of the products showed one major product (98.4%) identified as chlorobenzene. Two minor products were not identified, although neither had the retention time of benzene.

Acknowledgment. We gratefully acknowledge the Robert A. Welch Foundation (Grant C-490) for support of this work. Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. **5**, 56485-66-6; **6**, 91-58-7; **7**, 71436-63-0; **8**, 71436-64-1; **9**, 71436-65-2; **10**, 2050-69-3; **11**, 2050-75-1; **12**, 71436-66-3; **13**, 71436-67-4; **14**, 71436-68-5; **15**, 71436-69-6; **16**, 71436-70-9; **23**, 74925-43-2; **24**, 74925-44-3; **25**, 51526-36-4; **26**, 74925-45-4; **27**, 74925-46-5; **28**, 66768-81-8; **31**, 74925-47-6; indene, 95-13-6; 1,2-dibromoindan, 20357-79-3; 2-bromoindene, 10485-09-3; 2,3-benzobicyclo[3.1.0]hexane, 15677-15-3; 1,4-dihydronaphthalene, 612-17-9; 1,3-naphthalenediol, 132-86-5; chlorobenzene, 108-90-7; 1-bromo-2-aminonaphthalene, 20191-75-7; 2-chloro-1-naphthol, 606-40-6; 2-chloroindene, 18427-72-0; 1,2-dichloroindan, 74925-48-7; 4-bromocyclopentene, 1781-66-4; 2-chloronaphthalene-1,3-diyl, 74925-49-8.

Models for Glycoside Hydrolysis. Synthesis and Hydrolytic Studies of the Anomers of a Conformationally Rigid Acetal

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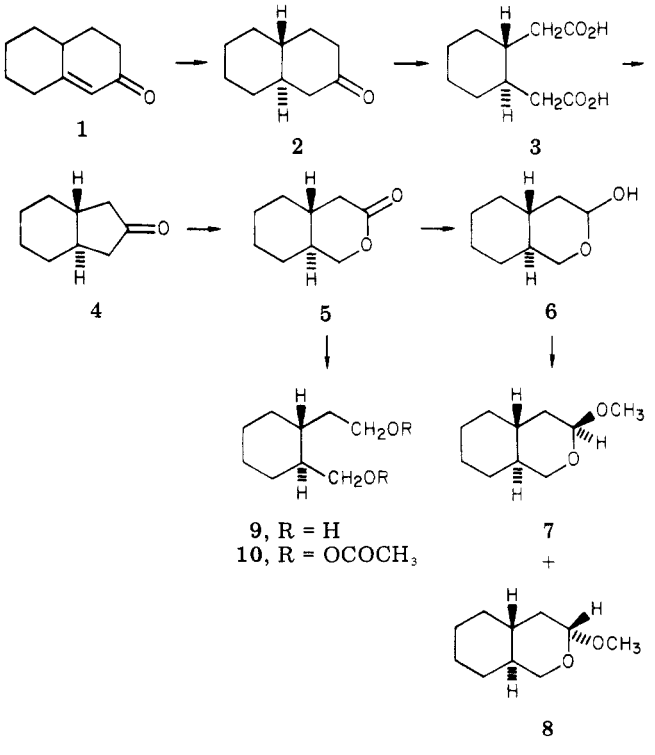
The methyl acetals of 2-hydroxy-3-oxa-*trans*-decalin were synthesized as models for conformationally rigid methyl glycosides. The compounds were prepared by Baeyer–Villiger oxidation of *trans*-hexahydrohydrindan-2-one followed by reduction of the resulting lactone with diisobutylaluminum hydride. Treatment of the hemiacetal with methanol and an acid catalyst afforded a mixture of acetals which were separated by chromatography and identified by NMR. Hydrolytic studies were carried out under a range of acid concentrations and temperatures. The mechanistic implications of the relative hydrolysis rates (axial/equatorial ratio of 1.51 ± 0.22) and activation parameters are discussed.

Due to the biological and commercial importance of the reaction, the acid-catalyzed hydrolysis of glycosides has been the object of extensive research as well as the subject of several reviews.[1,2] In spite of abundant data on glycoside hydrolysis, an in-depth understanding of the factors that affect the rate remains obscure. One of the factors which affects the rate of hydrolysis of glycosides is the configuration about the anomeric center. In an extensive study comparing the rates of hydrolysis of the anomers of methyl glycosides, Feather and Harris[3] found that the β anomers containing the equatorial methoxy group hydrolyzed more rapidly than the α anomers containing the axial methoxy group. Ten anomeric pairs were selected such that the major conformation of both members of the pair is the same. The hydrolysis ratio (axial to equatorial) was 0.52 ± 0.12. Since the equatorial isomer is more stable than the axial as a result of the anomeric effect,[4] the conformations of the initial state determined the relative rates of hydrolysis. This general conclusion appears to be contradicted by the observation that the β anomers of *O*-aryl glycosides frequently hydrolyze more slowly than the corresponding α anomer.[3] The contradiction may be resolved by proposing that the stable conformation of the α anomer of *O*-aryl glycosides contains the leaving group in the equatorial position. Hence, it becomes apparent that the interpretation of the relative rates of anomer hydrolysis rests on one's ability to determine the most stable conformation. Furthermore, although the assigned conformation is more stable than other possible conformations, the molecule is not compelled to react in that conformation. To overcome these difficulties, we synthesized the conformationally rigid methyl acetals **7** and **8** as models for a study of the hydrolysis of axial and equatorial methyl glycosides.

Scheme I



1 2 3 4 5 6

9, R = H
10, R = OCOCH3

7 + 8

Results and Discussion

The conformationally rigid acetals **7** and **8** were synthesized by the routes outlined in Scheme I. The starting material, $\Delta^{1,9}$-3-octalone (**1**), was prepared by a literature

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(4) Lemieux, R. U. "Molecular Rearrangements"; P. de Mayo, Ed.; Interscience: New York, 1964; p 735.

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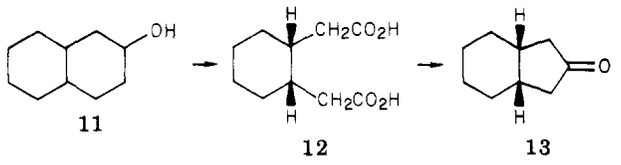
Scheme II



11 12 13

procedure[5] and reduced with lithium in liquid ammonia[6] to afford the pure *trans*-2-decalone (**2**). The ketone was oxidized with nitric acid to give the crystalline diacid **3** and pyrolyzed[7] to yield pure *trans*-hexahydrohydrindanone (**4**). Baeyer–Villiger oxidation of ketone **4** with peroxytrifluoroacetic acid afforded a smooth conversion to the lactone **5** in 68% yield. The lactone was characterized by reduction with sodium borohydride to give the expected diol, **9**, followed by acylation of the diol with acetic anhydride in pyridine to yield the diacetate **10**. The structures were consistent with their NMR spectra. Attempts to reduce the lactone with disiamylborane gave the desired hemiacetal, **6**, in poor yield. Reduction of **5** with a 30% molar excess of diisobutylaluminum hydride, however, provided the crystalline hemiacetal **6** in 55% yield. The hemiacetals were converted to an isomeric mixture of methyl acetals **7** and **8** in an 82% yield by refluxing **6** in absolute methanol with Dowex-50 (H^+ form) as an insoluble acid catalyst.

The axial (**7**) and equatorial (**8**) anomeric methyl acetals were separated by column chromatography and characterized by NMR. The mixture of anomers was separated on a column of silica gel eluted with a diethyl ether–pentane (15/85) solvent mixture. The column effluent was monitored by GC to reveal two well-resolved peaks designated as anomers "A" and "B". The structures of the anomers were assigned on the basis of the NMR splitting patterns of the coupling of the anomeric proton with the adjacent protons on the ring. The NMR of anomer A displayed a narrow doublet of doublets at 4.37 ppm with a primary splitting of 3.0 Hz and a secondary splitting of less than 0.5 Hz. The NMR of anomer B, on the other hand, displayed a broad doublet of doublets at 3.55 ppm with a primary splitting of 10.5 Hz and a secondary splitting of 2.5 Hz. NMR studies a α- (axial) and β- (equatorial) methyl glycosides[8] show that the equatorial anomeric proton of the α-methyl glycoside is associated with the smaller primary coupling to the hydrogen at C-2. The α-methyl glycosides typically show a primary coupling of 3.0–3.5 Hz and a secondary coupling of 1.5–2.5 Hz while the β-methyl glycosides show a primary coupling of 8.5–8.8 Hz and a secondary coupling of 1.5–2.5 Hz. Comparison of these splitting patterns to those observed for anomers A and B demonstrates that anomer A corresponds to the axial methoxy acetal (**7**) and anomer B corresponds to the equatorial methoxy acetal (**8**).

Prior to the successful synthesis described above, the preparation of **7** and **8** was attempted by starting with a commercially available mixture of *cis*- and *trans*-2-decalols (**11**, K&K Laboratories). The oxidation of **11** with nitric acid provided a mixture of the cis and trans isomers of 1,2-cyclohexanediacetic acid. Repeated crystallizations of the mixture from hexane–acetone afforded the pure, although undesired, cis isomer **12**, mp 159–160 °C (lit.[9] mp 159–161 °C). This conclusion was verified by the pyrolysis of **12** (Scheme II) to give *cis*-hexahydrohydrindan-2-one (**13**) whose oxime derivative gave the expected melting point of 79–80 °C (lit.[9] mp 80 °C).

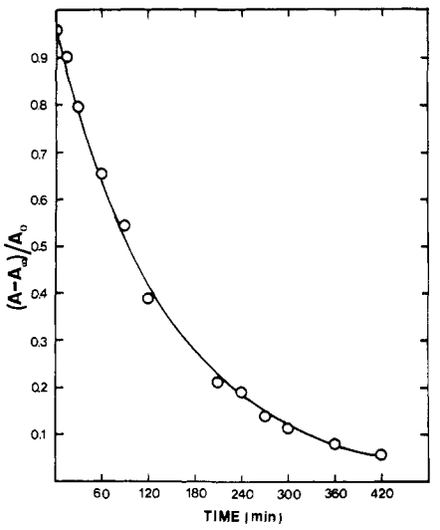


Figure 1. Time course of the hydrolysis of the axial isomer, **7**, carried out in a 0.010 M aqueous HCl/acetone solvent mixture (1/1 v/v) maintained at 35.2 °C. The line represents the theoretical curve with a rate constant of 6.9×10^{-3} min^{-1}.

The axial anomer (**7**) is more stable than the equatorial anomer (**8**). Time-dependent measurements of the axial to equatorial ratio assured that the mixture had reached equilibrium during their preparation. An equilibrium mixture of **7** and **8** contains 68 ± 1% of **7** and 32 ± 1% of **8**. This represents a $\Delta G°$ of 0.45 kcal for axial–equatorial interconversion at 25 °C. Similar observations have been made for the 3-methoxy-4-oxa-5α-cholestane[10] and 3-methoxy-4-oxa-5α-estrane[11] anomers at equilibrium. These results are consistent with the anomeric effect[4] resulting from an unfavorable interaction of the equatorial substituent dipole with the ring oxygen dipole.

The acid-catalyzed hydrolyses of the axial and equatorial anomers (**7**, **8**) of the conformationally rigid acetals were studied in aqueous hydrochloric acid–acetone solvent mixtures maintained at constant temperature in a water bath. The course of the reaction, monitored by GC, showed the disappearance of **7** and **8** and the appearance of the product hemiacetal **6**. The disappearance of **7** and **8** follows first-order kinetics of over 4 half-lives. A typical kinetic run is shown in Figure 1. Pseudo-first-order rate constants, k_{obsd}, were evaluated from the slopes of the semilogarithmic plots of the normalized GC peaks (normalized with respect to an internal standard and corrected for the infinity value) vs. time by the method of least squares. The correlation coefficients of all k_{obsd} values were 0.99 or better.

Any interpretation of the relative rates of axial vs. equatorial anomers must rest on a comparison of the rates measured under a variety of conditions. Since the conclusions are justified only if the anomers show similar variations in rate with changes in the catalyzing acid and temperature, the dependence of k_{obsd} on acid concentration and temperature was measured. The data are summarized in Table I. The variations of k_{obsd} for the axial and equatorial anomers with increasing acid concentration are

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Table I. Observed First-Order Rate Constants[a] for the Hydrolysis of 7 and 8 as a Function of Hydrogen Ion[b] Concentration and Temperature

10^3k_{Ax}, min^{-1}	10^3k_{Eq}, min^{-1}	$10^3[H^+]$, M	temp, °C
3.7	2.3	2.5	35.2
6.9	6.1	5.0	35.2
11.1	6.9	7.5	35.2
41.2	28.1	25.0	35.2
4.4	3.4	25.0	19.8
2.8	1.9	7.5	24.8
21.5	12.3	7.5	39.7
153.3	87.8	7.5	55.1

[a] Calculated from the slope of $(A_t - A_\infty)/A_0$ vs. time; slopes were determined by the method of least squares; correlation coefficients of all measured first-order rate constants are 0.99 or better. [b] Aqueous HCl/acetone mixtures (1/1 v/v). Ax = axial and Eq = equatorial.

linear (Figure 2) and provide the second-order rate constant (k_2) for acid-catalyzed hydrolysis by eq 1, yielding values of 1.65 and 1.10 M^{-1} min^{-1} for the axial and equatorial anomers, respectively, at 35.2 °C.

$$k_{obsd} = k_2[H^+] \quad (1)$$

In contrast to the results for alkyl glycosides,[3,12] a comparison of the second-order rate constants demonstrates that the axial anomer hydrolyzes 1.50 times faster than the equatorial anomer. If one considers all the data in Table II, which cover a broad range in acid concentration and temperature, the axial to equatorial rate ratio is 1.51 ± 0.22. Given the observation that the axial anomer is more stable than the equatorial anomer, one must conclude that the initial configuration does *not* determine the relative rates of anomer hydrolysis and further that the anomers hydrolyze by different transition states. The latter conclusion is of particular interest, because in the case of methyl glycosides, the data did not allow one to reach that conclusion.

The mechanism of acid-catalyzed hydrolysis of glycosides involves protonation of the glycoside to form the conjugate acid. Since glycosides (including models 7 and 8) are unsymmetrical acetals, there are two possible sites of protonation (the glycosidic bond and the ring oxygen), leading to two different mechanisms. Cleavage of the exocyclic carbon–oxygen bond results in the formation of an intermediate cyclic oxonium ion (cyclic mechanism), while the cleavage of the endocyclic carbon–oxygen bond results in the formation of an intermediate open-chain oxonium ion (ring-opening mechanism). Although the latter mechanism has not been rigorously excluded in all cases, the experimental evidence strongly favors the cyclic mechanism. In a study of the hydrolysis of methyl-α-D-glucopyranoside, Vernon and co-workers[13] have measured the kinetic isotope effect associated with the oxygen of the glycosidic bond. The observed isotope effect of 1.03 would only be expected if the methoxy glycosyl bond were broken in the rate-determining step via the cyclic mechanism. The observation[14] that *O*-aryl glucopyranosides hydrolyze faster than the corresponding *O*-methyl glucopyranosides argues *against* the ring-opening mechanism since the intermediate open-chain cation from *O*-aryl glucopyranosides is less stable than the corresponding cation from *O*-methyl glucopyranoside. Furthermore, studies of the anomerization of glucopyranosides also support the cyclic mechanism. An anomerization mechanism involving the open-chain cationic intermediate and nonspecific formation of acetals was excluded by tracer experiments[15] in CD_3OD. These experiments demonstrated that the anomerization of *O*-methyl glucopyranosides was accompanied by >98% exchange of the methoxy group with the solvent. The above evidence argues strongly against the open-chain mechanism, and, consequently, the acid-catalyzed hydrolysis of acetals 7 and 8 will be discussed in terms of the cyclic mechanism.

The observed first-order dependence on the acetal and acid during hydrolysis of acetals 7 and 8 is in accord with the general mechanism of glycoside hydrolysis. Given that the axial and equatorial anomers (7, 8) must hydrolyze via different transition states, the difference in their hydrolysis rates may be explained by postulating an early transition state for the equatorial anomer with little C–O bond breakage and a late transition state for the axial anomer with more extensive C–O bond breakage. This hypothesis is supported by an examination of the activation parameters for the hydrolysis of 7 and 8 (Table II). Both anomers exhibit positive enthalpies and entropies of activation as expected for a dissociative mechanism. Moreover, the observation that the axial anomer exhibits both a larger positive enthalpy and entropy of activation than the equatorial anomer is in accord with the hypothesis that the rate-determining transition state of the axial anomers involves more extensive C–O bond breakage.

In summary, kinetic studies of the hydrolysis of the conformationally rigid methyl acetals (7, 8) demonstrate the following: (a) in contrast to glycosides, the axial anomer hydrolyzes 1.50 times faster than the equatorial anomer; (b) the anomers hydrolyze via *different* transition states; (c) the rate-determining transition state of the axial anomer involves more extensive bond breakage than that of the equatorial anomer.

Experimental Section

General Methods. All melting points are uncorrected and were determined by using the capillary technique. Infrared spectra were taken on a Perkin-Elmer 237 grating spectrophotometer. NMR spectra were taken on a Varian 360-L or HA-100 instrument, and all chemical shifts are given in parts per million downfield from tetramethylsilane as internal standard. Gas chromatograms were made on a Varian Aerograph Model 1200 gas chromatograph with a flame-ionization detector. Analyses were performed by Midwest Microlab, Inc.

$\Delta^{1,9}$-2-Octalone (1) was prepared according to the procedure of Robinson[5] in a 40% yield. The distilled product [78–87 °C (2 torr)] gives a UV spectrum (λ_{max} 230 nm) which matches that of an authentic sample. GC (4 ft × $^1/_8$ in. column of 10% SE-30 on Chromosorb W at 175 °C) shows greater than 99% purity.

***trans*-2-Decalone (2)** was prepared by a modification of a published procedure.[6] A flamed-out, 2-L, three-necked flask was charged with 2.5 g of 1 (0.017 mol), 30 mL of dry diethyl ether, and 30 mL of purified dioxane (CaH dried and distilled). After the solution was cooled to −70 °C in a dry ice/acetone bath, anhydrous ammonia (800 mL) and lithium metal (0.28 g, 0.04 mol) were added with constant stirring. The blue solution was stirred for 1 h, the cooling bath was removed, and the ammonia was allowed to evaporate. After 15 h, water (100 mL) was added, and the mixture was extracted three times with ether. The extract was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The pale yellow liquid was distilled at 28 torr; the major fraction (bp 119–120 °C) gave 1.03 g of clear liquid (40% yield). GC (4 ft × $^1/_8$ in. column of 10%

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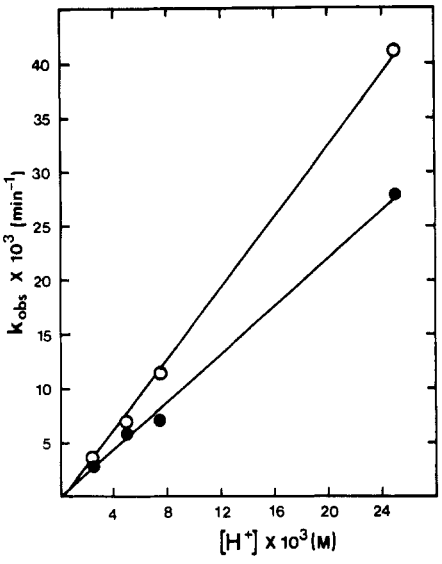

Figure 2. Variation of the observed pseudo-first-order rate constant of the hydrolysis of the axial anomer (**7**, ○) and the equatorial anomer (**8**, ●). The reactions were carried out in aqueous HCl/acetone solvent mixtures (1/1, v/v) maintained at 35.2 °C.

Table II. Activation Parameters[a] for the Hydrolysis of 7 and 8

[H$^+$],[b] M	$\Delta H^{\ddagger\circ}_{Ax}$, kcal/mol	$\Delta H^{\ddagger\circ}_{Eq}$, kcal/mol	$\Delta S^{\ddagger\circ}_{Ax}$, cal/mol K	$\Delta S^{\ddagger\circ}_{Eq}$, cal/mol K
7.5×10^{-3}	25.7	24.6	17	13
2.5×10^{-2}	26.1	24.6	21	16

[a] Calculated from the slope and intercept of ln k_2 vs. (temperature)$^{-1}$; temperature range 20–55 °C. Ax = axial and Eq = equatorial. [b] Aqueous HCl/acetone mixtures (1/1 v/v).

SE-30 on Chromosorb W at 175 °C) indicates greater than 99% purity. A semicarbazone derivative gave a melting point of 185–186 °C (lit.[6] mp 189–191 °C).

***trans*-1,2-Cyclohexanediacetic acid (3)** was prepared by a published procedure:[7] 51% yield; mp 166–166.5 °C (lit.[7] mp 167 °C).

***trans*-Hexahydrohydrindan-2-one (4)** was prepared by the published procedure of Vogel[7] in 47% yield. GC (5 ft × $^1/_8$ in. column of 10% Carbowax 20M on Chromosorb W, 60/80 mesh, heated with a linear temperature program of 170–200 °C at 4 °C/min) showed the presence of only one isomer: IR (neat) 2910 (s), 2840 (m), 1745 (s) cm^{-1}; NMR (neat) δ 3.0–1.0 (m).

***trans*-3-Oxa-2-decalone (5).** Trifluoroacetic acid anhydride (1.75 g, 0.012 mol) and 0.3 mL of 85% hydrogen peroxide were placed in a 25-mL pear-shaped flask cooled in an ice bath. The mixture was stirred constantly while 1.05 g (0.0095 mol) of **4** was slowly added. After 10 min, the reaction mixture was diluted with 5 mL of chloroform and the solution poured into a saturated potassium carbonate solution to neutralize the trifluoroacetic acid. The layers were separated, and the aqueous layer was extracted three times with 5 mL of chloroform. The chloroform layers were combined and dried over magnesium sulfate, and the solvent was removed under reduced pressure to yield 1.0 g of product (68%). The lactone was purified by sublimation at 0.2 torr (60 °C), yielding a white solid: mp 41–42 °C; IR (neat) 3000 (m), 2910 (s), 2840 (m), and 1735 (vs) cm^{-1}; NMR ($CDCl_3$) δ 4.4 (2 H, m), 1.0–3.4 (12 H, m). GC (a 5 ft × $^1/_8$ in. column of 10% Carbowax 20M on Chromosorb W, 60/80 mesh, heated with a linear temperature program of 170–200 °C at 4 °C/min) established the existence of only one isomer in greater than 99% purity. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.77; H, 9.21.

Characterization of *trans*-3-Oxa-2-decalone. A solution of 100 mg of **5** (0.65 mmol) in 25 mL of absolute ethanol was treated with 50 mg (1.3 mmol) of sodium borohydride. After the solution was stirred for 1 h at room temperature, the solvent was evaporated in vacuo; the resulting solid mass was treated with 10 mL of 0.1 M aqueous hydrochloric acid, and the aqueous mixture was extracted with two 10-mL portions of dichloromethane. The organic layers were combined and dried over anhydrous sodium sulfate, and the solvent was evaporated in vacuo. An IR examination of the resulting white solid showed a new band at 3500–3200 cm^{-1} and the disappearance of the 1735-cm^{-1} lactone band, consistent with the reduction of **5** to **9**. The white solid was treated with pyridine (1 mL) and acetic anhydride (1 mL) and stirred overnight. The mixture was poured into cold water and extracted with dichloromethane. The organic layer was washed with several portions of water and dried over anhydrous sodium sulfate, and the solvent removed in vacuo. An NMR examination of the oil showed two new singlets at 2.0 and 2.1 ppm (6 H), consistent with the structure of **10**.

2-Hydroxy-3-oxa-*trans*-decalin (6). A solution of 200 mg (1.3 mmol) of **5** in 25 mL of dry toluene was introduced to a dry 50-mL round-bottomed flask flushed with dry nitrogen. The flask was cooled to −20 °C, and 1.25 mL of diisobutylaluminum hydride in pentane (1.7 mmol) was added slowly with stirring. After 45 min, excess diisobutylaluminum hydride was destroyed by the addition of 6 mL of 2 M 2-propanol in toluene followed by the further addition of 0.75 mL of water. The reaction mixture was stirred for 20 min to give a cloudy gel; 0.75 g of magnesium sulfate and 0.75 g of Celite No. 535 fitering aid were then added and stirred vigorously; the resulting paste was filtered through a glass-fritted funnel and washed with THF. The filtrate was evaporated under reduced pressure to give 0.11 g (55% yield) of white, crystalline product, mp 75–77 °C. Recrystallization from benzene afforded clear plates, mp 83.5–85.0 °C. TLC (silica gel G, 1:2 cyclohexane–ethyl acetate) showed two spots representing the axial and equatorial hemiacetals: IR (perfluorokerosene mull) 3500–3200 (s), 2920 (s), 2860 (m) cm^{-1}; NMR ($CDCl_3$) δ 5.85 ($^1/_2$ H, t), 5.25 ($^1/_2$ H, m), 4.7 ($^1/_2$ H, d, J = 4 Hz), 4.6–3.4 (2.5 H, m), 2.6–1.1 (12 H, m); NMR ($CDCl_3$ plus D_2O) δ 5.80 ($^1/_2$ H, t), 5.20 ($^1/_2$ H, m), 4.6–3.4 (2 H, m), 2.6–1.1 (12 H, m). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.33. Found: C, 68.89; H, 10.64.

2-Methoxy-3-oxa-*trans*-decalins (7, 8). A 50-mL round-bottomed flask was charged with 100 mg of **6** (0.64 mmol), 300 mg of methanol-washed Dowex-50-X (H$^+$ form), and 15 mL of absolute methanol, and the mixture was heated at reflux for 3 h with constant stirring. The resin was removed by filtration and washed with a little methanol; the filtrate was evaporated under reduced pressure to yield a tarry residue. The residue was dissolved in 25 mL of chloroform and filtered through a mixture of silica gel G and Celite No. 535 (2:1). The filtrate was evaporated under reduced pressure to give 90 mg of pale yellow liquid (82%): IR (neat) 2920 (s), 2860 (m) cm^{-1}; NMR ($CDCl_3$) δ 4.4 (d), 3.9 (d), 3.15 (s), 3.06 (s), 2.2–1.0 (m). GC (5 ft × $^1/_8$ in. column of 10% Carbowax 20M on Chromosorb W, 60/80 mesh, heated with a linear temperature program of 130–180 °C at 6 °C/min) demonstrated the two isomers to be in a ratio of 2:1.

Separation and Identification of Isomers 7 and 8. The isomers were separated on a column (2 × 23 cm) packed with silica gel in pentane. A sample of the crude isomer mixture was loaded on the column and eluted with 300 mL of 15% diethyl ether in pentane (v/v). Fractions (3.5 mL) were collected by an automatic fraction collector and analyzed for products by GC on a 5 ft × $^1/_8$ in. column of 10% Carbowax 20M on Chromosorb W, 60/80 mesh, at 165 °C. Fractions 23–36 were pooled, and the solvent was removed under reduced pressure to yield 25 mg of isomer A. Similarly, fractions 30–35 were pooled, and the solvent was removed under pressure to yield 16 mg of isomer B. For A (**7**): NMR (HA-100, $CDCl_3$) δ 4.4 (1 H, dd, J_1 = 3.0 Hz, J_2 = 0.5 Hz), 3.06 (3 H, s). For B (**8**): NMR δ 3.9 (1 H, dd, J_1 = 10.5 Hz, J_2 = 2.5 Hz), 3.15 (3 H, s).

Kinetics of Hydrolysis. A mixture of **7** and **8** (8–10 mg) and *n*-undecyl alcohol (3–5 mg) as an internal standard were weighed out in a 25-mL round-bottomed flask equipped with a stirring bar and mixed with 4 mL of acetone. The flask was sealed with a No-Air stopper and submerged in a constant-temperature bath equipped with a magnetic stirrer. After 5 min of thermal equilibration, the hydrolysis was initiated by the addition of 4 mL of aqueous HCl. Aliquots (5–7 μL) were removed and analyzed by GC (5 ft × $^1/_8$ in. column of Carbowax 20M on Chromosorb W, 60/80 mesh, heated with a linear temperature program of

130–180 °C at 6 °C/min) for 6–8 and the internal standard. The GC areas were obtained with the aid of a planimeter (scanned four times and averaged) and normalized against the internal standard. The slope of semilogarithmic plots of $[(\text{area})_t - (\text{area})_\infty]/(\text{area})_0$ vs. time provided the observed first-order rate constant, k_{obsd}. All rate constants were evaluated by the method of least squares.

Registry No. 1, 1196-55-0; 2, 700-77-6; 2 semicarbazone, 74924-96-2; 3, 40599-78-8; 4, 16484-17-6; 5, 18335-58-5; 6 (axial isomer), 74924-97-3; 6 (equatorial isomer), 74924-98-4; 7, 74924-99-5; 8, 74925-00-1; 9, 24112-80-9; 10, 74925-01-2.

Selectivity of the Aromatic Plumbylation Reaction

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The plumbylation of toluene in dichloroacetic acid yields initially 5.4% 2-, 1.8% 3-, and 92.7% 4-methylphenyllead(IV) dichloroacetates. The toluene to benzene rate ratio under these conditions is 59.5. The partial rate factors are $o_f^{Me} = 9.64$, $m_f^{Me} = 3.21$, and $p_f^{Me} = 331$. The plumbylation of toluene in trifluoroacetic acid yields aryl trifluoroacetates and biaryls. Analysis of these products suggests that the plumbylation reaction yields 17.9% 2-, 3.2% 3-, and 78.9% 4-methylphenyllead(IV) trifluoroacetates in the initial step of the reaction. The toluene to benzene rate ratio is 114 under these conditions. The partial rate factors are $o_f^{Me} = 61.2$, $m_f^{Me} = 10.8$, and $p_f^{Me} = 540$. These observations suggest that the plumbylation reaction is a typical electrophilic substitution and that the reaction is significantly more selective than thallation or mercuration.

The use of lead(IV) acetates for the nuclear oxidation of benzene derivatives has been known for some time.[1] Subsequently attention has been drawn to the involvement of aryllead(IV) compounds as intermediates in these reactions. DeVos, Norman, and Sternhell and their associates have investigated the factors governing the formation of these compounds.[2-4] Their work has led to the development of good procedures for the preparation of a variety of aryllead(IV) compounds which are valuable synthetic intermediates. For example, the aryllead(IV) compounds react with other aromatic compounds to form biaryls[4e] and with 1,3-dicarbonyl compounds to form 2,2-diaryl-1,3-dicarbonyl derivatives.[5] The aryllead compounds also react quantitatively with halogens to form aryl chlorides, bromides, and iodides as well as substances with aryl sulfur, nitrogen, and carbon linkages.[6]

$$\text{ArH} + \text{Pb(OAc)}_4 \rightarrow \text{ArPb(OAc)}_3 + \text{HOAc}$$

It is intriguing that the isomer distributions in the plumbylation of toluene depend significantly upon the solvent. It may be inferred from the results of Sternhell and his co-workers that the reaction of lead(IV) trifluoroacetate with toluene in trifluoroacetic acid yields about 25% 2-, 5% 3-, and 70% 4-methylphenyllead(IV) trifluoroacetates.[4a] DeVos and his associates report that the reaction of lead(IV) acetate with excess toluene in the presence of dichloro- and trichloroacetic acids yields the 4-methylphenyllead(IV) derivatives exclusively.[3a] They suggest that further reactions may selectively consume the 2 and 3 isomers. In addition, there may be a substantial difference in the selectivity of lead(IV) dichloroacetate and lead(IV) trifluoroacetate as electrophilic reagents. These interpretations are certainly reasonable; however, the isomer distributions for the reaction in trifluoroacetic acid may differ because substitution occurs by an electron-transfer process in that solvent. The considerations coupled with our interest in the use of metallic reagents as catalysts in electrophilic aromatic substitution reactions prompted us to study the selectivity of the reaction of lead(IV) compounds with benzene and toluene in dichloroacetic acid and trifluoroacetic acid.[7]

Table I. Isomer Distribution for Plumbylation of Toluene in Dichloroacetic Acid at 25 °C

% reaction[a]	% $CH_3C_6H_4OH$[b]	isomer distribution, % 2-	3-	4-
26	8.2	4.6	1.0	94.3
32	13.9	6.3	2.1	91.5
40	13.4	5.2	2.3	92.4
	average value	5.4 ± 1.2	1.8 ± 0.7	92.7 ± 1.4

[a] Based on the consumption of lead(IV) acetate. [b] The average isomer distribution for the cresols was 40% 2-, 17% 3-, and 43% 4-isomers.

Results

Plumbylation in Dichloroacetic Acid. The plumbylation of benzene and toluene proceeded smoothly in dichloroacetic acid at 25 °C to yield a mixture of aryllead(IV) dichloroacetates and aryl dichloroacetates. Biaryls were not formed. The aryl dichloroacetates formed slowly from the aryllead(IV) dichloroacetates under the conditions of these experiments. In order to obtain ac-

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