copper sulfate in a rocking autoclave. The 4-bromoisoquinoline was obtained (445 g. or 71.5%) as a crude product (m. p., 39–42°) which on recrystallization from petroleum ether (b. p., 60–68°) melted at 42–42.5°. We observed that the yield was improved by completely mixing the molten isoquinoline perbromide hydrobromide prior to the prolonged heating.[11,13]

4-Hydroxyisoquinoline.—A mixture of 10.5 g. (0.05 mole) of 4-bromoisoquinoline, 5 g. (0.02 mole) of copper sulfate, 4.1 g. of copper bronze and 31.3 g. (0.75 mole) of sodium hydroxide in 17 cc. of water was heated in an autoclave at 210° for twelve hours. After cooling, the dark brown residue was extracted with hot water, and to the aqueous filtrate was added Dry Ice. The 4.5 g. (61%) of light brown 4-hydroxyisoquinoline which precipitated melted between 210–214°. Recrystallization from a 1:2 mixture of glacial acetic acid and ethyl ether raised the melting point to 223°. The yield of crude product using double the quantities of reactants was 60%.

Anal. Calcd. for C_9H_7ON: N, 9.65. Found: N, 9.67.

The yellow, crystalline *picrate* melted at 243–244° after recrystallization from 95% ethanol.

Anal. Calcd. for $C_{15}H_{10}O_8N_4$: N, 14.97. Found: N, 15.20.

p-(γ-Diethylaminopropylamino)-phenyl Bromide.—This compound was prepared incidental to an orienting experiment concerned with the synthesis of 1-[p-(γ-diethylaminopropylamino)-phenyl]-isoquinoline by a procedure like that described earlier for the preparation of 1-(p-aminophenyl)-isoquinoline.

In the first reaction, 34.4 g. (0.2 mole) of p-bromoaniline and 30 g. (0.2 mole) of freshly distilled γ-diethylaminopropyl chloride[14] were heated between 150–160° (internal temperature) for six hours. After cooling the dark brown solution, water was added, and the neutralization was effected by 20% sodium hydroxide. The ether extracts were dried, and after removal of the ether fractional distillation yielded 30 g. (52%) of a colorless liquid which boiled at 135–137° (0.2 mm.); n^{20}_D 1.5530; d^{20}_{20} 1.1178.

In a second preparation, to a melt of 156 g. (0.5 mole) of crude N-(p-bromophenyl)-benzenesulfonamide[15] and 41.5 g. (0.3 mole) of anhydrous potassium carbonate heated at 150° was added cautiously 90 g. (0.6 mole) of γ-diethylaminopropyl chloride. Heating was continued between 150–160° for six hours, and on pouring into cold water a brown, viscous oil separated. The oil was hydrolyzed by refluxing for twelve hours with 600 cc. of concentrated hydrochloric acid. Subsequent to neutralization by 40% sodium hydroxide solution and extraction with ether, there was obtained 88.5 g. (62%) of compound distilling at 155–157° (0.5 mm.); n^{20}_D 1.5528; d^{20}_{20} 1.1181.

Anal. Calcd. for $C_{13}H_{21}N_2Br$: N, 9.92. Found: N, 10.19.

The **dihydrochloride**, prepared by adding an excess of ethereal hydrogen chloride to a dry ether solution of p-(γ-diethylaminopropylamino)-phenyl bromide, melted at 185–186° after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{13}H_{23}N_2BrCl_2$: N, 7.83. Found: N, 7.72.

Summary

1-(p-Aminophenyl)-isoquinoline has been prepared by the addition of the lithium salt of p-aminophenyllithium to isoquinoline and shown to be identical with a compound prepared by cyclization. By the use of appropriate RLi compounds, other 1-(arylsubstituted)-isoquinolines have been synthesized in which some of the aryl groups are p-mercaptophenyl and p-(2,5-dimethyl-1-pyrryl)-phenyl.

AMES, IOWA RECEIVED JANUARY 17, 1947

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[13] Edinger and Bossung, *J. prakt. Chem.*, **43**, 191 (1891); Bergstrom and Rodda, THIS JOURNAL, **62**, 3030 (1940).

[14] Gilman and Shirley, *ibid.*, **66**, 888 (1944).

[15] v. Braun, *Ber.*, **40**, 3926 (1907).

[CONTRIBUTION FROM THE IPATIEFF HIGH-PRESSURE AND CATALYTIC LABORATORY, DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY]

Studies in the Terpene Series. VII. Destructive Hydrogenation of Bicyclic Dihydroterpenic Hydrocarbons[1,2]

BY V. N. IPATIEFF, HERMAN PINES AND MICHAEL SAVOY

The structure of bicyclic dihydroterpenic hydrocarbons, which are often formed during the catalytic treatment of mono- and bicyclic terpenes, is difficult to prove by heretofore described methods. It was of especial importance during our study to find a means of determining the type of rings present in bicyclic dihydroterpenic hydrocarbons. For that reason the study of the destructive hydrogenation of bicyclic dihydroterpenic hydrocarbons was undertaken with the purpose of splitting one of the rings and converting these dihydroterpenes to monocyclic hydrocarbons; the structure of the latter can usually be determined by means of dehydrogenation.

For that reason the following compounds were submitted to a ring rupture by means of destructive hydrogenation: pinane, isocamphane and isobornylane. The reaction was carried out in a rotating autoclave in the presence of a nickel–kieselguhr catalyst and under an initial hydrogen pressure of 100 atmospheres, measured at 25–28°. It was found that the temperature at which the fission of one of the rings takes place depends upon the size of the rings. In pinane, which is composed of a four- and a six-carbon atom ring, the rupture of the ring occurs as low as 175°. Bicyclic hydrocarbons composed of a six-carbon atom ring containing a bridge in the 1,4-position linked through a carbon atom are more stable toward hydrogenation than pinane; the cleavage of one of the rings takes place at 210–220°.

The destructive hydrogenation of pinane causes the rupture of the following bonds: 6–8 (I), 4–8 (II), 4–5 (III) and 5–6 (IV)

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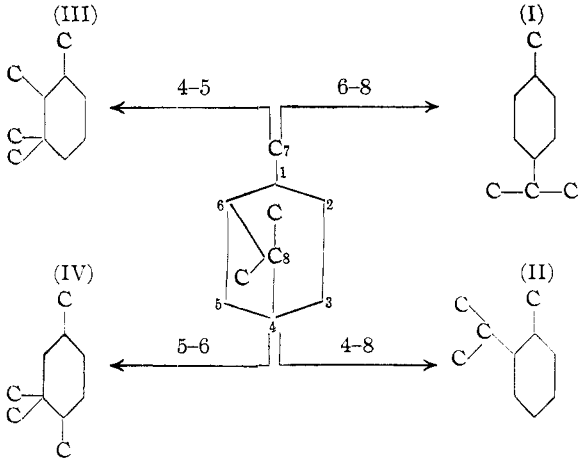
[1] This work was made possible through financial assistance of the Universal Oil Products Company, Riverside, Illinois.

[2] For Paper VI of this series see V. N. Ipatieff, H. Pines, V. Dvorkobitz, R. C. Olberg and M. Savoy, *J. Org. Chem.*, **12**, 34 (1947).



The product resulting from this destructive hydrogenation was composed of about 13% of 1-methyl-4-isopropyl- and 5% of 1-methyl-2-isopropylcyclohexane, 65% of 1,1,2,3- and 10% of 1,1,2,5-tetramethylcyclohexane. The separation of the disubstituted cyclohexanes from the polymethylated cyclohexanes was accomplished by means of selective dehydrogenation using platinized alumina as a catalyst; it was reported previously[3] that cyclic hydrocarbons containing a geminal carbon atom undergo dehydrogenation at higher temperature than alkylated cyclohexanes in which only one hydrogen atom attached to a carbon atom in the ring is substituted.

By carrying out the dehydrogenation at 230–240°, it was possible to convert only the methylisopropylcyclohexanes to the corresponding *o*- and *p*-cymene; the latter were separated from the tetramethylcyclohexanes by sulfur dioxide extraction. The aromatic hydrocarbons thus separated were identified by means of solid derivatives and infrared spectral analysis.

The cycloparaffinic hydrocarbons which remained after the removal of methylisopropylcyclohexanes and which consisted mainly of tetramethylcyclohexanes, were dehydrogenated by means of platinized alumina at 300°. Trimethylbenzenes composed of about 80% of 1,2,3- and 12% of 1,2,4-trimethylbenzene were formed with the liberation of hydrogen and methane in molar ratio of 2:1. The 1,2,3-trimethylbenzene formed was identified by means of its solid nitro and bromo derivatives. The presence of 1,2,4-trimethylbenzene was detected by comparing the infrared absorption spectra of the product with that of known samples of 1,2,3- and 1,2,4-trimethylbenzene.

Isocamphane and isobornylane, on destructive hydrogenation, yielded a mixture of monocyclic hydrocarbons which did not undergo dehydrogenation to aromatic hydrocarbons when passed over platinized alumina at 300°. The resistance toward dehydrogenation indicates that the monocyclic hydrocarbons formed through the destructive hydrogenation were probably composed of alkylcyclopentanes and not of alkylcyclohexanes. The results obtained demonstrate that the five-membered rings in bicyclic hydrocarbons are more resistant toward hydrogenation than are six-membered rings.

Experimental

Material.—*Pinane* was prepared by hydrogenating pinene dissolved in an equal volume of *n*-pentane in the presence of a nickel-kieselguhr catalyst at 60° and under an initial hydrogen pressure of 100 atmospheres measured at 20°. The pinane obtained distilled at 165–166°, n^{20}_D 1.4605; the distillation was made in a column of about ten-plate efficiency and at a reflux ratio of 30:1.

Isocamphane was synthesized from isoborneol according to the method described previously[4]; it melted at 62°.

Isobornylane was obtained by hydrogenating fenchyl alcohol using alumina–nickel catalyst.[5]

Apparatus and Procedure.—The destructive hydrogenations were carried out in an electrically heated rotating autoclave made of stainless steel. The hydrocarbon and the nickel-kieselguhr catalyst[6] equivalent to 10% by weight of the hydrocarbon were placed in an autoclave; the latter was then charged with hydrogen to a pressure of 100 atmospheres measured at room temperature. The autoclave was heated gradually to a temperature at which the hydrogen started to be absorbed and the autoclave was maintained at this temperature until the pressure remained constant for one hour. The autoclave was then cooled and the gaseous and liquid product analyzed.

Destructive Hydrogenation of Pinane.—One hundred and six grams of pinane was hydrogenated at 175° in a 450-cc. autoclave. According to the pressure drop it was calculated that one mole of hydrogen was absorbed per mole of hydrocarbons charged. The boiling range and the index of refraction of the destructively hydrogenated pinane is given in Fig. 1.

Dehydrogenation at 240°.—Forty-one grams of the destructively hydrogenated pinane was passed at 240° and at a rate of 15 ml. per hour over 75 g. of 10–14 mesh size catalyst, placed in a glass tube of 20 mm. diameter. The catalyst was composed of activated alumina containing 5% of platinum.[7] After the hydrocarbons were passed over the catalyst twice, the dehydrogenation was completed as could be judged from the evolution of gas; 19% of the hydrocarbons underwent dehydrogenation to aromatics. The gaseous products formed consisted of 95.1% of hydrogen and 4.9% of methane.

The aromatic hydrocarbons were separated from the naphthenes by means of liquid sulfur dioxide extraction. The procedure consisted of dissolving one volume of the hydrocarbons obtained from the dehydrogenation in 1.5 volumes of *n*-pentane; the solution was cooled to −75° and to it was added 2.5 volumes of liquid sulfur dioxide. The mixture was shaken vigorously, maintaining the temperature at −60 to −75°. The lower layer, which consisted of sulfur dioxide and dissolved aromatic hydrocarbons, was separated; the sulfur dioxide was allowed to evaporate, and the remaining liquid was washed with dilute aqueous sodium hydroxide solution, water and dried over calcium chloride.

The extracted aromatic hydrocarbons which distilled at 167–170° on oxidation yielded terephthalic acid which was converted to dimethylterephthalate melting at 141°.

The oxidation was carried out by treating at a reflux temperature, 1 g. of the aromatic hydrocarbons with 7 g. of chromium trioxide dissolved in a solution consisting of 30 ml. of acetic acid, 30 ml. of water and 10 ml. of 96% sulfuric acid.

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(3) V. N. Ipatieff, H. Pines and R. C. Olberg, This Journal, **68**, 1709 (1946).

(4) V. N. Ipatieff and H. Pines, This Journal, **66**, 1120 (1944).

(5) V. N. Ipatieff and H. Pines, *ibid.*, **67**, 1931 (1945), footnote 4.

(6) V. N. Ipatieff and B. B. Corson, *Ind. Eng. Chem.*, **26**, 1838 (1934).

(7) H. Pines and V. N. Ipatieff, This Journal, **61**, 1076 (1939).

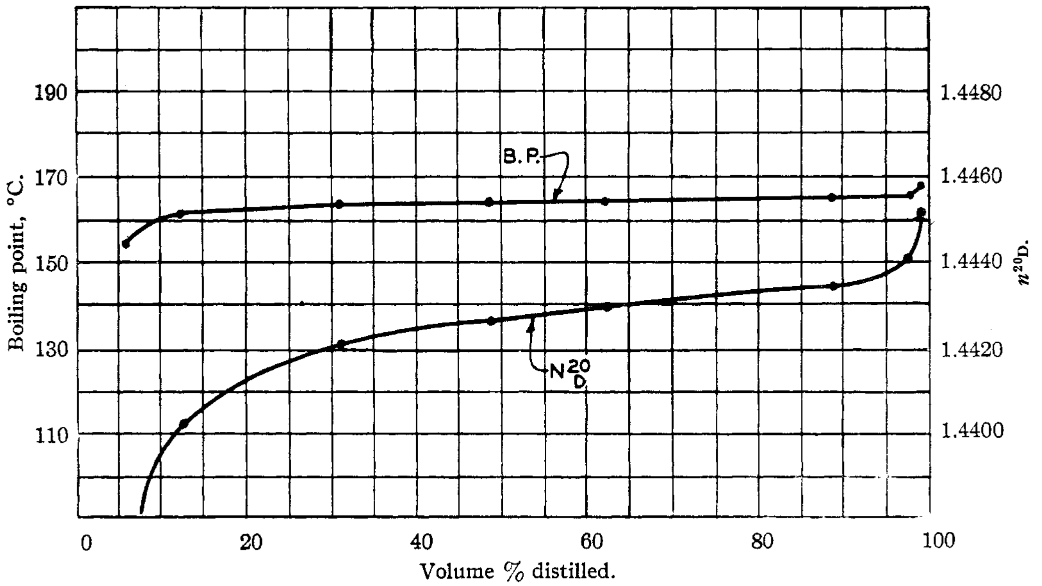

Fig. 1.—Distillation of the products obtained from the destructive hydrogenation of pinane.

The sulfonamide derivative,[8] prepared from the sulfur dioxide extract, melted at 115° and did not depress the melting point when mixed with a sulfonamide prepared from a known sample of *p*-cymene.

The infrared absorption analysis of the aromatic extract showed it to contain 67% of *p*-cymene and 27% of *o*-cymene (Fig. 4).

Dehydrogenation at 300°.—The raffinate (upper layer from sulfur dioxide extraction) freed by distillation of *n*-pentane, was treated with sulfuric acid containing 15% sulfur trioxide in order to remove any aromatic hydrocarbons present. The treated hydrocarbons were washed with dilute sodium hydroxide, water, dried over calcium chloride and distilled. They boiled at 164–166°, n^{20}D 1.4422.

Anal.[9] Calcd. for $C_{10}H_{20}$: C, 85.63; H, 14.37. Found: C, 85.55; H, 14.16.

Thirteen grams of the hydrocarbons was submitted to dehydrogenation at 300°. According to the gas liberated, 52% of the product underwent dehydrogenation in the first pass; the gases were composed of 65% of hydrogen and 35% of methane. The aromatic hydrocarbons formed were extracted with liquid sulfur dioxide according to the procedure described above, they distilled at 169–172°, n^{20}D 1.4970.

The bromo derivatives of the aromatic hydrocarbons melted at 246°.

The bromination was carried out by dropping 2 ml. of bromine into 0.3 ml. of the aromatic hydrocarbon at 0°. The mixture was allowed to stand for one hour at room temperature. The excess of bromine was removed and the bromide crystallized from ethanol.

Anal. Calcd. for $C_9H_9Br_3$: C, 30.25; H, 2.52; Br, 67.33. Found: C, 30.40; H, 2.89; Br, 66.24.

The bromo derivative did not show a depression in melting point when mixed with a synthetically prepared 4,5,6-tribromo-1,2,3-trimethylbenzene; a lowering in melting point was however observed when it was mixed with 3,5,6-tribromo-1,2,4-trimethylbenzene.

The nitro derivative of the aromatic hydrocarbon melted at 206°; a mixed melting point with a trinitro derivative of 1,2,3-trimethylbenzene caused no depression whereas with trinitro derivative of 1,2,4-trimethylbenzene considerable depression occurred.

Anal. Calcd. for $C_9N_3O_6H_9$: N, 16.46. Found: N, 15.69.

Infrared absorption spectra of the aromatic hydrocarbon showed that it consisted of about 80% of 1,2,3- and 12% of 1,2,4-trimethylbenzene and 8% of unidentified material.

The sulfur dioxide insoluble hydrocarbons, consisting of unchanged naphthenes, were recovered and repassed over platinized alumina at 300°; 59% of the hydrocarbons underwent dehydrogenation with the liberation of gases containing 66% of hydrogen and 34% of methane. The aromatic hydrocarbons recovered were identified through their bromo- and nitro derivatives as 1,2,3-trimethylbenzene, and through infrared analysis as a mixture of 1,2,3- and 1,2,4-trimethylbenzene (Fig. 5).

Destructive Hydrogenation of Isocamphane.—Fifty grams (0.38 mole) of isocamphane was destructively hydrogenated at 210°. One mole of hydrogen per mole of dihydroterpene charged was absorbed. The boiling range and the index of refraction of the destructively hydrogenated isocamphane are given in Fig. 2. Less than 5% of the destructively hydrogenated isocamphane underwent dehydrogenation when passed over platinized alumina at 300°.

Destructive Hydrogenation of Isobornylane.—Forty grams (0.25 mole) of isobornylane was treated with hydrogen at 215°; one mole of hydrogen per mole of hydrocarbon charged was absorbed. The boiling range and the index of refraction of the destructively hydrogenated isobornylane are represented in Fig. 3. The destructively hydrogenated product did not undergo dehydrogenation at 300° when passed over platinized alumina.

Infrared Spectra Analysis (by W. S. Gallaway[10]).—The infrared spectra were obtained by the use of a large Gaertner spectrometer very similar to the one described by McAlister.[11] The data are obtained as automatic recordings of the intensity of the light transmitted through a rock-salt cell of 0.10 mm. sample thickness. Direct comparison of these records with those for a blank cell yields the per cent. transmission at any desired wave length.

The compositions of the samples were determined by a two-step process. The first was to identify the components present by a comparison with the spectra of pure

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(8) E. H. Huntress and J. S. Autenrieth, *ibid.*, **63**, 3446 (1941).

(9) Analyses were made by Dr. T. S. Ma, University of Chicago.

(10) Universal Oil Products Company Research Laboratories, Riverside, Illinois.

(11) E. D. McAlister, G. L. Matheson and W. J. Sweeney, *Rev. Sci. Instruments*, **12**, 314 (1941).

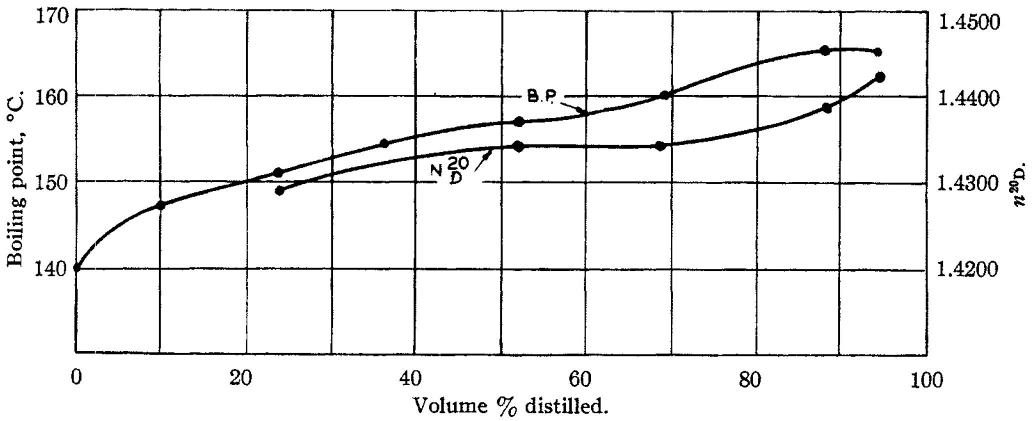

Fig. 2.—Distillation of the products obtained from the destructive hydrogenation of isocamphane.

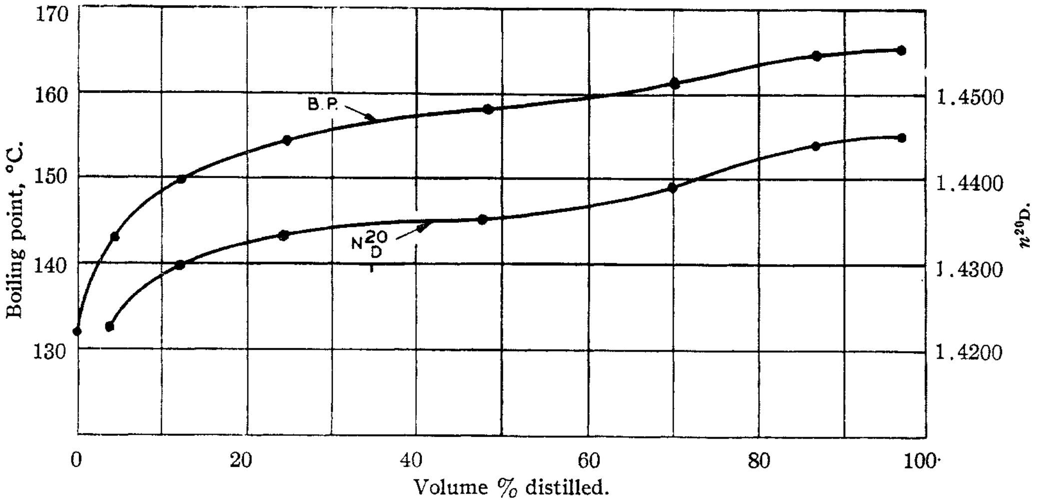

Fig. 3.—Distillation of the products obtained from the destructive hydrogenation of isobornylane.

materials. Then, after all the sample absorptions had been accounted for by such comparisons, the application of the Lambert-Beer absorption law at the proper wave lengths yielded the per cent. concentration of the various components. More complete details of this method may be found in the articles by Brattain,[12,13] Wright,[14] and Barnes.[15]

This procedure may be followed by a study of Figs. 4 and 5 wherein the intensities of the absorption maxima of the various materials are plotted at the proper wave lengths for the interval of 7.5 to 11 microns. It may be seen that the lines of the various pure compounds appear in the sample patterns with intensities approximately proportional to their concentrations. Further, it is seen that nearly all the sample absorptions are accounted for by these pure components. The few remaining lines are quite weak and represent a small amount of unknown material. The lack of identification may be due either to failure to find pure materials having these absorptions or to not being able to make a positive identification for such low concentrations.

These bar diagrams, while they show the data quite clearly, suffer from the disadvantage that they do not give the extent of the absorption between the peaks or the widths of the bands. Thus it is difficult to determine from these plots whether an absorption belonging to one component and lying close to a band of another component should appear as a separate resolved absorption or should be merged with its neighbor. For example, in the mixtures of the trimethylbenzenes, only one absorption appears at 8.02 μ and two are seen at 8.61 and 8.65 μ whereas two are expected in both cases. In the former, the bands are somewhat wide, while in the latter case, they are very sharp. Similarly, one line of the doublet in the *p*-cymene spectrum at 9.5 μ is not noticeable in the mixture patterns owing to the presence of the *o*-cymene band at 9.62 μ. These apparent difficulties are not troublesome when the original recordings are studied and intensities are determined from them.

The several wave lengths used for calculating the composition of the various samples are given in Table I.

TABLE I

WAVE LENGTHS OF CHARACTERISTIC INFRARED ABSORPTIONS, IN μ

1,2,3-Trimethylbenzene	1,2,4-Trimethylbenzene	*p*-Cymene	*o*-Cymene
9.14	8.88	9.45	9.20
9.31	8.79	9.80	9.63
9.91	10.01	12.23	13.19
10.13	12.41		13.78
13.05			

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[12] R. R. Brattain and O. Beeck, *Bull. Am. Phys. Soc.*, **16**, 9 (1941).

[13] R. R. Brattain and O. Beeck, *J. App. Phys.*, **13**, 699 (1942).

[14] N. Wright, *Ind. Eng. Chem., Anal. Ed.*, **13**, 1 (1941).

[15] R. B. Barnes, R. C. Gore, U. Liddel and V. F. Williams, *ibid.*, **15**, 659 (1943).

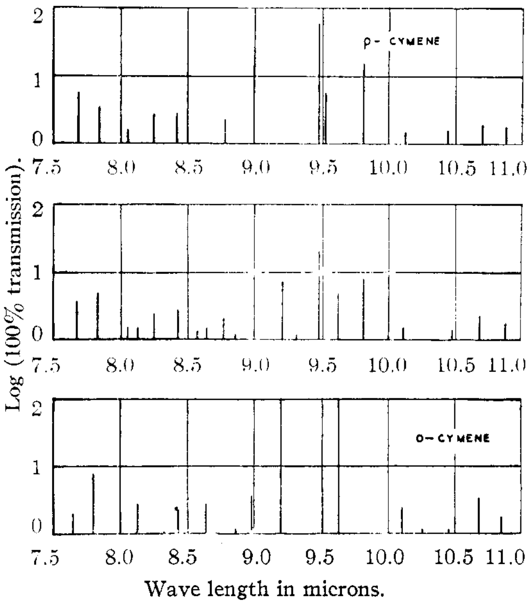

Fig. 4.—Infrared analysis: aromatics from the dehydrogenation at 240° of the destructively hydrogenated pinane.

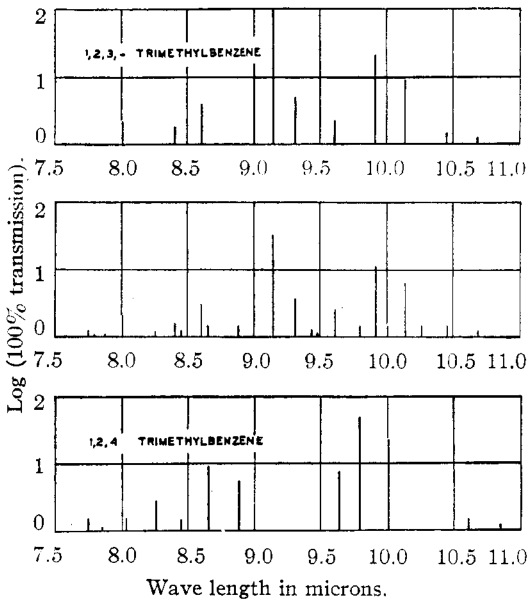

Fig. 5.—Infrared analysis: aromatics from the dehydrogenation at 300° of the destructively hydrogenated pinane.

Summary

The fission of one of the rings in pinane, isocamphane and isobornylane was investigated.

Pinane on destructive hydrogenation in the presence of a nickel–kieselguhr catalyst yielded about 13% of 1-methyl-4-isopropyl- and 5% 1-methyl-2-isopropylcyclohexane, 65% of 1,1,2,3- and 10% of 1,1,2,5-tetramethylcyclohexane. The disubstituted cyclohexanes were separated from the polymethylated cyclohexanes by selective dehydrogenation. The dehydrogenation of the tetramethylcyclohexanes yielded the corresponding 1,2,3- and 1,2,4-trimethylbenzene. The aromatic hydrocarbons were identified by chemical means and by infrared analysis.

Isocamphane and isobornylane yielded on destructive hydrogenation a mixture of compounds which consist probably of alkylated cyclopentanes.

EVANSTON, ILLINOIS RECEIVED[16] FEBRUARY 15, 1947

[16] Original manuscript received April 11, 1946.

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE, PITTSBURGH, PA.]

Hydroxyalkylation with Cyclic Alkylene Esters. I. Synthesis of Hydroxyethylapocupreine

BY WARNER W. CARLSON AND LEONARD H. CRETCHER

The hydroxyalkylation of phenolic cinchona alkaloid derivatives has been reported in previous publications[1] from this department. The reagents normally employed in such syntheses, alkylene oxides or halohydrins, were found to give low yields of the desired products, presumably because of quaternary salt formation. A two-step procedure finally was developed[1b] whereby a benzyloxyalkyl toluenesulfonate was treated with an alkali salt of the phenolic alkaloid to give a benzyloxyalkyl ether derivative; removal of the benzyl grouping by acid hydrolysis then afforded the desired hydroxyalkyl cinchona ether. The toluenesulfonate procedure, while it represented a definite improvement, in terms of yield, over methods previously employed, still was not found to be completely satisfactory. Accordingly, the search for new hydroxyalkylating agents was continued, and two such substances, the cyclic sulfite and carbonate esters of ethylene glycol, are now reported. Through the use of one of these, ethylene carbonate, the hydroxyethylation of a typical phenolic alkaloid, apocupreine, has been accomplished in good yield under mild conditions.

Only one previous instance of the use of a cyclic glycol ester as an alkylating agent has been found in the literature. By the action of silver sulfate on ethylene bromide in xylene, Baker and Field[2] prepared ethylene sulfate (I) in low yield,

[1] (a) Butler, Nelson, Renfrew and Cretcher, THIS JOURNAL, **57**, 575 (1935); (b) Butler and Renfrew, *ibid.*, **60**, 1473 (1938).

[2] Baker and Field, *J. Chem. Soc.*, 86 (1932).