Rearrangement of Δ^2-Dihydropyran over Hot Alumina

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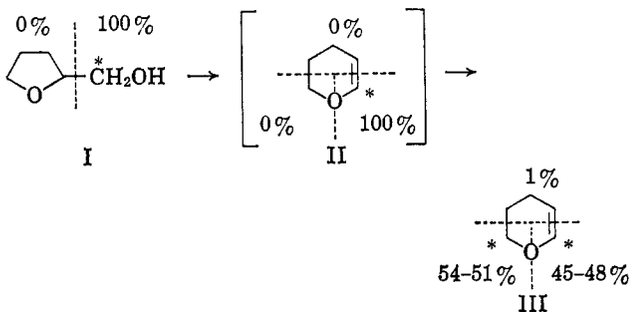
Exposure to alumina at 350° isomerizes Δ^2-dihydropyran-6-^{14}C to a mixture of Δ^2-dihydropyran-6-^{14}C and Δ^2-dihydropyran-2-^{14}C. The same kind of scrambling occurs when a mixture of Δ^2-dihydropyran-6-^{14}C and tetrahydrofurfuryl alcohol is passed over alumina. Δ^3-Dihydropyran cannot be an intermediate in the scrambling process, since Δ^3-dihydropyran on treatment with alumina under the same conditions gives no Δ^2-dihydropyran but only butadiene and carbon dioxide. The labeled Δ^2-dihydropyran was prepared by carbonating the Grignard reagent from 5-bromo-1-pentene with radioactive carbon dioxide, reducing the resulting 5-hexenoic-1-^{14}C acid to 5-hexenol-1-^{14}C, ozonizing the unsaturated alcohol to 5-hydroxypentanal-5-^{14}C, and dehydrating the tautomeric 2-hydroxytetrahydropyran-6-^{14}C to the desired Δ^2-dihydropyran-6-^{14}C.

When tetrahydrofurfuryl alcohol (I) labeled in the exocyclic methylene position with carbon-14 is passed over alumina at *ca.* 350°, Δ^2-dihydropyran (III) is formed with radioactivity at both the 2 and 6 position.[1] Conceivably, in this process, Δ^2-dihydropyran-2-^{14}C (II) forms first, but then, while still in contact with alumina, rearranges reversibly to Δ^2-dihydropyran-6-^{14}C to



give product III with the observed distribution of radioactivity. The present paper provides evidence demonstrating that this kind of rearrangement in Δ^2-dihydropyran can occur and, therefore, that the above interpretation for the tetrahydrofurfuryl alcohol process is admissable. As a beginning in defining the reaction pathway for this 2,6 interchange, we have now shown that Δ^3-dihydropyran cannot serve as an intermediate.

The 2,6-scrambling was demonstrated by locating the radioactivity in singly labeled Δ^2-dihydropyran before and after exposure to the alumina catalyst. It was more convenient to insert the label at the 6 rather than the 2 position. The synthesis proceeded by carbonating the Grignard reagent from 5-bromo-1-pentene (IV) with radioactive carbon dioxide and reducing the resulting 5-hexenoic-1-^{14}C acid to 5-hexenol-1-^{14}C (V). Ozonolysis of this unsaturated alcohol V gave 5-hydroxypentanal-5-^{14}C (VI) which on dehydration afforded the necessary Δ^2-dihydropyran-6-^{14}C (VII).

This specifically labeled material (VII) was passed over alumina under conditions similar to those used in converting tetrahydrofurfuryl alcohol into Δ^2-dihydropyran. The radioactivity in the dihydropyran was located by applying the degradation scheme used before[1]—that is, by ozonolysis of dihydropyran in order to separate position 2 from positions 3, 4, 5, and 6, and by oxidation of dihydropyran to glutaric acid followed by Schmidt degradation to 1,3-diaminopropane in order to separate positions 2 and 6 from 3, 4, and 5.

(1) W. J. Gensler and G. L. McLeod, *J. Org. Chem.*, **28**, 3194 (1963).

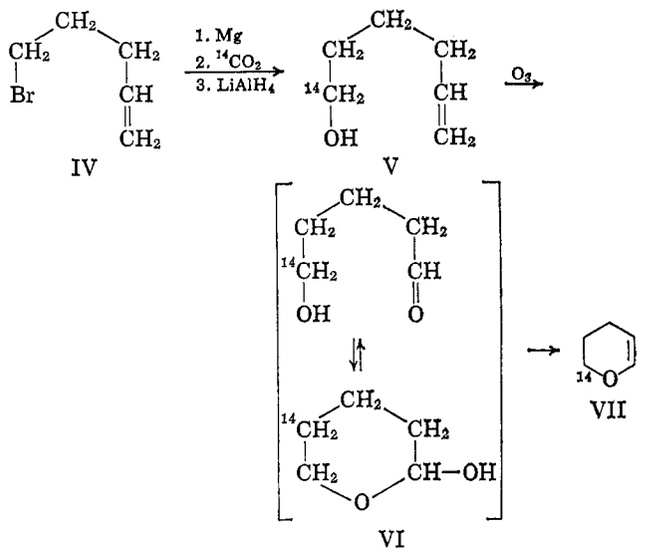


Table I summarizes the results. The first row of numbers, giving the distribution of radioactivity in the starting material VII, shows that *ca.* 99% of the activity resides at the 6 position. Accordingly, no premature rearrangement has occurred, and the activity distribution expected from the synthesis is validated. Note that different ways of handling the experimental numbers lead to slightly different distributions, but

TABLE I

PERCENTAGE DISTRIBUTION OF RADIOACTIVITY IN Δ^2-DIHYDROPYRAN

Dihydropyran	2 position *a*	2 position *b*	6 position *c*	6 position *d*	3, 4, and 5 positions, *e*
Before exposure to alumina	1.2	−1.8	97.5	100.4	1.4
Exposed to alumina	44.9	48.0	49.8	46.6	5.5
Mixed with tetrahydrofurfuryl alcohol and exposed to alumina	41.9	44.8	54.7	51.9	3.4

[a] Relative molar activity of formate divided by mean activity of dihydropyran. [b] (Mean activity of dihydropyran minus activity of 2,4-dinitrophenylhydrazone of 4-hydroxybutanal) divided by mean activity of dihydropyran. [c] (Mean activity of dihydropyran minus activity of formate minus activity of dibenzoyldiaminopropane) divided by mean activity of dihydropyran. [d] (Activity of 2,4-dinitrophenylhydrazone of 4-hydroxybutanal minus activity of dibenzoyldiaminopropane) divided by mean activity of dihydropyran. [e] Activity of dibenzoyldiaminopropane divided by mean activity of dihydropyran. In all cases, the mean activity of dihydropyran is taken as the average of the relative molar activities of the derived 2,4-dinitrophenylhydrazone of 5-hydroxypentanal and the derived glutaric acid.

TABLE II

Δ^3-DIHYDROPYRAN OVER HOT ALUMINA (SEE THE EXPERIMENTAL SECTION FOR DETAILS)

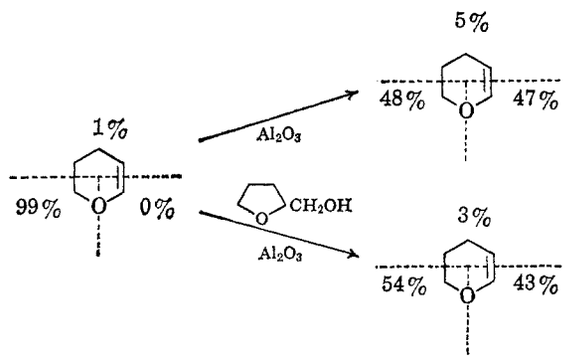
Material tested	Temp, °C	Collecting traps: Empty	Water	Bromine, %	Alcohol	$Ca(OH)_2$
Δ^3-DHP	350	*a, b*				
Δ^3-DHP[d]	320–370	DNP (−)[c]	DNP (−), dimedon (−)	65	DNP (−)	
Δ^3-DHP	270–320	DNP (−)[c]	DNP (−), dimedon (−)	40	DNP (−)	
Δ^3-DHP plus 1 mole of tetrahydrofurfuryl alcohol	350	*a, e*				
Δ^3-DHP plus $^2/_3$ mole of tetrahydrofurfuryl alcohol[f]	320–370	DNP (−)[g]	Dimedon (−), DNP (+) (mp 112–114°)	57	DNP (−)	CO_2 (+)
Tetrahydrofurfuryl alcohol[f]	320–370		DNP (+) (mp 112–113°)	0		
Δ^3-plus Δ^2-DHP[f]	320–370	*c*	DNP (+) (mp 111.5–116°)	50	DNP (−)	CO_2 (+)
Aqueous formaldehyde[h]	320–370	DNP (−)	DNP (−)[i]	0	DNP (−)	CO_2 (+)

[a] Held at Dry Ice–acetone temperature. [b] Fractionation of the trapped material gave a low-boiling material (butadiene), but no distillate that was a liquid at room temperature. [c] A small quantity of green material was noted. [d] About the same results were obtained when no carrier nitrogen was used. [e] Δ^2-Dihydropyran, isolated by the usual procedure, showed bp 85–87° and $n^{25}D$ 1.4315. The infrared absorption peak characteristic of vinyl ether double bonds was conspicuous. [f] The alumina was not pretreated. [g] The trap contained a small amount of green organic liquid plus a small, aqueous layer. [h] This 12% aqueous formaldehyde (15 g) was neutral to litmus and gave no precipitate with lime water. The same results were obtained with or without nitrogen carrier gas. When water alone was passed over hot alumina, the test for carbon dioxide was negative. [i] The solution was significantly acid to litmus and gave a positive test for carbon dioxide with limewater.

the discrepancies are relatively small and, at least for our present purpose, may be disregarded. The second row in Table I shows the distribution of activity after Δ^2-dihydropyran-6-^{14}C (VII) has been exposed to alumina. Much of the activity has moved from the 6 to the 2 position. The possibility that tetrahydrofurfuryl alcohol effects the course of the 2–6 scrambling in dihydropyran was checked by passing a mixture of tetrahydrofurfuryl alcohol and Δ^2-dihydropyran-6-^{14}C over the catalyst. Table I shows that the scrambling results with or without tetrahydrofurfuryl alcohol are about the same. Tetrahydrofurfuryl alcohol, accordingly, does not influence the process. Scheme I formulates the experimental findings.

SCHEME I

REDISTRIBUTION OF RADIOACTIVITY WHEN Δ^2-DIHYDROPYRAN-6-^{14}C IS PASSED OVER HOT ALUMINA IN THE ABSENCE AND IN THE PRESENCE OF TETRAHYDROFURFURYL ALCOHOL

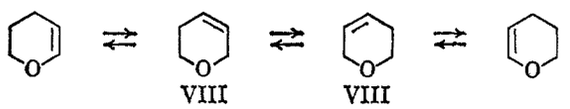


Whether our data are consistent with complete 2–6 equilibration has not been settled. Also remaining to be explained is the significance of the minor radioactivity at positions 3, 4, and 5. Notwithstanding these questions, the results show clearly that the 2 and 6 positions of Δ^2-dihydropyran do exchange and that under the conditions chosen, the exchange is either complete or close to completion. This behavior provides permissive evidence in support of the suggested tetrahydrofurfuryl alcohol reaction pathway, I → II → III.

How does the 2–6 scrambling process operate? One *a priori* possibility calls for a series of reversible interconversions between Δ^2- and Δ^3-dihydropyran (VIII) and between Δ^3- and Δ^4(= Δ^3)-dihydropyran. Scheme II shows how the 2–6 scrambling would then become not so much a matter of carbon atom exchange

SCHEME II

POSSIBLE PATHWAY FOR 2–6 SCRAMBLING IN Δ^2-DIHYDROPYRAN

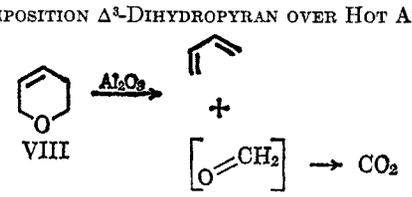


as of double-bond migration around the ring. If this is correct, Δ^3-dihydropyran must be able to rearrange to Δ^2-dihydropyran under the conditions of the 2–6 scrambling. With this in mind, we examined the behavior of Δ^3-dihydropyran over hot alumina.

Δ^3-Dihydropyran (VIII) was found to be unstable, decomposing under the influence of the hot alumina to butadiene and carbon dioxide. Since formaldehyde under the same conditions is transformed to carbon dioxide, the results are compatible with the destruction of Δ^3-dihydropyran through generation of butadiene plus formaldehyde[2] and by further oxidation of formaldehyde to carbon dioxide (*cf.* Scheme III). Table II

SCHEME III

DECOMPOSITION Δ^3-DIHYDROPYRAN OVER HOT ALUMINA



shows that when Δ^3-dihydropyran is taken alone over hot alumina either at 320–370° or at 270–320°, no sign of Δ^2-dihydropyran can be detected. Mixtures of Δ^3-dihydropyran and tetrahydrofurfuryl alcohol give

(2) The thermal decomposition at 600° of Δ^3-dihydropyran to butadiene and formaldehyde has been reported before by R. Paul and S. Tchelitcheff, *Compt. Rend.*, **224**, 1722 (1947).

Δ^2-dihydropyran, butadiene, and carbon dioxide. Evidently, the process converting tetrahydrofurfuryl alcohol to Δ^2-dihydropyran can occur simultaneous with the process decomposing Δ^3-dihydropyran. The results with a mixture of Δ^2- and Δ^3-dihydropyran again suggest independent processes. Accordingly, the interpretation offered in Scheme II is untenable and some other mechanism must be sought. This problem is being pursued.

Experimental Section

General.—The elemental analyses were reported by Carol K. Fitz, Needham Heights, Mass. Temperatures are not corrected.

5-Hexenoic Acid-1-^{14}C and 5-Hexenol-1-^{14}C (V) from 5-Bromo-1-pentene (IV).—A vacuum manifold was connected to a high-vacuum source, mercury manometer, nitrogen inlet, carbon dioxide generator,[3] and cold finger. A small flask fitted with a dropping funnel and magnetic stirrer and attached through a water-cooled condenser served as the reaction vessel. The flask containing 0.768 g (0.0316 g-atom) of magnesium was placed on the line and flushed thoroughly with pure nitrogen. A solution of 30 ml of ether (distilled from lithium aluminum hydride) plus 4.70 g (0.0315 mole) of 5-bromo-1-pentene (IV)[4] was added dropwise at a rate sufficient to maintain a gentle reflux. The mixture was stirred and boiled for 0.5 hr after the addition had been completed. This Grignard solution was frozen at liquid nitrogen temperature, evacuated, and closed off from the manifold.

Carbon dioxide generated from 5.9 g (0.030 mole) of dry barium carbonate-^{14}C by treatment with concentrated sulfuric acid, was collected at liquid nitrogen temperature in the cold-finger reservoir. After the carbon dioxide generator had been closed off, the stopcock to the frozen Grignard solution was opened, and the liquid nitrogen bath around the carbon dioxide reservoir was replaced with a Dry Ice–acetone bath. When all the carbon dioxide had frozen out on the Grignard solution, it was warmed until the resulting slurry was loose enough to stir. To bring as much as possible of the carbon dioxide into reaction, the carbonation mixture was again cooled with liquid nitrogen and then allowed to warm slightly. This process was repeated several times, then nitrogen was admitted and the reaction mixture was stirred under nitrogen at room temperature overnight.

A suspension containing 7 g (0.2 mole) of lithium aluminum hydride and 50 ml of ether was cautiously added to the stirred carbonation mixture. After an additional 5-hr period of stirring at room temperture, a saturated aqueous solution (200 ml) of sodium potassium tartrate was carefully added. The resulting mixture was continuously extracted with ether for at least 18 hr. The extract, dried with sodium sulfate, was concentrated, and the residual, pale yellow oil was distilled. 5-Hexenol-1-^{14}C (V) was collected at 158–159° in a 65% yield (1.96 g).

Practice runs according to this procedure gave 5-hexenol boiling at the same temperature and with n^{25}D 1.4322.[5]

Anal. Calcd for $C_6H_{12}O$: C, 71.95; H, 12.08. Found: C, 72.2; H, 12.3.

Ozonolysis of 5-Hexenol-1-^{14}C (V) to 5-Hydroxypentanal-5-^{14}C (VI) and Its Dehydration to Δ^2-Dihydropyran-6-^{14}C (VII).—Ozonized oxygen[6] was bubbled into a solution of 1.52 g (0.0152 mole) of radioactive 5-hexenol dissolved in 50 ml of methylene chloride that had been dried and distilled over calcium hydride. The ozonolysis mixture was kept in an acetone–Dry Ice bath. After 45 min, a deep blue color appeared in the reaction mixture simultaneous with liberation of iodine from potassium iodide by the escaping gases. In pilot experiments in which the output of ozone was known, both of these end-point indicators served satisfactorily to signal the equivalence point. The flow of ozone was interrupted and replaced with a stream of pure, dry nitrogen. When, after a few minutes, the blue color disappeared, the cold bath was removed and 5 g of zinc dust and 10 ml of water were added. Warming the mixture evaporated the organic solvent. The mixture was then heated on the steam bath for 2 hr with occasional shaking, and then allowed to stand overnight at room temperature.

Filtration removed the solids, which were rinsed with several portions of warm water. The combined aqueous filtrates were extracted continuously with ether for periods ranging from 6 hr to 2–3 days. Saturating the aqueous layer with sodium chloride proved expeditious. The ether extract was dried and concentrated, and the oily residual 5-hydroxypentanal-5-^{14}C (VI, *ca.* 3 ml) was then transferred to a small still provided with a 2-in. Vigreux column. Pure Δ^2-dihydropyran (1 g) was used conveniently here to complete the transfer. A few small chips of porous clay plate were added, and the flask was slowly heated to 265–290°. Distillate was collected in a receiver containing a small amount of sodium carbonate or potassium carbonate and held at 0°. When no more distillate appeared, the flask was cooled, 1 ml of Δ^2-dihydropyran was added, and the heat treatment was repeated.

The combined distillates were transferred to another small still provided with a short column. Rinsing the receiver with Δ^2-dihydropyran (*ca.* 1 ml) facilitated the removal of as much as possible of the upper organic layer. The product was dried by adding very small portions of lithium aluminum hydride (care!) until gas was no longer evolved. In later runs, preliminary addition of calcium hydride before the lithium aluminum hydride was found convenient. Distillation afforded 3.39 g of Δ^2-dihydropyran-6-^{14}C (VII), bp 83–84° and n^{25}D 1.4378.

Anal. Calcd for C_5H_8O: C, 71.39; H, 9.58. Found: C, 71.1; H, 9.5.

In runs of 0.1 mole, the yield of dihydropyran was approximately 40–45%.

The 2,4-dinitrophenylhydrazone of the hydroxypentanal obtained by hydrolyzing this radioactive dihydropyran (VII) was prepared essentially as described before.[1] The final recrystallization from 50% aqueous methanol gave the derivative, mp 110.5–111.0°, in 71% yield.

Anal. Calcd for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00. Found: C, 46.9; H, 5.1; relative molar activity, 4933 ± 33.

Clay chips are not essential in dehydrating 5-hydroxypentanal to dihydropyran. Thus, in a pilot experiment, 2.0 g (0.020 mole) of 5-hexenol was ozonized as described above, and the derived hydroxypentanal was distilled without clay chips at pot temperatures up to 315°. The redistilled dihydropyran product, bp 84–87° and n^{25}D 1.4380, weighed 0.79 g. Since no extraneous dihydropyran was used here, the yield from hexenol was 47%.[7] Δ^2-Dihydropyran could also be formed (44%) by treating 5-hydroxypentanal in dry, cold 2-methyl-5-ethylpyridine first with *p*-toluenesulfonyl chloride to form 2-tosyloxytetrahydropyran and then heating the reaction mixture at *ca.* 160°.

Δ^2-Dihydropyran-6-^{14}C (VII) over Hot Alumina.—The procedure in general was the same as that described for the conversion of tetrahydrofurfuryl alcohol to dihydropyran.[1] The same Alcoa activated alumina (Grade F-1, 8–14 mesh) and the same pretreatment with dihydropyran and tetrahydrofurfuryl alcohol were employed. With the center of the catalyst bed at 355°, 0.45 g of Δ^2-dihydropyran-6-^{14}C (VII) was passed through the catalyst tube at the rate of 1 drop per 6 sec followed directly by 10 ml of nonradioactive dihydropyran. A slow stream of nitrogen was passed through the tube before, during, and for 20 min after passage of the dihydropyran. The green organic layer in the first receiver was treated essentially as described before[1] to give 3.8 g of radioactive dihydropyran, bp 83–84° and n^{25}D 1.4381.

Anal. Calcd for C_5H_8O: C, 71.39; H, 9.58. Found: C, 71.2; H, 9.9.

Δ^2-Dihydropyran-6-^{14}C (VII) plus Tetrahydrofurfuryl Alcohol over Hot Alumina.—A mixture of Δ^2-dihydropyran-6-^{14}C (0.9 g), tetrahydrofurfuryl alcohol (1 ml), and water (1 drop) was passed over the hot alumina just as before. The dropping funnel and the catalyst tube were then rinsed and flushed by passing three-

(3) M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert, and P. F. Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949.

(4) Prepared from 4-pentenol and phosphorus tribromide essentially according to the directions of P. Gaubert, R. P. Linstead, and H. N. Rydon, *J. Chem. Soc.*, 1971 (1937). Note also M. S. Kharasch and C. F. Fuchs, *J. Org. Chem.*, **9**, 359 (1944). The 5-bromo-1-pentene prepared here showed bp 125–128° and n^{25}D 1.4587.

(5) V. P. Gol'mov [*Chem. Abstr.*, **48**, 1240 (1954); *Zh. Obshch. Khim.*, **22**, 2132 (1952)] reported bp 155.5–156° (718 mm) and n^{20}D 1.4364 for 5-hexenol.

(6) L. I. Smith, F. L. Greenwood, and O. Hudrlik, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 673.

(7) Unpublished work by Dr. T. P. Manos has shown that dihydropyran forms smoothly on dropping 5-hydroxypentanal into diphenyl ether at 230–240°.

1-ml portions of tetrahydrofurfuryl alcohol in succession through the catalyst tube. Processing the combined emergent products gave 2.8 g of pure radioactive dihydropyran with bp 84.5–86° and $n^{25}D$ 1.4392.

Anal. Calcd for C_5H_8O: C, 71.39; H, 9.58. Found: C, 71.1; H, 9.7.

Δ^2-Dihydropyran Degradation.—The distribution of radioactivity in dihydropyran before and after exposure to hot alumina was determined by chemically dissecting the molecule according to a procedure worked out before.[1] In each case, the total activity of the dihydropyran was found by hydrating it to 5-hydropentanal and taking the mean activity of the derived 2,4-dinitrophenylhydrazone and the derived glutaric acid. The 2,4-dinitrophenylhydrazone was routinely purified by recrystallization from aqueous methanol, the glutaric acid from benzene. Cleaving Δ^2-dihydropyran by ozonolysis presented the number 2 carbon atom in the form of zinc formate and the 3, 4, 5, and 6 carbon atoms in the form of 4-hydroxybutanal, which was isolated as its 2,4-dinitrophenylhydrazone. This derivative was recrystallized from aqueous ethanol. The ozonolysis was performed much as described before, except that the reaction mixture was kept in an acetone–Dry Ice bath. Also in connection with isolation of the 4-dihydroxybutanal, Mr. S. H. Stein has found that batch extraction with methylene chloride from the aqueous solution is feasible and can take the place of the less convenient continuous extraction with ether. The activity of the 3, 4, and 5 carbon atoms of Δ^2-dihydropyran was found from the activity of the dibenzoyl derivative of 1,3-diaminopropane derived from the glutaric acid by a Schmidt degradation. The dibenzoyl derivative was recrystallized from benzene.

Table III gives the relative molar activity of the several compounds as well as other pertinent information.

Radioactivity Measurements.—The method of Schwebel, Isbell, and Moyer[8] was adapted for radioactivity determinations. For each compound in a related series, counts were taken in five to seven sets of three, referring, respectively, to compound, standard, and background. These counts were reduced to "relative molar activities," which are proportional to the molar activities of the compounds. The errors given for each determination are standard deviations and refer only to the counting uncertainty. The counting standard deviations ranged from 2 to 5%, so that the combined weighing and dilution uncertainty, estimated at 0.5%, was neglected. Table III presents the results.

Δ^3-Dihydropyran (VIII).—Δ^3-Dihydropyran was prepared by a Prins reaction with paraformaldehyde, propylene, acetic acid, and sulfuric acid, followed by acid-catalyzed elimination of acetic acid from the resulting 4-acetoxytetrahydropyran.[9] To make sure that this material was free of Δ^2-dihydropyran, the product was shaken with 0.1 *N* hydrochloric acid at room temperature under conditions known to convert Δ^2-dihydropyran to the higher boiling 5-hydroxypentanal. Fractionation gave Δ^3-dihydropyran, bp 92–93° and $n^{25}D$ 1.4481–1.4426.

Anal. Calcd for C_5H_8O: C, 71.39; H, 9.58. Found: C, 70.9; H, 9.9.

The Δ^3-dihydropyran (VIII) showed no infrared absorption in the 1630–1650-cm^{-1} region. With the same infrared absorption sample cell, the intense double-bond vibration of Δ^2-dihydropyran at 1640 cm^{-1} could be detected at a concentration of 0.1%. Accordingly, an upper limit of approximately 0.1% for the possible content of Δ^2-dihydropyran in the Δ^3-dihydropyran was established. Under conditions giving an immediate 2,4-dinitrophenylhydrazone derivative from hydrated Δ^2-dihydropyran, no sign of any precipitate was obtained from the Δ^3-dihydropyran.

Δ^3-Dihydropyran (VIII) over Hot Alumina.—With the exception of the collecting units, the apparatus and directions were the same as those described above. For most of the experiments with Δ^3-dihydropyran, the effluent gases were led through a series of traps. The first trap (at 0°) was empty, the second contained 100 ml of water, the third (0°) contained 50 ml of chloroform plus 10–24 g of bromine, the fourth contained 100 ml of 95% ethanol, and the fifth contained 100 ml of a clear, saturated, calcium hydroxide solution. In some of the runs, one or more of these traps were left out.

Several tests were applied to the contents of the traps. The first, second, and fourth were checked for material producing a 2,4-dinitrophenylhydrazone under conditions that converted Δ^2-dihydropyran to the corresponding derivative of 5-hydroxypentanal. Negative results with this test limited the Δ^2-dihydropyran to trace amounts (*ca.* 0.02 g). The dimedon test for formaldehyde was applied to the contents of the second trap.

TABLE III

ANALYTICAL DEGRADATION OF Δ^2-DIHYDROPYRAN

Compound	Yield, %	Mp, °C	Anal,[a] % C	Anal,[a] % H	Relative molar activity
A. Δ^2-Dihydropyran-6-^{14}C before Exposure to Hot Alumina					
2,4-DNP of 5-hydroxypentanal	71	110.5–111	46.9	5.1	4933 ± 33
Glutaric acid	33	93.5–95	45.2	5.9	4764 ± 24
Zinc formate dihydrate	96		12.6	3.1[b]	57 ± 1[c]
2,4-DNP of 4-hydroxybutanal	26	114.2–115	45.0	4.5	4930 ± 17
N,N′-Dibenzoyl-1,3-diaminopropane	22	149.5–150	72.5	6.2	66 ± 2
B. Δ^2-Dihydropyran-6-^{14}C Exposed to Hot Alumina					
2,4-DNP of 5-hydroxypentanal	50	107.5–108	46.9	5.0	139 ± 3
Glutaric acid	42	93–95	45.3	5.9	136 ± 8
Zinc formate dihydrate	93		12.4	3.0[d]	62 ± 5[c]
2,4-DNP of 4-hydroxybutanal	45	114–115	44.9	4.6	72 ± 4
N,N′-Dibenzoyl-1,3-diaminopropane	25	148–151	72.5	6.6	7.5 ± 1.5
C. Δ^2-Dihydropyran-6-^{14}C Mixed with Tetrahydrofurfuryl Alcohol and Exposed to Hot Alumina					
2,4-DNP of 5-hydroxypentanal	65	106.5–107.5			1273 ± 13
Glutaric acid	54	93–95	45.3	5.9	1241 ± 12
Zinc formate dihydrate	97		12.7	3.3[e]	526 ± 6[c]
2,4-DNP of 4-hydroxybutanal	43	115–115.5	44.8	4.5	694 ± 5
N,N′-Dibenzoyl-1,3-diaminopropane	28	147–150	72.4	6.5	43 ± 8

[a] Theoretical values for the compounds are as follows. *Anal.* Calcd for 2,4-DNP of 5-hydroxypentanal ($C_{11}H_{14}N_4O_5$): C, 46.81; H, 5.00. Calcd for glutaric acid ($C_5H_8O_4$): C, 45.45; H, 6.10. Calcd for zinc formate dihydrate ($C_2H_6O_6Zn$): C, 12.55; H, 3.16; Zn, 34.15. Calcd for 2,4-DNP of 4-hydroxybutanal ($C_{10}H_{12}N_4O_5$): C, 44.78; H, 4.51. Calcd for N,N′-dibenzoyl-1,3-diaminopropane ($C_{17}H_{18}N_2O_2$): C, 72.32; H, 6.43. [b] Found for Zn, 34.3. [c] This figure is half the relative molar activity of the zinc formate dihydrate. [d] Found for Zn, 34.2. [e] Found for Zn, 33.8.

A negative test here limited the formaldehyde content to less than 1 mg. In the calcium hydroxide solution a milky precipitate that dissolved with evolution of gas on acidification with hydrochloric acid was accepted as evidence for carbon dioxode. In the bromine trap, butadiene was converted into 1,2,3,4-tetrabromobutane, which was isolated by first evaporating all volatile

(8) A. Schwebel, H. S. Isbell, and J. D. Moyer, *J. Res. Natl. Bur. Std.*, **53**, 221 (1954); *cf.* W. J. Gensler and W. R. Koehler, *J. Org. Chem.*, **27**, 2754 (1962).

(9) S. Olsen, *Acta Chem. Scand.*, **5**, 1168 (1951). See also E. Hanschke, *Chem. Ber.*, **88**, 1053 (1955), and M. I. Farberov, E. P. Tepenitsyna, and N. K. Shemyakina, *Chem. Abstr.*, **49**, 8315 (1955); *Zh. Obshch. Khim.*, **25**, 133 (1955).

material and then recrystallizing the residue from ligroin and from 85% aqueous ethanol[10] until the melting point of the white crystals was 115.5–116.5°. When pure butadiene was bubbled into a solution of bromine in chloroform, the recrystallized racemic form of 1,2,3,4-tetrabromobutane,[11] mp 115.5–116.5°, could be isolated in 59% yield. Accordingly, the yields of butadiene given in Table II in the column headed "bromine" were calculated by multiplying the yield of pure crystalline 1,2,3,4-tetrabromobutane product by 100/59.

(10) M. Lespieau and Ch. Prévost, *Bull. Soc. Chim. France*, [4] **37**, 704 (1925).

(11) W. M. Schubert and W. A. Lanka, *J. Am. Chem. Soc.*, **76**, 1956 (1954). Ya. M. Slobodin and S. A. Zaboev, *Chem. Abstr.*, **46**, 7433 (1952); *Zh. Obshch. Khim.*, **22**, 603 (1952).

Chlorination of Benzylic Sulfides with N-Chlorosuccinimide[1]

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The chlorination of benzylic sulfides by N-chlorosuccinimide has been investigated. The resulting α-chloro sulfides have been characterized by nmr and by conversion into the chloro sulfones. Mechanistic interpretation is offered for the results of competitive reactions of mixtures of sulfides, the directive effect in the chlorination of benzyl *p*-chlorobenzyl sulfide, and a large primary kinetic isotope effect in the chlorination of α-*d*-benzyl phenyl sulfide.

The two most generally applicable methods for the synthesis of α-chloro sulfides cited in the literature are the sulfuryl chloride chlorination of sulfides[2] and the condensation of aldehydes with mercaptans in the presence of hydrogen chloride.[3] The efficacy of N-chlorosuccinimide (NCS) for the conversion of sulfides into α-chloro sulfides has recently been reported.[4] This paper describes the reaction of NCS with benzylic sulfides.

Results

Chlorination of sulfides **1a–d** with NCS at room temperature in carbon tetrachloride afforded α-chloro sulfides **2a–d** with no detectable ring halogenation or chlorinolysis. The chloro sulfides were not isolated, but were identified by their nmr spectra (Table I) and by conversion on treatment with *m*-chloroperbenzoic acid[2d] into the corresponding sulfones (**3a–d**) (Scheme I).

TABLE I

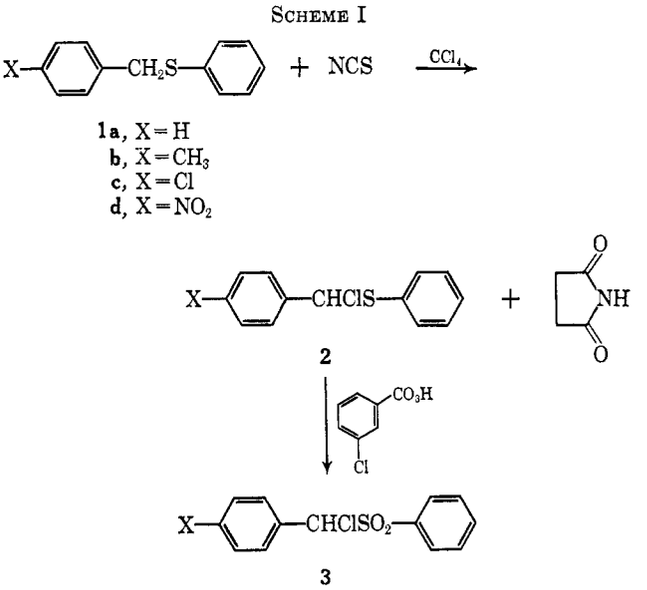
CHEMICAL SHIFTS[a] OF METHYLENE AND METHINE HYDROGENS IN COMPOUNDS 1 AND 2

X	CH_2S[b]	CHClS	Δ, ppm
H	4.00	6.15	2.15
CH_3	3.98	6.13	2.15
Cl	3.96	6.10	2.14
NO_2	4.09	6.20	2.11

[a] In parts per million downfield from internal tetramethylsilane. [b] 15% w/v solution in CCl_4.

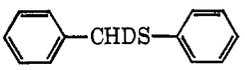
In Table I are collected the chemical shifts of the methylene and methinyl singlets observed in the nmr spectra of compounds **1** and **2**. The change in chemical shift brought about by chlorination appears reasonable when compared with a shielding constant of 2.53 for chlorine for disubstituted methylenes.[5]

SCHEME I



The relative reactivities of sulfides **1a–d** with NCS were determined. Samples of a carbon tetrachloride solution of two of the sulfides containing a few drops of cyclohexane as an internal standard were taken before the addition of NCS and after chlorination was complete. Quantitative nmr analysis indicated the relative amounts of the two sulfides before and after the reaction. The results of these competitions are summarized in Table II. The relative rates so obtained were correlated by the Hammett $\sigma\rho$ treatment (Figure 1) with a visually determined ρ value of −0.8.

The isotope effect in the chlorination of α-*d*-benzyl phenyl sulfide (**4**) was determined by quantitative nmr spectrometry. Data from the chlorination of benzyl phenyl sulfide were used as a calibration for the experiments on **4**. A comparison of the area of the methylene resonance of **4** to that of the methinyl peak



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