

terized by its 2,4-dinitrophenylhydrazone, together with about 0.35 g. of acetone peroxide isolated by filtration. The total amount of acetone and its derivatives isolated accounted for about 40% of the theoretical.

3,8(9)-*p*-Menthadiene (IV). Maleic Anhydride Adducts.
A. 4,7-Dimethyl-1,2,3,5,6,7,8,9-octahydronaphthalene-1,2-dicarboxylic Acid (XI).—The residue obtained from the steam distillation during the purification of compound III by treatment with maleic anhydride (see above) consisted of about 15 g. of heavy oil which crystallized on standing. The solid thus obtained was dissolved in ether and nearly quantitatively extracted from it with a 10% aqueous potassium hydroxide. Extraction of the acidified aqueous layer with ether and trituration with 40% aqueous acetic acid gave 12 g. of a white crystalline powder, m.p. 170–190°. Recrystallization from 40% aqueous acetic acid gave colorless cubes, m.p. 203–204°.

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.66; H, 7.94. Found: C, 66.4; H, 7.82.

The adduct m.p. 203–204° was formed also when both pure 3,8(9)-*p*-menthadiene²¹ and a synthetic sample of IV prepared according to Perkin and Wallach¹³ were treated with an ether solution of maleic anhydride at reflux.

B. 4,7-Dimethyl-1,2,3,4,6,7,8,9-octahydronaphthalene-1,2-dicarboxylic Acid Anhydride.—Six grams of the dicarboxylic adduct XI was refluxed for 4 hours with 28 ml. of acetic anhydride. The mixture then was distilled until the liquid temperature reached 155–160° and then distilled under vacuum; b.p. 178° at 7 mm., yield 5 g. The resulting oil solidified when treated with pentane and was recrystallized from this solvent by stirring the solution while cooling. The amorphous precipitate melted at 68–69°.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 71.79; H, 7.60. Found: C, 71.8; H, 7.69.

(21) Obtained through the courtesy of Hercules Powder Co., Wilmington, Del.

The anhydride dissolved slowly when treated with a hot solution of 10% potassium hydroxide. The dicarboxylic acid XI was recovered, m.p. 203–204°; no depression with the starting material.

Chromatography of Cut 2 (Table I).—Five ml. of cut 2 dissolved in 10 ml. of *n*-pentane was passed over 25 ml. of 60 to 200 mesh silica gel²² in a water-jacketed column, 8 mm. i.d., according to the described procedure.²³ Figure 3 shows the eluate reaches a minimum refractive index which corresponded to a maximum optical rotation. The ultraviolet spectra of the successive eluate fractions showed first a continuous decrease with a final disappearance of the 235 m μ peak of IV; second, the appearance at 25% elution proceeding through a maximum, of the 243 m μ peak of III; and third, the appearance at 40% elution of the 273 m μ peak of V. This peak increased in absorbancy consistently to the end of the process. The elution of I and II was followed by observing the optical rotation of the eluate. It proceeded through a maximum at about 38% elution (Fig. 3).

The infrared spectrum of the first few drops of the eluate showed that they consisted of IV, practically free from III.

The estimation of components in each portion of the eluate was determined by means of ultraviolet and infrared spectroscopy and optical rotation as described under "Analytical Procedure."

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EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WASHINGTON]

Azulene. V. Alkylation Experiments. Chloromercuration^{1,2,3}

BY ARTHUR G. ANDERSON, JR., EDWARD J. COWLES, JAMES J. TAZUMA AND JERRY A. NELSON⁴

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The Friedel-Crafts alkylation of azulene has been attempted with a number of reagents and catalysts and under a wide range of conditions. Some evidence for the formation of 1-alkylazulenes was obtained from a number of runs but only two products, a 1-hexylazulene and 1-benzylazulene, were obtained in sufficient yield and purity for analysis. Chloromercuration gives a dichloromercuriazulene in high yield.

Since the theoretical considerations previously discussed⁵ had led us to expect that electrophilic substitution would occur predominantly at the 1-position, it was felt that the alkylation of azulene would lead to mono- and (or) dialkyl derivatives which could be readily identified, even if formed in quite low yield, by their characteristic absorption spectra.⁶ Consequently some of our earliest experiments on the electrophilic substitution of azulene involved alkylation reactions.

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(2) From the Ph.D. theses of J. A. Nelson, J. J. Tazuma and E. J. Cowles; supported in part by a grant from the Research Corporation.

(3) Paper IV, A. G. Anderson, Jr., and E. J. Cowles, *THIS JOURNAL*, **77**, 4617 (1955).

(4) Shell Oil Fellow, 1949–1950.

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(6) Pl. A. Plattner and E. Heilbronner, *Helv. Chim. Acta*, **30**, 910, 1320 (1947); **31**, 804 (1948). See also T. Wagner-Jauregg, H. Arnold, F. Hüter and J. Schmidt, *Ber.*, **74B**, 1522 (1941).

As naphthalene⁷ and thiophene,⁸ in contrast to benzene, give low yields (5–10%) of alkyl derivatives in the Friedel-Crafts reaction, it was suspected that the yields of alkylazulenes realized might be small but it was hoped that isolation of the products, which would differ in color from azulene, by chromatography would be possible. As the yields, for the most part, proved to be very low (<1%), a large number of trial reactions were run (using *ca.* 5 mg. of azulene) in which the conditions of time and temperature were varied over a wide range and different solvents and catalysts were tried. The following discussion includes only illustrative examples chosen from runs performed on a somewhat larger scale (20–320 mg. of azu-

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lene) to verify the tentative results of certain trial runs.

Methylation.—One group of experiments on methylation involved methyl chloride, methyl bromide or methyl iodide and aluminum chloride or aluminum bromide with the alkyl halide also serving as the solvent or with carbon disulfide added. From reactions with methyl chloride or bromide and aluminum bromide at -70° for a few minutes or with methyl bromide and aluminum bromide at 0° for 24 hours were obtained trace amounts (*ca.* 1 mg.) of a blue liquid which appeared from its absorption spectra in the ultraviolet and visible regions to be 1-methylazulene.⁹ Similar results were obtained from a reaction with methyl chloride and aluminum chloride in carbon disulfide. With the latter solvent it was observed that azulene formed a somewhat insoluble complex with the aluminum chloride and it was necessary that the alkyl halide be present when the catalyst was added. Treatment of azulene dissolved in methylene chloride with trimethyloxonium fluoborate at room temperature gave a barely detectable yield of the blue product. A similar run using triethyloxonium fluoborate gave no product corresponding to 1-ethylazulene. The principal product from the reaction of methyl iodide and azulene in the presence of aluminum chloride was thought originally⁹ to be 1-methylazulene as its ultraviolet and visible absorption spectra were almost identical with those of a 1-alkylazulene. Subsequent mixed chromatography with an authentic sample has shown the two compounds to be different and the identity of the substitution product is not known.

Attempts to obtain the product from the reaction with methyl chloride or bromide and aluminum bromide analytically pure by chromatography were unsuccessful and its infrared spectrum differed slightly from that of a pure synthetic sample of 1-methylazulene. As the impurity present appeared, from the spectral and analytical data, to be azulene, a study of the separation of 1-methylazulene from azulene was undertaken. Four general methods were investigated: adsorption chromatography, partition chromatography, countercurrent distribution and evaporative distillation. In the experiments with adsorption chromatography eight different adsorbents were tried. In no case was a clean separation of a mixture of azulene and 1-methylazulene achieved. For partition chromatography potato starch columns were prepared and tested in accordance with the procedure of Stein and Moore.¹⁰ No solvent was found which would effect the desired separation. After a countercurrent extraction procedure involving fifty-three transfers, all of the color was in thirty-seven of the upper layer fractions but was so distributed that the separation was not satisfactory. Collection of a number of fractions from the evaporative distillation of mixtures of azulene and 1-methylazulene at several different temperatures and pressures likewise afforded only a partial separation. It was concluded from these experiments that any 1-meth-

ylazulene formed in methylation reactions could not be separated completely from unreacted azulene.

Isopropylation.—Almost all of a number of reactions of isopropyl chloride or isopropyl bromide with azulene in the presence of aluminum chloride, aluminum bromide, zinc chloride or stannic chloride at $-5, 0, +10, +25^{\circ}$, or under reflux and with reaction times ranging from two minutes to nineteen hours gave from one to four products in very low yield. Only the reaction with aluminum chloride at 25° for two minutes gave a sufficient quantity of products to enable even partial identification. Two blue liquid substances were obtained, both of which were thought to be 1-alkylazulenes from their ultraviolet and visible absorption spectra. One was obtained in pure form and its analysis corresponded to that of a 1-hexylazulene. Treatment of azulene with isopropyl alcohol or propylene and boron trifluoride etherate gave only trace amounts of a blue oil and extensive decomposition of the azulene. It was noted that azulene and boron trifluoride formed a violet complex.

Benzylation.—The benzylation of azulene was attempted in the hope that the product would be a solid and readily separable from unreacted azulene. After a number of experiments under a variety of conditions it was found that reaction of azulene with a tenfold excess of benzyl chloride and a fourfold excess of stannic chloride in chloroform provided the best yield (5.6%) of a crystalline product which was identical (m.p., m.m.p., infrared spectrum) with the 1-benzylazulene previously synthesized.³ The amounts of other products formed were too small to permit identification.

Other studies⁵ had indicated that further reaction of 1-substituted azulenes occurred at the 3-position. It was of interest to study this further, particularly with groups which are definitely *ortho*-, *para*- or *meta*-directing in the benzene series and which had been shown to give substitution on the 1-position of azulene. Benzylation of 1-acetylazulene gave an olive green solid and this same compound, 1-acetyl-3-benzylazulene, was obtained by acetylation of 1-benzylazulene. In both cases the 1,3-disubstituted compound was the major product and only very small amounts of other substances were formed.

Chloromercuration.—The observation that azulene formed colored complexes with aluminum halide (light blue), stannic chloride (purple) and boron trifluoride (violet) indicated that a reaction should occur with mercuric chloride. As azulene had been shown⁵ to be quite reactive, the rate of chloromercuration would make possible a comparison with reactive aromatic heterocyclic systems which form chloromercuri derivatives. Treatment of azulene with mercuric chloride and sodium acetate resulted in an immediate reaction and, after fifteen minutes, a dichloromercuriazulene was isolated in quantitative yield as an amorphous light blue solid. Thus azulene is considerably more reactive toward mercuric chloride than thiophene¹¹ or

(9) These results were reported in a preliminary communication: A. G. Anderson, Jr., and Jerry A. Nelson, *THIS JOURNAL*, **72**, 3824 (1950).

(10) W. H. Stein and S. Moore, *J. Biol. Chem.*, **176**, 337 (1948).

(11) F. C. Whitmore, "Organic Compounds of Mercury," Am. Chem. Soc. Monograph No. 3, Chemical Catalog Co. (Reinhold Publ. Corp.), New York, N. Y., 1921.

furan¹² and at least as reactive as pyrrole.¹³ The dichloromercuriazulene is almost completely insoluble in organic solvents and attempts to convert it (e.g., by reaction with acetic anhydride, acetyl chloride or ketene) into other disubstituted azulenes in order to show the positions occupied by the substituents have not been successful. Treatment with acetic anhydride gave a low yield of 1-acetylazulene but no diacetylazulene was formed. Reaction with sirupy phosphoric acid regenerated azulene in 69% yield.

Experimental

1-Methylazulene.—1-Methyl-3,4,5,6,7,8-hexahydroazulene was synthesized from cycloheptanone and converted to 1-methylazulene as described by Plattner¹⁴ and the product purified by chromatography of a petroleum ether solution on an alumina column.

Friedel-Crafts Reaction of Azulene with Isopropyl Chloride.—A solution of C.P. isopropyl chloride (2 ml.) and C.P. aluminum chloride (500 mg., 0.28 mmole) was added to a solution of azulene (36 mg., 0.28 mmole) in 5 ml. of isopropyl chloride and the combined mixture shaken vigorously for two minutes. After the addition of ice-water (10 ml.) the isopropyl chloride solution was separated, washed with 20 ml. of water and evaporated to dryness. Sublimation of the unreacted azulene (20 mg.) at room temperature and 10 mm. pressure left a green residue which was taken up in petroleum ether and chromatographed on activated alumina. Two blue bands separated on the column and were eluted separately with petroleum ether. Evaporation of the solvent from the first eluate left 4 mg. (19% net yield) of a blue oil which, even after repeated chromatographic purification on alumina and Florisil, did not give an exact analysis for monoisopropylazulene. The absorption spectrum (λ_{\max} in $m\mu$ at 233, 280, 338, 347, 533, 608, 660 and 732) was very similar to that reported for a 1-alkylazulene⁶ and for 1-isopropylazulene.¹⁵

From the second eluate fraction was obtained in like manner 2.5 mg. (9.4% net yield) of a blue oil which was purified by chromatography on activated alumina. Its absorption spectrum (λ_{\max} in $m\mu$ (log ϵ) at 239 (4.15), 278 (4.47), 3.40 (3.41), 347 (3.50), 364 (3.46), 583, 607, 660 and 735) and analysis corresponded to that of a 1-hexylazulene.

Anal. Calcd. for $C_{16}H_{20}$: C, 90.5; H, 9.49. Found: C, 90.6; H, 9.24.

1-Benzylazulene.—To a cooled (ice-bath) solution of 320 mg. (2.4 mmoles) of azulene in 2.9 ml. (3.2 g., 25 mmoles) of benzyl chloride was added in small portions a solution of 0.88 ml. (1.96 g., 7.5 mmoles) of stannic chloride in 25 ml. of chloroform. During the addition the color of the reaction mixture changed from blue to violet and then became yellow as a yellow precipitate separated.

Treatment with 30 ml. of ice-water regenerated the blue color and the colored products were extracted with chloroform. Chromatography of the concentrated organic solution on alumina with chloroform as the eluent and removal of the solvent from the blue eluate fraction (a small more strongly adsorbed green fraction was not investigated) left an impure liquid. Further purification was accomplished by rechromatographing six times (petroleum ether), each time collecting the dark front portion of the rather broad band. The material so obtained was freed of solvent and treated with 30 ml. of a warm, saturated solution of 1,3,5-trinitrobenzene. The crystals collected after cooling were washed with cold alcohol and chromatographed (petroleum ether) on alumina. The concentrated blue eluate fraction was again chromatographed. Three bands (blue-violet, blue, faint blue) separated and the first two were collected. The same fractions were obtained in different proportions (more of the blue band) from the concentrate of the trailing portions of the first petroleum ether chromatographs. The corresponding fractions were combined and rechromato-

graphed to give a total of 203 mg. (63.5% recovery) of azulene (blue-violet band) and 30.7 mg. (5.6%) of 1-benzylazulene, m.p. 75–77°. The latter product was identical (mixed melting point and infrared spectrum) with the material previously synthesized.⁸

1-Acetyl-3-benzylazulene. A. From 1-Acetylazulene.—A mixture of 1.3 ml. (1.4 g., 11 mmoles) of benzyl chloride, 0.52 ml. (1.16 g., 4.4 mmoles) of anhydrous stannic chloride and 6 ml. of chloroform was added dropwise to a cooled (ice-bath) solution of 190 mg. (1.1 mmoles) of 1-acetylazulene⁶ in 5 ml. of chloroform. The mixture was allowed to stand at room temperature for 15 minutes and was then shaken with ice and water. The separated chloroform layer was washed with saturated salt water and the solvent removed (air stream). The residue was taken up in 10 ml. of petroleum ether and chromatographed on alumina with petroleum ether-acetone (95:5) as the solvent. Three moving bands (blue, red-violet, blue-violet) separated. Rechromatography of the material from the second band yielded 159 mg. (84% recovery) of 1-acetylazulene. The residue from the third band was rechromatographed three more times whereupon 22.9 mg. (7.8%) of olive green platelets, m.p. 103–104°, were obtained. A cyclohexane solution of this product showed absorption maxima in $m\mu$ (log ϵ) 238 (4.38), 267 (4.18), 297 (4.49), 308 (4.58), 380 (3.87), 395 (3.89), 538 (ϵ 307), 570 (ϵ 366), 680 (ϵ 99) and points of inflection at 311 (4.37), 320 (3.58), 355 (3.58), 505 (ϵ 189), 525 (ϵ 259) and 612 (ϵ 292). The infrared spectrum of a carbon tetrachloride solution was taken.

Anal. Calcd. for $C_{16}H_{16}O$: C, 87.66; H, 6.47. Found: C, 87.52; H, 6.34.

B. From 1-Benzylazulene.—A solution of 0.45 ml. (0.625 g., 6.1 mmoles) of acetic anhydride, 0.05 ml. (0.09 g., 0.34 mmole) of anhydrous stannic chloride and 4.5 ml. of chloroform was added in small portions to 46 mg. (0.21 mmole) of 1-benzylazulene. The resulting solution was treated with ice-water after 15 minutes. After shaking with a few milliliters of 6 *N* sodium hydroxide, the organic layer was separated and extracted with small portions of the 6 *N* base until the aqueous layer remained clear and strongly alkaline. The residue from the chloroform solution was chromatographed on alumina with petroleum ether-acetone (95:5) as the eluent. The material from the first (blue) band was unstable to air and was discarded. The second (violet-blue) band contained the major portion of the products. This fraction was rechromatographed several more times and the final solution found to contain 11.8 mg. (21%) of 1-acetyl-3-benzylazulene by colorimetric analysis. Removal of the solvent and recrystallization (several times) from petroleum ether-chloroform (90:10) and then from *n*-hexane followed by sublimation at 0.004 mm. gave olive green platelets which were identical with the product obtained in A.

Chloromercuration of Azulene.—To a solution of azulene (7 mg., 0.055 mmole) in 1 ml. of ethanol and 0.5 ml. of 33% sodium acetate was added 0.5 ml. of saturated mercuric chloride solution at room temperature. The azulene color disappeared immediately and a light brown precipitate formed. After 15 minutes the precipitate, the color of which had changed gradually to a light blue-gray, was collected and washed repeatedly with small volumes of hot water until the filtrate gave a negative test for chloride ion. After further washing with 10 ml. of hot ethanol and 30 ml. of acetone, the solid was dried at 56° and 1 mm. pressure for four hours. The product, a dichloromercuriazulene, proved to be insoluble in common organic solvents but was slightly soluble in 1,6-dioxane or tetrahydrofuran. On heating, the compound darkened slowly above 250° but did not melt below 300°. The yield (34 mg.) was quantitative.

Anal. Calcd. for $C_{10}H_6Cl_2Hg$: C, 20.05; H, 1.01; Cl, 11.8. Found: C, 20.24; H, 1.17; Cl, 11.8.

Regeneration of Azulene from Dichloromercuriazulene.—Finely powdered dichloromercuriazulene (28 mg., 0.047 mmole) was shaken vigorously with 10 ml. of cold 85% phosphoric acid until all of the solid had dissolved (15 minutes). The solution was diluted with 20 ml. of ice-water and then extracted with 10 ml. of 20–40° petroleum ether. The blue organic layer was separated, evaporated to dryness and the residue sublimed at room temperature and 10 mm. pressure to give 4.2 mg. (69%) of crystalline azulene.

SEATTLE 5, WASH.

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