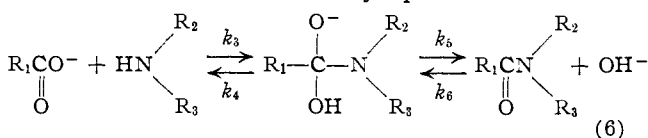


intermediate, we have to modify eq. 4 to



With the usual steady state assumptions, the observed rate constant for amide formation is  $k_1 = k_3/[1 + (k_4/k_6)]$  while the observed rate constant for amide hydrolysis is  $k_2 = k_6/[1 + (k_5/k_4)]$ . Bender and Ginger found for the hydrolysis of benzamide at 109° that a substitution of two-thirds of the water with dioxane reduced  $k_2$  by a factor of 6 while  $k_5/k_4$  was increased from 10 to 34. The reduction of the hydrolysis rate is therefore due both to a decrease in  $k_6$  and an increase in the ratio  $k_5/k_4$ . As for amide formation, the data of Bender and Ginger show that  $k_4/k_6 \ll 1$  for amide hydrolysis both in the presence and the absence of an organic cosolvent and we are, therefore, justified in approximating  $k_1 \approx k_3$ . It is then the rate of formation of the tetrahedral intermediate from propionate and ammonia or methylamine which is being observed in studies of the rate of amide formation. The striking difference in the result obtained with the water-1-propanol and the water-2-propanol system suggests that the solvation of the transition state complex is surprisingly sensitive to the details of the structure of the cosolvent.

### Experimental

**Reagents.**—Reagent grade ammonia (Allied Chemical Co.), methylamine (Eastman Organic Chemicals) and ethylamine (Matheson) were received as aqueous solutions. Reagent grade anhydrous dimethylamine, isopropylamine, ethanolamine, formic acid and acetic acid (Eastman) were used without purification. Reagent grade propionic, butyric and isobutyric acids (Eastman), 1-propanol and 2-propanol (Brothers Chem. Co.) were purified by fractional distillation. Succinic acid (Eastman, reagent grade) melted at 186.8°. Reagent grade (Eastman) N-methylformamide, N-methylacetamide and N-methylpropionamide were fractionally distilled; propionamide was recrystallized from acetone-water. N-Isopropylformamide was prepared from an equimolar mixture of methyl formate and isopropylamine which was allowed to stand at room temperature for 3 hours. The fraction boiling at 220° (lit.<sup>26</sup> 220°) was collected. The other amides used (N-methylisobutyramide, m.p. 20°, lit.<sup>27a</sup> 20°, N-isopropylacetamide, b.p. 89–90°, lit.<sup>27b</sup> 89–90°, N,N-dimethylpropionamide, 81–82°, N-ethylpropionamide 105–110°, N-isopropylpropionamide (hygroscopic crystals)) were made by a reaction of the appropriate acid chloride and amine. N-Methylsuccinamic acid (m.p. 111°) was made from succinic

(26) J. Parker, A. L. Thomson and J. Waughan, *J. Chem. Soc.*, 2601 (1955).

(27) (a) A. P. N. Franchimont, *Chem. Zentr.*, **84**, **II**, 1960 (1913); (b) K. G. Wyness, *J. Chem. Soc.*, 2934 (1958).

(28) W. P. Ratchford and C. H. Fisher, *J. Org. Chem.*, **15**, 317 (1950).

(29) H. Meerwein, *et al.*, *Ber.*, **89**, 209 (1956).

anhydride and methylamine; its acid number was 96.5% of theory, the amine released on base hydrolysis 101% of theory.

**Determination of Hydrolysis Rates.**—Evacuated sealed tubes containing 30 ml. of solutions 0.01 M in both NaOH and amide were placed into a thermostated bath. Sample tubes were removed at intervals and the ammonia or amine liberated was distilled under vacuum from a water-bath at 5–8° into a known amount of dilute H<sub>2</sub>SO<sub>4</sub> in water-1-propanol at –15°. When about one-third of the reaction solution had distilled over, the excess H<sub>2</sub>SO<sub>4</sub> was titrated with 0.01 N NaOH using either phenolphthalein indicator or conductometry. This method was not applicable to the amides of formic and acetic acids, since they reacted at appreciable rates even at the low temperature of the distillation step. In these cases the partially hydrolyzed amide solutions were passed through an Amberlite IR 120 cation exchange column and the carboxylic acid was determined conductometrically in the eluate.

**Determination of the Rate of Amide Formation.**—Unless otherwise specified, the formation of amide was followed in aqueous solutions containing initially 1 N amine and 0.2 N carboxylic acid. Sealed evacuated tubes containing 20 ml. of the solution were placed into a thermostated bath. At specified times, a sample tube was cooled to room temperature and most of the excess amine was distilled off under a pressure of 10–20 mm. The solution was then diluted and passed through a cation exchange column which was subsequently washed with 200 ml. of distilled water. The eluate was made basic with 20 g. of NaOH and was heated. The amine liberated was distilled into a H<sub>2</sub>SO<sub>4</sub> solution of known concentration adjusted so as to represent a moderate excess over the expected amount of amine. The acid was then back-titrated conductometrically with NaOH.

In the case of amide formation from the non-volatile ethanolamine, a different procedure had to be employed. The unreacted acids and amine were removed by successive passage through columns of the anion exchanger Amberlite IR 400 and the cation exchanger Amberlite IR 120 followed by a second passage over the anion exchanger. A quantity of NaOH equivalent to the initial amount of carboxylic acid was added to the eluate, which was heated to hydrolyze the amide. After removal of sodium ions and amine by passage through a cation exchanger, the carboxylic acid was determined conductometrically in the effluent.

**Evaluation of Analytical Methods.**—A solution containing 1 M ammonia, 0.2 M ammonium propionate and 0.002 M propionamide in 50 ml. was subjected to the analysis for amide used in following rates of amide formation. The results of the analysis carried out in triplicate was 95%, 96% and 105% of theory. A solution containing 0.0075 M N-methylpropionamide, 0.0075 M sodium hydroxide and 0.00375 M N-methylammonium propionate was analyzed for methylamine by the procedure used in following rates of amide hydrolysis. The results of a triplicate analysis were 96%, 98% and 99% of theory.

**Characteristics of Kinetic Runs.**—The amide formation was followed to conversions which were in most cases below 1% but never more than 4%. In this range the amide hydrolysis is not yet significant and the amide content is linear in time. Analyses carried out at zero time gave apparent amide concentrations corresponding to apparent conversions of 0.02–0.09%. Amide hydrolyses were first order in amide and first order in hydroxide ion. In one case, that of propionamide hydrolysis at 50°, our second-order rate constant of  $2.57 \times 10^{-4}$  l.-mole<sup>-1</sup> sec.<sup>-1</sup> could be compared with the value of  $1.97 \times 10^{-4}$  obtained by extrapolation of the data obtained by Willems and Bruylants<sup>10</sup> in the temperature range of 65–85°. The discrepancy may be due to the much lower ionic strength used in our study.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY 4, CALIF.]

## The Preparation of Cyclic Cyclopropylcarbinols<sup>1</sup>

BY WILLIAM G. DAUBEN<sup>2</sup> AND GILBERT H. BEREZIN<sup>3</sup>

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The reaction of cyclic allyl alcohols or related methyl ethers with methylene iodide and zinc-copper couple has been shown to give cyclopropylcarbinols (or methyl ethers) in high yield. The reaction has been found to be stereospecific, yielding only the *cis* isomer. The mechanism of the reaction is discussed.

The synthesis of the cyclopropylcarbinyl system has been widely studied since such a system occurs in various natural products and in many materials pro-

duced by photochemical reactions and since reactions of such a system permit evaluation of the conjugative ability of a cyclopropyl ring. Many methods have been utilized for the preparation of such a system, but most of the methods either demanded complex starting materials or were not general in scope.<sup>4</sup> In

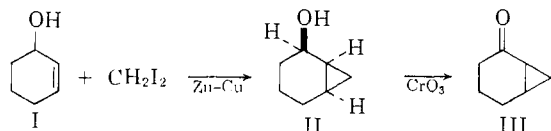
(1) This work was supported in part by Grant No. CY-4284, U. S. Public Health Service.

(2) Miller Research Professor, 1961–1962.

(3) Shell Oil Company Summer Fellow, 1960.

1958, Simmons and Smith reported a new general stereospecific synthesis of cyclopropanes which involved the treatment of olefins with methylene iodide and a zinc-copper couple.<sup>4b</sup> When this reaction was employed with an acetate of an allyl<sup>4b</sup> or a homoallyl alcohol<sup>6</sup> in order to prepare a cyclopropylcarbinyl or the homo related system, the yield of product was poor. Using the free homoallylic alcohol, however, it was found that the reaction was excellent and that the free hydroxyl group not only greatly catalyzed the reaction but played a role in the stereospecificity of the reaction.<sup>5</sup> It, therefore, seemed likely that the Simmons-Smith reaction should also be useful with allylic alcohols to prepare substituted cyclopropylcarbinols.

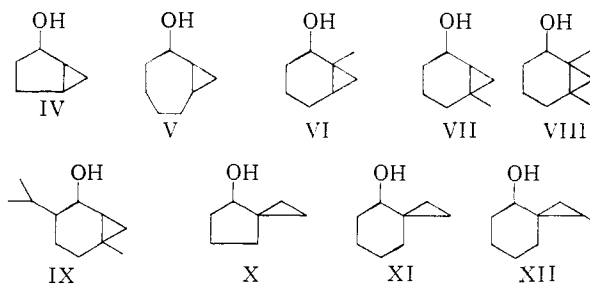
It was found that addition of one mole of  $\Delta^2$ -cyclohexene-1-ol (I) to iodomethylzinc iodide prepared from 2.2 moles of methylene iodide and 2.4 moles of zinc-copper couple gave in a 63% yield a single saturated alcohol contaminated with traces of methylene iodide.



The absence of any starting alcohol in the reaction product was demonstrated by gas-liquid chromatography. The removal of the trace amount of methylene iodide was best accomplished by allowing the crude reaction product to stand for 24 hours with an excess of sodium methoxide in methanol. Subsequent distillation of the crude product yielded pure *cis*-bicyclo[4.1.0]heptane-2-ol (II). The spectral properties of II are those expected of such a structure. In the infrared spectrum there are bands at 3060 and 1010  $\text{cm}^{-1}$  and in the nuclear magnetic resonance spectrum there are bands above 9.3  $\tau$ , absorptions characteristic of a cyclopropyl ring.<sup>6-8</sup> The saturated character of the material follows from the absence of vinyl protons in the n.m.r. spectrum and from the absence of end absorption in the ultraviolet spectrum.

Oxidation of II in acetone at  $-25^\circ$  with chromium trioxide solution<sup>9</sup> gave the known bicyclo[4.1.0]heptane-2-one (III).<sup>10</sup> Reduction of the ketone with lithium aluminum hydride gave a mixture of the two isomeric bicyclo[4.1.0]heptane-2-ols in a ratio of 7:3, as measured by gas-liquid chromatography. The lesser isomer was identical with the product formed in the Simmons-Smith reaction. Thus, as was found earlier with the homoallylic alcohol, the reaction of an allylic alcohol with iodomethylzinc iodide proceeds with complete stereospecificity.

The synthetic procedure outlined above for the preparation of II was found to be a general method for the preparation of cyclic cyclopropylcarbinols. The generality is best indicated by reference to the wide variety of compounds IV-XII, which were prepared by this method. It is to be noted specifically that when flexible cyclic allyl alcohols are used, tri- and tetra-substituted double bonds readily react. In their original study, Simmons and Smith reported that the tri-substituted olefinic bond in limonene did not react,<sup>4a</sup>



but it has now been found that reaction does occur at this position but at a slower rate.<sup>11</sup>

In all of the above ring systems, the same specificity of reaction was found in the formation of the cyclopropylcarbinol *via* the Simmons-Smith reaction on the related allyl alcohol. As mentioned earlier, a similar stereospecificity has been reported when the homoallyl alcohol,  $\Delta^3$ -cyclopentenol, was studied.<sup>5</sup> On the basis of finding anchimeric acceleration of ionization of one isomer as compared to the other and by consideration of conformational concepts of hydride reduction of ketones and of the equilibrating Meerwein-Ponndorf reaction, the product formed in the iodomethylzinc iodide reaction should possess the hydroxyl group *cis* to the cyclopropyl ring. However, the much different geometric relationship between the carbon-carbon double bond and the hydroxyl function in a cyclic allyl alcohol as compared to  $\Delta^3$ -cyclopentenol made it essential to establish again the stereochemistry of the various alcohols prepared in the present study.

The first indication of the stereochemistry of these materials was gained by the finding that the reaction product from the Simmons-Smith reaction on  $\Delta^2$ -cycloheptenol was identical with the major bicyclo[5.1.0]octane-2-ol formed in the solvolysis of  $\Delta^3$ -cyclooctene-1-yl brosylate.<sup>12</sup> In this solvolysis, Cope and his co-workers found that both isomeric bicyclo[5.1.0]octane-2-ols were formed and assigned the *cis* configuration to the major product.<sup>13</sup> The stereochemical assignment was based on the assumption that if the solvolysis was a concerted process or proceeded *via* a bridged ion intermediate, the major product should be a *cis* isomer. In agreement with such an assignment were the lesser thermodynamic stability of this isomer and the axial nature of the hydroxyl group as indicated by shorter g.l.c. retention time and lesser hydrogen bonding as shown in the infrared spectrum. Also, the minor alcohol was synthesized by reaction of iodomethylzinc iodide with  $\Delta^2$ -cycloheptenyl acetate and the alcohol was assigned a *trans* configuration since it was assumed in this reaction that the cyclopropyl ring is usually formed by addition of a methylene group to the lesser hindered side of the unsaturated compound—that is, the side opposite the acetoxy group. If such be the case, then it must be that the presence of a free hydroxyl system directs the introduction of the cyclopropane in a *cis* manner and the related ester in a *trans* manner.

The correctness of this last proposal as well as the establishment of a *cis* relationship between the hydroxyl group and the cyclopropyl ring on the bicyclic alcohols present in this work has been proved in an unambiguous manner. Bicyclo[4.1.0]heptane-2-ol (II) was converted to its methyl ether XIII with sodium hydride and methyl iodide. Hydrogenolysis of XIII over Raney nickel at  $220^\circ$  and 2800 pounds pressure gave rise to the methyl ethers of *cis*-2-methylcyclohexanol (XIV) and the *cis*-3-methyl isomer XIV in a

(11) H. E. Simmons and E. P. Blanchard, Jr., private communication.

(12) A. C. Cope, S. Moon and P. E. Petersen, *J. Am. Chem. Soc.*, **84**, 1935 (1962).

(13) The major product was called *endo* in ref. 12.

(4) For reviews of the synthetic methods, see (a) N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957), (b) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959).

(5) S. Winstein and J. Sonnenberg, *ibid.*, **83**, 3235 (1961).

(6) A. H. R. Cole, *J. Chem. Soc.*, 3807 (1954).

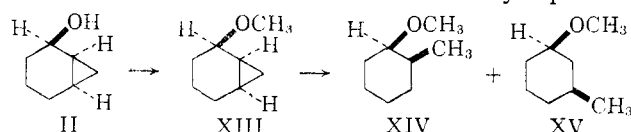
(7) J. M. Derfer, E. E. Pickett and C. E. Boord, *J. Am. Chem. Soc.*, **71**, 2483 (1949).

(8) K. B. Wiberg and B. J. Nist, *ibid.*, **83**, 1226 (1961).

(9) K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); C. Djerassi, R. R. Engle and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

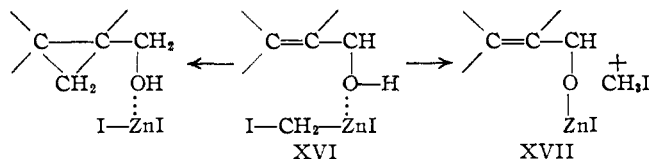
(10) G. Stork and J. Ficini, *J. Am. Chem. Soc.*, **83**, 4678 (1961).

ratio of 3:1. The absence of any *trans* isomer was shown by g.l.c. of authentic samples of the four isomeric methyl ethers of these two series and in each case it was found that the *cis* isomer was cleanly separated



from its *trans* isomer. The presence of only the thermodynamically unstable *cis*-2-methyl isomer clearly indicated that no equilibration had taken place in this degradation. Thus, in the Simmons-Smith reaction on cyclic allyl alcohols only the *cis* isomer is formed.

The high degree of stereospecificity exhibited by the iodomethylzinc iodide reagent in the reaction with cyclic allyl alcohols has definite mechanistic implications. As has been pointed out previously in the  $\Delta^2$ -cyclopentenol case, such a stereospecific effect of the hydroxyl group must be due to some coordination of the hydroxyl group with the reagent prior to reaction with the double bond. In addition to the stereospecificity aspects, the hydroxyl groups also strongly facilitate the reaction. For example, when cyclohexene,  $\Delta^2$ -cyclohexenol, methylene iodide and zinc-copper couple in a ratio of 1:1:1.2:1.2 were allowed to react, methylene addition occurred only on the hydroxylated moiety and the bicyclic alcohol II was formed in the usual yield of 45% (based upon the methylene iodide used). Also, this yield of cyclopropylcarbinol shows that the hydroxyl group, in contrast to its reaction with a Grignard reagent, does not quantitatively destroy the iodomethylzinc iodide reagent. A direct measure of the yield of the reaction between this iodomethylzinc iodide reagent and allyl alcohol was made by allowing a known amount of the reagent (determined by iodometric analysis) to react with an equivalent amount of  $\Delta^2$ -cyclopentenol. This alcohol was chosen since starting material, product and methylene iodide are readily separated by g.l.c. It was found that a 78–82% yield of bicyclo[3.1.0]pentene-2-ol was obtained. Since it has been reported that the iodomethylzinc iodide reagent is decomposed rapidly by water<sup>14</sup> and by a saturated alcohol,<sup>14</sup> there is no question that a competition exists between methylene transfer and destruction of the reagent. It is suggestive that the first



stage in the reaction is the formation of a complex like XVI; this complex than can undergo decomposition to form the alkoxyzinc iodide XVII and methyl iodide or when the geometry is favorable by insertion of the methylene group onto a double bond. All the allyl alcohols so far studied possessed a flexible ring system in which the hydroxy group can adopt an axial conformation which would seem well suited for this favorable competition as well as the stereospecificity. It would appear that such a conformation may well be needed to retain these two features of the reaction.

The suggestion of the formation of a complex such as XVI involving an unshared electron pair on the oxygen of the hydroxyl function was further indicated by the isolation of only *cis*-2-bicyclo[4.1.0]heptylmethyl ether from the Simmons-Smith reaction with  $\Delta^2$ -cyclohexenylmethyl ether. The yield of the ether was approximately the same as found with the free alcohol,

(14) H. E. Simmons and E. P. Blanchard, Jr., private communication.

clearly showing the competition of the allyl double bond for the coordinated reagent. The importance of a complex for facilitation of the reaction explains why the related esters do not follow the same reaction course but react with the double bond from the unhindered side and form product in low yield.

### Experimental<sup>15</sup>

For all gas-liquid chromatography analyses and separations, except as otherwise noted, an Aerograph master A-100 gas liquid chromatographic apparatus equipped with a 0.25 in.  $\times$  5 ft. diethylene glycol succinate column was employed. A column temperature of 100–110° and an injector temperature of 135–150° were used.

The anhydrous ether used in the reactions was distilled from  $P_2O_5$  directly into the reaction flask.

$\Delta^2$ -Cyclohexene-1-ol.—Following the procedure described using the chloro isomer,<sup>16</sup> 59 g. (0.36 mole) of 3-bromo- $\Delta^1$ -cyclohexene<sup>17</sup> yielded 23 g. (65%) of the alcohol, b.p. 62–64° (11 mm.),  $n_D^{25}$  1.4859 [lit.<sup>18</sup> b.p. 85° (25 mm.),  $n_D^{25}$  1.4861].

$\Delta^2$ -Cycloheptene-1-ol.—Using the method described above for the cyclohexene analog, from 178 g. (1 mole) of N-bromo-succinimide and 98 g. (1 mole) of cycloheptene, there was obtained 18 g. (16%) of the alcohol, b.p. 75–76° (17 mm.),  $n_D^{25}$  1.4885 [lit.<sup>18</sup> b.p. 72° (7 mm.),  $n_D^{25}$  1.4890].

2-Methyl- $\Delta^2$ -cyclohexene-1-ol.—To a well-stirred mixture of 4.5 g. (0.3 mole) of lithium aluminum hydride in 200 ml. of anhydrous ether, there was added a solution of 30 g. (0.27 mole) of 2-methyl- $\Delta^2$ -cyclohexene-1-one<sup>19</sup> in 60 ml. of anhydrous ether over a 30-minute period. The mixture was stirred at room temperature for 1 hour and then under reflux for 2 hours. The mixture was cooled and a solution of 20 g. of methanol in 20 ml. of ether was added over a 15-minute period with stirring. When the gentle reflux subsided, saturated ammonium chloride solution was added until the salts precipitated. The ethereal solution was decanted and the salts were washed by decantation with two 100-ml. portions of ether. The combined ethereal extracts were dried, the ether evaporated, and the product distilled; yield 25 g. (82%), b.p. 76–78° (18 mm.),  $n_D^{25}$  1.4816 [lit.<sup>20</sup> b.p. 73–75° (18 mm.),  $n_D^{25}$  1.4823].

2,3-Dimethyl- $\Delta^2$ -cyclohexene-1-ol.—Using the method described for the preparation of 2-methyl- $\Delta^2$ -cyclohexene-1-ol, from 10 g. (0.08 mole) of 2,3-dimethyl- $\Delta^2$ -cyclohexene-1-one<sup>21</sup> and 5 g. (0.13 mole) of lithium aluminum hydride in 250 ml. of anhydrous ether, there was obtained 8.0 g. (79%) of product, b.p. 80–81° (8 mm.),  $n_D^{25}$  1.4844.

Anal. Calcd. for  $C_8H_{14}O$  (126.10): C, 76.14; H, 11.18. Found: C, 76.39; H, 11.18.

2-Ethylidenecyclohexane-1-ol.—Using the method described for the preparation of 2-methyl- $\Delta^2$ -cyclohexene-1-ol, from 7.0 g. (0.056 mole) of 2-ethylidenecyclohexane-1-one<sup>22</sup> and 3.5 g. (0.092 mole) of lithium aluminum hydride in 200 ml. of anhydrous ether, there was obtained 6.8 g. (95%) of product, b.p. 68–69° (5 mm.),  $n_D^{25}$  1.4856.

Anal. Calcd. for  $C_8H_{14}O$  (126.19): C, 76.14; H, 11.18. Found: C, 76.32; H, 11.24.

*cis*-Bicyclo[4.1.0]heptane-2-ol.—A typical procedure for the preparation of the bicyclic alcohols is described. This procedure has been utilized for the synthesis of the other related alcohols.

To a well-stirred mixture of 250 ml. of anhydrous ether, 36 g. (0.55 mole) of zinc-copper couple<sup>23</sup> and 0.2 g. of iodine there was added 115 g. (0.43 mole) of methylene iodide. The reaction mixture was warmed with an infrared lamp until a spontaneous reaction began, as evidenced by continued refluxing of the ether when the lamp was removed. The flask containing the reaction mixture was then immersed in a water-bath whose temperature was maintained at 35° and the mixture stirred for 30 minutes. To this gently refluxing mixture there was added a solution of 20 g. (0.2 mole) of  $\Delta^2$ -cyclohexene-1-ol in 40 ml. of anhydrous ether over a period of 20 minutes. The temperature of the water-bath was raised to 38° and the mixture stirred under reflux for an additional hour. The mixture was cooled to room temperature

(15) Analyses by the Microanalytical Laboratory, University of California, Berkeley.

(16) P. D. Bartlett and G. F. Woods, *J. Am. Chem. Soc.*, **62**, 2933 (1940).

(17) R. E. Buckles, R. C. Johnson and W. J. Probst, *J. Org. Chem.*, **22**, 55 (1957).

(18) A. C. Cope, T. A. Liss and G. W. Wood, *J. Am. Chem. Soc.*, **79**, 6287 (1957).

(19) E. W. Warnhoff and W. S. Johnson, *ibid.*, **75**, 494 (1953).

(20) A. S. Dreiding and J. A. Hartman, *ibid.*, **75**, 3723 (1953).

(21) L. N. Nazarov, S. N. Ananchenko and I. V. Torgov, *J. Gen. Chem. USSR, Eng. Trans.*, **26**, 939 (1956).

(22) A. S. Dreiding and S. N. Nickel, *J. Am. Chem. Soc.*, **76**, 3965 (1954).

(23) R. E. Shank and H. Shechter, *J. Org. Chem.*, **24**, 1825 (1959). The washings were done in a beaker with a porcelain spatula, each acid washing being done for only 10 seconds.

and a saturated ammonium chloride solution was added (~50 ml.) until the complex inorganic salts precipitated to the bottom of the reaction flask. The ethereal solution was decanted into a separatory funnel and the precipitated salts were washed by decantation with two 150-ml. portions of ether. The combined ethereal solution was extracted with four 100-ml. portions of saturated potassium carbonate solution, and two 100-ml. portions of saturated sodium chloride solution. The ether solution was dried over anhydrous magnesium sulfate and the ether removed at 40 mm. pressure. The residual oil was added, in a nitrogen atmosphere, to 75 ml. of a saturated methanolic solution of sodium methoxide and the resulting solution allowed to stand for 24 hours. The methanolic solution was added to 500 ml. of ether and the resulting solution was washed with saturated sodium chloride solution until the washings were no longer basic, the ethereal solution was dried, the ether and methanol removed at reduced pressure and the residual oil distilled; yield 14 g. (63%), b.p. 76–77° (10 mm.),  $n_D^{25}$  1.4886;  $\nu_{\text{max}}^{\text{CCL}_4}$  3060, 1010, 974  $\text{cm}^{-1}$ ; no bands 1800–1500  $\text{cm}^{-1}$ ; n.m.r. no vinyl proton absorption, complex series of bands with principal high field peaks at 9.35, 9.42, 9.67, 9.75, 9.77  $\tau$ .

Anal. Calcd. for  $\text{C}_7\text{H}_{12}\text{O}$  (112.17): C, 74.95; H, 10.78. Found: C, 75.09; H, 10.62.

The phenylurethan was recrystallized from carbon tetrachloride; m.p. 109–110.5°.

Anal. Calcd. for  $\text{C}_{14}\text{H}_{17}\text{O}_2\text{N}$  (231.32): C, 72.70; H, 7.41. Found: C, 72.69; H, 7.61.

*trans*-Bicyclo[4.1.0]heptane-2-ol.—Using the method described for the preparation of 2-methyl- $\Delta^2$ -cyclohexene-1-ol, from 13 g. (0.12 mole) of bicyclo[4.1.0]heptane-2-one and 4 g. (0.1 mole) of lithium aluminum hydride in 250 ml. of anhydrous ether there was obtained 11.5 g. (86%) of product; g.l.c. analysis showed two materials in the ratio of 3:7. Gas-liquid chromatographic separation of the first and lesser peak gave a material whose infrared spectrum and refractive index were the same as *cis*-bicyclo[4.1.0]heptane-2-ol. Collection of the second and major product gave the *trans* isomer;  $\nu_{\text{max}}^{\text{CCL}_4}$  3070, 1020, 974  $\text{cm}^{-1}$ ; no bands between 1800–1500  $\text{cm}^{-1}$ ; n.m.r. no vinyl proton absorption, high field multiplet between 9.34 and 9.93  $\tau$ .

Anal. Found: C, 74.95; H, 10.78.

The phenylurethan was recrystallized from hexane; m.p. 98–99°, mixed m.p. with *cis* isomer, 91–93°.

Anal. Found: C, 72.97; H, 7.22.

Bicyclo[4.1.0]heptane-2-one.—To a solution of 6.0 g. (0.053 mole) of *cis*-bicyclo[4.1.0]heptane-2-ol in 250 ml. of acetone (distilled from potassium permanganate) cooled to 25°, there was added with stirring over a 5-minute period, 24.5 ml. (0.065 mole) of a stock chromium trioxide solution (prepared from 26.72 g. of chromium trioxide in 23 ml. of concentrated sulfuric acid and diluted to 100 ml. with water).<sup>9</sup> Nitrogen was bubbled through all the solvents, reagents and reaction solution before and during the oxidation. The reaction solution was allowed to stir for an additional 5 minutes, 10 ml. of methanol added to reduce the unused chromium trioxide, the solution decanted from the chromium salts, and the salts were washed with two 150-ml. portions of acetone. The acetone was evaporated, the residue dissolved in ether, the ethereal solution washed twice with saturated sodium chloride solution and dried. The ether was evaporated at reduced pressure and the remaining oil distilled; b.p. 85.0–85.5° (10 mm.), yield 3.7 g. (63%),  $n_D^{25}$  1.4878;  $\nu_{\text{max}}^{\text{CCL}_4}$  3070, 1695, 1005  $\text{cm}^{-1}$ ; n.m.r. complex high field band between 8.75 and 8.93  $\tau$ . It has been reported<sup>10</sup> that this ketone shows a  $\lambda_{\text{max}}^{\text{EtOH}}$  220  $\mu$ ; we have found only a  $\lambda_{\text{max}}^{\text{HO}}$  200  $\mu$  ( $\epsilon$  5950) and the spectra of this and related ketones will be discussed separately.

Anal. Calcd. for  $\text{C}_7\text{H}_{10}\text{O}$  (110.15): C, 76.32; H, 9.15. Found: C, 76.66; H, 9.37.

The 2,4-dinitrophenylhydrazone was recrystallized from ethanol, m.p. 159.5–161.5° [lit.<sup>10</sup> m.p. 158°].

*cis*-Bicyclo[5.1.0]octane-2-ol.—Using the standard method described above, from 17 g. (0.14 mole) of  $\Delta^2$ -cycloheptene-1-ol, 81 g. (0.3 mole) of methylene iodide, 28 g. (0.43 mole) of zinc-copper couple and 0.2 g. of iodine, there was obtained 12.1 g. (63%) of product, b.p. 90.5–91.5° (10 mm.), m.p. 39–40°;  $\nu_{\text{max}}^{\text{CCL}_4}$  3070, 3000, 1027  $\text{cm}^{-1}$ , no bands between 1800 and 1500  $\text{cm}^{-1}$  [lit.<sup>12</sup> m.p. 42.8–43.8°,  $\nu_{\text{max}}^{\text{CCL}_4}$  3080, 2990, 1025  $\text{cm}^{-1}$ ].

The phenylurethan was recrystallized from petroleum ether; m.p. 79–80° [lit.<sup>12</sup> m.p. 76–77°].

*cis*-Bicyclo[3.1.0]hexane-2-ol.—Using the standard method described above, from 21 g. (0.25 mole) of  $\Delta^2$ -cyclopentene-1-ol,<sup>24</sup> 140 g. (0.53 mole) of methylene iodide, 39 g. (0.60 mole) of zinc-copper couple and 0.2 g. of iodine, there was obtained 18.5 g. (75%) of product, b.p. 78.0–79.5° (20 mm.),  $n_D^{25}$  1.4742;  $\nu_{\text{max}}^{\text{CCL}_4}$  3060, 1050, 1020  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_6\text{H}_{10}\text{O}$  (98.14): C, 73.43; H, 10.27. Found: C, 73.21; H, 10.27.

(24) K. Alder and F. H. Flock, *Chem. Ber.*, **89**, 1732 (1956).

*cis*-1-Methylbicyclo[4.1.0]heptane-2-ol.—Using the standard method described above, from 18 g. (0.16 mole) of 2-methyl- $\Delta^2$ -cyclohexene-1-ol, 85 g. (0.34 mole) of methylene iodide and 23 g. (0.36 mole) of zinc-copper couple in 200 ml. of ether there was obtained 10 g. (50%) of product, b.p. 68–70° (10 mm.),  $n_D^{25}$  1.4784;  $\nu_{\text{max}}^{\text{CCL}_4}$  3065, 1035, 1010  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_8\text{H}_{14}\text{O}$  (126.19): C, 76.14; H, 11.18. Found: C, 76.07; H, 11.38.

*cis*-6-Methylbicyclo[4.1.0]heptane-2-ol.—Using the standard procedure described above, from 20 g. (0.18 mole) of 3-methyl- $\Delta^2$ -cyclohexene-1-ol,<sup>25</sup> 102 g. (0.38 mole) of methylene iodide and 27 g. (0.40 mole) of zinc-copper couple in 200 ml. of ether, there was obtained 13 g. (57%) of product, b.p. 74–75° (10 mm.),  $n_D^{25}$  1.4765;  $\nu_{\text{max}}^{\text{CCL}_4}$  3050, 1040, 1000  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_8\text{H}_{10}\text{O}$  (126.19): C, 76.14; H, 11.18. Found: C, 75.87; H, 11.10.

3-Isopropyl-6-methylbicyclo[4.1.0]heptane-2-ol.—Using the standard method described above from 20 g. (0.13 mole) of a mixture of *cis*- and *trans*-3-methyl-6-isopropyl- $\Delta^2$ -cyclohexene-2-ol, prepared by lithium aluminum hydride reduction of the related ketone,<sup>26</sup> 76 g. (0.28 mole) of methylene iodide and 21 g. (0.32 mole) of zinc-copper couple in 250 ml. of ether, there was obtained 12 g. (60.5%) of a mixture of the two stereoisomeric alcohols, b.p. 71–72° (1 mm.), solidified after distillation, m.p. 58–60°;  $\nu_{\text{max}}^{\text{CCL}_4}$  3070, 1025, 1005  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{11}\text{H}_{20}\text{O}$  (168.27): C, 78.51; H, 11.98. Found: C, 78.24; H, 11.97.

*cis*-1,6-Dimethylbicyclo[4.1.0]heptane-2-ol.—Using the standard procedure described above from 6.7 g. (0.053 mole) of 2,3-dimethyl- $\Delta^2$ -cyclohexene-1-ol, 32 g. (0.12 mole) of methylene iodide and 10 g. (0.15 mole) of zinc-copper in 250 ml. of ether, there was obtained 3.5 g. (47%) of product, b.p. 73–80° (10 mm.),  $n_D^{25}$  1.4769;  $\nu_{\text{max}}^{\text{CCL}_4}$  3070, 1030, 1010  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_9\text{H}_{16}\text{O}$  (140.21): C, 77.09; H, 11.50. Found: C, 77.03; H, 11.54.

Spiro[2.5]octane-2-ol.—Using the standard procedure described above, from 17.5 g. (0.14 mole) of 2-methylenecyclohexane-1-ol,<sup>27</sup> 81 g. (0.30 mole) of methylene iodide and 28 g. (0.43 mole) of zinc-copper couple in 200 ml. of ether, there was obtained 12 g. (68%) of product, b.p. 76–78° (20 mm.),  $n_D^{25}$  1.4772;  $\nu_{\text{max}}^{\text{CCL}_4}$  3080, 1015, 1000  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_8\text{H}_{14}\text{O}$  (126.19): C, 76.14; H, 11.18. Found: C, 75.88; H, 10.91.

Spiro[2,4]heptane-2-ol.—Using the standard procedure described above, from 7.6 g. (0.078 mole) of 2-methylenecyclopentane-1-ol,<sup>27</sup> 48 g. (0.18 mole) of methylene iodide and 14.5 g. (0.22 mole) of zinc-copper couple in 150 ml. of ether, there was obtained 6.5 g. (74%) of product, b.p. 100° (68 mm.),  $n_D^{25}$  1.4717;  $\nu_{\text{max}}^{\text{CCL}_4}$  3080, 1080, 1012, 992  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_7\text{H}_{12}\text{O}$  (112.17): C, 74.95; H, 10.78. Found: C, 74.64; H, 10.52.

7-Methylspiro[2,5]octane-2-ol.—Using the standard procedure described above, from 6.5 g. (0.052 mole) of a stereoisomeric mixture of 2-ethylidenecyclohexane-1-ols, 35 g. (0.13 mole) of methylene iodide and 10 g. (0.15 mole) of zinc-copper couple in 200 ml. of ether, there was obtained 3.5 g. (49%) of product, b.p. 73–74° (5 mm.),  $n_D^{25}$  1.4760;  $\nu_{\text{max}}^{\text{CCL}_4}$  3060, 1010, 990  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_9\text{H}_{16}\text{O}$  (140.21): C, 77.09; H, 11.50. Found: C, 77.35; H, 11.63.

*cis*-2-Bicyclo[4.1.0]heptyl Methyl Ether.—To a well-stirred suspension of 6 g. (0.25 mole) of sodium hydride powder in 300 ml. of anhydrous ether, there was added a solution of 10 g. (0.09 mole) of *cis*-bicyclo[4.1.0]heptane-2-ol in 50 ml. of anhydrous ether over a period of 30 minutes and the mixture was allowed to stir for an additional 2 hours. To this mixture there was added 45 g. (0.32 mole) of methyl iodide and the stirring was continued for an additional 48 hours. At the end of this period, the excess sodium hydride was decomposed by cautious addition of a 1:1 ether-methanol solution until no further exothermic reaction was noted and then saturated ammonium chloride solution was added until the inorganic salts precipitated. The ethereal solution was decanted and the inorganic salts were washed by decantation with two 150-ml. portions of ether. The combined ethereal decantations were washed with three 200-ml. portions of saturated sodium chloride solution and dried over magnesium sulfate. The ether and excess methyl iodide were removed by distillation at atmospheric pressure and the residual oil distilled, b.p. 60° (40 mm.), yield 9 g. (80%),  $n_D^{25}$  1.4746;  $\nu_{\text{max}}^{\text{CCL}_4}$  3060, 1190, 1100, 1025, 970  $\text{cm}^{-1}$ .

(25) M. Mousseron, R. Jacquier, M. Mousseron-Canet and R. Zagdoun, *Bull. soc. chim. France*, **19**, 1042 (1952).

(26) A. K. Macbeth, B. Milligan and J. S. Shannon, *J. Chem. Soc.*, 901 (1953).

(27) A. S. Drieding and J. A. Hartman, *J. Am. Chem. Soc.*, **75**, 939 (1953).

*Anal.* Calcd. for  $C_8H_{14}O$  (126.19): C, 76.14; H, 11.18. Found: C, 76.21; H, 11.30.

A g.l.c. of the product on a 50-ft. capillary column coated with Apiezon and run at 80° showed only one peak. A chromatogram of a mixture of *cis*- and *trans*-2-bicyclo[4.1.0]heptyl methyl ether (prepared using the above etherification method on a mixture of *cis*- and *trans*-bicyclo[4.1.0]heptane-2-ol) showed the expected two peaks.

*cis*- and *trans*-2-Methylcyclohexyl Methyl Ether.—Using the above etherification method, from 5.0 g. (0.044 mole) of commercial 2-methylcyclohexanol (shown to contain 90% *trans* and 10% *cis* isomer by g.l.c. with a glycerol column at 100°), 3.0 g. (0.125 mole) of sodium hydride powder and 22 g. (0.150 mole) of methyl iodide, there was obtained 4.8 g. (86%) of product.

Gas-liquid chromatographic separation of the product at 50° gave two fractions, of which the first was present to the extent of 10% and was assigned the *cis* configuration. A portion of this fraction was isolated and showed  $n_D^{25}$  1.4334;  $\nu_{max}^{C-Cl}$  2940, 1215, 1190, 1150, 1100, 925, 890, 860  $cm^{-1}$ .

*Anal.* Calcd. for  $C_8H_{16}O$  (128.20): C, 74.94; H, 12.58. Found: C, 74.74; H, 12.83.

The second fraction was present to the extent of 90% and was assigned the *trans* configuration. A portion of this fraction was collected and shown to have  $n_D^{25}$  1.4302;  $\nu_{max}^{C-Cl}$  2940, 1190, 1160, 1110, 995, 985, 920  $cm^{-1}$ , no band between 900 and 850  $cm^{-1}$ .

*Anal.* Found: C, 74.69; H, 12.42.

*cis*- and *trans*-3-Methylcyclohexyl Methyl Ether.—Using the above etherification process, from 11.4 g. (0.1 mole) of an isomeric mixture of 3-methylcyclohexanols (shown to contain 30% *trans* and 70% *cis* isomer by g.l.c. at 100°), 5.0 g. (0.21 mole) of sodium hydride powder and 40 g. (0.28 mole) of methyl iodide, there was obtained 10.7 g. (85%) of product.

Gas-liquid chromatographic separation of the product at 70° gave two fractions of which the first was present to the extent of 30% and assigned a *trans* configuration. A portion of this fraction was isolated and shown to have  $n_D^{25}$  1.4303;  $\nu_{max}^{C-Cl}$  1250, 1195, 1150, 1090, 985, 925  $cm^{-1}$ .

*Anal.* Calcd. for  $C_8H_{16}O$  (128.20): C, 74.94; H, 12.58. Found: C, 75.04; H, 12.73.

The second fraction was present to the extent of 70% and assigned the *cis* configuration. A portion of this fraction was collected and shown to have  $n_D^{25}$  1.4300;  $\nu_{max}^{C-Cl}$  1200, 1165, 1110, 1080, 985, 970, 925  $cm^{-1}$ .

*Anal.* Found: C, 75.04; H, 12.73.

**Raney Nickel Used in Hydrogenolysis.**—A 20-g. portion of commercial<sup>28</sup> Raney nickel stored under water was washed five times with 100-ml. portions of water, five times with 100-ml. portions of 95% ethanol, and stored under 95% ethanol. Best results were obtained when the catalyst was used immediately.

**Hydrogenolysis of *cis*-2-Bicyclo[4.1.0]heptyl Methyl Ether.**—A mixture of 2 g. of *cis*-2-bicyclo[4.1.0]heptyl methyl ether and 1 g. of Raney nickel was placed in a glass liner and the liner placed in a high pressure bomb. The temperature was raised to 220° and the initial pressure of hydrogen at this temperature was 2800 pounds. The mixture was shaken at this temperature for 12 hours, the bomb cooled, and the contents diluted with 20 ml. of ether, and the suspension filtered. The ether was distilled and there was obtained a residue of 1.7 g. of liquid.

Gas-liquid chromatographic separation of the residue at 70° gave three fractions, the first of which was present to the extent of 40%. A portion of this fraction was collected and shown to have  $n_D^{25}$  1.4333 and the same infrared spectrum as *cis*-2-methylcyclohexyl methyl ether. The second fraction was present to

the extent of 10%. A portion of this fraction was collected and shown to have  $n_D^{25}$  1.4300 and an identical infrared spectrum as *cis*-3-methylcyclohexyl methyl ether. The third fraction was present to the extent of 50% and collection of a portion of the fraction showed the material to be identical with the starting bicycloheptyl methyl ether.

**Reaction of Equimolar Quantities of  $\Delta^2$ -Cyclohexene-1-ol and Cyclohexene with Methylene Iodide and Zinc-Copper Couple.**—To a mixture of 26.7 g. (0.12 mole) of methylene iodide and 9.3 g. (0.14 mole) of zinc-copper couple in 150 ml. of ether, there was added 9.8 g. (0.1 mole) of  $\Delta^2$ -cyclohexene-1-ol and 8.2 g. (0.1 mole) of cyclohexene. The mixture was stirred vigorously and heated with an infrared lamp. When the reaction became self-supporting, as indicated by continued refluxing of the ether, the lamp was removed and the reaction flask immersed in a water-bath held at 40°. The stirring was continued and the reaction allowed to continue for an additional 2 hours. The reaction was processed in the usual fashion and removal of the ether at atmospheric pressure gave 16.5 g. of liquid residue. This material was distilled to yield 6.4 g. of distillate, b.p. 70–83°, and 10.1 g. of residual material.

Gas-liquid chromatography of the distillate at 30° showed only one peak. This compound was isolated and shown to have the same infrared spectrum as cyclohexene. The residual product was separated by g.l.c. at 100° and shown to contain two fractions, the first of which was present to the extent of 40%. A portion of this fraction was isolated and shown to have the same infrared spectrum as  $\Delta^2$ -cyclohexene-1-ol. The second fraction was present to the extent of 60% and a portion of this fraction was collected and shown to have the same infrared spectrum as *cis*-bicyclo[4.1.0]heptane-2-ol. The chromatograms of the distillate and the residue gave no indication of the presence of bicyclo[4.1.0]heptane.

**Reaction of  $\Delta^2$ -Cyclopentene-1-ol with a Stoichiometric Amount of Iodomethylzinc Iodide.**—To a well-stirred mixture of 8 g. (0.12 mole) of zinc-copper couple in 200 ml. of anhydrous ether, there was added 27 g. (0.10 mole) of methylene iodide. The reaction was initiated in the usual manner and heated under reflux for 3.5 hours. The mixture was cooled to room temperature, the insoluble material allowed to settle and 150 ml. of the clear solution was pipetted through a cotton plug into a clean dry flask. A 5-ml. portion of this solution was allowed to react with a solution of iodine in ether and the unreacted iodine titrated with thiosulfate solution. It was found that there was 0.94 mmole of reagent per 5 ml. of solution; thus in the reaction flask there was 27 mmoles of reagent. To this solution was added 2.3 g. (27 mmoles) of  $\Delta^2$ -cyclopentene-1-ol and the solution was heated under reflux for 12 hours. The reaction mixture was worked-up in the usual fashion and there was obtained 2.4 g. of crude product (free of ether but containing about 10% of methylene iodide); g.l.c. analysis showed the presence of 21–22 moles of product, or a yield of 78–82%. In this analysis it is to be noted that the starting material gives twice the peak height as the product.

**Reaction of  $\Delta^2$ -Cyclohexenyl Methyl Ether with Methylene Iodide and Zinc-Copper Couple.**—Using the standard procedure, from 8.0 g. (0.07 mole) of  $\Delta^2$ -cyclohexenyl methyl ether, 24 g. (0.084 mole) of methylene iodide and 6.5 g. (0.098 mole) of zinc-copper couple, there was obtained 7 g. of product.

Gas-liquid chromatographic separation of the material at 95° gave two fractions, the first of which was present to the extent of 30% and shown to be starting ether. The second fraction was present to the extent of 70% and collection of a portion of the material showed it to be *cis*-2-bicyclo[4.1.0]heptyl methyl ether.

In an identical run using the same molar proportions, there was obtained from  $\Delta^2$ -cyclohexene-1-ol a yield of 60% of bicyclic product and 40% of starting material was recovered.

(28) Raney Catalyst Co., Chattanooga, Tenn.