Lead Tetraacetate. VI. Stereochemical Studies on the Formation of Bicyclic Ethers from Alicyclic Primary Alcohols[1]

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The reactions of lead tetraacetate with 2-cyclohexylethanol, 3-cyclohexylpropanol, 2-cyclopentylethanol, and 3-cyclopentylpropanol were studied to determine the stereochemistry of the tetrahydrofurans formed. The oxidation of 2-cyclohexylethanol yielded both *cis*- and *trans*-7-oxabicyclo[4.3.0]nonanes, while 2-cyclopentylethanol yielded only the *cis* isomer of 2-oxabicyclo[3.3.0]octane. The oxidation of 3-cyclohexylpropanol yielded an oxaspiran, 1-oxaspiro[4.5]decane, in low yield, while the oxidation of 3-cyclopentylpropanol yielded a saturated oxaspiran, 1-oxaspiro[4.4]nonane, and an unsaturated oxaspiran, 1-oxaspiro[4.4]non-6-ene. The oxymercuration–demercuration of 2-(2-cyclohexenyl)ethanol (18) and 2-(2-cyclopentenyl)ethanol (19) yielded isomerically pure *cis*-7-oxabicyclo[4.3.0]nonane (2) and *cis*-2-oxabicyclo[3.3.0]octane (9).

In 1959 Jeger and his coworkers[3] treated pregnane-3β,20β-diol-3-acetate with lead tetraacetate and obtained a cyclic ether. Various steroids were subsequently treated with lead tetraacetate (LTA), yielding tetrahydrofurans in up to 50% yield.[4]

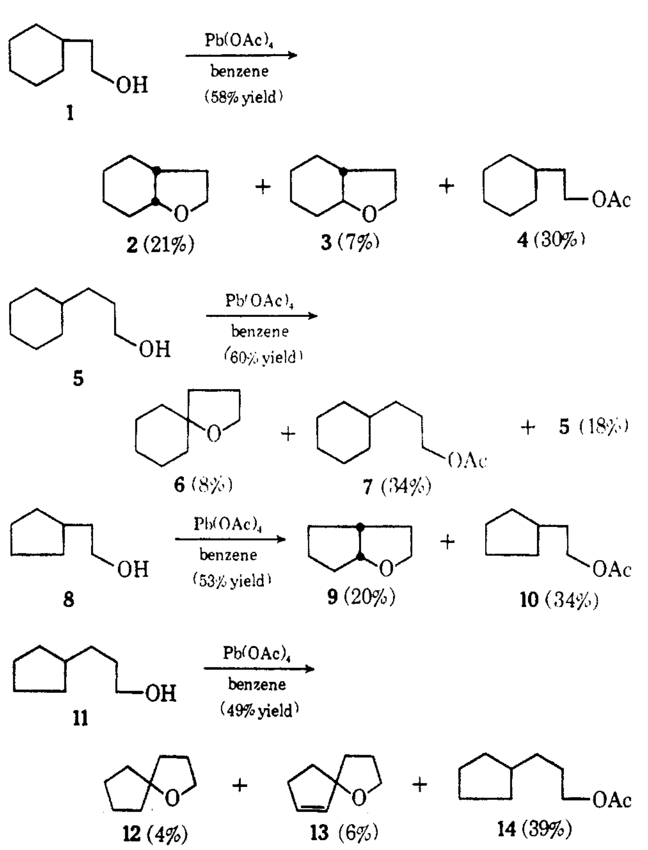
Micovic, *et al.*,[5] later discovered that treatment of saturated aliphatic alcohols with lead tetraacetate yielded tetrahydrofurans in up to 50% yield, accompanied by minute amounts of tetrahydropyrans. The oxidation of optically active (4*R*)-4,8-dimethylnonanol by Jeger and his coworkers[6] led to racemized tetrahydrofurans, indicating that the reaction involved either a free-radical or carbonium-ion intermediate. The ion or free-radical character of this intermediate has not as yet been conclusively established.

While the work by Jeger's[6] group indicated that the reaction proceeds through an intermediate capable of inversion, no attempt to correlate ring strain and product formation has been made previously. The systems we have chosen afford the opportunity to determine the stereochemistry of tetrahydrofuran ring formation and to study the reaction in relation to the geometry of the starting materials.

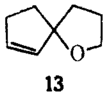
Results

The alcohols were treated with lead tetraacetate from a 1:1 to a 1:2 (ROH:LTA) molar ratio in refluxing benzene from 11 hr to 2 days. The composition of the products was determined by gas chromatography and products were identified by comparison of their ir and nmr spectra and retention times on a gas chromatograph with those of authentic samples. The results are summarized in Scheme I.

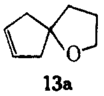
Scheme I



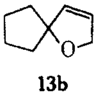
The structure **13** was assigned on the basis of elemental analysis, spectroscopic evidence, and hydrogenation data. The infrared (ir) spectrum indicated unsaturation and an ether group. The nuclear magnetic resonance (nmr) spectrum of **13** showed a multiplet at τ 4.3 (2 H), a triplet at 6.25 (2 H), a multiplet at 7.7 (2 H), and a multiplet at 7.9–8.3 (6 H). Hydrogenation of **13** generated **12**. Assuming that the double bond is disubstituted, as indicated by nmr, there are only four places where a double bond can be placed



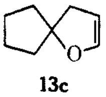
13



13a



13b



13c

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[1] (a) Part V: S. Moon and P. R. Clifford, *J. Org. Chem.*, **32**, 4017 (1967). (b) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

[2] NASA Trainee, 1964–1967.

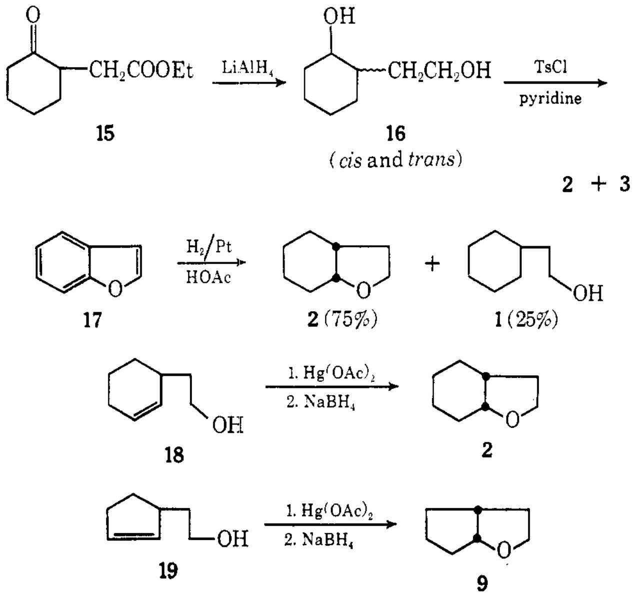
[3] G. Gainelli, M. L. Mihailovic, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **42**, 1124 (1959).

[4] For leading references, see R. Criegee, "Oxidation in Organic Chemistry," part A, K. B. Wiberg, Ed., Academic Press, New York, N. Y., 1965, pp 278–366.

[5] V. M. Micovic, R. I. Mamuzic, D. Jeremic, and M. L. Mihailovic, *Tetrahedron*, **20**, 2279 (1964).

[6] D. Hauser, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **47**, 1883 (1964).

SCHEME II



in **12**, namely, **13**, **13a**, **13b**, and **13c**. Only **13** is consistent with the nmr spectrum.[7]

Synthesis and Stereochemistry of Products.—The synthesis of compounds **2**, **3**, and **9** is outlined in Scheme II.

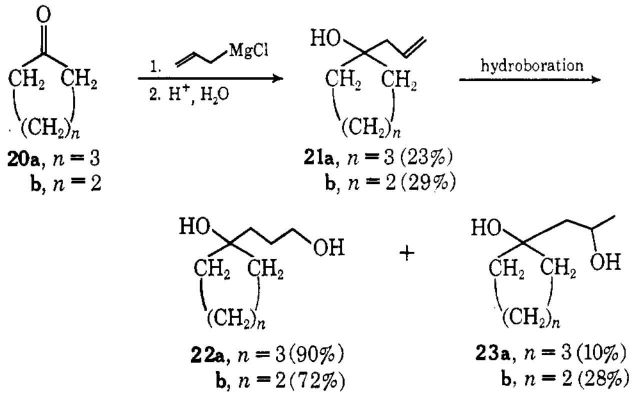
Treatment of a mixture of *cis*- and *trans*-2-(2-hydroxycyclohexyl)ethanol with tosyl chloride in pyridine afforded a mixture of **2** and **3**. Hydrogenation of benzofuran yielded 75% **2** and 25% hydrogenolysis product, the alcohol **1**. The bicyclic ether **2** was therefore characterized as the *cis* isomer and **3** was accepted to be the *trans* isomer.

Treatment of 2-(2-cyclohexenyl)ethanol (**18**) with mercuric acetate yielded **2** in 100% isomeric purity. On the premise that the cyclopentenyl system would react analogously, 2-(2-cyclopentenyl)ethanol (**19**) was treated with mercuric acetate, and **9** was obtained, pure. On the basis of the stereoselectivity of the mercuric acetate oxidation of the cyclohexenyl alcohol, **9** was concluded to be the *cis* isomer. Since the mercuric acetate oxidation of **18** and **19** was shown to yield **2** and **9** in 67% and 75% yield and with 100% isomeric purity, the treatment of the olefinic alchols **18** and **19** with mercuric acetate is an excellent preparative method for the pure ethers **2** and **9**.

The synthesis of compounds **6** and **12** is outlined in Scheme III. Hydroboration of **21a** yielded two diols, **22a** and **23a**, in a 9:1 ratio. Diol **23a** was identified by its nmr as 1-(1-hydroxycyclohexyl)-2-propanol. It was independently synthesized by the mercuric acetate oxidation of **21a**. Diol **22a** was treated with tosyl chloride in pyridine, forming **6**.

Hydroboration of the alcohol **21b** yielded the diols

SCHEME III



22b and **23b** in a 3:1 ratio. The diols were characterized by their ir and nmr spectra. Treatment of the mixture of **22b** and **23b** with tosyl chloride in pyridine yielded **12** and unchanged **23b**.

Discussion

The lead tetraacetate oxidation of 2-cyclohexylethanol (**1**) yielded the ethers **2** and **3** in a 3:1 ratio. The presence of both isomers indicates that the reaction is less stereospecific than the analogous mercuric acetate oxidation of 2-(2-cyclohexenyl)ethanol (**18**). The predominance of the *cis* isomer is an indication of a preference for formation of the less strained system. A variation of the alcohol to lead tetraacetate ratio did not materially change the distribution of the *cis* and *trans* isomers. (See Table I.)

TABLE I

RELATIVE YIELDS OF MAJOR PRODUCTS FROM THE LTA OXIDATION OF 2-CYCLOHEXYLETHANOL (1)

Molar ratio of alcohol to LTA	Solvent	Products, % 2	3	1	4
1:1	Benzene[a]	42	12	29	17
1:2	Benzene[b]	51	17	0	32
1:1.5	Benzene[c]	36	12	0	52

[a] Alcohol (2 g) in benzene (50 ml). [b] Alcohol (2 g) in benzene (70 ml). [c] Alcohol (10 g) in benzene (100 ml).

The lead tetraacetate oxidation of 2-cyclopentylethanol (**8**) yielded only the *cis* isomer of 2-oxabicyclo[3.3.0]octane. The lack of the *trans* isomer is probably due to the prohibitive strain of the system.

The lead tetraacetate oxidation of 3-cyclohexylpropanol produced the oxaspiran **6** in low yield. Variation of the conditions did not significantly change the amount of oxaspiran formed. Unlike the other reactions, addition of excess lead tetraacetate did not result in total consumption of starting material (see Table II). When the reaction was carried out in cyclohexane, cyclohexyl acetate was formed, which strongly suggests that a free-radical intermediate is produced in the reaction.

When cyclohexene was used as the solvent, in the presence of anhydrous calcium carbonate, 60% of the alcohol **5** was converted to the acetate **7** with just trace amounts of the ether being formed. Also found

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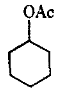
[7] One of the referees has suggested that the nmr spectrum is also compatible with **13a**. It was pointed out that the two allylic protons *cis* to the oxygen may be shielded and hence submerged in the rest of the ring protons with values of approximately τ 8.3. However, a study of some models shows that the analogous protons of the saturated system are positioned exactly as the two protons questioned above. In the saturated system there is no observed absorption of two protons upfield as expected from such shielding. We submit, therefore, that such shielding does not exist in either case, and that the nmr spectrum is compatible only with **13**.

Table II

Relative Yields of Major Products from the LTA Oxidation of 3-Cyclohexylpropanol (**5**)

Molar ratio of alcohol to LTA	Solvent	Products, %			
		OAc 	**6**	**5**	**7**
1:1	Cyclohexane[a]	5	14	41	40
1:1.5	Cyclohexane[a]	5	11	25	59
1:1.5	Cyclohexane[b]	5	11	37	46
1:1.5	Cyclohexane[c]	7	17	19	58
1:1	Benzene[a]		10	52	38
1:2	Benzene[a]		13	30	43

[a] Run in 25 ml of solvent. [b] Run in 200 ml of solvent. [c] Solvent (25 ml) with anhydrous calcium carbonate (2.11 g). [d] Yields were determined by integration of vapor phase chromatographic curves.

were 2-cyclohexen-1-ol, 2-cyclohexen-1-one, and 2-cyclohexen-1-yl acetate in a 1:1:2 ratio. The lead tetraacetate oxidation of neat cyclohexene yielded[8] 1.4% 2-cyclohexan-1-ol, 6.7% 2-cyclohexan-1-one, 80.4% 2-cyclohexen-1-yl acetate, 7.3% 1,2-cyclohexane diacetates, and 4% unknown mixture.

The observation that 60% of the alcohol was consumed when 1 g of **5** was treated with 4.5 g of lead tetraacetate in 200 ml of cyclohexene affords valuable information as to the relative reactivity of the double bond and the alcohol group. The 80.4% yield of 2-cyclohexen-1-yl acetate from the lead tetraacetate oxidation of neat cyclohexene demonstrates that this is a convenient procedure for the preparation of 2-cyclohexen-1-yl acetate from cyclohexene.

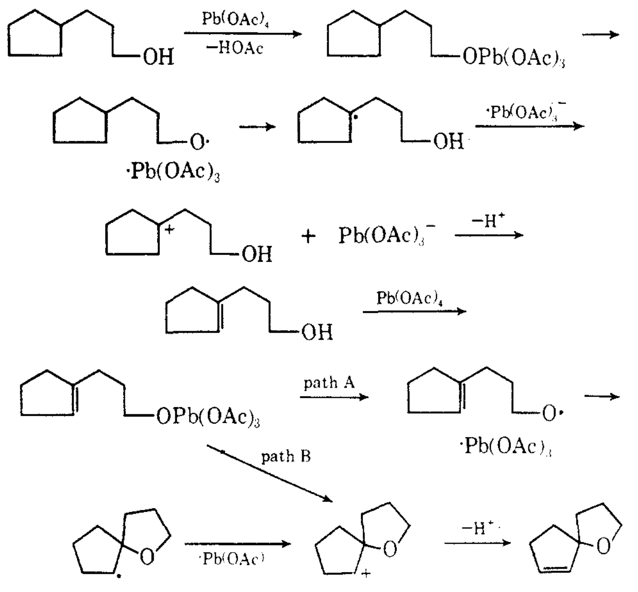
The lead tetraacetate oxidation of 3-cyclopentylpropanol (**11**) yielded **12** and **13**. The presence of **13** suggests that the process of tetrahydrofuran ring formation not only proceeds with inversion[6] and isomerization,[1] but also with elimination. The presence of **13** indicates that an intermediate with substantial carbonium-ion character may exist (see Scheme IV).

Heusler[9] was the first to suggest the oxidation of the carbon free radical to the carbonium ion as a plausible route to ring formation. Heusler proposed the lead tetraacetate free radical (generated from alcohol–lead bond homolysis) as the oxidizing agent for the conversion of the carbon radical into the carbonium ion. Recent work by Heiba,[10] however, suggests that lead tetraacetate itself is capable of oxidizing the carbon free radical to the carbonium ion.

Experimental Section[11]

Reaction of 2-Cyclohexylethanol with LTA.—A mixture of 10 g of 2-cyclohexylethanol and 60 g of LTA was refluxed in 100 ml of benzene for 19 hr. The mixture was cooled to room temperature and filtered. The precipitate was washed with benzene and the washings were added to the filtrate. The combined organic layer was washed with water, 10% sodium bicarbonate solution, and water, dried ($MgSO_4$), concentrated, and distilled, yielding 6.19 g (62% yield), bp 39–62° (1.5 mm). The fractions were analyzed by gas chromatography [ethylene glycol adipate (EGA) (programmed from 50 to 150°)] and showed five components, three of which were identified[12] as *cis*-7-oxabicyclo[4.3.0]nonane (**2**, 21%), *trans*-7-oxabicyclo[4.3.0]octane (**3**, 7%), and 2-cyclohexylethyl acetate (**4**, 30%). No starting alcohol was found in the reaction mixture.

Scheme IV



Reaction of 3-Cyclohexylpropanol with LTA. A. In Benzene.—3-Cyclohexylpropanol (5 g) was treated with 20 g of LTA in 100 ml of refluxing benzene for 2 days. The mixture was cooled to room temperature and treated with 10 ml of ethylene glycol to remove any unchanged LTA. The ethylene glycol was removed and the benzene layer was washed with 10% sodium carbonate solution and water, dried ($MgSO_4$), concentrated, and distilled through a short-path distillation column, yielding 2.99 g (60% yield), bp 55° (40 mm) to 85° (0.7 mm). Gas chromatography showed three major products which were identified[12] as 1-oxaspiro[4.5]decane (**6**, 8%), 3-cyclohexylpropanol (**5**, 18%), and 3-cyclohexylpropyl acetate (**7**, 34%).

B. In Cyclohexane.—3-Cyclohexylpropanol (1 g) was treated with 4.7 g of LTA in 200 ml of refluxing cyclohexane for 18 hr. The product was isolated as above. Gas chromatography of the crude product mixture indicated four components which were identified[13] as cyclohexyl acetate (5%), **6** (11%), **5** (37%), and **7** (46%).

C. In Cyclohexene.—3-Cyclohexylpropanol (1 g) was treated with 4.7 g of LTA and 1.0 g of calcium carbonate in 200 ml of refluxing cyclohexene for 18 hr. The products were isolated as described above. Gas chromatography indicated that the alcohol to acetate ratio was almost 1:2 with just trace amounts of the ether being formed. Integration of peak areas indicated that the alcohol had been at least 60% consumed during the reaction. Gas chromatography also indicated the presence of three additional peaks which were identified[12] as 2-cyclohexen-1-ol, 2-cyclohexen-2-one, and 2-cyclohexen-1-yl acetate in a 1:1:2 ratio. The oxidation products of 3-cyclohexylpropanol and cyclohexene were found in about a 1:1 ratio.

Reaction of 2-Cyclopentylethanol (8) with LTA.—Cyclopentylethanol (**8**, 1 g) was treated with 6 g of LTA in 25 ml of refluxing benzene for 11 hr. The product was isolated as above.

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[8] Based on lead tetraacetate.

[9] K. Heusler and J. Kalvoda, *Angew. Chem. Intern. Ed. Engl.*, 525 (1964).

[10] E. I. Heiba, R. M. Dessau, and W. J. Koehl, Jr., *J. Amer. Chem. Soc.*, **90**, 2706 (1968).

[11] For gas chromatography analysis, an F & M Model 720 thermal conductivity gas chromatograph was used. Ir spectra were recorded with a Perkin-Elmer Infracord, Model 337, and a Varian A-60 spectrometer was used to record the nmr spectra. The chemical shifts are shown in τ values from tetramethylsilane (TMS).

[12] The products were isolated by gas chromatography and identified by comparison of their ir spectra, nmr spectra, and retention times on gas chromatography with those of authentic samples.

[13] Product ratios were obtained by integration of peak areas. The products were identified by comparison of their ir spectra with those of authentic samples.

The product was distilled through a short-path distillation column yielding 0.56 g (56%), bp 40° (65 mm) to 75° (6 mm). Gas chromatography of the distillate showed two products which were identified[12] as 2-oxabicyclo[3.3.0]octane (**9**, 22%) and 2-cyclopentylethyl acetate (**10**, 34%).

Reaction of 3-Cyclopentylpropanol (11) with LTA.—3-Cyclopentylpropanol (10 g) was treated with 80 g of LTA in 250 ml of refluxing benzene for 17 hr. The product was isolated as above. The product was distilled through a short-path distillation column and collected, yielding 6.25 g (63% yield), bp 50° (15 mm) to 100° (0.4 mm). Gas chromatography of the product mixture showed three major peaks which were identified[11] as 1-oxaspiro[4.4]nonane (**12**, 4%), 1-oxaspiro[4.4]non-6-ene (**13**, 6%), and 3-cyclopentylpropyl acetate (**14**, 39%).

Anal. Calcd for $C_8H_{12}O_1$ (**13**): C, 77.37; H, 9.85. Found: C, 77.07; H, 9.86.

13 (50 mg) was isolated by gas chromatography and hydrogenated at room temperature and atmospheric pressure in 10 ml of anhydrous ethanol in the presence of 0.1 g of platinum oxide. After 15 hr, 60% of **13** had been converted into **12** and a small quantity of higher boiling material.

3-Cyclopentylpropanol.—β-Cyclopentylpropionic acid (20 g) was treated with 4 g of lithium aluminum hydride in 100 ml of anhydrous ether, yielding 7.25 g (41%) of 3-cyclopentylpropanol, bp 63° (1.0 mm).

Reaction of LTA in Neat Cyclohexene.—LTA (10 g) was refluxed in 100 ml of cyclohexene for 2 days. The reaction mixture was concentrated by distillation of excess cyclohexene. Gas chromatography (silicone rubber) showed five products which were identified[11] as 2-cyclohexen-1-ol (1.4%), 2-cyclohexen-1-yl acetate (80%), 2-cyclohexen-1-one (7%), an unknown mixture (4%), and diacetates (7%).[14]

1-Cyclohexen-1-ylmorpholine.—Cyclohexanone (98 g, 1 mol) and morpholine (87 g, 1 mol) were refluxed in 220 ml of benzene for 18 hr. Water (25 ml) was collected in a Dean-Stark trap. The benzene was removed by distillation, and the residue was distilled, yielding 125 g (75%) of 1-cyclohexen-1-ylmorpholine, bp 78-81° (0.3-0.15 mm).

Ethyl (2-Oxocyclohexyl)acetate (15).—1-Cyclohexen-1-ylmorpholine (40 g) and 55 g of ethyl bromoacetate were stirred overnight in 160 ml of benzene at 50°. The mixture was cooled to room temperature and concentrated under reduced pressure. The crude product was diluted with 100 ml of methanol and treated with 50 ml of water at refluxing temperature for 15 hr. The product was condensed *in vacuo*, treated with 100 ml of 1.0 *M* hydrochloric acid for 10 min, and extracted with ether. The ethereal extract was washed with water, 10% sodium carbonate, and water, dried ($MgSO_4$), concentrated, and distilled, giving 3 g of the acetoxy ketone **15**: bp 73-74° (0.34-0.40 mm) [lit.[15] bp 131-134° (13 mm)]; ir (CS_2) 1710 (C=O), 1740 cm^{-1} (ester C=O). Gas chromatography (silicone rubber at 200°) showed the product to be homogeneous.

2-(2-Hydroxycyclohexyl)ethanol (16).—The acetate **15** was treated with 5 g of lithium aluminum hydride in 25 ml of refluxing ether for 22 hr. The mixture was cooled to room temperature and treated with 5 ml of water, 5 ml of 10% sodium hydroxide, and 15 ml of ether. The product was filtered and the precipitate was washed with ether. The washings were added to the filtrate and the ethereal layer was dried ($MgSO_4$) and concentrated. Gas chromatography (silicone rubber) of the crude product showed only one peak. The ir spectrum (CS_2) showed a strong band for associated hydroxyl group but little free absorption. The product is assumed to be a mixture of the *cis* and *trans* isomers.

***cis*- and *trans*-7-Oxabicyclo[4.3.0]nonanes (2 and 3).**—Compound **16** (1 g, crude mixture) was treated with 0.7 g of tosyl chloride in 15 ml of pyridine for 24 hr at 35-40°. The product was poured onto cracked ice and extracted with ether. The ethereal layer was washed with 10% sodium carbonate, water, 3 *M* hydrochloric acid, and water, dried ($MgSO_4$), and concentrated. Gas chromatography of the crude product (EGA) showed two peaks.

The first peak was identified as **2** (29%), and the second peak was identified as **3** (71%). The ir spectrum (CS_2) of **2** showed 1180, 1155, 1120, 1080, 1045, 1020, 985, 930, 880, 200 cm^{-1}; that (CS_2) of **3** showed 1190, 1150, 1142, 1070, 985, 935, 860 cm^{-1}. Cantor and Tarbell[16] give 1184, 1160, 1142, 1090 cm^{-1} as characteristic absorption peaks for **3**.

***cis*-7-Oxabicyclo[4.3.0]nonane (2).**—Benzofuran (**17**, 0.5 g) was hydrogenated at room temperature and atmospheric pressure in 50 ml of glacial acetic acid in the presence of 0.11 g of platinum oxide. After 4.5 hr, 575 ml of hydrogen[17] was taken up and the reaction was stopped.

The catalyst was removed by filtration and the product was diluted with water and extracted with ether. The ethereal extract was washed with water, 10% sodium carbonate solution, and water, dried ($MgSO_4$), and concentrated. Gas chromatography (silicone rubber and EGA) showed that the benzofuran was totally consumed in the reaction. Two products were found which were identified[13] as **2** (75%) and **1** (25%). None of the *trans* isomer **3** was found.

***cis*-7-Oxabicyclo[4.3.0]nonane (2).**—Mercuric acetate (12.8 g) was dissolved in 40 ml of water. Tetrahydrofuran (40 ml) was added, producing a yellow suspension. 2-(β-Cyclohexenyl)-ethanol was added rapidly (no heat developing), and the yellow color cleared within a minute. The solution was stirred for 45 min at room temperature after which time the solution gave a negative test for mercuric ion.[18] The solution was treated with 40 ml of 3 *M* sodium hydroxide, followed by 2 g of sodium borohydride in 40 ml of 3 *M* sodium hydroxide. The reaction, which was strongly exothermic, produced a black precipitate immediately upon the introduction of the sodium borohydride solution, which upon stirring settled into a silvery mercury lake. The water layer was saturated with sodium chloride and the product was extracted with ether. The ethereal extract was dried ($MgSO_4$), concentrated, and distilled, giving 3.36 g (67%) of the bicyclic ether **2**, bp 71° (28 mm) [lit.[16] bp 66-68° (15 mm)].

***cis*-2-Oxabicyclo[3.3.0]octane (9).**—2-(2-Cyclopentenyl)ethanol (**19**, 5.6 g) was treated with 16 g of mercuric acetate in 100 ml of 50% THF in water for 0.5 hr. The product was treated with 50 ml of 3 *M* sodium hydroxide and demercurated with 2.5 g of sodium borohydride in 50 ml of 3 *M* sodium hydroxide. The water layer was saturated with sodium chloride and the product was dried ($MgSO_4$), concentrated, and distilled, giving 4.2 g (75%) of the bicyclic ether **9**, bp 49-50° (28 mm).

1-Allylcyclohexanol (21a).—Allyl chloride (38 g) was slowly added to 12 g of magnesium in 100 ml of dry ether. The reaction flask was kept at 0° by means of an ice-water bath and the addition of the allyl chloride was made at the rate of 1 drop/10-12 sec. The addition took 7 hr. Cyclohexanone (49 g) in 50 ml of ether was added slowly to the Grignard reagent with vigorous stirring. The reaction mixture was allowed to stir overnight at room temperature. Water (20 ml) was added to decompose unchanged the Grignard reagent. Saturated ammonium chloride solution (23 ml) was added to the reaction mixture. The mixture was stirred at room temperature for 15 min. A white solid formed, and the ethereal layer was decanted. The ethereal extract was dried ($MgSO_4$), concentrated, and distilled, giving 32 g (23%) of the unsaturated alcohol **21a**, bp 58.0-58.5° (1.4 mm). Gas chromatography (silicone rubber at 125°) showed the product to be homogeneous.

3-(1-Hydroxycyclohexyl)propanol (22a).—1-Allylcyclohexanol (**21a**, 7 g) was dissolved in 50 ml of THF (dried over sodium). Sodium borohydride (1 g) was added, and the mixture was treated with 5 g of 47% boron trifluoride etherate at room temperature. After addition was complete the solution was stirred at room temperature for 1 hr. Water (5 ml) was added to decompose excess diborane. The reaction mixture was treated with 30 ml of 3 *M* sodium hydroxide, followed by 30 ml of 30% hydrogen peroxide. The mixture was stirred for 1 hr at room temperature and extracted with ether. The ethereal extract was washed with 20% sodium hydroxide and water, dried ($MgSO_4$), concentrated, and distilled, giving 3.65 g (51%) of a very viscous liquid, bp 100-115° (0.2 mm). Gas chromatography (silicone rubber at 140°) showed two products. The first product (10% of the mixture) was identified as 1-(1-hydroxycyclohexyl)-2-

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[14] Absolute yields were determined by introduction of 0.1863 g of ethyl cyclohexylcarboxylate into the product mixture for use as an internal standard, and based on LTA.

[15] A. Segre, R. Viterbo, and G. Parisi, *J. Amer. Chem. Soc.*, **79**, 3503 (1957).

[16] S. E. Cantor and D. S. Tarbell, *ibid.*, **86**, 2902 (1964).

[17] It was calculated that 399 ml of hydrogen would be necessary to hydrogenate the sample totally, and 23 ml would be necessary to reduce the platinum oxide.

[18] A few drops of the reaction mixture was added to a 3 *M* sodium hydroxide solution. A yellow color indicates that the reaction is incomplete.

propanol (**23a**). The second product was identified as 3-(1-hydroxycyclohexyl)propanol (**22a**): ir (CS_2) strong hydrogen bonding and little free OH absorption; nmr (CCl_4) τ 6.2 (t, 2), 5.0 (broad s, 2), 8.5 (m, 14). After 4 days, large crystals developed in the ethereal solution. They were found to be **22a**, mp 66–68° (lit.[19] mp 60°).

Anal. Calcd for $C_9H_{18}O_2$ (**23a**): C, 68.3; H, 11.4. Found: C, 68.0; H, 11.6.

1-Oxaspiro[4.5]decane (6).—The diol **22a** (1.0 g) was treated with 2 g of tosyl chloride in 10 ml of pyridine for 18 hr at 40–50°. The product was poured onto cracked ice and extracted with ether. The ethereal extract was washed with 6 *M* hydrochloric acid, water, 10% sodium bicarbonate solution, and water, dried ($MgSO_4$), and concentrated. The crude mixture (0.5 g) was shown to be homogeneous on gas chromatography (silicone rubber programmed from 50 to 100°): ir (CS_2) 1145, 1120, 1085, 1050, 925, 905 cm^{-1}. 1-Oxaspiro[4.5]decane (**6**) was previously prepared by the treatment of 3-(1-hydroxycyclohexyl)propyl *n*-pentyl ether with tosyl chloride in pyridine.[20]

1-(1-Hydroxycyclohexyl)-2-propanol (23a).—1-Allylcyclohexanol (1.4 g) was treated with 3.12 g of mercuric acetate in 20 ml of THF–water. The yellow suspension disappeared in 10 sec and the reaction was stirred at room temperature for 15 min. Sodium hydroxide (3 *M*, 10 ml) was added, followed by 0.5 g of sodium borohydride in 10 ml of 3 *M* sodium hydroxide. The product was extracted with ether (the water layer being saturated with sodium chloride). The ethereal extract was washed with water, dried ($MgSO_4$), and concentrated. Gas chromatography of the crude product showed one major peak: ir (CS_2) 3400 (strong hydrogen-bonded OH absorption), 2960, 2925, 2850 cm^{-1}; nmr (CCl_4) τ 4.3 (s, 2), 6.0 (m, 1), 8.5 (m, 10), 8.8 (d, 3).

1-Allylcyclopentanol (21b).—The reaction of allylmagnesium chloride (23 g of allyl chloride and 15 g of magnesium turnings) and cyclopentanone (25 g) gave 10.9 g (29%) of the alcohol **21b**, bp 71–73° (20 mm) [lit.[21] bp 63° (10 mm)].

3-(1-Hydroxycyclopentyl)propanol (22b).—1-Allylcyclopentanol (5.3 g) was treated with 1.5 g of sodium borohydride and 5.0 g of 47% boron trifluoride etherate in 200 ml of THF (dried over sodium) under a nitrogen atmosphere. The mixture was stirred at room temperature overnight. Unchanged diborane was destroyed with 10 ml of water; the mixture was treated with 30 ml of 3 *M* sodium hydroxide, followed by addition of 30% hydrogen peroxide. The product was extracted with ether. The ethereal extract was washed with 6 *M* sodium hydroxide and water, dried ($MgSO_4$), concentrated, and distilled, yielding 1.25 g (20%) of a viscous liquid, bp 122–130° (5 mm). Gas chromatography (silicone rubber programmed from 50 to 180°) showed two peaks. The first peak (28%) on the basis of its retention time, ir, and the analogous reaction in the preparation of **22a** was tentatively assigned as the diol **23b**. The second peak (72%) was assigned as the diol **22b**, mainly because of the nmr signal at τ 6.4 (triplet corresponding to the methylene hydrogens α to the primary hydroxyl group).

1-Oxaspiro[4.4]nonane (12).—A mixture of **22b** and **23b** (0.8 g) was treated with 2.0 g of tosyl chloride in pyridine for 18 hr at 50°. The product was poured onto cracked ice and extracted with ether. The ethereal extract was washed with water, 6 *M* hydrochloric acid, water, sodium bicarbonate solution, and water, dried ($MgSO_4$), and concentrated. Gas chromatography (diethylene glycol succinate) of the crude product showed only one major product: ir (CS_2) 1165, 1100, 1050, 970, 945, 920, 900 cm^{-1}; nmr (CCl_4) τ 6.3 (t, 2), 8.1–8.5 (m, 12).

Anal. Calcd for $C_8H_{14}O$: C, 76.2; H, 11.1. Found: C, 76.2; H, 11.2.

Registry No.—Lead tetraacetate, 546-67-8; **1,** 4442-79-9; **5,** 1124-63-6; **8,** 766-00-7; **9,** 18320-80-4; **11,** 767-05-5; **12,** 176-10-3; **21a,** 1123-34-8; **23a,** 18321-43-2; 1-cyclohexen-1-ylmorpholine, 670-80-4.

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The Synthesis of Imidate Hydrochlorides by Reaction of Ethyl Chloroformate with Amides and Thionamides

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The scope of the reaction of ethyl chloroformate with amides as a preparation of ethyl imidate hydrochlorides has been investigated. The imidate salts have been prepared successfully in good yields from aliphatic amides containing from one to eight carbon atoms, both straight and branched chain. The N-methyl and N-ethyl derivatives of these aliphatic amides reacted in the same way to give N-substituted imidate hydrochlorides. Attempts to employ the reaction with aromatic amides or N-substituted amides in which the substituent is larger than ethyl were unsuccesful. In certain cases a side reaction occurred. Thus the hemihydrochlorides of acetamide and N-methylcaprylamide were obtained as a second product from acetamide and N-methylcaprylamide, respectively. N-Methylacetamide gave its hemihydrochloride as the only product of the reaction. Thionamides have been found to react with ethyl chloroformate in a similar way, giving the ethyl imidate hydrochloride and carbonyl sulfide as products. The hydrochloride salts of ethyl acetimidate, ethyl propionimidate, ethyl isobutyrimidate, ethyl benzimidate, and ethyl N-phenylacetimidate have been prepared from thioacetamide, thiopropionamide, thioisobutyramide, thiobenzamide, and thioacetanilide, respectively. The reactivity of thionamides is considerably greater than that of the analogous oxygen compounds. The rate curve for the reaction, using propionamide, shows it to be autocatalytic. A possible mechanism for the reaction is suggested.

Although imidates (imino ethers, imido esters) and their salts have been known for nearly a century,[2] and are useful intermediates for the synthesis of a variety of compounds,[3] there has been only one general direct method for their preparation, namely, the method of Pinner,[4] which involves synthesis of the imidate hydrochloride from the appropriate nitrile and alcohol with anhydrous hydrogen chloride (eq 1). The salt

$$RCN + R'OH + HCl \longrightarrow RC(=NH_2Cl)OR' \qquad (1)$$

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