope, R. S. Bly, M. M. Martin, and R. C. Petterson, *J. Am. Chem. Soc.*, 87, 3111 (1965).

(3) G. Gainelli, M. Lj. Mihailovic, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, 42, 1124 (1959).

(4) See ref. 5, 6, and 8 for partial listings.

(5) V. W. Micovic, R. I. Mamuzic, D. Jeremic, and M. Lj. Mihailovic, *Tetrahedron Letters*, 2091 (1963).

(6) S. Moon and J. M. Lodge, *J. Org. Chem.*, 29, 3453 (1964).

(7) R. M. Moriarty and K. Kapadia, *Tetrahedron Letters*, 1165 (1964).

(8) K. Kitahonoki and A. Matsuura, *ibid.*, 2263 (1964).

(9) See ref. 2.

(10) A. C. Cope and B. C. Anderson, *J. Am. Chem. Soc.*, 79, 3892 (1957).

(11) Treatment of *cis, cis*-1,5-cyclooctadiene with formic acid gave a mixture of 1,4- and 1,5-epoxycyclooctane with the latter predominating. See A. C. Cope and P. E. Peterson, *ibid.*, 81, 1643 (1959).

(12) (a) G. Gainelli, B. Kamber, J. Keller, M. Lj. Mihailovic, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, 44, 518 (1961); (b) J. Kalvoda and K. Heusler, *Chem. Ind.* (London), 1431 (1963).

(13) R. Criegee, *Ann.*, 481, 263 (1930).

(14) (a) G. H. Whitham, *J. Chem. Soc.*, 2232 (1961); (b) H. J. Kabbe, *Ann.*, 656, 204 (1962); (c) B. A. Arbuzov, Z. G. Isaeva, and V. V. Ratner, *Bull. Acad. Sci. USSR, Div. Chem. Sci* (English Transl.), 594 (1962); (d) I. Alkonyi, *Chem. Ber.*, 96, 1873 (1963); (e) C. B. Anderson and S. Winstein, *J. Org. Chem.*, 28, 605 (1963); (f) R. Criegee, *Angew. Chem.*, 70, 173 (1958).

that norbornene and norbornadiene on treatment with lead tetraacetate give only the rearranged products formulated below and none of the vicinal glycols.[15] Since it is known that a cation intermediate in a medium-sized ring gives transannular products, it was of interest to investigate the reactions of cyclooctene and cycloheptene with lead tetraacetate. On treatment of cis-cyclooctene with lead tetraacetate in acetic acid at 64° for 2 hr. the total yield of product was 45%, and it was composed of 2-cycloocten-1-yl acetate (10%), 4-cycloocten-1-yl acetate (31%), cis-1,2-cyclooctanediol diacetate (15%), and cis-1,4-cyclooctanediol diacetate (44%). The same reactants heated in refluxing benzene for 3 hr. gave only 9.4% of the same products in relative amounts of 26, 12, 30, and 32% (in the order listed above).

The most striking result is the predominance of transannular products. It is also worthy of note that the 1,2-cyclooctanediol diacetate was exclusively the cis isomer; none of the trans isomer was formed. A slower rate of reaction in benzene compared to acetic acid is indicative of a polar mechanism.

Cycloheptene was treated with lead tetraacetate in acetic acid at 64° for 3 hr. and gave a 42% yield of products, composed of 2-cyclohepten-1-yl acetate (41%), trans-1,2-cycloheptanediol diacetate (41%), cis-1,3-cycloheptanediol diacetate (4%), trans-1,3-cycloheptanediol diacetate (4%), and an unidentified compound (10%). Neither of the isomeric 1,4-cycloheptanediol diacetates nor cis-1,2-cycloheptanediol diacetate could be detected among the products.

Experimental[16]

Reaction of Lead Tetraacetate with Cyclooctanol. A mixture of cyclooctanol (0.5 g.) and lead tetraacetate (2 g.) in dry benzene (20 ml.) was refluxed with stirring for 48 hr. The mixture was cooled and the excess lead tetraacetate was decomposed by adding ethylene glycol (5 ml.). The mixture was stirred for 15 min., water was added, and the organic layer was separated. It was washed with potassium iodide solution, sodium thiosulfate, and water, and dried over magnesium sulfate. Removal of the solvent under reduced pressure yielded 0.37 g. of crude material that according to gas chromatographic analysis (TCEP at 142°) consisted of 1,4-epoxycyclooctane (18%), cyclooctyl acetate (56%), cyclooctanone (5%), and cyclooctanol (20%). The products were isolated by gas chromatography and identified by comparison of retention times and infrared spectra with those of authentic samples. The above experiment was repeated on a larger scale (20 times). The product mixture (8.5 g.) was analyzed as above. It contained 1,4-epoxycyclooctane (26%), cyclooctyl acetate (45%), cyclooctanone (5%), and cyclooctanol (24%). Distillation of the crude product through a semimicro column gave 1.56 g. (7.9%) of 1,4-epoxycyclooctane, b.p. 57–60° (3.5 mm.), as the lowest boiling fraction.

Reaction of Lead Tetraacetate with 1-Methylcyclooctanol. A mixture of 1-methylcyclooctanol[17] (0.7 g.),

(15) K. Alder, F. H. Flock, and H. Wirtz, *Chem. Ber.*, **91**, 609 (1958).
(16) Melting points are corrected and boiling points are uncorrected. Microanalyses were performed by Dr. S. M. Nagy and his associates. Footnote 24 of A. C. Cope and P. E. Peterson, *J. Am. Chem. Soc.*, **81**, 1643 (1959), describes the conditions and equipment used for gas chromatography.
(17) H. C. Brown and M. Borkowski, *ibid.*, **74**, 1894 (1952).

lead tetraacetate (3 g.), and dry benzene (30 ml.) was refluxed for 48 hr. The product mixture (0.68 g.), isolated as described above, was analyzed by gas chromatography (TCEP at 120°). It contained 1,4- and 1,5-epoxy-1-methylcyclooctane[9] (23%) in a proportion of 1 to 3, respectively, and 1-methylcyclooctanol (77%). At higher temperatures the alcohol dehydrated on the gas chromatographic column. The mixture of 1,4- and 1,5-epoxy-1-methylcyclooctane was isolated by gas chromatography at 100°, and then was separated at a lower temperature (75°). The oxides were identified by comparison of their infrared spectra with those of authentic samples.[9]

Reaction of Lead Tetraacetate with Cycloheptanol. Cycloheptanol (1.0 g.) was treated with lead tetraacetate (4 g.) in benzene and the crude product (1.5 g., containing some benzene), isolated as described above, was analyzed by gas chromatography (TCEP at 120°). It contained an epoxide (5%) later shown to be 1,4-epoxycycloheptane, cycloheptyl acetate (62%), and a mixture of cycloheptanone and cycloheptanol (29%); cycloheptanone and cycloheptanol were not separated under the conditions used. The infrared spectrum of the epoxide displayed no hydroxyl or acetate bands, but had a band at 1027 cm.$^{-1}$ indicative of an epoxide.

The above experiment was repeated using cyclohexane as a solvent instead of benzene, according to the procedure of Jeger.[12a] Cycloheptanol (20 g.) was treated with lead tetraacetate (80 g.) (subjected to reduced pressure to remove acetic acid present) in cyclohexane (900 ml.) to which 8 g. of calcium carbonate had been added. The products (14.5 g.), isolated as described above, consisted of 1,4-epoxycycloheptane (5%), cycloheptyl acetate (52%), and cycloheptanone and cycloheptanol (40%), as shown by gas chromatography (TCEP at 145°). The mixture was fractionally distilled through a semimicro column. Redistillation of the first fraction gave the epoxide, 0.34 g., b.p. 54–62° (20 mm.). A sample for microanalysis, m.p. 46.5–47.0°, was isolated by gas chromatography (TCEP at 125°).

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 75.00; H, 10.78.

Structure Proof of 1,4-Epoxycycloheptane. A mixture of 80 mg. of the epoxide obtained from treatment of cycloheptanol with lead tetraacetate, 300 μl. of acetic anhydride, and 25 μl. of boron trifluoride etherate was heated on a steam cone for 1.5 hr., then cooled, diluted with 3 ml. of water, and extracted with ether. The combined ether extracts were washed with water, 5% sodium carbonate solution, and saturated sodium chloride solution, and dried over magnesium sulfate. The solvent was removed and the residue was passed through 10 g. of activity II acid-washed alumina. The ether eluate was concentrated to 100 mg. of a pale yellow liquid which was shown to contain 50% of trans-1,4-cycloheptanediol diacetate and 50% of 4-cyclohepten-1-yl acetate, identified by gas chromatography (silicone oil at 180°) and by comparison of their infrared spectra with those of authentic samples.

Reaction of Lead Tetraacetate with 1-Methylcycloheptanol. 1-Methylcycloheptanol (3.4 g.), prepared from cycloheptanone and methyl magnesium iodide, was treated with lead tetraacetate (13 g.) and calcium carbonate (1.3 g.) in cyclohexane (140 ml.), and the

crude products (2.25 g.) were isolated as described above. Gas chromatography (TCEP at 125°) showed that the mixture contained an epoxide (1.5%) and the unchanged alcohol. Distillation through a semi-micro column yielded 0.37 g. of a mixture, b.p. 78–83° (22 mm.), from which the pure epoxide, n^{25}D 1.4523, was obtained by gas chromatography (TCEP at 125°).

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.25; H, 11.11.

Reaction of Lead Tetraacetate with Cyclohexanol. Treatment of cyclohexanol (1.0 g.) with lead tetraacetate (4 g.) and benzene (40 ml.) as described above yielded 0.7 g. of a crude mixture. Gas chromatography (TCEP at 123°) showed that the mixture contained 77% of cyclohexyl acetate and 23% of cyclohexanol. No cyclohexanone was detected. The products were isolated by gas chromatography and identified by comparison of their infrared spectra with those of authentic samples.

Reaction of Cyclooctene with Lead Tetraacetate. A. A mixture of 4.43 g. of lead tetraacetate (containing *ca.* 5% of acetic acid) and 1.05 g. of cyclooctene in 10 ml. of acetic acid was stirred at room temperature for 3 hr. The mixture was cooled to 10° and 2.5 ml. of ethylene glycol was added, and the mixture was stirred at 15–25° for 15 min. It was then diluted with 80 ml. of water and extracted with four 25-ml. portions of ether. The combined ether extracts were washed with water, 20% potassium iodide solution, 20% sodium thiosulfate solution, saturated sodium bicarbonate solution, water, and saturated sodium chloride solution, and dried over magnesium sulfate. Removal of the solvent yielded 1 g. which was largely unchanged starting material. The product mixture (3.2%) was shown to contain 9% of 2-cycloocten-1-yl acetate, 28% of 4-cycloocten-1-yl acetate, 10% of *cis*-1,2-cyclooctanediol diacetate, and 53% of *cis*-1,4-cyclooctanediol diacetate, which were identified by gas chromatography (silicone oil at 200°) and by comparison of their infrared spectra with those of authentic samples. *trans*-1,2-Cycloheptanediol diacetate was used as an internal standard in estimating the yields in this case and in the two described below.

B. A mixture of 4.43 g. of lead tetraacetate and 1.05 g. of cyclooctene in 44 ml. of dry benzene was heated under reflux for 3 hr. and then was cooled to 10°. Ethylene glycol (2.5 ml.) was added and the mixture was stirred at room temperature for 30 min. The benzene layer was washed with water, 20% potassium iodide solution, 20% sodium thiosulfate solution, saturated sodium bicarbonate solution, water, and saturated sodium chloride solution, and dried over magnesium sulfate. Removal of the solvent yielded 0.8 g. of material which contained unchanged cyclooctene and 9.4% of a mixture of products. The products were 2-cycloocten-1-yl acetate (26%), 4-

cycloocten-1-yl acetate (12%), *cis*-1,2-cyclooctanediol diacetate (30%), and *cis*-1,4-cyclooctanediol diacetate (32%), identified as described in section A.

C. The procedure was the same as in A except that the reaction mixture was heated at 64 ± 1° for 3 hr. A mixture (1.43 g.) of unchanged cyclooctene (55%) and products (45%) was obtained. The products were 2-cycloocten-1-yl acetate (10%), 4-cycloocten-1-yl acetate (31%), *cis*-1,2-cyclooctanediol diacetate (15%), and *cis*-1,4-cyclooctanediol diacetate (44%), identified as described in section A.

Preparation of cis-1,2-Cyclooctanediol Diacetate. *cis*-1,2-Cyclooctanediol diacetate (87 mg., 92%) was obtained from the corresponding glycol (60 mg.) by treatment with acetic anhydride in pyridine. A sample collected by gas chromatography (silicone oil at 200°) was analyzed.

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.17; H, 8.86.

Reaction of Cycloheptene with Lead Tetraacetate. A mixture of 0.96 g. of cycloheptene and 4.65 g. of lead tetraacetate (containing 5% of acetic acid) in 10 ml. of acetic acid was heated at 64 ± 1° for 3 hr. Treatment as described for the reaction of lead tetraacetate with cyclooctene (A) gave cycloheptene and 42% of a mixture of products. The products were 2-cyclohepten-1-yl acetate (41%), *trans*-1,2-cycloheptanediol diacetate (41%), *cis*-1,3-cycloheptanediol diacetate (4%), and *trans*-1,3-cycloheptanediol diacetate (4%), identified by gas chromatography on silicone oil at 180° and by comparison of their infrared spectra with those of authentic samples. *trans*-1,2-Cyclohexanediol diacetate was used as an internal standard in estimating the yields. An unidentified product (10%) was also found, but none of the isomeric 1,4-cycloheptanediol diacetates or *cis*-1,2-cycloheptanediol diacetate were present in the mixture.

Preparation of cis-1,2-Cycloheptanediol Diacetate. *cis*-1,2-Cycloheptanediol diacetate (155 mg.) was prepared in 94% yield from the corresponding glycol (100 mg.) by treatment with acetic anhydride in pyridine. A sample collected by gas chromatography (silicone oil at 180°) was analyzed.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 62.03; H, 8.34.

Preparation of cis- and trans-1,3-Cycloheptanediol Diacetates. *cis*- and *trans*-1,3-cycloheptanediol diacetates were prepared from the corresponding glycols[18,19] as described above. Samples collected by gas chromatography (silicone oil at 180°) were analyzed.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found (*cis* isomer): C, 61.74; H; 8.64; (*trans* isomer): C, 61.76; H, 8.29.

(18) A. C. Cope, T. A. Liss, and G. W. Wood, *J. Am. Chem. Soc.*, **79**, 6287 (1957).
(19) A. C. Cope, J. K. Heeren, and V. Seeman, *J. Org. Chem.*, **28**, 516 (1963).