[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE FLORIDA STATE UNIVERSITY]

Azulenes. VI. A Further Instance of Isopropyl Group Migration[1a]

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The synthesis of 3-isopropyl-4,5-dimethylindan is described. The usual diazoacetic ester treatment of this indan, followed by decarboxylation and dehydrogenation, resulted in the formation of 2-isopropyl-4,5-dimethylazulene by migration of an isopropyl group and the isolation, in an impure state, of what is believed to be 3-isopropyl-4,5-dimethylazulene.

The isoprenoid 3-isopropyl-4,5-dimethylazulene (I) is of some interest since it may represent an azulene occurring in nature or may appear among the dehydrogenation products of sesquiterpenes of unknown structure.[2] Although the most noteworthy of these, chamazulene, recently has been identified[3-5] as 1,4-dimethyl-7-ethylazulene, the structures of helenazulene,[6] and a number of others[7] remain to be established. The present communication reports our work dealing with the synthesis of I.

The preparation of 3-isopropyl-4,5-dimethylindan from hemimellityl chloride is outlined in the accompanying flow sheet and needs no further discussion. Treatment of this indan with diazoacetic ester, saponification of the resulting carboxylic ester, decarboxylation and dehydrogenation with palladium–charcoal furnished primarily a *violet-blue* azulene accompanied by a *blue* fraction. The visible spectrum of the violet-azulene (see experimental part) was very similar to the spectrum of 2-isopropyl-4,5-dimethylazulene (II) whose synthesis has been reported previously.[8] However, the m.p. of its trinitrobenzene complex was somewhat low, probably due to difficulties in separating the isomers. Maxima in the spectrum of the blue azulene (λ_{max} 583, 600, 736 and shoulders at 548, 562, 630, 660, 695 mμ) were in excellent agreement with the maxima to be expected of 3-isopropyl-4,5-dimethylazulene on the basis of Plattner's rules.[9] However, the bands remained somewhat less sharply defined than usual, although the usual purification steps were repeated numerous times. This suggests[10] that we were not completely successful in removing the contaminants, principally II.[11]

These results furnish another example of the ease with which the isopropyl group migrates from position 1 (or 3) to position 2 of the azulene nucleus under the conditions of palladium–charcoal dehydrogenation and render unlikely the presence of I among the high-temperature dehydrogenation products of sesquiterpene derivatives. It is not clear yet whether, as in earlier instances,[12] the presence of a methyl group at position 8 (or 4) is necessary to induce migration. The isolation of unrearranged 1-isopropyl- and 1-isopropyl-5-methylazulene by Arnold[13] from dehydrogenations carried out under similar conditions suggests that this may be the case.

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Experimental[14]

2,3-Dimethylphenylacetonitrile.—A solution of 48 g. of hemimellityl chloride in 60 ml. of ethanol was added dropwise, with stirring and heating, to a hot solution of 25 g. of potassium cyanide in 25 ml. of water. Stirring and refluxing was continued for three hours, the ethanol was removed by distillation, water was added and the organic layer was extracted with ether. Distillation of the ether extract yielded 43 g. (90%) of a fraction boiling at 98–105° (3 mm.) which solidified on standing. The product melted at 49.5° after recrystallization from petroleum ether.

Anal. Calcd. for $C_{10}H_{11}N$: C, 82.71; H, 7.65. Found: C, 82.76; H, 7.46.

2,3-Dimethylphenylacetic Acid.—A mixture of 2 g. of the nitrile, 25 ml. of ethanol, 5 ml. of water and 4 g. of potassium hydroxide was refluxed until the evolution of ammonia ceased (nine hours). The solvent was distilled, water was added, the aqueous layer was extracted with ether, acidified and the solid acid which precipitated in quantitative yield was recrystallized from hexane to a constant m.p. of 118.5–119.5°.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.15; H, 7.38. Found: C, 73.28; H, 7.30.

α-(2,3-Dimethylphenyl)-isovaleronitrile.—To a solution of 14.5 g. of 2,3-dimethylphenylacetonitrile in 50 ml. of dry toluene was added 3.9 g. of sodamide. The mixture was heated and stirred for one hour until ammonia evolution ceased. It was allowed to cool to room temperature and 12.3 g. of isopropyl bromide was added dropwise. After one additional hour stirring and heating the mixture was decomposed with a little methanol and diluted with water. The organic layer was washed with water, dilute base and acid and again with water, dried and distilled. The product was collected at 105–115° (2 mm.), wt. 14.9 g. (80%). The analytical sample boiled at 103–104° (1.6 mm.), $n^{26}D$ 1.5159.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.86; H, 9.15. Found: C, 83.56; H, 9.15.

α-(2,3-Dimethylphenyl)-isovaleric Acid.—A mixture of 101 g. of the nitrile, 750 ml. of amyl alcohol and 200 g. of

(1) (a) Previous paper, W. Herz, THIS JOURNAL, **76**, 3349 (1954). (b) Abstracted from the thesis of Bruce E. Cleare, submitted in partial fulfillment of the requirements for the degree Master of Science, 1954.

(2) A. J. Haagen-Smit, Azulenes, "Fortschritte der Chemie Organischer Naturstoffe," Vol. 5, Springer Verlag, Vienna, 1948, p. 40.

(3) A. Meisels and A. Weizmann, THIS JOURNAL, **75**, 3866 (1953).

(4) F. Sorm, J. Novak and V. Herout, *Collection Czechoslov. Chem. Communs.*, **18**, 527 (1953).

(5) E. Stahl, *Ber.*, **87**, 202 (1954).

(6) R. Adams and W. Herz, THIS JOURNAL, **71**, 2354 (1949).

(7) M. Gordon, *Chem. Revs.*, **30**, 127 (1952). However, linderazulene has recently been identified as chamazulene (K. Takeda and W. Nagata, *Pharm. Bull. Japan*, **1**, 164, 241 (1953); F. Sorm, V. Herout and K. Takeda, *Collection Czechoslov. Chem. Communs.*, **19**, 186 (1954)) and lactarazulene appears to be dehydro-S-guaiazulene (F. Sorm, V. Benešova and V. Herout, *ibid.*, **19**, 357 (1954)).

(8) W. Herz and J. L. Rogers, THIS JOURNAL, **75**, 4498 (1953).

(9) Pl. A. Plattner, *Helv. Chim. Acta*, **24**, 283E (1941); compare with the maxima of S-guaiazulene, chamazulene and lactarazulene given in ref. 7.

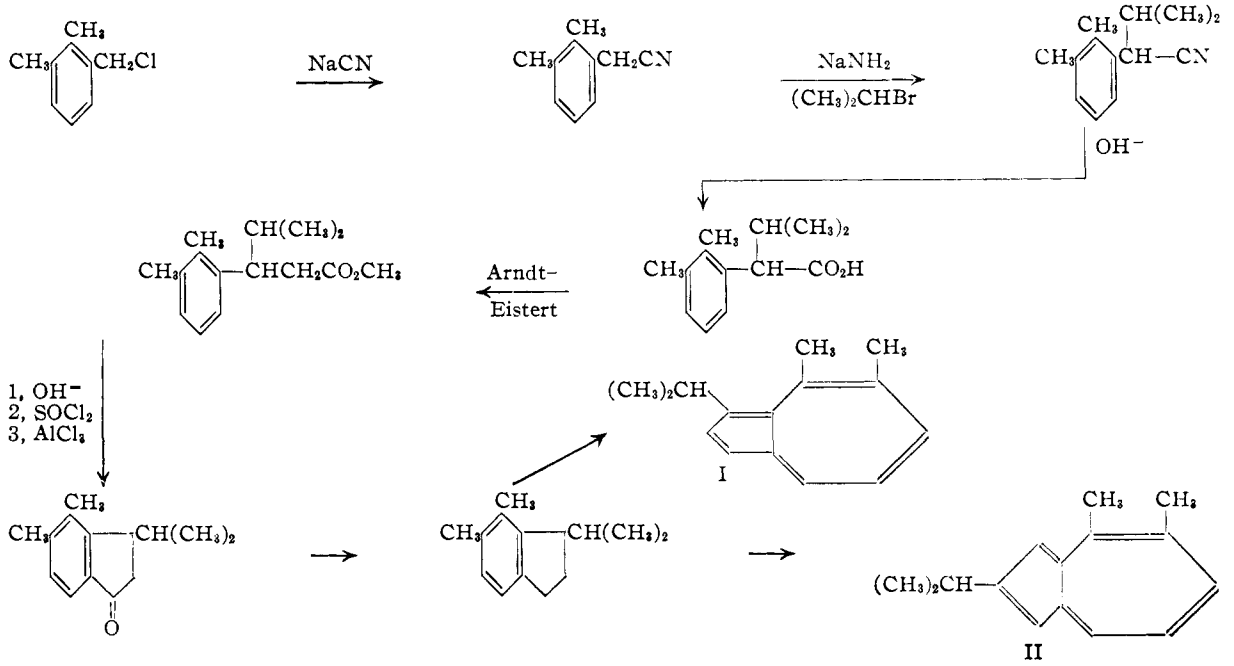
(10) H. Arnold and H. Schachtner, *Ber.*, **86**, 1445 (1953).

(11) It is suspected that some of the difficulties encountered during the purification process arose because of isomerization on the alumina columns. Repeated passage through alumina of a solution of the blue azulene resulted in a final eluate appearing to retain a violet tinge.

(12) W. Herz, THIS JOURNAL, **75**, 73 (1953); T. Ukita, H. Watanabe and M. Miyazaki, *ibid.*, **76**, 4585 (1954).

(13) H. Arnold, *Ber.*, **80**, 172 (1947).

(14) Melting and boiling points are uncorrected. Analyses by Drs. Weiler and Strauss, Oxford.



potassium hydroxide was refluxed for two days in a copper flask until the evolution of ammonia had ceased. Water was added and the mixture of amyl alcohol and water was distilled until the organic solvent was removed. The residual aqueous solution was acidified and yielded 118 g. of crude acid. Recrystallization from ligroin afforded colorless crystals, m.p. 132–132.5°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.68; H, 8.79. Found: C, 75.76; H, 8.71.

α-(2,3-Dimethylphenyl)-isocaproic Acid.—A mixture of 18.3 g. of the preceding acid and 18.3 g. of thionyl chloride was heated on the steam-bath for 20 hours. Distillation furnished 20.5 g. of a light yellow liquid, b.p. 112–115° (2 mm.).

A solution of 20.5 g. of the acid chloride in 50 ml. of anhydrous ether was added to a diazomethane solution prepared from 40 g. of nitrosomethylurea. After 14 hours the ether was removed at reduced pressure. The residual yellow diazoketone which did not crystallize weighed 19 g.

The Wolff rearrangement, carried out under the conditions recommended by Newman and Beal,[15] yielded a total of 92.2 g. of methyl ester, b.p. 106° (0.25 mm.), $n^{25}D$ 1.5076, from 134.6 g. of crude diazoketone. This represents a 64% over-all yield based on the original acid.

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.36; H, 9.01.

Saponification furnished 85.5 g. of the crude acid (98% yield based on methyl ester, 63% over-all). Recrystallization from ligroin gave colorless crystals, m.p. 74–74.5°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.58; H, 9.07.

3-Isopropyl-4,5-dimethylindanone.—A mixture of 80 g. of the previous acid and 80 g. of thionyl chloride was heated on the steam-bath for four hours. Distillation furnished 61.5 g. of acid chloride, b.p. 121° (1 mm.), which was added cautiously to 80 g. of anhydrous aluminum chloride suspended in thiophene-free benzene. After one day the product was worked up in the usual way. The yield was 46.5 g. (63%), m.p. 88° after recrystallization from *n*-hexane.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.35; H, 9.08.

The dinitrophenylhydrazone was recrystallized from ethyl acetate and melted at 255–255.5°.

Anal. Calcd. for $C_{20}H_{22}N_4O_4$: N, 14.7. Found: N, 15.4.

(15) M. S. Newman and P. F. Beal, THIS JOURNAL, **72**, 5163 (1950).

3-Isopropyl-4,5-dimethylindan.—Reduction of 45 g. of the indanone in the manner described earlier[16] resulted in 36.5 g. (87%) of a liquid boiling at 93.5–94° (1 mm.), $n^{24}D$ 1.5243.

Anal. Calcd. for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.10; H, 11.02.

2- and 3-Isopropyl-4,5-dimethylazulene.—Repeated treatment of 17 g. of 3-isopropyl-4,5-dimethylindan with diazoacetic ester gave 18 g. of crude product boiling above 120° (3 mm.). Saponification of this material yielded 5.5 g. of a green oil, b.p. 165–200° (1 mm.), which was decarboxylated and dehydrogenated in the usual manner[16] with 10% palladium–charcoal. The resulting violet-blue liquid, b.p. 100–145° (1.5 mm.), wt. 2.0 g., was taken up in ethanol and mixed with 1.5 g. of trinitrobenzene in 30 ml. of warm ethanol. When the solution was concentrated somewhat and allowed to cool, there precipitated 1.5 g. of violet-black trinitrobenzene complex. Decomposition of the solid by chromatography over alumina (eluant cyclohexane) yielded a violet-blue eluate which was concentrated and reconverted to the trinitrobenzene complex. Repeated crystallization of the complex from ethanol furnished needles of m.p. 134–135°. Although this m.p. is somewhat lower than the m.p. of authentic 2-isopropyl-4,5-dimethylazulene–TNB complex,[8] the visible spectrum of an isoöctane solution, prepared by decomposing 8.3 mg. of the complex over alumina, exhibited almost identical maxima (shoulder at 545; maxima at 563, 575, 609, 672 mμ; ϵ_{max} 298, 293, 257, 100; minima at 600 and 670 mμ; ϵ_{min} 252, 99). The peaks were not quite as sharp as observed earlier.[17] A mixed m.p. with the TNB complex of authentic 2-isopropyl-4,5-dimethylazulene was 136°.

Anal. Calcd. for $C_{21}H_{21}N_3O_6$: C, 61.34; H, 5.14. Found: C, 61.46; H, 5.33.

The ethanolic mother liquor from the first preparation of the trinitrobenzene complex was concentrated to dryness *in vacuo*. When the residue was chromatographed (eluant cyclohexane), the eluate was considerably more blue than a solution of 2-isopropyl-4,5-dimethylazulene. This suggested that the TNB complex of the 3-isopropyl derivative was somewhat more soluble in ethanol than that

(16) W. Herz, *ibid.*, **73**, 4295 (1951).

(17) A redetermination of the visible spectrum of authentic 2-isopropyl-4,5-dimethylazulene on an automatic recording Beckman model DK spectrophotometer gave the following values: shoulder at 535–540; maxima at 566, 575, 612 and 672 mμ; ϵ_{max} 388, 373, 343 and 133; minima at 600 and 665 mμ; ϵ_{min} 337, 129). The considerable decrease in ε shown by the rearranged azulene is characteristic of slightly contaminated azulenes.[10]

of the isomeric 2-substituted compound. The blue eluate, wt. 0.9 g., was dissolved in ethanol and treated with 0.3 g. of trinitrobenzene. The complex which separated on standing was recrystallized from ethanol and melted at 105°. The visible spectrum of a solution prepared by decomposition of this fraction (λ_{max} 583, 600, 736 mμ; shoulders at 548, 562, 630, 660, 695 mμ; ϵ_{max} 221, 218, 49; λ_{min} 595; ϵ_{min} 216) indicated that this material consisted largely of the desired azulene, but the bands were less well pronounced than would be expected if it were pure.[10] The mother liquor was concentrated to dryness, rechromatographed and the eluate reconverted to the TNB complex. This was repeated three times in an effort to free the azulene from the less soluble contaminant. The trinitrobenzene complex separating from the last treatment melted at 92–95°, but the visible spectrum indicated no greater degree of purity.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE VIRGINIA POLYTECHNIC INSTITUTE]

The Synthesis of 10-Phenyl-1,2-benzanthracene and the Three Isomeric 10-Monomethylphenyl-1,2-benzanthracenes[1,2]

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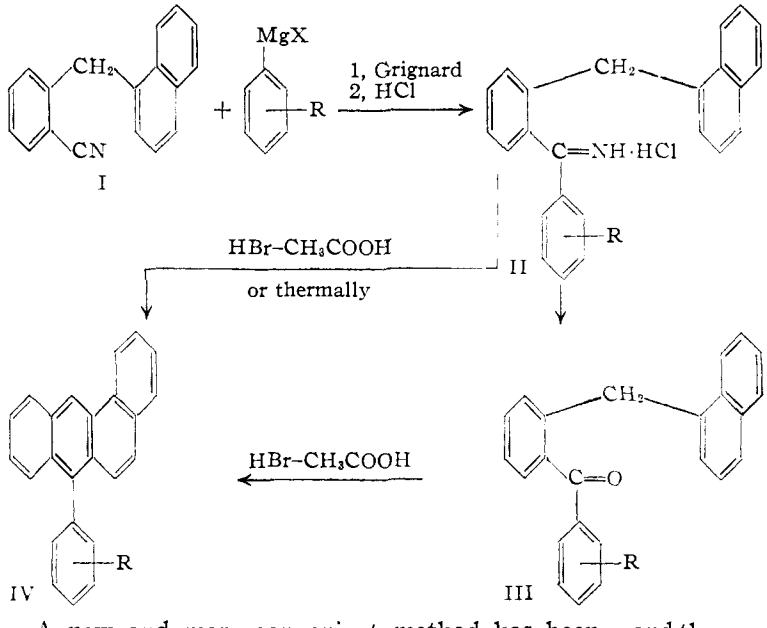
The synthesis of four new ketimine hydrochlorides, four new ketones and four new hydrocarbons has been accomplished. Bradsher's aromatic cyclodehydration reaction[3] has been extended to the 10-phenyl-1,2-benzanthracene system.

In 1940, Bradsher[3] presented a new method for synthesizing aromatic hydrocarbons. In a later publication[4] he extended this aromatic cylodehydration reaction to the preparation of 9-methyl- and 10-methyl -1,2- benzanthracene and suggested that his method might prove useful for the synthesis of other new carcinogenic compounds. We have now extended Bradsher's synthesis to the preparation of hydrocarbons in the 10-aryl-1,2-benzanthracene system.



A new and more convenient method has been found for obtaining the 1-(2-cyanobenzyl)-naphthalene (I) required in the synthesis. Bradsher[4] began with crude 2-chlorophenyl- 1-naphthylcarbinol prepared by the Grignard reaction and reduced this with phosphorus and hydriodic acid to the corresponding *o*-chlorobenzylnaphthalene. Although we were able to isolate the intermediate carbinol,[5] it was found that the reduction step gave variable results. The new method involves the direct condensation of *o*-chlorobenzyl chloride with naphthalene. Previous reports concerning the condensation of naphthalene with benzyl chloride indicate that considerable quantities of di- and tribenzylnaphthalenes are formed concurrently and that the monobenzylnaphthalenes are obtained as a mixture of isomers almost impossible to separate.

We have found that losses due to dibenzylation can be suppressed by adding the high-boiling products to subsequent runs along with the recovered naphthalenes. In this way over-all yields of 79% of monobenzyl derivative (based on the halide) were obtained.

Using zinc dust as a catalyst we were able to produce a mixture of isomers which was 70% 1-(2-chlorobenzyl)-naphthalene.[6] This mixture could not be separated conveniently, so it was converted directly to a mixture of nitriles by the Rosenmund–von Braun method with isolation of the pure 1-(2-cyanobenzyl)-naphthalene (I) being accomplished by fractional crystallization from 90% ethanol.

The reaction between the nitrile I and the appropriate Grignard reagent led to an excellent yield of the ketimine which was isolated as the hydrochloride.[7] This was hydrolyzed quantitatively to the ketone III using dilute sulfuric acid and subsequently cyclodehydrated to the hydrocarbon IV using a mixture of hydrobromic and acetic acids. The established procedure for this last reaction

(1) Presented before the Division of Organic Chemistry at the 126th Meeting of the American Chemical Society, New York, N. Y., September, 1954.

(2) This paper has been abstracted from the Masters' theses presented to the Virginia Polytechnic Institute by Joseph Shulman in 1950 and by Alexej Bořkovec in 1953.

(3) C. K. Bradsher, THIS JOURNAL, **62**, 486 (1940).

(4) C. K. Bradsher, *ibid.*, **62**, 1077 (1940).

(5) F. A. Vingiello, *ibid.*, **73**, 1887 (1951).

(6) In a future communication we will describe a modified experiment which leads to predominantly the 2-isomer.

(7) Higher yields of the ketones were obtained if the ketimine hydrochlorides, which hydrolyze easily, were not isolated but hydrolyzed directly.