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THE CYCLO-ADDITION OF 1,3-BUTADIENES TO AROMATIC HYDROCARBONS TO FORM INDANS[1]

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In 1955 Carpenter gave a survey of research on polycyclic musks carried out in these Laboratories.[2] One of the compounds reported was the acetyl derivative of the hydrocarbon resulting from the sulfuric acid-catalyzed reaction of p-cymene with 2,3-dimethyl-2-butene. Subsequent study with this hydrocarbon and with other methods of synthesis has led to a revision of its assigned structure and has resulted in the discovery of a new reaction for the synthesis of indan derivatives starting from isoprene or from 2,3-dimethyl-1,3-butadiene. We now wish to report on this novel reaction and the chemistry involved in its discovery.

It has been well established that p-cymene reacts with many olefins in the presence of sulfuric

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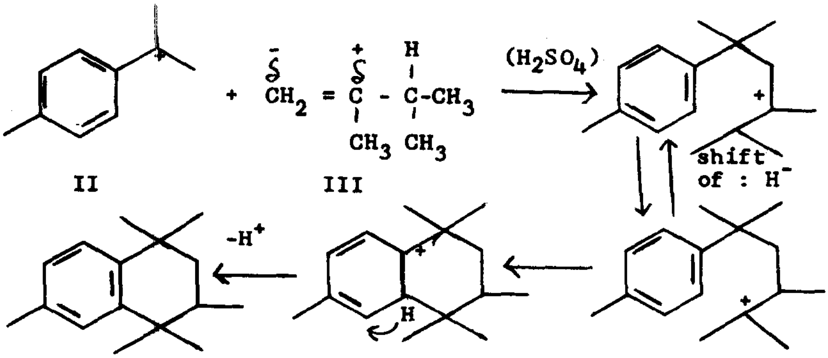
[1] Methods of conducting the novel reactions described in this and in subsequent papers are the subject of United States and foreign patent applications. Much of the work was carried out in 1959 and 1960.

[2] M. S. Carpenter, Proc. Sci. Sect. Toilet Goods Assoc. 23, 1 (1955).

or hydrofluoric acids to yield indan derivatives.[3] In this reaction hydride-transfer[4] occurs between p-cymene and the protonated form of the olefin. With 2,3-dimethyl-1-(or-2-) butene an additional hydride-transfer occurs resulting in a tetralin (I), rather than the indan structure which was originally proposed.[2] The p-cymyl carbonium ion (II), resulting from the first hydride-transfer, seems to react as follows:



II

III

I (m. p. 66-67°)

The structure of I has been confirmed by alternate syntheses[5] as well as by study of its NMR spectrum.

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[3] V. N. Ipatieff, H. Pines, and R. C. Olberg, J. Amer. Chem. Soc. 70, 2123 (1948). A. V. Grampoloff, Helv. Chim. Acta 38,1263 (1955). S. H. Weber, D. B. Spoelstra and E. H. Polak, Rec. trav. chim. 74, 1179 (1955). M. J. Schlatter, Amer. Chem. Soc. Div. Petrol. Chem. Preprints Symposia 1 No. 2. (Chemicals from Petrol.) 77-82 (1956).

[4] Hydride-transfer reactions are discussed in a review paper by N. C. Deno, H. J. Peterson, and G. S. Sainer, Chem. Rev. 60, 7 (1960).

[5] More on this reaction and alternate synthetic routes will be included in a later publication on polycyclic musks.

The NMR trace shows a total of six methyl groups identified as follows: one doublet centered at 0.95 ppm., four saturated methyls at 1.03, 1.22, 1.25 and 1.30 ppm., and one benzylic methyl at 2.25 ppm. There appear protons, giving a multiplet centered at 1.6 ppm., similar to those of β-saturated-ring protons of previously studied tetralin structures. These appear up field compared to analogous protons of indan structures. The three protons on the aromatic ring show as a quartet for two ortho protons plus a third peak superimposed.[6] Infrared spectrum analysis suggests a tetralin structure. The band at 7.60 - 7.65 μ, characteristic of indans,[7] is lacking.

In the mechanism discussed above the olefin, 2,3-dimethylbutene (III), functions, in its protonated form, as hydride-acceptor, becoming 2,3-dimethylbutane. As a result only half of the olefin, at best, can be utilized for the desired cyclialkylation[8] process. With the object of simultaneously providing hydride-acceptor and cyclialkylation agent there was substituted 2,3-dimethyl-1,3-butadiene for III in the sulfuric acid-catalyzed reaction

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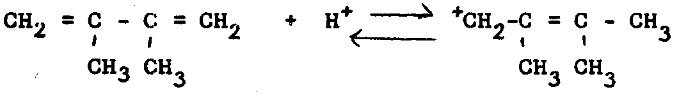
[6] We are indebted to Dr. Martin Saunders of Yale University for the NMR measurement and interpretation.

[7] Unpublished infrared data on indans and tetralins.

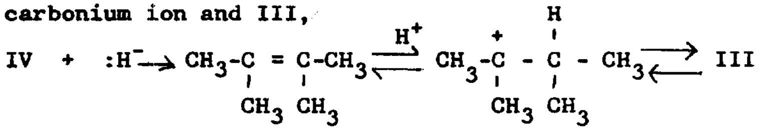
[8] The term "cyclialkylation" was coined by H. A. Bruson and J. W. Kroger to describe the formation of a "new cycle by attachment of a saturated divalent alkyl group to the aromatic nucleus". (J. Amer. Chem. Soc. **62**, 37 (1940)).

with p-cymene. It was postulated that the reaction might proceed with the formation of the methylprenyl carbonium ion,



$$CH_2=\underset{CH_3}{C}-\underset{CH_3}{C}=CH_2 + H^+ \rightleftharpoons {}^+CH_2-\underset{CH_3}{C}=\underset{CH_3}{C}-CH_3 \qquad (IV)$$

Then this carbonium ion would withdraw the hydride ion from p-cymene resulting in the formation of the p-cymyl carbonium ion and III,



$$IV + :H^- \rightarrow CH_3-\underset{CH_3}{C}=\underset{CH_3}{C}-CH_3 \overset{H^+}{\rightleftharpoons} CH_3-\underset{CH_3}{\overset{+}{C}}-\underset{CH_3}{\overset{H}{C}}-CH_3 \rightleftharpoons III$$

which would then react by the same route as before yielding I. However, the reaction took a different course yielding a novel hydrocarbon, IV. This product, a colorless liquid, b.p. 99° (2 mm.), n_D^{20} 1.5175, d_4^{25} 0.9206, gave an elemental analysis indicating a bicyclic compound, $C_{16}H_{24}$. Vapor phase chromatograms of the hydrocarbon indicated a purity of about 95%. Its infrared spectrum shows the pattern for 1,2,3,4-tetrasubstitution in the 5 to 6 μ range.[9] The absence of appreciable absorption in the 11.0 to 11.6 μ range along with the strong band at 12.28 μ supports this.

Similarly from isoprene there was obtained in good yield (62% of theory) a homolog V, ($C_{15}H_{22}$). The vapor phase chromatogram indicated 95% purity. Here again the infrared spectrum points to a tetrasubstituted

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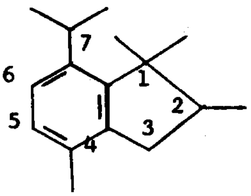
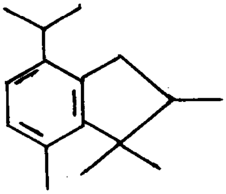
[9] C. W. Young, R. B. DuVall, and N. Wright, Anal. Chem., 23, 709 (1951).

benzene derivative. In addition there appears a well-defined medium band at 7.62 μ in the region where indans usually absorb.[7]

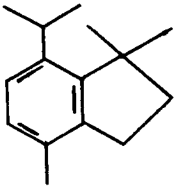
NMR spectra, correlated with the infrared spectra of the novel bicyclic hydrocarbons, indicate as possible structures the following[10]



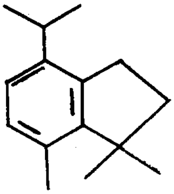
IV-a



IV-b



V-a



V-b

From consideration of probable reaction mechanism the structure IV-a and V-a are favored. The NMR spectrum of IV shows multiplets, centered at 3.30 and 2.78 ppm. characteristic of benzylic hydrogens. The trace shows a total of six methyl groups : one doublet centered at 1.00 ppm., produced by the "split-methyl" on position 2 (of IV-a), peaks at 0.97 and 1.37 ppm. representing the geminal methyls at position 1, the two overlapping doublets, centered at 1.14 and 1.18 ppm., produced by the methyls of the isopropyl group (at position 7), and the benzylic methyl group at 2.15 ppm. (position 4). The quartet centered at 6.88 ppm. is produced by the ring protons at positions 5 and 6. The NMR spectrum of V shows it to be a homolog of IV lacking the methyl group in position 2. The trace lacks the

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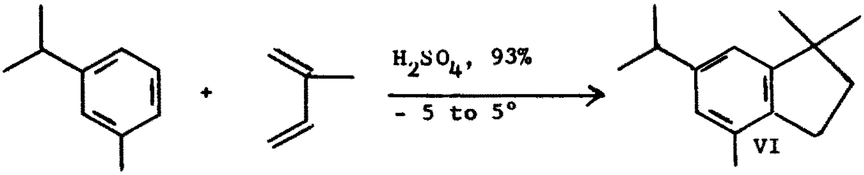
[10] We are grateful to Dr. Martin Saunders of Yale University and Dr. Seymour Lemberg of International Flavors and Fragrances, Inc. for assistance in interpreting the NMR spectra.

doublet centered at 1.00 ppm. shown above. In this case the methyls of the isopropyl group are equivalent and produce doublets that coincide. Otherwise it is similar to the spectrum of IV. The spectra of the purified acetyl derivatives differ from those of the corresponding hydrocarbons only by the additional methyl peak produced by the acetyl group and by the single 1-proton peaks of the aromatic protons.

m-Cymene reacts with isoprene under identical conditions, giving an indan derivative, VI, a colorless liquid, b.p. 82° (1 mm.), n_D^{20} 1.5106 (76% of theory).



The infrared spectrum shows the typical pattern for 1,2,3,5-tetrasubstitution on the aromatic ring[9,11] with medium bands at 12.97 μ and 13.96 μ, and the weaker pattern in the 5 to 6 μ region. In addition there is medium absorption at 7.60 μ, characteristic of indans. The vapor phase chromatogram shows one compound present to the extent of about 96%. Acetylation gave a solid derivative, m.p. 68.5 - 69°.

This cyclialkylation type of reaction, yielding indan derivatives, readily occurs when alkyl derivatives of benzene, having at least two adjacent positions on the aromatic ring

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[11] Cl. Ferrero and R. Helg, Helv. Chim. Acta **42**, 2113 (1959).

unsubstituted, are reacted with isoprene or with 2,3-dimethyl-1,3-butadiene in the presence of concentrated sulfuric acid. From mono-alkylbenzenes are obtained 6-alkyl-1,1-dimethylindans, with cumene and t-butylbenzene giving the best yields (53 and 61% of theory respectively). Vapor phase chromatograms of these 6-isopropyl-and 6-t-butyl-1,1-dimethylindans showed purities of about 95%. They were identical with the two hydrocarbons synthesized from cuminaldehyde and from p-t-butylbenzaldehyde. Beets and co-workers,[12] who first prepared these, reported acetyl derivatives, melting at 48.1° - 48.6° and 77.1° - 77.4° respectively, which had strong musk odors. Acetyl derivatives of the isoprene-derived products have identical properties.

Cyclialkylation of the xylenes, as well as other dialkyl-and trialkylbenzenes, with isoprene and with 2,3-dimethyl-1,3-butadiene proceeds very well. Pseudocumene reacts with isoprene to produce 70% of theory of a solid hydrocarbon, which is probably 1,1,4,6,7-pentamethylindan. The infrared spectrum shows a medium band at 7.62 μ, indicating indan structure. A band at 11.65 μ is in the region where pentasubstituted benzenes absorb.[13]

Benzene is cyclialkylated with isoprene to produce a low yield of 1,1-dimethylindan plus a considerable amount of a colorless solid, m.p. 92-94°, believed to be 1,1,7,7-tetramethyl-s-hydrindacene.

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[12] M. G. J. Beets, H. Van Essen, and W. Meerburg, Rec. trav. chim. 77, 854 (1958).

[13] L. J. Bellamy, The Infra-red Spectra of Complex Molecules, Second Edition, Chapt. 5, p. 79. John Wiley & Sons, Inc., New York, N.Y. (1960).

Further studies are being made on the structures and mechanism of formation of the "isoprene-cyclialkylation" indan derivatives. This will be reported on in the future.

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