the liquid state are associated through the formation of hydrogen bonds. The OH band appears at longer wave lengths and is much broader in the liquid than in the vapor state.[5] The changes in the character of this band as the alcohol passes from the vapor state to the liquid state are evidence that the OH group participates in the association process. Although in ethyl acetate and in ethyl formate the OH band is shifted to the shorter wave lengths, and this may indicate the breaking of hydrogen bonds between the alcohol molecules, the band does not become sharp, as it does for alcohol in the vapor state. It may be possible to interpret these results by assuming that as the ester content in the mixture is increased the polymerization of the alcohol is decreased and that the alcohol becomes associated to some degree with the ester through the formation of weak hydrogen bonds between the hydroxyl group of the alcohol and the carbonyl group of the ester. This would account for the shift to the longer wave lengths and the increase in intensity of the band associated with the carbonyl group, and it is in accord with the results of the previous investigations.[3]

The writers wish to express gratitude to Dr. E. K. Plyler for the use of his laboratory facilities.

Summary

Ethyl formate and ethyl acetate were found to shift the OH band of methyl alcohol to the shorter wave lengths and to increase its intensity. The CO band of the esters was shifted to the longer wave lengths by the alcohol, and its intensity was increased correspondingly. As a possible means of accounting for these results it was suggested that the esters may tend to decrease the polymerization of the alcohol, and to become associated with it, to some degree, through the formation of weak hydrogen bonds.

CHAPEL HILL, N. C. RECEIVED JANUARY 6, 1937

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[5] E. L. Kinsey and J. W. Ellis, *Phys. Rev.*, **49**, 105 (1936).

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Pinacol Rearrangement of *cis*- and *trans*-1,2-Dimethylcyclohexanediol-1,2 and the Relationship of the Walden Inversion to the Mechanism of Molecular Rearrangements

BY PAUL D. BARTLETT AND IRVING PÖCKEL

The course of a molecular rearrangement has been observed in some cases to depend upon the conditions of the rearrangement[1] and upon the configuration of the rearranging compound.[2] The dependence of the course of reaction upon configuration in the alicyclic series has been studied hitherto only for cases of *semi*-pinacolic rearrangements such as that of 1-methylcyclohexanediol-1,2. When the *cis*-isomer of this compound forms 2-methylcyclohexanone on dehydration, it is ascribed to a direct elimination of water, molecular rearrangement occurring to an important extent only in the *trans*-isomer, where ring contraction makes the rearrangement evident.

We have undertaken the study of an actual pinacol rearrangement, where vinyl dehydration is impossible, and where the results tell us directly the effect of configuration upon the relative ease of migration of two organic radicals. There is little doubt of the configurations of the 1,2-diols in the cyclohexane series. The ultimate criterion in this series is the resolution of the *trans*-cyclopentanediol and *trans*-cyclohexanediol into optical isomers.[3] A number of independent criteria, most of them due to Böeseken and his co-workers, support the generalization that where the two isomeric diols can be prepared, one by hydration of the corresponding epoxide and the other by aqueous permanganate oxidation of the corresponding cyclohexene, the former has the *trans* and the latter the *cis* configuration. The isomeric 1,2-dimethylcyclohexanediols-1,2 have been prepared by these methods, and hence although neither of them has been resolved, their configurations are known with a high degree of probability.

The *trans*-pinacol, m. p. 92–92.5°, prepared by hydrolysis of the oxide, was rearranged by Namet-

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[1] Bartlett and Rosenwald, THIS JOURNAL, **56**, 1990 (1934).

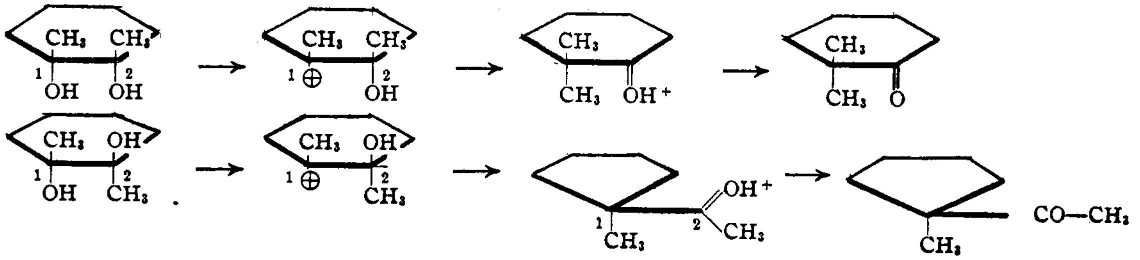
[2] Tiffeneau and Tchoubar, *Compt. rend.*, **199**, 360, 1624 (1934); *ibid.*, **202**, 1931 (1936).

[3] Derx, *Rec. trav. chim.*, **41**, 333 (1922); Van Loon, Thesis, Delft, 1929, p. 51; Helferich, Burkhardt and Hiltmann, *Ber.*, **70**, 308 (1937).

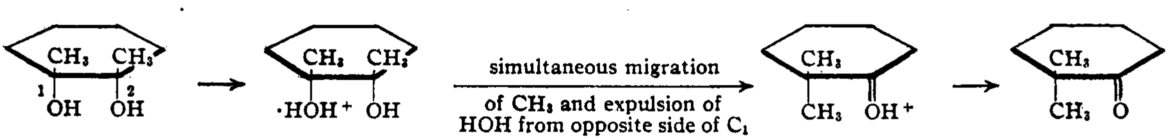
kin and Delektorsky[4] and found to give 1-methyl-1-acetylcyclopentane in 78% yield (semicarbazone, m. p. 140.5–141°). We repeated this experiment for the sake of standardizing our conditions and then, using the same procedure (boiling with 20% sulfuric acid), carried out the rearrangement of the *cis*-pinacol, m. p. 38.5–39.1°, prepared by the action of aqueous permanganate on 1,2-dimethylcyclohexene-1. The sole product of this rearrangement was 2,2-dimethylcyclohexanone, whose semicarbazone, m. p. 202–204° with decomposition, was isolated in 74% yield and unmixed with any of its lower melting isomer.

These observations have an important bearing on the mechanism of the pinacol rearrangement. This reaction is included by Whitmore among those rearrangements which proceed because a carbon atom exists with an "open sextet" of electrons,[5] which becomes completed by the migration of an organic radical with its electron pair. Despite the success of this theory in correlating facts and predicting the course of reactions, its users have been rather cautious not to speak literally of positive carbonium ions. Recently skepticism has been growing concerning the actual existence of such ions in metathetical reactions.[6]

In the present reaction we are dealing with the relative migration aptitudes of two groups, the methyl group and that group which is a part of the cyclohexane ring.



The space relations cannot be pictured exactly, since the cyclohexane ring is non-planar and the *cis* groups may be at any angle to each other within a range of angles determined by the mobility of the ring. However, the *average* positions of the groups, if the ring is mobile, are shown in the formulas. In the *cis*-pinacol, the ring carbon atom and the methyl group which migrates are about equally remote from the hydroxyl group which is eliminated in the reaction. In the *trans*-pinacol, the ring carbon atom which migrates is much more remote from the replaced hydroxyl group than the methyl. In other words, a group migrates by preference which is located in space near the ***opposite side*** of carbon atom No. 1 to that occupied by the hydroxyl group which is to be replaced. This is inconsistent with the idea that the hydroxyl group is actually removed before the migration occurs, for then the radical most accessible to the open spot on carbon No. 1 would surely be the one to migrate. The fact that different products result from the two stereoisomers also excludes the formation of a racemizable "open sextet," as do the pinacolic and semi-pinacolic deaminations of McKenzie,[7] which yield optically active products. There remains only the possibility that the migration of carbon and the expulsion of the hydroxyl are simultaneous processes. The preferred migration of the radical situated near the back side of the carbon atom No. 1 brings out a very strong resemblance between the pinacol rearrangement and those replacement reactions[8] in which it has been so elegantly shown that Walden inversion attends every act of replacement. Whether or not a Walden inversion mechanism is the only one by which a pinacol rearrangement occurs, this case in which the inversion mechanism is the preferred one seems to justify the modification of the "open sextet" theory as indicated in the scheme



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[4] Nametkin and Delektorsky, *Ber.*, **57**, 583 (1924).

[5] Whitmore, THIS JOURNAL, **54**, 3274 (1932).

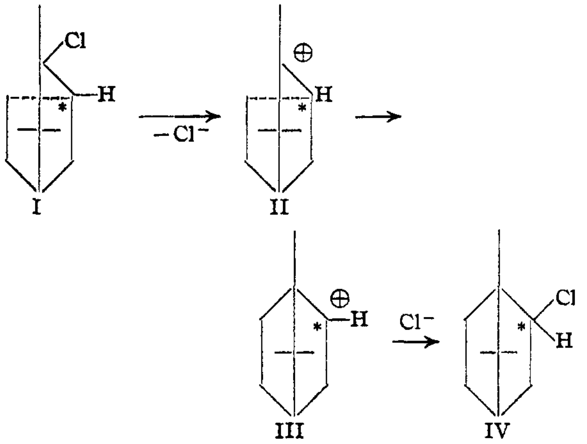
[6] Ogg, paper presented at the Symposium on Molecular Structure, Princeton, N. J., January 2, 1937; Wallis and Bowman, *J. Org. Chem.*, **1**, 383 (1936), especially p. 387.

[7] McKenzie, Roger and Wills, *J. Chem. Soc.*, 779 (1926); Roger and McKenzie, *Ber.*, **62**, 272 (1929).

[8] Olson and Long, THIS JOURNAL, **56**, 1294 (1934); Hughes, Juliusburger, Masterman, Topley and Weiss, *J. Chem. Soc.*, 1525 (1935).

A similar mechanism was written by Wallis and Bowman[6] for the more complicated case of a dehydration by thionyl chloride.

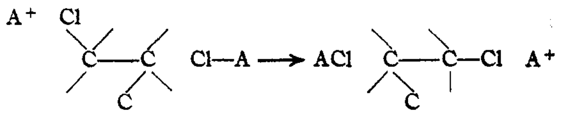
The "open sextet" theory has been of the greatest service in correlating the facts of the Wagner–Meerwein rearrangement. The extensive and careful work of Meerwein and van Emster[9] showed that the conversion of camphene hydrochloride (I) into isobornyl chloride (IV), which is promoted by solvents like sulfur dioxide, cresol, and nitromethane, and by such catalysts as hydrogen chloride, stannic and ferric chlorides, could be formulated as follows



From the standpoint of the existence of free ions, it is a most remarkable property of this rearrangement that of the two possible stereoisomeric chlorides, differing in the configuration of the starred carbon atom, only one—isobornyl chloride—is the direct product. Its isomer, bornyl chloride, is nevertheless the more favored at equilibrium, and is produced very slowly by the same reagents on long standing. The bond represented by the dotted line in the camphene formulas is, in space, behind the vertical bond which it crosses in the diagram. Therefore, if the simple ionization picture were correct, the only explanation for the formation of isobornyl chloride would be that the chloride ion caught the ion III with its open face still to the rear, in the place vacated by the migrating bond. This demands that isobornyl chloride should have the "endo" configuration, advocated by Lipp,[10] rather than the "exo" assignment of Vavon[11] and Hückel.[12] The recent work of Asahina, Ishidate and Sano[13] has shown that isoborneol in fact possesses the "exo" configuration.

It is not rigorously certain that isobornyl chloride is configuratively related to isoborneol, but all evidence points in this direction. This chloride is produced from borneol under conditions normally leading to Walden inversion.[14] Furthermore, the Wagner–Meerwein rearrangement can be duplicated with an acetate radical instead of the chlorine, by treating camphene with acetic and sulfuric acids (Bertram–Walbaum reaction), and the product in this case is isobornyl acetate, which can be hydrolyzed normally to isoborneol, almost certainly without change of configuration.

We can only conclude that the Wagner–Meerwein rearrangement involves complete Walden inversion at the starred carbon atom. This is incompatible with any reasonable deductions from the literal open sextet theory, and is equally incompatible with a series of steps involving solvated carbonium ions which undergo inversion at every reaction. It is completely compatible with a "push and pull" theory analogous to the one advanced by Lowry[15] for acid–base catalysis, in which donors and acceptors of protons are replaced by donors and acceptors of chloride ions, and a Walden inversion occurs at each replacement involving the halogen ion. Such a mechanism may be represented schematically thus



In this representation ACl is any compound capable of yielding a chloride ion, and the three carbon atoms are those three of the camphene-isobornyl system which actually participate in the rearrangement.

Meerwein and van Emster state that the rearrangement is a first order reaction, and this can of course not be literally true if the mechanism we have outlined is correct. Two observations of these authors show the way to the explanation. In the first place, hydrogen chloride is a powerful catalyst for the rearrangement;

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(9) Meerwein and van Emster, *Ber.*, **53**, 1815 (1920); **55**, 2500 (1922).

(10) Lipp, *Ann.*, **480**, 298 (1930).

(11) Vavon, *Bull. soc. chim.*, [4] **39**, 925 (1926).

(12) Hückel, *Ann.*, **477**, 157 (1930).

(13) Asahina, Ishidate and Sano, *Ber.*, **69**, 343 (1936).

(14) Wallach, *Ann.*, **230**, 231 (1885); Wagner and Brykner, *Ber.*, **32**, 2307 (1899).

(15) Lowry and Faulkner, *J. Chem. Soc.*, 2883 (1925); Lowry, *Chem. Rev.*, **4**, 231 (1927).

and in the second place, hydrogen chloride is always present in any solution of camphene hydrochloride, for this compound dissociates rapidly and reversibly into hydrogen chloride and camphene. In most of the solutions used by Meerwein the degree of dissociation was determined as being between 5 and 10%, and the dissociation equilibrium was established rapidly enough to be maintained throughout the reaction.

Now, either hydrogen chloride or the free chloride ion might act as a chloride donor, and either hydrogen chloride or solvated hydrogen ion might act as a chloride acceptor. The purpose of the present discussion is not to decide among these possibilities, but to present a recalculation of the kinetic data of Meerwein and van Emster, showing that two different kinetic formulations, based upon the "push and pull" theory, both fit these data better than the first order formulation used by the original investigators.

If x is the concentration of camphene hydrochloride, at equilibrium with a small concentration y of hydrogen chloride and of camphene, then at all times

$$y^2 = K^2x$$

where K^2 is the equilibrium constant of dissociation. In most of the solvents employed, it is proper to treat the hydrogen chloride thus as completely non-ionized, for they are solvents of far less basicity than water or the alcohols. We may now suppose two alternative kinetic situations, which are representative but do not exhaust the possibilities.

CASE I.—Suitable collision between the camphene hydrochloride and a single hydrogen chloride molecule, acting as either donor or acceptor (or a hydrogen and a chloride ion), is sufficient to bring about reaction. In this case

$$-\mathrm{d}x/\mathrm{d}t = kxy = kx \times K\sqrt{x} = kKx^{3/2}$$
$$\text{and} \quad 1/\sqrt{x} - 1/\sqrt{x_0} = (1/2)kKt$$

where x_0 is the initial value of x.

CASE II.—The reaction is brought about by suitable collision between a camphene hydrochloride molecule and *two* hydrogen chloride molecules (one acting as donor and one as acceptor). Then

$$-\mathrm{d}x/\mathrm{d}t = kxy^2 = kK^2x^2, \quad \text{and}$$
$$(1/x) - (1/x_0) = kK^2t$$

These assumptions lead, respectively, to 3/2-order and to second-order kinetic equations.

Meerwein and van Emster report the original data for reaction in ten solvents, of which one run, that with petroleum ether as solvent, was so slow that it was carried only to about 10% of total reaction. The other nine were followed to about 60% reaction. In order to make the fairest possible comparison between the first, three-halves, and second order formulations for these nine runs we have used the method of normal equations to pass the best straight line, in each of the twenty-seven cases, through the points which are supposed to lie on a straight line. The mean deviations of the points from the straight line have then been reduced to a common scale, with the slope of each line taken as the unit, so that the reduced mean deviations represent the fractional error in the value of k which would be made by computing k from two points an hour apart, one of which was in error by the mean deviation. This procedure eliminates the undue emphasis on the initial point of each curve which is inherent in the method used by Meerwein and van Emster.[15a] In each case the first value of k as determined by them is much lower than those determined from subsequent points. This is in accordance with the "push and pull" mechanism, which demands a short incubation period while the camphene hydrochloride is dissociating, but the least squares treatment shows that the second point is by no means so far off the curve as is suggested by the successive constants of Meerwein and van Emster.

As an example of this treatment we may show the fitting of a second order kinetic equation to the data on the rearrangement in benzene at 40°. The solution of the normal equations leads to the most probable straight line given by

$$1/x = 0.00995 + 0.0000496t$$

in which for convenience the unit of x is taken as one-hundredth of the initial concentration (Meerwein's results are tabulated in terms of per cent.). In the following table, the values in the "calculated" column are those obtained with the use of this equation.

The superiority of this formulation over the 3/2-order and first order is shown both by its lower reduced mean deviation (Table II) and by the

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[15a] Even the method used by Meerwein and van Emster leads to the same conclusions with regard to the order of the reaction. We have also applied a more exact formulation taking into account the fact that not x, but $x + y$, is the quantity whose rate of change determines the order of the reaction. This formulation also produces no change in the conclusions, and makes such a minor correction in each case that for our present purpose the simpler formulation seems preferable.

TABLE I

RATE OF REARRANGEMENT OF CAMPHENE HYDROCHLORIDE IN BENZENE AT 40°

Hours	1/x (obsd.)	1/x (calcd.)	Deviation × 10^5
0	0.01000	0.00995	− 5
17	.01066	.01079	+13
42	.01205	.01203	− 2
66	.01310	.01322	+12
95	.01502	.01466	−36
143	.01696	.01704	+ 8
192	.01941	.01947	+ 6
		Average	12

Reduced mean deviation = 0.00012/0.0000496 = 2.36

fact (Table I) that the deviations alternate in sign, indicating that the points are without trend, while the signs of the deviations in the other two formulations clearly indicate a curvature.

Table II summarizes the results of the comparison of formulations for the nine solvents.

TABLE II

COMPARISON OF FIRST, THREE-HALVES AND SECOND-ORDER FORMULATIONS FOR THE WAGNER–MEERWEIN REARRANGEMENT IN VARIOUS SOLVENTS

Solvent	Temp., °C.	Reduced mean deviation for order of reaction First	Three-halves	Second
Chlorobenzene	40	3.17	1.16	0.79
Benzene	40	6.69	3.81	2.36
Nitromethane	20	0.12	0.06	0.05
Ethyl bromide	40	3.08	1.89	.84
Acetonitrile	20	0.52	0.15	.08
Benzonitrile	20	.97	.51	.20
Nitrobenzene	20	.40	.17	.25
Anisole	40	1.45	.54	.73
Bromobenzene	40	1.36	.58	.67

It should be mentioned that as measures of precision the reduced mean deviations as we have taken them are only horizontally comparable; multiplication for each run by the total number of hours of the run would make them vertically comparable in the table, but would not affect the comparison between different methods of formulation.

It is seen that for the first six solvents in the table the second-order formulation is the best; for the last three solvents, the three-halves order formulation is the best; and in all cases the first-order is much the worst. Further experimental work, which is being undertaken in this Laboratory, will be necessary to decide specifically the mechanism of this process, and to sort out the various types of "pushes and pulls" which might lead to these or intermediate orders of reaction.[16] Meanwhile, we can only be impressed with the excellence of the pioneer experimental work of Meerwein, which after fifteen years of accumulated experience still throws new light on this difficult problem.

Experimental

cis-1,2-Cyclohexanediol-1,2 was prepared by the method of Wallach.[17] It was crystallized from hexane with the aid of solid carbon dioxide, and melted at 38.5–39.1°.

Rearrangement of the *cis*-Pinacol.—0.43 g. of the *cis*-pinacol was boiled with 20% sulfuric acid and the product, a ketone of peppermint-like odor, was removed by steam distillation. The semicarbazone was prepared directly by allowing the product to stand with 0.34 g. of semicarbazide hydrochloride and 0.40 g. of sodium acetate in 40 cc. of water. The semicarbazone was obtained in a yield of 0.41 g. (74.2% based on the pinacol) and melted at 202–204° (dec.). 2,2-Dimethylcyclohexanone-1 and its semicarbazone have been made by Meerwein,[18] and by Auwers and Lange.[19] The melting point given by Meerwein is 200–201°. The isomeric ketone from the rearrangement of the *trans*-pinacol yields a semicarbazone melting at 140.5–141°.[20]

Summary

1. The pinacol rearrangement of 1,2-dimethylcyclohexanediol-1,2 takes different courses for the *cis*- and *trans*-isomers, a carbon atom migrating in each case which is, on an average, remote in space from the adjacent hydroxyl group which it replaces.

2. An interpretation of the pinacol rearrangement as involving Walden inversion at the carbon atom where replacement occurs is derived from these facts.

3. The modification of the "open sextet" theory so introduced, if extended to the Wagner–Meerwein rearrangement of camphene hydrochloride into isobornyl chloride, is consistent with the configurations of borneol and isoborneol recently assigned by chemical methods, while a literal "open sextet" theory is not.

4. It now becomes necessary to regard this Wagner–Meerwein rearrangement, not as a spontaneous intramolecular process, but as one involving donors and acceptors of chloride ion, quite analogous to the acid–base catalysis of Lowry.

5. A thorough recalculation of the kinetic data of Meerwein and van Emster shows that

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(16) A hydrogen ion as acceptor and a hydrogen chloride molecule as donor would lead to a reaction of the 7/4 order.

(17) Wallach, *Ann.*, **396**, 280 (1913).

(18) Meerwein, *ibid.*, **405**, 143 (1914).

(19) Auwers and Lange, *ibid.*, **401**, 321 (1913).

(20) Nametkin and Delektorsky, *Ber.*, **57**, 583 (1924).

either a three-halves order or a second order formulation of this rearrangement, derivable from the donor-acceptor theory, will fit the facts better than the first-order formulation used by these authors.

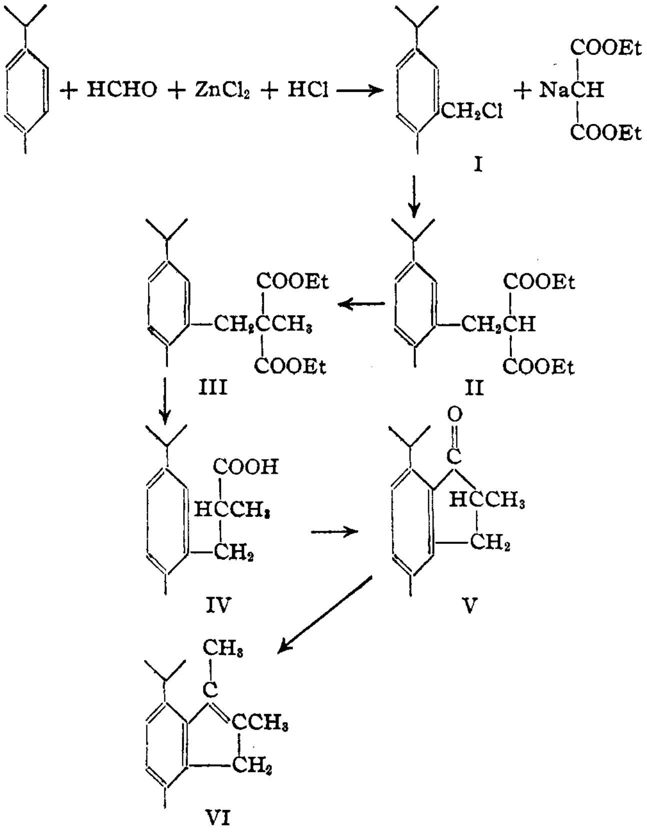
CAMBRIDGE, MASS. RECEIVED MARCH 8, 1937

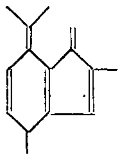
[CONTRIBUTION FROM THE NEW ZEALAND COÖPERATIVE RENNET CO., LTD.]

The Synthesis of 1,2,4-Trimethyl-7-isopropylindene

BY WALTER G. WHITTLESTON

The following equations represent the manner in which the synthesis of 1,2,4-trimethyl-7-isopropylindene was carried out



The synthesis was carried out with the object of producing a substance which on reduction and dehydrogenation would yield a compound of the structure 

Owing to shortage of materials and time, this was not completed.

The Introduction of the Chloromethyl Group into *p*-Cymene.—The first method attempted was that of Rapson and Short[1] in which *p*-cymene, anhydrous zinc chloride and paraformaldehyde were stirred into an emulsion and dry hydrogen chloride bubbled through the rapidly stirred mixture. This method was unsuccessful. It may be mentioned here that the yield obtained by the above authors, calculated on the basis of the amount of *p*-cymene taken at the start of the preparation, was 43%, and not the higher figure which they give.

The method due to Blanc[2] was finally employed, 40% aqueous formaldehyde being used in the place of paraformaldehyde. By employing apparatus in which the hydrogen chloride was distributed to the reaction mixture by a rapidly rotating hollow paddle stirrer, and keeping the temperature at 60° in a thermostatic bath, together with the use of nickel chloride as a catalyst, it was possible to get better yields than those of Blanc. The use of a small amount of nickel chloride reduced the production of tarry by-products in the reaction, and so made it much more efficient and convenient.

The preparation of diethyl methyl-(2-*p*-cymylmethyl)-malonate was carried out using the usual methods. This substance was saponified and decarboxylated. The acid chloride was prepared by the use of thionyl chloride, and after removal of the hydrogen chloride and sulfur dioxide by boiling, ring closure was effected by the addition of anhydrous aluminum chloride. The resultant ketone on treatment with methylmagnesium iodide gave 1,2,4,-trimethyl-7-isopropylindene.

Experimental

All temperatures are uncorrected. I. 2-*p*-Cymylmethyl Chloride.—Fifty grams of *p*-cymene, 20 g. of zinc chloride (anhyd.), 1 g. of nickel chloride and 40 g. of 40% formalde-

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[1] Rapson and Short, *J. Chem. Soc.*, 128 (1933).

[2] Blanc, *ibid.*, Ai, 549 (1923).