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Methanolysis of Optically Active Hydrogen 2,4-Dimethylhexyl-4-phthalate[1,2]

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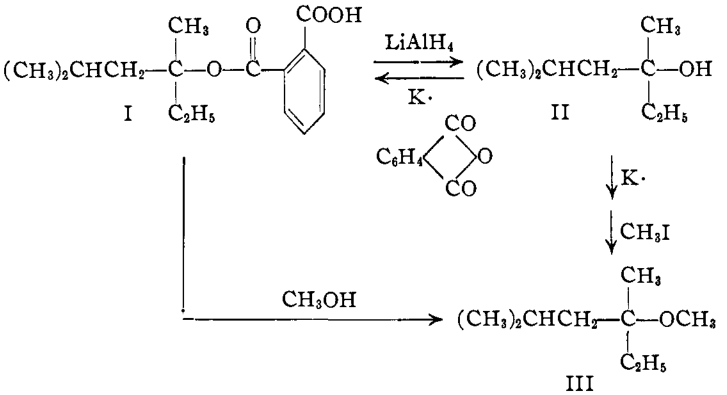
The optically active tertiary alkyl ester, hydrogen 2,4-dimethylhexyl-4-phthalate (I), has been solvolyzed in methanol to 4-methoxy-2,4-dimethylhexane (III) with about 54% inversion and 46% racemization of configuration. This outcome is so different from the 100% racemization demanded by a free carbonium ion intermediate that a new structural hypothesis for the intermediate is proposed.

The stereochemical characteristics of the displacement reaction about a tertiary carbon atom being presently unknown, an investigation has been initiated by observing the methanolysis of the recently resolved hydrogen 2,4-dimethylhexyl-4-phthalate (I).[4]

Among the prerequisites for mechanistic significance are knowledge of the configurational and specific rotational relationships of I, 2,4-dimethylhexan-4-ol (II) and 4-methoxy-2,4 dimethylhexane (III), the product of methanolysis, and knowledge of the behavior of I, II and III in boiling methanolic phthalic acid, essentially the condition of the methanolysis.

The stereochemical relationship of I and II has been derived from two experiments[4]; the one in which I (+7.35°)[5] is converted with lithium aluminum hydride to II (−2.72°), and the other in which repetition of the experiment with I (−1.64°) was followed by treatment of the resulting II as its potassium salt with phthalic anhydride, I (−1.62°) being recovered.



Having thus demonstrated that these reactions proceed without racemization and, to a high degree of probability, without alteration of configuration, one concludes that +I and −II are configurationally identical and that the ratio of rotations of II and I is −0.37.

The configurational identity of −II and −III is derivable from the fact that II (−0.30°) as its potassium salt is transformed by methyl iodide to III (−0.78°), a reaction which is so similar to that of the potassium salt of II with phthalic anhydride in which complete retention of configuration obtains, that there is no reason to doubt the absence of stereochemical alteration. The ether produced is infrared-spectroscopically free of carbinol (Fig. 1, curve II).[6] Thus +I, −II and −III are configurationally related with the ratio of rotation of III and II being +2.6 and that of III and I being −0.96.

That the methanolysis of I, a reaction in which methyl ether III is obtained infrared-spectroscopically free of carbinol II (Fig. 1, curve I), proceeds without simultaneous racemization of I is shown by the fact that I of substantially unchanged rotation (+2.9°) is recovered in 25% yield from an incomplete (36 hr.) methanolysis of I (initial rotation +3.1°).

Optically active ether III is slowly racemized in boiling absolute methanol containing one molar equivalent of phthalic acid. On 9 days' boiling the rotation decreases from +1.43 to +1.01°, corresponding to 29% racemization. In subsequent calculations the very approximate assumption is made that III is racemized 3 1/3% per day under the methanolysis conditions.

The question of whether ether III is the primary isolable product of the methanolysis or whether it is produced by way of an intermediate cannot be answered generally, but specifically the possible intervention of carbinol II or conjugate olefins can be excluded. The hypothesis of carbinol as intermediate is inconsistent, first, with the fact that no carbinol can be detected in the ether isolated and, second, with the observation that 9 days' boiling of carbinol with methanolic phthalic acid leads to ether III, but in a degree (25%) which cannot account for the isolation of pure ether in the methanolysis. The other hypothesis that III is produced to an important extent by way of primary formation of the mixed olefins which then add methanol is inconsistent with the fact that both I and III react with boiling methanol and a stronger catalyst (0.7% hydrogen chloride) to give the mixed olefins in high yield. Consequently, olefin is stable thermodynamically with respect both to starting material and product in the usual methanolysis and cannot be intermediate in the ether formation.

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(1) Taken fron a dissertation submitted April 18, 1949, in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

(2) Presented at the 117th Meeting of the American Chemical Society, Philadelphia, Pa., April 9, 1950; "Abstracts of Papers," p. 7L.

(3) Sterling Chemistry Laboratory, Yale University, New Haven, Connecticut.

(4) (a) W. von E. Doering and H. H. Zeiss, THIS JOURNAL, **70**, 3966 (1948); (b) **72**, 147 (1950).

(5) Although little doubt exists that I of this rotation is close to optical purity, neither the qualitative nor the quantitative interpretation of the present work depends upon the use of optically pure materials.

(6) Infrared spectra of 2,4-dimethylhexan-4-ol (II) are reproduced in Fig. 2 of reference 3b.

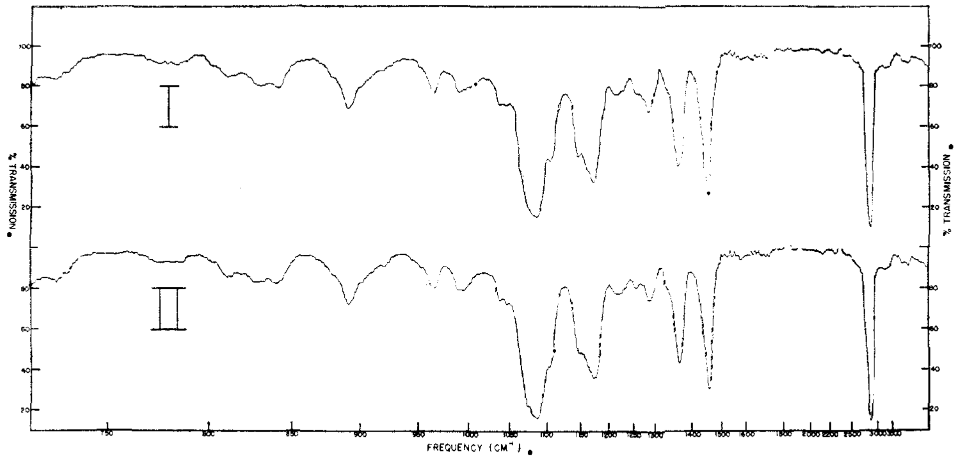

Fig. 1.—Curve I represents the infrared spectrum of optically active (+2.53°) 4-methoxy-2,4-dimethylhexane (III) from the methanolysis of hydrogen phthalate (I) and curve II represents that of racemic methyl ether (III) from methylethylisobutylcarbinol (II).

Choice between a mechanism involving alkyl–oxygen or acyl–oxygen fission is resolved simply and almost unequivocally on the basis of the product criterion employed by Cohen and Schneider in their investigation of the hydrolysis of esters of *t*-butyl alcohol.[7] In methanol, methyl ether III can arise only by alkyl–oxygen cleavage, provided the ether be the primary product, which appears well substantiated. The alternate acyl–oxygen fission must produce carbinol II as initial product, a consequence which is realized in the reaction of I (−2.2°) with methanolic sodium methoxide to give exclusively carbinol II, +0.77°, with essentially complete retention of configuration.

The methanolysis of optically active I (+6.1°), effected by refluxing in absolute methanol for 9 days produced III (+2.53°), the theoretical value for complete retention of configuration being −5.85°. The stereochemical course of this methanolysis is therefore 43% inversion and 57% racemization, or 71.5% inversion and 28.5% retention, the two modes of expression being equivalent. These figures combine the stereochemistry of the methanolysis process (in which one is primarily interested) and the subsequent racemization of the ether. Correction for this latter process can be made from the fact that ether is 29% racemized in 9 days under similar conditions, but this correction will, of course, be exaggerated in magnitude. The corrected values are 61% inversion and 39% racemization with the true value being intermediate.

In order better to approximate the stereochemistry of the methanolysis process, the reaction was repeated for 36 hr., I (+3.1°) giving III (+1.54°). This result corresponds to 52% inversion and 48% racemization, or 76% inversion and 24% retention. Corrected for a maximum of 5% (one-sixth of 29%) racemization, these values become 54.5% inversion and 45.5% racemization, or 77% inversion and 23% retention.[8]

These facts can be considered to constitute a stereochemical condition which must be imposed on a mechanistic hypothesis for the methanolysis of hydrogen 2,4-dimethyl-4-phthalate (I). In general, the imposition of this condition excludes single-step, stereochemically specific hypotheses and admits two (or more) step hypotheses in which the individual steps follow differing and possibly opposing stereochemical courses.

Recently, communications[9] have appeared employing methylethylisohexylcarbinol as the optically active tertiary carbinol in experiments similar to ours and stemming from the earlier experiments of Stevens and McNiven.[10] The carbinol was apparently obtained from naturally occurring linalool of undisclosed optical and structural purity. In the absence of these and other essential details, no comment is possible.

Of the numerous specific hypotheses satisfying the general stereochemical condition imposed by the experiments described here, we wish to discuss two. The first of these, developed fragmentarily and modified frequently, involves the life-time of the intermediate carbonium ion, the formation of which is rate-determining in the S_N1 mechanistic hypothesis.[11] If this life-time be long, the carbonium ion becomes flat and racemic but if the length of life "is comparable to the period of molecular oscillation of the solute within the enclosing solvent, the recession of the anion ejected from its former partner will produce a dissymmetric shielding of the latter during the period in which the course of substitution is being determined, and the result will be that substitutions with inversion will outnumber those which retain configuration."[11c]

With the extent of inversion being in fact so surprisingly large in the tertiary case investigated here, it seems unconvincing to us that a shielding

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[7] S. G. Cohen and A. Schneider, This Journal, **63**, 3382 (1941).

[8] In this experiment precision in measuring the specific rotation of the viscous I probably introduces more error than the racemization of ether.

[9] (a) E. D. Hughes, C. K. Ingold, R. J. L. Martin and D. F. Meigh, *Nature*, **166**, 679 (1950); (b) C. A. Burton, E. D. Hughes, C. K. Ingold and D. F. Meigh, *ibid.*, **166**, 680 (1950).

[10] P. G. Stevens and N. L. McNiven, This Journal, **61**, 1295 (1939).

[11] (a) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 244 (1935); (b) W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott, *ibid.*, 1252 (1937); (c) E. D. Hughes, *Trans. Faraday Soc.*, **34**, 202 (1938); (d) L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold and N. A. Taher, *J. Chem. Soc.*, 979 (1940); (e) I. Dostrovsky, E. D. Hughes and C. K. Ingold, *ibid.*, 173 (1946).

effect operating at a comparatively large distance should be the responsible factor. "It would seem that if ionization were complete enough to permit the reaction to be called unimolecular, then the ion R^+ would be free enough from shielding effects so that a completely racemic product would result from the reaction of R^+ with solvent molecules."[12]

The stereochemistry of the solvolysis reaction can more profitably be discussed in terms of a hypothesis[13] which is similar in part to those being developed to accommodate new kinetic conditions.[14,15] These hypotheses are concerned with the assignment to the solvent of a theoretically sound and necessary role in the solvolysis reaction. The kinetic investigations are necessarily focused on the description of the species generating the rate-determining transition state, whereas the stereochemical observations shed light on the details of the structural changes occurring in the solvolysis reaction. The highly contentious feature of freedom in the Ingold–Hughes hypothesis of a carbon cation intermediate is incidentally removed. in part. The hypothesis recognizes a gradual progression in the free energy diagram from the concerted, one-transition type[16] of which primary halides and secondary halides with complete Walden inversion are examples (Fig. 2, curve 1) and the two-step type with intermediate[17] (Fig. 2, curve 3) of which a clear example is the reaction of tri-*p*-anisylcarbinol with alcoholic sodium bisulfite to give tri-*p*-anisylmethanesulfonic acid in which the red color of the intermediate carbonium ion appears until the end of the reaction.[18]

The one-step displacement of methyl halide in water, for example, is considered at present to involve no intermediate and has been described by a single transition state,[19] t^1 (represented by formula B) where the minimum solvation suggested by the investigation of Swain[14] has been included to avoid ejecting a bare, unsolvated halide ion.

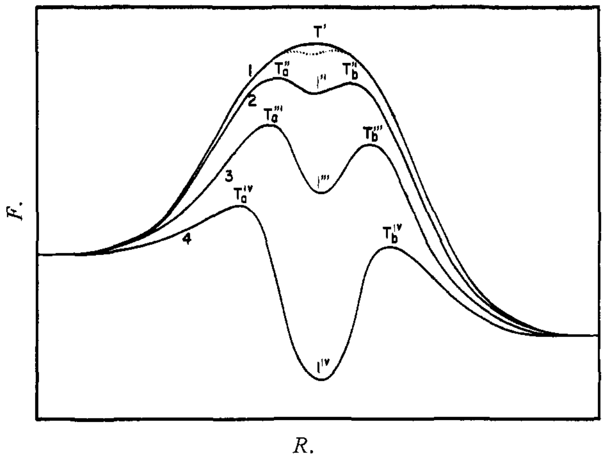

Fig. 2.—*R* represents the projection of points of minimum free energy in the free energy surface of reaction (the reaction coördinate); and *F* represents free energy. The curves 1, 2, 3 and 4 represent displacement reactions of the B: + R-X type.

In this transition state the sp^2-bonded methyl group, if free, would represent a carbonium ion of excessive energy and reactivity inappreciably mitigated by electron access from the carbon–hydrogen bonds; but, being unfree, is instead covalently bonded to the two Lewis bases (water in the rear, X at the front) by two bonds each having a pair of electrons (from the base) and involving overlap of one half of the p-orbital of carbon with a (presumably but not necessarily) sp^3-orbital of the base (described as a $^1/_2p$-sp^3 hybrid type). This bonding has also been described in resonance pictures by Winstein, *et al.*[15]

As the methyl group is varied structurally in a systematic series in which the energy of the free, hypothetical carbonium ion is decreased continuously by increasing resonance access of electrons from the substituents to the p-orbital, the arrangement of atoms corresponding to t^1 is transformed from a transition state to an intermediate (Fig. 2; i^{II}, i^{III}, i^{IV}) of increasing stability and operational significance[19]; the $^1/_2p$-sp^3 bonds to solvent and leaving group, strong bonds and a major stabilizing factor in the transition state (t^1), become longer and weaker as the p-orbital is filled increasingly with electrons from within the carbonium ion until, in the terminal cases (i^{IV}), bonds to the leaving group are ionic and to a particular solvent molecule non-existent[20]; and non-specific solvation, larger with compact ions and transition states, presumably decreases somewhat with the wider distribution of charge usually associated with resonance stabilization.[21] The two distinct types of solvation (decrease in the free energy of an ion, here positively charged), conveniently called "dielectric or non-specific solvation" and "covalent or specific solvation," can be expected to vary widely and independently with solvent.

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[12] S. Winstein, THIS JOURNAL, **61**, 1635 (1939).

[13] Presented briefly by Doering and Zeiss[3] and by W. von E. Doering and A. Streitwieser, Jr., "Abstracts of Papers," 119th Meeting, American Chemical Society, Boston, Mass., April 1, 1951, p. 45M; this hypothesis has recently been outlined by M. J. S. Dewar, *Ann. Repts. on Progress Chem.* (*Chem. Soc. London*), **48**, 121 (1951).

[14] (a) C. G. Swain, THIS JOURNAL, **70**, 1119 (1948); (b) C. G. Swain and R. W. Eddy, *ibid.*, **70**, 2989 (1948). See these for other references.

[15] S. Winstein, E. Grunwald and H. W. Jones, *ibid.*, **73**, 2700 (1951).

[16] M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **34**, 11 (1938).

[17] E. Wigner, *ibid.*, **34**, 29 (1938).

[18] A. Baeyer and V. Villiger, *Ber.*, **35**, 3013 (1902).

[19] Theoretically a transition state is defined as the configuration of lowest free energy that a system of atoms must attain in order to pass from one minimum to another in the free energy surface (or space), and an intermediate (I) in the reaction (A ⇄ B) where A and B are minima is defined as a third minimum bounded by two transition states, one between A and I, the other between I and B, the passing of both being necessary for the interconversion of A and B. Operationally an intermediate (I) between A and B is defined as, an *observed* system which appears necessarily (within the limits of observation) in the interconversion of A and B, whereas a transition state is defined as a postulated system necessarily traversed in A ⇄ B which observations have been unable to detect. The operational definition seems more appropriate at the moment despite the admitted possibilities that a reaction described as single transition-state without an intermediate on the basis of present observations will acquire an intermediate on the basis of future experiments and that one type of observation may indicate an intermediate whereas another may indicate none.

[20] A pertinent inorganic analogy involves the change in type of bond to solvent (*e.g.*, liquid ammonia or water) in a series beginning, for example, with silver cation (corresponding to CH_3^+) and ending with sodium cation (corresponding to crystal violet).

[21] A. G. Evans, "The Reactions of Organic Halides in Solution," The Manchester University Press, Manchester, England, 1946.

The first phase of the displacement reaction with intermediate is the change of the bonding orbital on carbon in A from sp^3 to p, the bond between carbon and X changing from the overlap of two sp^3-orbitals (sp^3-sp^3) to the overlap of one-half the p-orbital of carbon with the sp^3-orbital of X ($^1/_2p$-sp^3). The ionic character of the bond increases with this change but to a degree that is determined by the structure of the molecule. The activation energy of this process presumably originates in the fact that the carbon covalent bonds in the transition state (t_a and also t_b of Fig. 2) are neither sp^3 nor sp^2 but a higher energy intermediate type. Whether the rate-determining process is a single, termolecular step giving B directly, or whether the rate-determining step involves a unimolecular ionization giving B′ or a bimolecular process giving B″ are questions which probably have no general answer and require individual solution. With most X the pull of hydrogen-bond formation or other interaction with the solvent would make B″ lower in free energy than B′ (Fig. 3) but if X were trimethylamine, for example, this relationship might not be true. Covalent solvation in the rear, would make B lower in free energy than B″ in a manner depending inversely on the stability of the carbonium ion *per se*. But even when B is more stable than B″ the process might be two-step if the stabilization by covalent solvation in the rear only became significantly effective *after* the transition state configuration had been passed. This situation could arise if there were a large steric factor in the sp^3 starting situation which prevented effective access of solvent from the rear[21] until the sp^2 configuration had almost been reached. These situations are pictured in Fig. 3 where curve A → B″ is without covalent solvation in the rear, A → Ta″ → B is with late and A → Ta → B is with early covalent solvation.

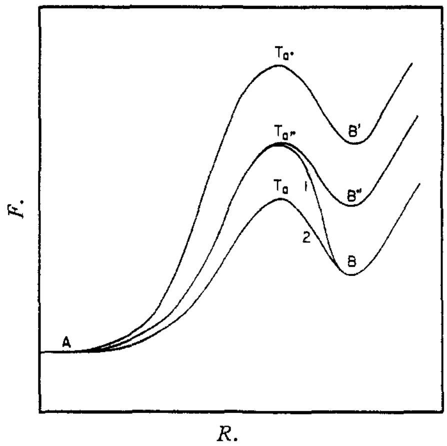
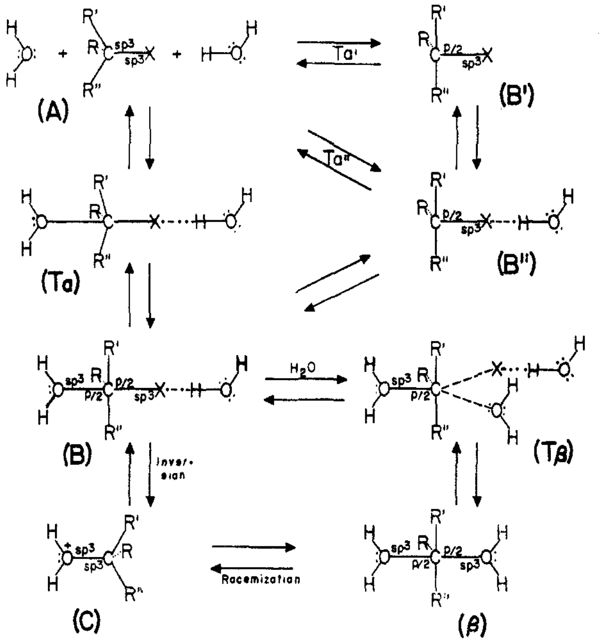


Fig. 3.—*R* represents the reaction coördination and *F* the free energy of the reactions of A to the three intermediates, B, B′ and B″ *via* transition states T_a, T_a' and T_a''.

Winstein, *et al.*,[15] have presented experimental work showing that the effectiveness with which the nucleophilic character of a solvent contributes to the energy of the transition state varies markedly with the structure of the organic reactant. These observations (which relate to that part of the curves in Fig. 3 from A to T) serve as the basis for a new classification of displacement reactions into "limiting" (A–T_a'') and "nucleophilic" (cases between A–T_a and A–T_a'').



The intermediate B (or B″) may proceed to the product C, revert to A (two reactions which are essentially identical in character), or be transformed to a new intermediate (β) by displacement of one base from its $^1/_2p$-sp^3 bond by another. If A is optically active, B (or B″) retains optical activity and gives C with complete inversion of configuration, A with complete retention and β with loss of optical activity. Products derived from β will therefore be racemic. The stereochemistry of the product is controlled by the relative activation energies of the processes B → C and B → β. Increasing the inherent stability of the free carbonium ion increases the activation energy of the former process and lowers that of the latter leading to increased racemization. On the same reasoning increased stability of the carbonium ion will lead to increased appearance of added, non-solvent bases in the product, or to its mechanistic equivalent, an increased "common ion effect."[22] According to this hypothesis reaction with retention may occur when the front-side group (X + reagent) in B′, B″ or B undergoes rotation followed by reformation of a covalent bond with another nucleus of (X + reagent). This occurrence becomes feasible when the solvent either by its nature or because of peculiar structural features is playing no effective role at the rear (B′ or B″) or when the solvent at the rear in B is non-reacting, although the rate of rotation and reformation of covalent bond must then be faster than the rate of conversion to an intermediate of the β-type.

The stereochemistry of the methanolysis of hydrogen 2,4-dimethylhexyl-2-phthalate finds qualitative explanation in terms of this hypothesis, constitutes

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(22) Compare A. G. Ogston, E. R. Holiday, J. St. L. Philpot and L. A. Stocken, *Trans. Faraday Soc.*, **44**, 45 (1948).

support for the structure of the hypothetical intermediate and consequently gives structure to the transition state in a way which complements the results of the kinetics.[14,15]

Experimental[23]

4-Methoxy-2,4-dimethylhexane (III).—To a suspension of 3.9 g. of potassium metal in 250 ml. of dry benzene at 70° was added 13 g. of racemic 2,4-dimethylhexan-4-ol (II). After stirring and warming the mixture for 4 hr., a solution of 14.4 g. of methyl iodide in 150 ml. of benzene was dropped into the benzene solution of the potassium salt of II. The slow precipitation of potassium iodide was allowed to proceed overnight. The mixture, under a blanket of nitrogen, was cautiously treated with water which dissolved the inorganic salt and destroyed any unreacted potassium. The aqueous layer was removed, and the benzene solution was washed with water. The water washes were extracted with fresh benzene, and the combined benzene solutions were dried over anhydrous potassium carbonate, and distilled. The main fraction, b.p. 151–152° at 760 mm. and n^{20}_{D} 1.4133, was refluxed over potassium metal and redistilled to give 2.6 g. of pure III: b.p. 151.5–152°, n^{20}_{D} 1.4130, n^{25}_{D} 1.4152, d^{25}_{4} 0.809.

Anal. Calcd. for $C_9H_{20}O$: C, 74.9; H, 14.0. Found: C, 75.0; H, 13.8.

The infrared spectrum of this substance is shown in Fig. 1, curve II.

The procedure was repeated with 5.2 g. of (−)-II, $[\alpha]^{25}_{\mathrm{D}}$ −0.30°, 1.6 g. of potassium and 6.3 g. of methyl iodide in 100 ml. of benzene to give 1.5 g. (26%) of (−)-III. This product was distilled from potassium: b.p. 151–152°, n^{25}_{D} 1.4150, $[\alpha]^{24}_{\mathrm{D}}$ −0.78°. The infrared spectrum of this methyl ether was identical with that of racemic III.

Methanolysis of Hydrogen 2,4-Dimethylhexyl-4-phthalate (I).—Absolute methyl alcohol, prepared by distilling from magnesium methoxide, was used in all methanolyses. A solution of 17.3 g. of (+)-hydrogen 2,4-dimethylhexyl-4-phthalate (I), $[\alpha]^{27}_{\mathrm{D}}$ +0.7°, in 150 ml. of methanol was refluxed for 9 days and then poured into 1500 ml. of water, separating an oily layer which was extracted with ether. The ether solution was extracted with 2% aqueous sodium carbonate, washed with water, dried over potassium carbonate, and concentrated. (Acidification of the alkaline extracts produced no isolable quantity of unreacted I.) Distillation of the residual liquid at atmospheric pressure gave 1.1 g. (12%) of (+)-III, b.p. 151–152°: n^{26}_{D} 1.4150, $[\alpha]^{26}_{\mathrm{D}}$ +0.26° (α +0.21°, l = 1). This methyl ether gave an infrared spectrum which was superimposable on that of racemic III. Redistillation of the considerable amount of forerun yielded an additional quantity (1.5 g.) of the (+)-III, bringing the total amount to 2.6 g. (29%).

The methanolysis was now repeated with (+)-I of much higher rotation, $[\alpha]^{22}_{\mathrm{D}}$ +6.1° (α +0.54°, c 8.87). A solution of 15.0 g. of this hydrogen phthalate was refluxed for 9 days in 150 ml. of methanol. The product, (+)-III, was isolated as described in the preceding experiment, and, after distillation and exhaustive redistillations of the foreruns, was obtained in the amount of 2.7 g. (35%): b.p. 151–152°, n^{23}_{D} 1.4148, $[\alpha]^{23}_{\mathrm{D}}$ +2.53° (α +2.05°, l = 1). The infrared spectrum of this methyl ether is given by curve I, Fig. 1, and is identical with authentic ether (Fig. 1, curve II) except for the possible presence of a small amount of olefin (*ca.* 1720 cm.$^{-1}$).

Acidification of the alkaline aqueous extracts from the above experiments, ether extraction of the acidic mixture and removal of the ether left 1 g. of methyl hydrogen phthalate, m.p. 82–84°.

Limited Methanolysis of (+)-I.—A solution of 19.5 g. of (+)-I ($[\alpha]^{23}_{\mathrm{D}}$ +3.1°, c 9.97), in 150 ml. of methyl alcohol was refluxed for 36 hr., and poured into water, (+)-III being isolated in the usual way: b.p. 152°, n^{20}_{D} 1.4131, $[\alpha]^{22}_{\mathrm{D}}$ +1.54° (α +1.25°, l = 1). Acidification of the alkaline aqueous extracts produced an oil which was dissolved in ether. The ether solution was washed with copious amounts of water, dried over sodium sulfate and concentrated *in vacuo* leaving 4.8 g. (25%) of unreacted (+)-I; $[\alpha]^{25}_{\mathrm{D}}$ +2.9° (α +0.31°, c 10.58).

Racemization of (+)-III.—A solution of 50 ml. of methyl alcohol, 3.2 g. of 4-methoxy-2,4-dimethylhexane, $[\alpha]^{26}_{\mathrm{D}}$ +1.43° (α + 1.16°, l = 1), and 3.7 g. of phthalic acid was refluxed for 9 days. The methyl ether (III) was recovered in the usual way, distillation of the neutral fraction giving 1.6 g. (50%) of (+)-III: b.p. 151–152°, n^{21}_{D} 1.4143, $[\alpha]^{30}_{\mathrm{D}}$ +1.01° (α + 0.82°, l = 1).

Behavior of 2,4-Dimethylhexan-4-ol (III) in Methanolic Phthalic Acid.—A solution of 5 g. of racemic II and 3.9 g. of phthalic acid in 50 ml. of methanol was refluxed for 9 days, poured into water and worked in the usual fashion. Distillation of the neutral fraction gave 3.1 g. of distillate; b.p. 151–153°, n^{26}_{D} 1.4216. The refractive indices of pure II and III measured at the same time were 1.4241 and 1.4151, respectively. Calculation on the basis of these figures indicated the distillate to be 72% II and 28% III. A more accurate determination of the composition based on the infrared spectra of synthetic mixtures of the carbinol and the methyl ether and of the distillate resulted in a figure of 25% (by volume) for the amount of III formed from II under the conditions of the methanolysis.

Base-catalyzed Methanolysis of (−)-I.—A solution of 20 g. of (−)-hydrogen 2,4-dimethylhexyl-4-phthalate (I), $[\alpha]^{23}_{\mathrm{D}}$ −2.2° (α −0.20°, c 9.16), in 150 ml. of methanol, to which 4.2 g. of sodium metal had been added, was refluxed for 7 days, the reaction products being isolated by the general procedure employed in the other methanolyses. The neutral fraction, when distilled at atmospheric pressure, yielded 3.5 g. (38%) of (+)-II distilling between 152–153°: n^{25}_{D} 1.4241, $[\alpha]^{26}_{\mathrm{D}}$ +0.77° (α +0.64°, l = 1).

Methanolysis of Methyl 2,4-Dimethylhexyl-4-phthalate.—(−)-Hydrogen 2,4-dimethylhexyl-4-phthalate (18.5 g.), $[\alpha]^{26}_{\mathrm{D}}$ −0.8°, in ether was esterified with diazomethane. The ether solution of the diester was extracted with dilute sodium hydroxide, washed with water and dried over potassium carbonate. Removal of the ether at the aspirator left 17 g. of methyl 2,4-dimethylhexyl-4-phthalate as an oil. This product was boiled in 140 ml. of methanol for 8 days, after which the major part of the methanol was removed by atmospheric distillation and the residual liquid was subjected to distillation under reduced pressure. Only a small quantity of distillate was obtained when the pressure was reduced to 1 mm. and the bath temperature was raised to 65°, but neither II nor III could be isolated. The oil remaining in the distillation flask (14.5 g.) was dissolved in ether and extracted with 1% sodium hydroxide. From the ether layer 12 g. of diester was recovered. The alkaline extract was acidified with dilute hydrochloric acid and extracted with ether. Upon washing and drying the ether solution and replacing the solvent ether with hot benzene, there was obtained 0.3 g. of crystalline methyl hydrogen phthalate, m.p. 82–83.5°.

Acid-catalyzed Methanolysis of Methyl 2,4-Dimethylhexyl-4-phthalate.—The unreacted diester (12 g.) from the preceding experiment was dissolved in 150 ml. of methyl alcohol containing 0.7% of dry hydrogen chloride. After refluxing the solution for 7 days, the methanol was removed in large part on the steam-bath, and the residual oil was distilled at 20 mm. At 70° a distillate was obtained which was poured into water, extracted with ether and recovered by distilling the dried ether solution at atmospheric pressure. Three fractions, totalling 1.5 g., distilled between 100–130°. The low boiling points and the refractive indices, which lay between 1.4062 and 1.4109, indicated that these fractions were chiefly composed of olefin. The optical rotation of the combined fractions was zero.

The residual material from the distillation at 20 mm. was dissolved in ether, and extracted with 5% sodium carbonate. After drying the ether solution over sodium sulfate and concentration at reduced pressure, there remained 6.5 g. of yellow oil, $[\alpha]_{\mathrm{D}}$ 0. This oil, when distilled, yielded 4.7 g. of dimethyl phthalate: b.p. 275–277° (760 mm.), n^{26}_{D} 1.5124. The alkaline solution was acidified and extracted with ether. Replacement of the ether with benzene and repeated concentration of the benzene solution gave no crystalline methyl hydrogen phthalate.

Reaction of 4-Methoxy-2,4-dimethylhexane (III) with Methanolic Hydrogen Chloride.—Racemic III (2 g.) was dissolved in 50 ml. of methanol containing 0.7% of dry hydrogen chloride. After being refluxed for 1 week, the meth-

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[23] The rotations of optically active II and III were measured uniformly without solvent. The hydrogen phthalates (I) were dissolved in 95% ethanol for this measurement.

anol solution was poured into 500 ml. of water. Extraction of the aqueous mixture with ether and removal of the ether gave olefinic material boiling between 108–110°: 0.5 g., n^{20}_D 1.4001. Olefin, having the same properties, is obtained from the dehydration of II.

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[CONTRIBUTION FROM CHANDLER LABORATORY, COLUMBIA UNIVERSITY]

2- and 3-Vinylpyridines as Dienophiles in the Diels–Alder Reaction[1]

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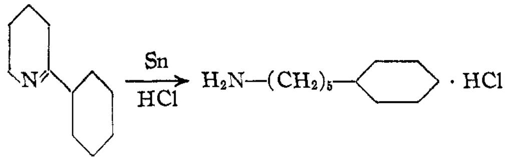
The Diels–Alder reactions of 2-vinylpyridine and of 3-vinylpyridine (the preparation of which has been improved) with butadiene and of 2-vinylpyridine with 2,3-dimethylbutadiene have been effected and compared with the styrene–butadiene reaction. The three dienophiles react at comparable temperatures. The structures of the adducts are 4-(α-pyridyl)-cyclohexene-1, 4-(β-pyridyl)-cyclohexene-1 and 4-(α-pyridyl)-1,2-dimethylcyclohexene-1.

The comparative reactivity of 2-vinylpyridine and 3-vinylpyridine as dienophiles in the Diels–Alder reaction is of theoretical interest in view of the marked electrophilicity of 2-vinylpyridine in contrast to the essentially neutral character of 3-vinylpyridine.[4] Until the recent report of the reaction of isoprene and 2-vinylpyridine to give 1-methyl-4-(α-pyridyl)-cyclohexene-1,[5] there have been no examples of the Diels–Alder reaction with vinylpyridines.

2-Vinylpyridine (I) and butadiene react to give an adduct, to which the structure, 4-(α-pyridyl)-cyclohexene-1 (II), is assigned on the basis of dehydrogenation with chloranil,[6] palladium black,[7] or, best with palladium-black and maleic acid[8] to 2-phenylpyridine and by analogy with the usual position assumed by the double bond in a Diels–Alder reaction. From the catalytic reduction of II in dilute hydrochloric acid a compound, m.p. 251–252.5°, is obtained, which is almost certainly 2-cyclohexylpiperidine hydrochloride (III), although Salathiel, *et al.*,[9] claim that this structure is to be assigned to a compound, m.p. 197–198°, which is the major product of the reduction of IV with tin and hydrochloric acid. Their compound is presumably V and not III.[10]



IV V

With 2,3-dimethylbutadiene, I reacts smoothly to give an adduct, 4-(α-pyridyl)-1,2-dimethylcyclohexene-1 (VI), which can be dehydrogenated to 4-(α-pyridyl)-1,2-dimethylbenzene (VII) and can be hydrogenated to a mixture of stereoisomers of 4-(α-piperidyl)-1,2-dimethylcyclohexane (VIII), the structural assignments being based on analogy and elementary analysis.

3-Vinylpyridine (IX) has been prepared in better yield by using a lower temperature (80°) in the reaction of trimethylamine and α-(3-pyridyl)-ethyl chloride hydrochloride, than that (125°) previously recommended,[4] the improvement being due to a large reduction in the amount of the undesirable by-product, α-(3-pyridyl)-ethyldimethylamine. IX reacts with butadiene, giving 4-(β-pyridyl)-cyclohexene-1 (X) which is converted by dehydrogenation to the known 3-phenylpyridine, and by hydrogenation to 3-cyclohexylpiperidine hydrochloride.

Styrene itself, reported by Alder and Rickert[11] to react with butadiene at 170–180°, in fact reacts appreciably at 125°.

From the data of Table I, which summarizes all of our experiments, it is apparent that 2- and 3-vinylpyridine and styrene react with butadiene at comparable orders of magnitude and 2-vinylpyridine with its easily polarizable double bond[4] is not much more reactive than the other two.

Experimental[12]

Procedure for the Diels–Alder Reactions.—In Table I, reaction times and temperatures for the various reactions are listed. In a typical procedure, a charge of 10.5 g. (0.10 mole) of freshly distilled vinylpyridine, 10 cc. (0.12 mole) of butadiene and 0.1 g. of hydroquinone was heated in a sealed tube. The reaction mixture, a dark, viscous oil, was leached with ether to yield a turbid solution which deposited appreciable quantities of ether-insoluble polymers on standing. It was found advisable to dilute the ethereal solution to a volume of *ca.* 300 cc. in order to remove as much of the polymeric material as possible; otherwise, emulsion formation in subsequent steps rendered the working of the product extremely tedious. The clear ethereal solution, decanted from insoluble polymers, was extracted with 2 *N* hydrochloric acid. Treatment of the acid extracts with excess 10% sodium hydroxide, liberated an oil which was dissolved in

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[8] S. Akabori and T. Suzuki, *Bull. Chem. Soc. Japan*, **4**, 200 (1929); S. Akabori and K. Saito, *Ber.*, **63**, 2245 (1930).

[9] R. Salathiel, J. M. Burch and R. M. Hixon, THIS JOURNAL, **59**, 984 (1937).

[10] They report the isolation of a small amount of material, characterized only by m.p. 250°, which may well have been III.

[11] K. Alder and H. F. Rickert, *Ber.*, **71**, 379 (1938).

[12] Microanalyses were performed by Miss Lois May, Columbia University. Melting points are corrected. The purity of the 2-vinylpyridine, obtained from the Reilly Tar and Chemical Corporation, was confirmed by boiling point and conversion to the picrate.