

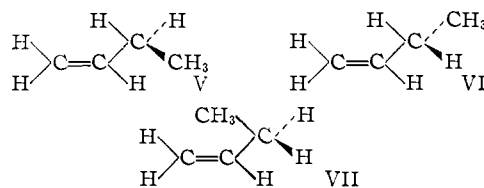
or about twice that when $\phi = 0^\circ$. In the H-C_{III}-C_{III}-H case, two situations may be distinguished: when a formal double bond joins the carbons, ϕ can assume only the values 0° and 180° , and $J_{III,III}$ then possesses values of about 10 and 17 c.p.s., respectively; alternatively, the trigonal carbons may be joined by a single bond, and in this case.⁶ $J_{III,III} \cong 16$ c.p.s. when $\phi = 180^\circ$.

The $J_{III,IV}$ coupling observed in propene (6.40 c.p.s.) is the average of that for the three protons, two of which are found²⁰ at $\phi = \pm 60^\circ$ and one at $\phi = 180^\circ$. The spectra of cyclohexene and cyclopentene²⁵ indicate that $J_{III,IV}$ ($\phi = \pm 60^\circ$) is of the order of one-three cycles, which requires $J_{III,IV}$ ($\phi = 180^\circ$) to be of the order of 16 c.p.s. All of these observations are consistent with the postulate that the coupling constant for the H-C-C-H system depends primarily on the dihedral angle, and that the change in hybridization of the carbons from sp^3 to sp^2 introduces only a small perturbation on the form of the functional dependence.

It was noted above that $J_{1,4}$ in propene, butene-1 and hexene-1 are roughly equal. If the functional dependence postulated above is accepted, then the

(25) To be published.

observed $J_{1,4}$ would depend steeply on the relative populations of the conformers V-VII.



For example, if the butene were entirely V and VI, one would predict the value $(2 + 16)/2 = 9$ c.p.s. for $J_{1,4}$. On the other hand, equal population of all states V-VII, would lead to equality with that observed for propene. Such an equality is at variance with previous suggestions^{18,19} based on Raman spectroscopy and heat capacity measurements.

Attempts to obtain definite evidence on the form of the functional dependence of $J_{III,IV}$ on ϕ will continue.

Acknowledgments.—We should like to thank Mr. Carl Saalbach for assistance in writing and revising the IBM program, Miss Nancy Free and Mr. H. Crawford for assistance in the laboratory and in the preparation of the illustrations.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY, EVANSTON, ILL.]

The Behavior of Ketene toward Acetals, Hemiacetal Chlorides, Acylals, Mixed Acetal-Acylals and Hemiacylal Halides

BY CHARLES D. HURD AND RAYMOND D. KIMBROUGH, JR.¹

RECEIVED JUNE 30, 1960

Ketene reacts not only with acetals and hemiacetal chlorides if catalyzed by Lewis acids but also with mixed acetal-acylals thereby increasing the length of the chain by two carbons. Ketene fails to add to full acylals or to hemiacylal halides under comparable conditions. Study of the reaction of ketene with acetals and hemiacetal chlorides has been extended to determine its limitations and to include heterocyclic members. Mixed acetals react according to both of the possible paths. Electron-withdrawing groups exert an inductive effect in lessening or even inhibiting this reaction. Hemiacetal chlorides in the carbohydrate series such as triacetyl-arabinosyl chloride or triacetyl-xylosyl chloride failed to react. A mechanism covering these findings is included.

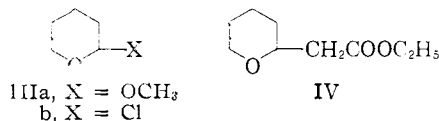
Certain aldehyde derivatives, namely, hemiacetal chlorides² (I) and acetals³ (II), have been shown to react with ketene when catalyzed by zinc chloride,



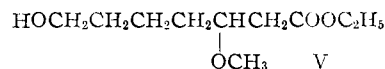
and these reactions were reported to be general, at least for simple members of the series. When ethyl alcohol was used in the step of purification the products were β -alkoxy esters, $\text{RCH}(\text{OR}')\text{-CH}_2\text{COOC}_2\text{H}_5$.

In the present study this reaction was extended to include cyclic acetals, cyclic hemiacetal chlorides and acylals. Limitations of the reaction were investigated also.

Ketene (ZnCl_2 , then $\text{C}_2\text{H}_5\text{OH}$) reacted with both 2-methoxytetrahydropyran (IIIa) and tetrahydropyran-2-yl chloride (IIIb) to form ethyl 2-tetra-



hydropyranacetate (IV). The yield of IV from IIIb was 60%, whereas that from IIIa was only 11%; but it will be noticed that IIIa is a mixed acetal, hence IV is but one of the predicted products. The other anticipated product would be ethyl 3-methoxy-7-hydroxyheptanoate (V) and it was formed in 24% yield.



Extension of this study to derivatives of tetrahydropyran-2,3-diol⁴ required the synthesis of certain new compounds. The known diacetate VIa was converted by means of hydrogen chloride into 3-acetoxytetrahydropyran-2-yl chloride (VIb).⁵

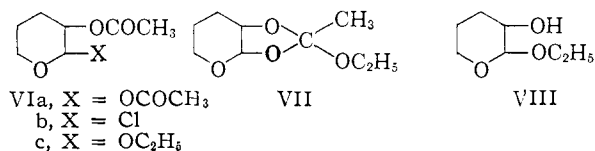
(1) American Viscose Fellow, 1955-1957; International Nickel Fellow, 1957-1958.

(2) A. T. Blomquist, R. W. Holley and O. J. Sweeting, *THIS JOURNAL*, **69**, 2356 (1947).

(3) F. Šorm and J. Smrť, *Chem. Listy*, **47**, 413 (1953); *C. A.*, **49**, 175 (1955).

(4) C. D. Hurd and C. D. Kelso, *THIS JOURNAL*, **70**, 1484 (1948).

(5) C. D. Hurd and R. D. Kimbrough, Jr., *ibid.*, **82**, 1373 (1960).



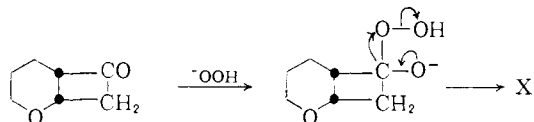
This compound was found to distil some 20° lower than VIa. It gave an instantaneous precipitate with alcoholic silver nitrate and showed infrared absorption bands at 5.75 μ (carbonyl) and 13.8 μ (C-Cl).

Conversion of the diacetate into 2-ethoxytetrahydropyran-3-yl acetate (VIc) was readily accomplished by refluxing with ethanol in the presence of zinc chloride. A strong absorption band at 5.75 μ ruled out the possibility that this might be the ortho ester VII. It was found that both acetate groups of VIa were cleaved if the zinc chloride was replaced with boron fluoride etherate. The product then was 2-ethoxytetrahydropyran-3-ol (VIII). Infrared on VIII showed no carbonyl absorption between 5.0-6.4 μ but there was a hydroxyl band at 2.9 μ .

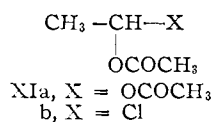
We have already described⁶ the reaction of ketene with the hemiacetal chloride VIb to give 2-(3-hydroxytetrahydropyran)-acetic γ -lactone (IX) in 43% yield. Both the structure and the stereochemistry of IX are assured in view of its inde-



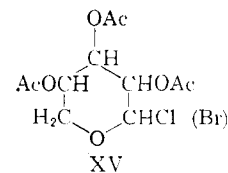
pendent synthesis⁵ from the adduct of ketene and dihydropyran by reaction with alkaline hydrogen peroxide. Since the adduct surely was formed by cis fusion, and since the lactone formation proceeds by a 1,2-shift wherein the migrating group (the no. 3 carbon of the tetrahydropyran ring) retains its configuration,⁶ it is evident that the pair of fused carbons of IX also are cis as in X



Acylals, hemiacylal chlorides and mixed acetal-acylals, until now, have not been tested with ketene. No addition of ketene was observed with ethylidene acetate (XIa), a full acylal, or with 1-chloroethyl acetate (XIb) which is a hemiacylal



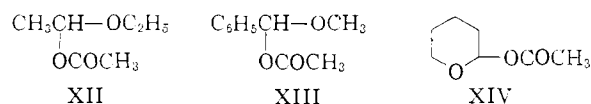
chloride. The latter was prepared from paraldehyde and acetyl chloride.⁷ About nine-tenths of both XIa and XIb were recovered after treating tenth-molar quantities (in 15 ml. of ethyl acetate containing 1 g. of zinc chloride) with 0.4 mole of ketene. No product was found resulting from



addition of ketene. Except for the liberation of acetaldehyde, the same non-reaction was observed using boron fluoride etherate, titanium tetrachloride or aluminum chloride as Lewis acids. The implications of these non-reactions bear on the mechanism of the general reaction and will be commented on later.

In contrast to the full acylals the simple mixed acetal-acylals were found to react smoothly with ketene when catalyzed by zinc chloride. They have also been observed to react⁸ with aromatic compounds when catalyzed by aluminum chloride. Thus, anisole and 1-ethoxyethyl acetate (XII) yielded *p*-methoxyacetophenone and 4,4'-ethylidenedianisole, as well as 4,4'-vinylidenedianisole if an excess of aluminum chloride was used. Similarly, toluene and XII yielded *p*-methylacetophenone and 1,1-di-*p*-tolylethane.

In the reaction with ketene (ZnCl₂, then EtOH) we found that XII changed readily into ethyl 3-ethoxybutyrate CH₃CH(OC₂H₅)CH₂COOC₂H₅, and



that α -methoxybenzyl acetate (XIII) gave rise to ethyl 3-phenyl-3-methoxypropionate C₆H₅CH(OCH₃)CH₂COOC₂H₅. A cyclic mixed acetal-acylal, namely, tetrahydropyran-2-yl acetate (XIV) also reacted by displacement of the acylal function giving a good yield of ethyl 2-tetrahydropyranacetate (IV).

Since ketene reacted with VIb to a lesser extent than with IIIb, it was anticipated that VIa should be more sluggish than XIV. Experiment confirmed this. The yield of IV from XIV was 70% whereas only a trace of IX came from VIa under comparable conditions with zinc chloride as catalyst: the chief product was VIc showing simple conversion of the acylal to the acetal as though ketene were not even present. If boron fluoride etherate was used instead of zinc chloride in the ketene-VIa-alcohol reaction again no more than a trace of IX was formed. The chief product was VIII.

In view of the retarding effect of the 3-acetyl group in VI on the reactivity at the 2-position, little hope was held that pentosyl halides (XV) would react with ketene in spite of the relationship of their structure to III. Triacetyl- α -D-xylosyl chloride, triacetyl- α -L-arabinosyl chloride and triacetyl- α -D-xylosyl chloride were synthesized from the corresponding tetraacetates and titanium tetra-

chloride, a method developed by Pacsu⁹ for the hexoses but not extended to pentoses. No γ -

(8) C. D. Hurd and T. Iwashige, *J. Org. Chem.*, **24**, 1321 (1959).

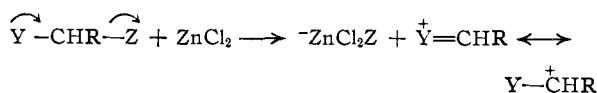
(6) G. W. Wheland, "Advanced Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1951, pp. 521-526.

(7) L. Ulich and R. Adams, *THIS JOURNAL*, **43**, 606 (1921).

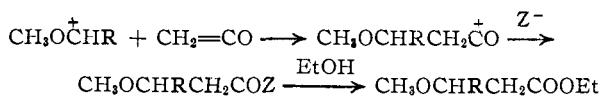
(9) (a) E. Pacsu, *Ber.*, **61**, 1508 (1929). See also, (b) H. Ohle, W. Marecek and W. Bourjau, *ibid.*, **62**, 833 (1929); (c) C. D. Hurd and S. M. Cantor, *THIS JOURNAL*, **60**, 2677 (1938).

lactone (in other words, no infrared absorption at 5.6μ) was found in the reaction mixture after treatment with ketene (ZnCl_2 , alcohol); hence, it may be assumed that these hemiacetal halides failed to react.

The aldehyde derivatives used in this investigation all possess the generalized structure $\text{Y}-\text{CHR}-\text{Z}$. To explain their reactions or non-reactions with ketene one must consider the electron-donating or the electron-withdrawing effects of the groups Y , Z and R on the aldehydic carbon. If this carbon can be changed into a carbonium ion, then one could expect reactivity with ketene. This would happen if Y donates electrons by resonance causing Z to leave as an anion



This situation holds for the simple acetals II, IIIa, hemiacetal chlorides I, IIIb and the mixed acetal-acylals $\text{CH}_3\text{O}-\text{CHR}-\text{Z}$, wherein $\text{Z} = \text{OR}$, Cl , OAc , respectively. The carbonium ion $\text{CH}_3\text{O}-\overset{+}{\text{C}}\text{HR}$ (either free or potential by a sufficiently weakened bond) reacts with ketene



If both Y and Z are electron-withdrawing groups (as Cl or OAc), this would tend to militate against

the carbonium ion: $\overset{+}{\text{Y}}-\text{CHR}-\text{Z}$. In other words, the inductive effect of Y would promote retention of Z , thus making ionization from the aldehydic carbon difficult or impossible. This situation would obtain for the full acylals and the hemiacylal halides.

If the R group contains an electron-withdrawing group, as acetate in VI or XV, the inductive effect operating at the aldehydic carbon also will lessen the tendency for the carbonium ion and this effect should lower the yield of product from ketene, perhaps even to a zero yield. The general findings support this proposed mechanism.

Experimental

All microanalyses were performed by Miss H. Beck.

Ketene was prepared by pyrolysis of acetone.¹⁰ 1-Ethoxyethyl acetate (XII) was synthesized from 1-ethoxyethyl chloride and sodium acetate.¹¹

Reaction of Ketene with XII.—Ketene was bubbled into a mixture of 15 ml. of 1-ethoxyethyl acetate, 15 ml. of ethyl acetate and 1 g. of anhydrous zinc chloride at a rate of about 0.1 mole per hour for 4 hours. The vessel was kept in ice-water during this time. The brown product was added to 50 ml. of absolute ethanol and the mixture was refluxed for 3 hours. Some ethanol and ethyl acetate were boiled off (about 40 ml.) and the residue was poured into 30 ml. of saturated sodium bicarbonate solution. The resulting mixture was extracted thrice with 30 ml. of ether. The combined ether extracts were dried with magnesium sulfate and the ether was removed on a steam-bath. The residue was vacuum distilled and 3 g. (18%) of ethyl 3-ethoxybutyrate was collected at $77-79^\circ$ (26 mm.).

α -Methoxybenzyl acetate (XIII) was prepared from α -methoxybenzyl chloride¹² and sodium acetate.¹¹ The

substance was isolated by distillation, b.p. $115-117^\circ$ (15 mm.). From 30 g. of the starting chloride, 20 g. (60%) of XIII was obtained.

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{O}_3$: C, 66.67; H, 6.67. Found: C, 66.78; H, 6.58.

Reaction of Ketene with XIII.—Ketene (0.4 mole, added during 4 hours) was bubbled into XIII (15 g. dissolved in 15 ml. of ethyl acetate). The procedure was then the same as for reaction of ketene with XII. The ethyl 3-phenyl-3-methoxypropionate was isolated by vacuum distillation, b.p. $78-80^\circ$ at 0.1 mm., yield 9 g. or 52%.

Anal. Calcd. for $\text{C}_{12}\text{H}_{16}\text{O}_3$: C, 69.2; H, 7.70. Found: C, 69.36; H, 7.57.

Tetrahydropyran-2-yl Chloride (IIIb).—Dihydropyran (84 g.) was cooled to 0° and dry hydrogen chloride was passed into it until 34 g. (95% of theory) had been absorbed. Temperature was controlled by ice-water during this period. The mixture was then distilled at 16 mm. and the IIIb was collected at $45-46^\circ$; yield 53 g. (45%). This compound may be kept in a closed container for about a week before appreciable decomposition occurs.

Anal. Calcd. for $\text{C}_6\text{H}_8\text{ClO}$: C, 49.8; H, 7.5. Found: C, 51.08; H, 7.7.

Reaction of Ketene with IIIb.—Ketene (0.48 mole) was bubbled during 4 hours into a mixture of 15 ml. (0.12 mole) of IIIb, 30 ml. of benzene and 0.8 g. of anhydrous zinc chloride. The mixture was cooled in ice-water. The dark brown product was added to 50 ml. of absolute ethanol and refluxed for an hour. The more volatile substances were boiled off on the steam-bath and 10% sodium bicarbonate solution was added until the mixture was neutral to litmus. Then the mixture was extracted thrice with 50 ml. of ether and the combined extracts were dried (MgSO_4) and distilled. The fraction boiling at $73-79^\circ$ (2-3 mm.) was collected; yield 12 g. (60%). This ethyl 2-tetrahydropyranacetate (IV) was redistilled, b.p. $66-68^\circ$ (1.5 mm.), n_D^{25} 1.4422.

Anal. Calcd. for $\text{C}_9\text{H}_{16}\text{O}_3$: C, 62.8; H, 9.30. Found: C, 62.81; H, 9.22.

2-Methoxytetrahydropyran (IIIa) was prepared from dihydropyran and methanol containing a trace of dry hydrogen chloride.¹³ These substances must be mixed slowly due to the large amount of heat evolved.

Reaction of Ketene with IIIa.—Ketene (0.6 mole) was added during 6 hours to 25 ml. (0.22 mole) of IIIa containing 1 g. of zinc chloride. The vessel was kept in ice-water during this period. The brown product was added to 200 ml. of absolute ethanol containing 3 ml. of concd. sulfuric acid and the mixture was refluxed overnight. Then 150 ml. of the alcohol was removed by distillation and the remaining black oil was poured into 200 ml. of 5% sodium bicarbonate solution. This mixture was extracted three times with 50 ml. of ether and the combined extracts were dried (MgSO_4). The ether was distilled off and the residue was distilled under vacuum with a 6-inch fractionating column. The fraction of IV was collected at $50-60^\circ$ (0.3-0.5 mm.) and the fraction of V was obtained at $100-120^\circ$ at the same pressure; yield of IV, 4 g. (11%), and of V 12 g. (24%). On redistillation the V was found to boil at $101-102^\circ$ (0.3 mm.).

Anal. Calcd. for $\text{C}_{10}\text{H}_{20}\text{O}_4$: C, 58.9; H, 9.79. Found: C, 59.14; H, 9.36.

3-Methoxy-7-hydroxyheptanoic hydrazide was prepared from V (1 ml.) and hydrazine hydrate (1 ml.) by refluxing the two reactants together for 2 hours. The product solidified on cooling and was recrystallized from ethyl acetate; m.p. $81.0-81.5^\circ$.

Anal. Calcd. for $\text{C}_8\text{H}_{18}\text{N}_2\text{O}_5$: C, 50.52; H, 9.47. Found: C, 50.51; H, 9.22.

Tetrahydropyran-2-yl acetate (XIV) was prepared from dihydropyran and acetic acid.¹⁴

Reaction of Ketene with XIV.—Ketene (0.4 mole) was added during 4 hours to a solution of 15 ml. of XIV, 15 ml. of ethyl acetate and 1 g. of anhydrous zinc chloride. The vessel was kept in ice-water during the addition of ketene.

(13) W. E. Parham and E. L. Anderson, *THIS JOURNAL*, **70**, 4187 (1948).

(14) J. G. MacKay-Bremmer and D. G. Jones, *British Patent* 606,764; *C. A.*, **43**, 1442 (1949).

(10) J. W. Williams and C. D. Hurd, *J. Org. Chem.*, **5**, 122 (1940).

(11) C. D. Hurd and F. O. Green, *THIS JOURNAL*, **63**, 2201 (1941).

(12) F. Straus and H. Heine, *Ann.*, **493**, 191 (1932).

The brown reaction product was added to 50 ml. of absolute ethanol and refluxed for 3 hours, after which solvents were removed on a steam-bath and the residue was poured into 30 ml. of saturated sodium bicarbonate solution. The resulting mixture was extracted 3 times with 30 ml. of ether. The combined extracts were dried (MgSO₄) and distilled. The product (IV) was collected at 65–70° (0.5 mm.), yield 12 g. or 70%.

2-Tetrahydropyranacetic Acid.—To 36 g. of XIV was added 2 g. of anhydrous zinc chloride dissolved in 5 ml. of ethyl acetate. Ketene was bubbled into the above mixture at a rate of about 0.2 mole per hour for 8 hours. The vessel was kept in ice-water during this time. The volume of the reaction mixture almost doubled during the addition of ketene and the color became dark brown. The mixture was added to 50 ml. of water, shaken well, and allowed to stand overnight. The mixture was then distilled. The fraction boiling between 100–120° at 0.5 mm. contained 22 g. of 2-tetrahydropyranacetic acid, m.p. 49–53°. This is a 61% yield. After recrystallization from a little hexane the m.p. was 55–56°.

Anal. Calcd. for C₇H₁₂O₃: C, 58.33; H, 8.33. Found: C, 58.50; H, 8.35.

Derivatives. Acyl Chloride.—A 3-molar excess of thionyl chloride (45 g.) was added to 18 g. of the above crude acid. Reaction was spontaneous. After this reaction had subsided, the black mixture was refluxed for 10 minutes. The excess of thionyl chloride was distilled off at reduced pressure and 2-tetrahydropyranacetyl chloride was collected at 45–47° and 0.3 mm., yield 18 g. (88%).

Anal. Calcd. for C₇H₁₁ClO₂: C, 51.6; H, 6.83. Found: C, 51.77; H, 6.86.

Amide.—Two grams of the above acid chloride was added to 10 ml. of ice-cold concd. ammonia. The resulting clear solution was kept at 0° for 24 hours, whereupon 0.8 g. of crystals formed. More solid was obtained when the solution was concentrated to 2 ml. and recooled. Total crude yield, 1.6 g. (80%). The 2-tetrahydropyranacetamide was recrystallized in good yield from hexane; m.p. 98–99°.

Anal. Calcd. for C₇H₁₃NO₂: N, 9.78. Found: N, 9.69.

Anilide.—Two grams of the above acid chloride was added to 4 ml. of aniline and 30 ml. of benzene. The solution was shaken with 10 ml. of water, 10 ml. of 5% hydrochloric acid, then 10 ml. of 5% sodium hydroxide, after which the benzene was evaporated. The dry residue was crystalline, yield 2.7 g. (90%). The 2-tetrahydropyranacetanilide was recrystallized from hexane in good yield, m.p. 84–85°.

Anal. Calcd. for C₁₃H₁₇NO₂: C, 71.2; H, 7.76. Found: C, 71.01; H, 8.05.

Tetrahydropyran-2,3-diol diacetate (VIa) was prepared by the oxidation of dihydropyran with hydrogen peroxide in *t*-butyl alcohol in the presence of osmium tetroxide, and acetylation with acetic anhydride.⁴ In this method 30% aqueous hydrogen peroxide was mixed with *t*-butyl alcohol and the water was removed with anhydrous sodium sulfate. In the present work only about half of the water was removed in this way, yet the results were the same as those earlier described.

3-Acetoxytetrahydropyran-2-yl Chloride (VIb).—To 10 g. of VIa was added 15 g. of a 25% solution of hydrogen chloride in anhydrous ether. The mixture turned light brown in a few minutes. It was stored for 3 days at 0° and then was distilled; b.p. 51–54° (0.2 mm.), yield 7.0 g. or 77%.

Anal. Calcd. for C₇H₁₁ClO₃: Cl, 19.9. Found: Cl, 17.7.

2-Ethoxytetrahydropyran-3-yl acetate (VIc) was prepared by refluxing 10 g. of VIa with 50 ml. of ethanol containing 2 g. of zinc chloride for 16 hours. Then the low boiling fraction was distilled off and the residue was neutralized with 5% sodium bicarbonate solution. The resulting mixture was extracted three times with 25 ml. of ether. The combined extracts were dried (MgSO₄) and distilled. The acetate was collected at 115–117° (22 mm.), yield 8.0 g. (90%).

Anal. Calcd. for C₉H₁₆O₄: C, 57.5; H, 8.50. Found: C, 57.54; H, 8.59.

2-Ethoxytetrahydropyran-3-ol (VIII) was synthesized from VIa (10 g.) by refluxing for 16 hours with 50 ml. of absolute ethanol which contained 2 ml. of boron fluoride etherate. The low-boiling cut was distilled off and the residue was neutralized with 5% sodium bicarbonate solution. The resulting mixture was extracted thrice with 25 ml. of ether. The ether extracts were dried (MgSO₄) and distilled; b.p. 85–87° (17 mm.), yield 5 g. (65%).

Anal. Calcd. for C₇H₁₄O₃: C, 57.5; H, 9.60. Found: C, 57.47; H, 9.53.

Triacetyl- α -D-xylosyl Chloride.—To 8.0 g. of D-xylose tetraacetate¹⁵ dissolved in 50 ml. of chloroform was added dropwise, with stirring, 4.5 ml. (8.0 g.) of titanium tetrachloride in 20 ml. of chloroform. During this addition the reaction mixture warmed up a bit. Stirring was continued for 2 hours and the mixture was kept at room temperature. This clear yellow solution was then poured onto 75 g. of ice, and the chloroform layer was separated. The latter was washed twice with iced water, filtered and dried (K₂CO₃). After removal of the chloroform at reduced pressure the residue solidified. The mixture was triturated with 10 ml. of anhydrous ether, cooled to –80°, and the solid triacetylxylosyl chloride was filtered with suction. (No attempt was made to cool the suction funnel before filtration, nor were precautions taken to prevent the condensation of water on the cold crystals; but as soon as the solvent was removed, the product was put in a vacuum desiccator.) The yield was 6.0 g. (80%), m.p. 95–98°. Melting points listed in the literature are 95–97°¹⁶ and 105°.¹⁷

Triacetyl- α -L-arabinosyl Chloride.—To 5.0 g. of L-arabinose was added 20 g. of acetic anhydride and 25 g. of dry pyridine. The mixture was shaken well until solution was complete, during which time (2 hours) the solution warmed up. This mixture was kept overnight and then was poured into 50 ml. of iced water and allowed to stand for an hour at room temperature. The insoluble oil was taken up in 50 ml. of chloroform and was washed with 50 ml. of water, 50 ml. of 5% hydrochloric acid, and then was dried over anhydrous calcium chloride.

To one-half of the above solution, corresponding to 0.0125 mole of the arabinose, was added dropwise with stirring 3.0 ml. of titanium tetrachloride in 10 ml. of chloroform. A precipitate formed which partially dissolved as the solution was heated in a water-bath at 70° for an hour. Then the brown reaction mixture was poured onto 50 g. of ice. Processing this material followed the procedure given for the xylose analog. The yield was 3.5 g. (70%), m.p. 146–148°. The m.p. in the literature is 146°.¹⁸

Attempted Reaction of Ketene with Ethylidene Acetate.—Ketene (0.4 mole) was added to a solution of 15 g. of XIa, 15 ml. of ethyl acetate and 1 g. of zinc chloride. After processing as described for the reaction of ketene and XII, about 80% of the XIa was recovered and no product was obtained in the distillate representing addition of ketene.

Acetaldehyde was released in about 90% amounts when boron fluoride etherate (1 ml.) or aluminum chloride (1 g.) or titanium tetrachloride (0.5 ml.) was used in place of the zinc chloride. Acetaldehyde was released also when XIb was treated with ketene and zinc chloride. No reaction with ketene was observed.

Attempted Reaction of Ketene with Triacetylxylosyl Chloride.—Ketene (0.4 mole) was passed into a mixture of 3 g. of triacetyl- α -D-xylosyl chloride, 30 ml. of ethyl acetate and 0.5 g. of zinc chloride at ice temperature. The product was poured into 100 ml. of absolute ethanol containing 1 ml. of concentrated sulfuric acid. Half of the solvent was distilled away and the distillate no longer smelled of ethyl acetate. The residue was refluxed for 10 hours, then was concentrated to 30 ml. and poured into 100 ml. of water. After neutralization (NaHCO₃), filtration, extraction with 10 ml. of chloroform, and evaporation to dryness under reduced pressure the residue was mixed with 15 ml. of acetic anhydride and 5 g. of sodium acetate and heated at 100° for an hour. Then it was poured into 100 ml. of water and, after an hour, was thrice extracted with chloroform. The dried (MgSO₄) extracts were evaporated. The resulting oil showed no absorption at 5.6 μ . The oil crystal-

(15) W. E. Stone, *Am. Chem. J.*, **15**, 653 (1893).

(16) C. S. Hudson and J. M. Johnson, *THIS JOURNAL*, **37**, 2751 (1915).

(17) Yu. A. Zhdanov and L. I. Shcherbakova, *Doklady Akad. Nauk, S. S. S. R.*, **90**, 185 (1953).

lized after several days. After recrystallizations from water, it melted at 102–104°. This was ethyl triacetylxyloside, known¹⁸ to melt at 106°.

(18) L. Asp and B. Lindberg, *Acta Chem. Scand.*, **4**, 1446 (1950).

The behavior of ketene toward the arabinosyl chloride was similar. Also, other catalysts, as boron fluoride etherate, gave no evidence of promoting a reaction between ketene and the glycosyl halide.

[CONTRIBUTION NO. 966 FROM THE DEPARTMENT OF CHEMISTRY, INDIANA UNIVERSITY, BLOOMINGTON, IND.]

The Effects of Deuterium Substitution on the Rates of Organic Reactions. VI. Secondary Isotope Effects on the Solvolysis Rates of γ -Methyl Substituted *t*-Alkyl Chlorides¹

BY V. J. SHINER, JR.²

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Deuterium substitution β to the chlorine of tertiary alkyl chlorides has previously been observed to have a marked decelerating influence on the rate of solvolysis of the alkyl chloride. This paper continues the study of these secondary isotope rate effects with particular reference to the influence of alkyl substitution on them. The 3,3-dideuterio analogs of all and the 1,1,1-trideuterio analogs of all but the second member of the following series of compounds have been synthesized and their solvolysis rates in "80%" aqueous alcohol at 25° measured: 2-chloro-2-methylbutane, 2-chloro-2-methylpentane, 2-chloro-2,4-dimethylpentane and 2-chloro-2,4,4-trimethylpentane. The secondary isotope rate effects of the 1-deuterio substitution do not show large variations in the series while the effects of 3-deuterio substitution are about the same for all but the last member of the series where only a small effect is evident. This result is thought to be due to steric inhibition of hyperconjugation in the neopentyl group of the last compound. The rate constants have been calculated by a statistical method programmed for an electronic computer.

The substitution of deuterium for β -situated hydrogen has been shown to have a marked retarding effect on the rates of solvolysis of certain derivatives of secondary and tertiary aliphatic alcohols.^{3,4,5} The effect has been shown to be cumulative as the degree of deuterium substitution increases and, per deuterium atom, is larger in a tertiary position than a secondary and is smallest in a primary position.^{3,4} It has also been observed to operate only slightly more effectively from a fixed *cis* than from a fixed *trans* position in the acetolysis of deuterated cyclopentyl tosylates.⁶ Further, the effect can be transmitted across a molecule through unsaturated linkages^{7,8} and has been shown to be solvent dependent.^{5,8} In a preliminary communication¹ it has been reported that deuterium substitution in the 3-position of 2-chloro-2,4,4-trimethylpentane had an abnormally *small* effect on the solvolysis rate. The present paper reports the details of that work and extends the observations to include secondary isotope rate effects of methylene deuteration through a complete series of compounds with increasing γ -methyl substitution. Some additional effects of methyl group deuteration are included for purposes of comparison. The series then gives the effects of deuterium substitution on the rates of solvolysis of 2-chloro-2-methylbutane,³ 2-chloro-2-methylpentane, 2-chloro-2,4-dimethylpentane and 2-chloro-2,4,4-trimethylpentane in 80% aqueous ethanol. Effects of complete deuteration of the 3-position are now available for each member of the

series and of the complete deuteration of the 1-position of all save the second member.

The starting point in the synthesis of the 3,3-dideuterioalkyl chlorides in each case was the reduction of the appropriate ethyl ester with lithium aluminum deuteride to give an α,α -dideuterio alcohol. The alcohols were converted to alkyl halides with phosphorus tribromide or with a triphenyl phosphite adduct⁹ and finally through the Grignard reagents to the alkyl- α -*d*₂-dimethylcarbinols.

The 1,1,1-trideuterio alkyl chlorides were made *via* the tertiary alcohols from the Grignard reagents starting with the methyl alkyl ketone and methyl-*d*₃ iodide. Methyl-*d*₃ iodide was made *via* the alcohol from lithium aluminum deuteride and diethyl carbonate. Deuterium analyses on a number of the compounds used are given in Table I.

TABLE I
DEUTERIUM ANALYSES

Compound	Av. atoms D/molecule
2-Methylpentane-3,3- <i>d</i> ₂ -2-ol	1.76
2-Chloro-2-methylpentane-3,3- <i>d</i> ₂	1.72
2,4-Dimethylpentane-3,3- <i>d</i> ₂ -2-ol	1.76
2-Chloro-2,4-dimethylpentane-3,3- <i>d</i> ₂	1.82
2,4-Dimethylpentane-1,1,1- <i>d</i> ₃ -2-ol	2.61
2-Chloro-2,4-dimethylpentane-1,1,1- <i>d</i> ₃	2.62
2,4,4-Trimethylpentane-3,3- <i>d</i> ₂ -2-ol	1.70
2-Chloro-2,4,4-trimethylpentane-3,3- <i>d</i> ₂	1.79
2,4,4-Trimethylpentane-1,1,1- <i>d</i> ₃ -2-ol	2.58
2-Chloro-2,4,4-trimethylpentane-1,1,1- <i>d</i> ₃	2.70, 2.69

Nuclear magnetic resonance (n.m.r.) spectral measurements at 60 mc. have been used to establish that the deuterium substitution is essentially complete at the sites indicated in the last four compounds listed in Table I. The 2,4,4-trimethylpentyl residue shows three unsplit bands. In order of increasing field these are: (1) a band of relative

(1) A preliminary communication on part of this work appeared in *THIS JOURNAL*, **78**, 2653 (1956). Presented in part at the XVIth International Congress of Pure and Applied Chemistry, Paris, 1957.

(2) Alfred P. Sloan Research Fellow.

(3) V. J. Shiner, Jr., *THIS JOURNAL*, **75**, 2925 (1953).

(4) V. J. Shiner, Jr., *ibid.*, **76**, 1603 (1954).

(5) E. S. Lewis and C. E. Boozer, *ibid.*, **76**, 791 (1954).

(6) A. Streitwieser, Jr., R. H. Jagow and S. Suzuki, *ibid.*, **77**, 6713 (1955).

(7) E. S. Lewis and G. M. Copinger, *ibid.*, **76**, 4495 (1954).

(8) V. J. Shiner, Jr., and C. J. Verbanic, *ibid.*, **79**, 373 (1957).

(9) D. G. Coe, S. R. Landauer and H. N. Rydon, *J. Chem. Soc.*, 2281 (1954).