Some Synthetic Studies for Benzazulenes[1]

C. W. MUTH, M. L. DEMATTE,[2a] A. R. URBANIK,[2b] AND W. G. ISNER[2c]

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506

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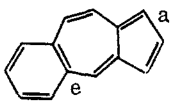
The results of several attempts for the preparation of the benzazulenes are reported including a successful method which afforded benz[*f*]azulene in 3–4% yield.

Benz[*f*]azulene (I)[3] has been prepared in 3–4% yields by modifying a Ziegler–Hafner method[4] for preparing azulenes. In the present synthesis 1 mole of 2-methylisoquinolinium iodide is allowed to react with a solution prepared by addition of 2 g-atoms of sodium and 2 moles of cyclopentadiene to absolute ethanol. The mixture is concentrated to yield a residue containing benz[*f*]azulene (I); however, if the residue after dilution with diethylene glycol[5] is subjected to superheated steam, the yield of I is higher.



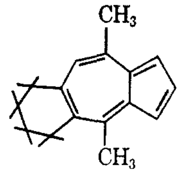
I

In this synthesis apparently cyclopentadiene anion undergoes reaction with 2-methylisoquinolinium iodide to form a dihydroisoquinoline which undergoes ring opening. Subsequently a seven-membered ring forms and methylamine is eliminated to yield benz[*f*]azulene (I). Methylamine was identified from its reaction product with phenyl isothiocyanate.

The reaction of benz[*f*]azulene (I) with alkaline potassium permanganate yielded *o*-phthalic acid indicating that the azuleno portion of the molecule is more susceptible to oxidation than is the benzo portion. Benz[*f*]azulene (I), also, underwent reaction with phenyldiazonium chloride.

To determine whether the fused benzene ring was responsible for the low yield of benz[*f*]azulene (I), the synthesis of 5,6-dimethylazulene was attempted from 1,3,4-trimethylpyridinium iodide and cyclopentadienyl sodium by a procedure analogous to that used for making I. The yields of 5,6-dimethylazulene were 1–2%; consequently, the low yield of benz[*f*]azulene (I) cannot be entirely due to the fused benzene ring in the starting material.

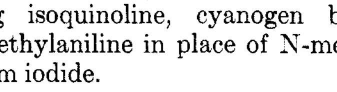
As an alternate method to prepare a substituted benz[*f*]azulene the dehydrogenation of 4,10-dimethyl-5,6,7,8-tetrahydrobenz[*f*]azulene (II) was attempted. This represents an attempt to dehydrogenate the tetrahydrobenzo group in the final synthetic step, instead of a hydroazuleno group as has been done previously. All dehydrogenation attempts were unsuccessful. The attempts included (1) refluxing a mixture of II with chloranil in benzene, (2) refluxing a mixture of II with palladium on charcoal in nitrobenzene, (3) slowly dropping II onto palladium on charcoal in a tube[6] the temperature of which was constant in individual runs but which varied in different runs from 190–500°.



II

All other methods tried for the synthesis of benz[*f*]azulene were unsuccessful. The unsuccessful methods follow.

(1) The successful procedure was modified by using isoquinoline, cyanogen bromide, and N-methylaniline in place of N-methylisoquinolinium iodide.
(2) A mixture made from 2-methylisoquinolinium iodide and sodium cyclopentadiene in tetrahydrofuran and subsequently benzidine was distilled under reduced pressure.
(3) A mixture made from 2-methylisoquinolinium bromide, sodium ethoxide, and cyclopentadiene in ethanol and subsequently benzidine was distilled under reduced pressure.
(4) Sodium ethoxide, cyclopentadiene and 2-methylisoquinolinium iodide in diphenyl ether were heated under reflux.
(5) Treatment of 2-(2′,4′-dinitrophenyl)isoquinolium chloride and 2-methylisoquinolinium iodide, respectively, with N-methylaniline.
(6) 2-{3-[(N-2,4-Dinitrophenyl)amino]vinyl}benzaldehyde[7] (III) did not condense with cyclopentadiene to yield a fulvene which by heating conceivably could be converted to benz[*f*]azulene (I).



III

In an effort to form a precursor for benz[*e*]azulene, N-(2′,4′-dinitrophenyl)quinolinium fluoride was treated with N-methylaniline. The product was N-methyl-N-phenyl-2,4-dinitroaniline instead of the desired dianil salt.

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[2] (a) From Ph.D. Dissertation, 1966; (b) from M. S. Thesis, 1963; (c) from M. S. Thesis, 1962.

[3] The synthesis of I has been reported by (a) A. Plattner, A. Furst, and W. Keller, *Helv. Chim. Acta*, **32**, 2464 (1949); (b) K. H. Heinlein, Ph.D. Dissertation, University of Marburg, Marburg/Lahn, West Germany, 1958; (c) J. Mayer and F. Sondheimer, *J. Am. Chem. Soc.*, **88**, 603 (1966).

[4] K. Ziegler and K. Hafner, U. S. Patent 2,805,266 (1957); K. Hafner, *Angew. Chem.*, **67**, 302 (1955).

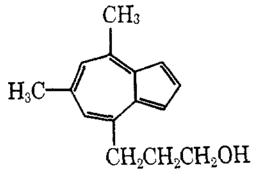
[5] J. F. Tilney-Bassett and W. A. Waters, *J. Chem. Soc.*, 3123 (1959).

[6] A. G. Anderson, J. A. Nelson, and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4980 (1953).

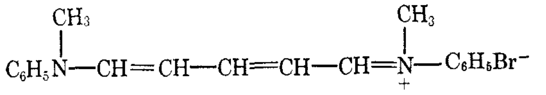
[7] D. Beke and C. Szantoy, *Ann.*, **640**, 127 (1961).

Secondly, it was observed that isobenzopyrylium ferrichloride did not undergo reaction with cyclopentadienyl sodium to yield benz[*e*]azulene. Homophthalaldehyde did not undergo reaction with cyclopentadienyl sodium to yield benz[*e*]azulene.

Thirdly, 4-(γ-hydroxypropyl)-6,8-dimethylazulene (IV) was prepared from a lithium salt of 4,6,8-trimethylazulene and ethylene oxide. Compound IV underwent reaction with hydrobromic acid to yield the corresponding bromide. Low yields in the foregoing reactions precluded this approach for the preparation of a benz[*e*]azulene or a heptalene. Likewise, exploratory work on the reaction of the lithium salt of 4,6,8-trimethylazulene with β-propio lactone did not yield promising results.



IV



$$C_6H_5\overset{CH_3}{\overset{|}{N}}-CH{=}CH-CH{=}CH-CH{=}\underset{+}{\overset{CH_3}{\overset{|}{N}}}-C_6H_5Br^-$$

V

Efforts to prepare benz[*a*]azulene (I)[8] from N-methyl-N-phenyl-5-(N′-methylanilino)penta-2,4-dienylideneammonium bromide (V) and indenyl sodium were unsuccessful. Also, we were unable to prepare 1,2-benz-4,6,8-trimethylazulene from 2,4,6-trimethylpyrylium perchlorate and indenyl sodium.

The structure assignment for 5,6-dimethylazulene (IV) is supported by visible spectral evidence. The calculated wavelength[9] for maximum number five of 5,6-dimethylazulene is 577 mμ; whereas, the observed value is 578 mμ.

The visible spectrum of 4,10-dimethyl-5,6,7,8-tetrahydrobenzazulene (VII) has little fine structure with broad maximum at 558 mμ. The calculated wavelength[9] for maximum number five of 4,10-dimethyl-5,6,7,8-tetrahydroazulene is 554 mμ.

Experimental Section[10]

Benz[*f*]azulene (I).—Freshly prepared cyclopentadiene (73.3 g, 1.11 moles) was added dropwise during 45 min to a stirred solution which was under a nitrogen atmosphere and which was prepared by dissolving 25.5 g (1.11 g-atoms) of sodium in 600 ml of absolute ethanol. After the solution was stirred for 0.5 hr, 150 g (0.553 mole) of isoquinoline methiodide was added in small portions. The reaction mixture was stirred overnight and refluxed for 3 hr during which time methylamine was liberated. The methylamine was characterized from its reaction product with phenyl isothiocyanate. Ethanol was removed *in vacuo*. The residue was diluted with 300 ml of diethylene glycol[5] and the mixture was steam distilled with superheated steam (250°). A blue solid and later a blue oil steam distilled. Twenty-six liters of distillate were collected and extracted with pentane. The pentane extract was washed three times with 1 *N* hydrochloric acid and then three times with water, concentrated, and dried over calcium chloride. The resulting solution was chromatographed on alumina with pentane as the eluent. Concentration of the eluent yielded a dark blue solid which was crystallized from pentane to yield 3.6 g (3.6%) of dark blue plates, mp 162–163.5° (lit. mp 159°,[8a,b] 164–165°[8c]). Recrystallization of I from ethanol gave brown solid, as well as blue solid.

Benz[*f*]azulene (I) in cyclohexane has ultraviolet and visible spectra similar to those reported.[11] The nmr spectrum of I in deuteriochloroform has a singlet at τ 1.56 and complex absorption at 2.0–2.9.

1,3,4-Trimethylpyridinium Iodide.—To 9.7 g (0.08 mole) of 3,4-lutidine in 100 ml of absolute ethanol was added with stirring 12.8 g (0.09 mole) of iodomethane during 45 min. The mixture was refluxed for 15 min and concentrated to yield a yellow solid which was dissolved in ethanol. The addition of anhydrous ether to the ethanolic solution afforded pale yellow crystals (15.5 g, 69%), mp 119–122°.

Anal. Calcd for $C_8H_{12}NI$: C, 38.70; H, 4.83; N, 5.64; I, 50.80. Found: C, 38.61; H, 4.91; N, 5.61; I, 50.65.

5,6-Dimethylazulene.—Freshly prepared cyclopentadiene (14.5 g, 0.22 mole) was added to a stirred solution which was prepared from 5.1 g (0.22 g-atom) of sodium and 110 ml of anhydrous ethanol, which was under a nitrogen atmosphere. To this solution was added 17.0 g (0.0676 mole) of 1,3,4-trimethylpyridinium iodide, and the mixture was refluxed for 1 hr. The solvent was evaporated, the residue was diluted with 150 ml of diethylene glycol, and the solution was distilled with superheated steam. The distillate was acidified with hydrochloric acid and extracted with hexane. The hexane solution was twice washed with 3 *N* hydrochloric acid, washed with water, and dried over magnesium sulfate. The solution was concentrated and the residue was chromatographed on alumina using hexane both as the solvent and developer. A bright blue band was developed followed by a brownish green band. The eluent from the blue band was evaporated and the residue was recrystallized from ethanol to yield 105 mg (1%) of 5,6-dimethylazulene as blue crystals, mp 67–70°.

An analytical sample, mp 68.5–71.5°, was prepared by crystallization from absolute ethanol: λ_{max}, mμ (log ε), in cyclohexane, 241 (4.12), 281 (4.69), 287 (4.66), 299 (3.91), 577 (2.51), 600 (2.49), 639 (2.50), 658 (2.26), 695 (2.21).

Anal. Calcd for $C_{12}H_{12}$: C, 92.30; H, 7.69. Found: C, 92.28; H, 7.82.

5,6-Dimethylazulene in ethanol reacted with 1,3,5-trinitrobenzene in ethanol to yield dark reddish brown needles, mp 138–141°.

Anal. Calcd for $C_{18}H_{15}N_3O_6$: C, 58.53; H, 4.06; N, 11.38; O, 26.01. Found: C, 58.65; H, 4.22; N, 11.30; O, 25.83.

1(3)-Phenylazo-5,6-dimethylazulene.—In a procedure adapted from that of Anderson, Nelson, and Tazuma,[6] 97.5 mg of 5,6-dimethylazulene was treated with phenyldiazonium chloride prepared from 95 mg of aniline hydrochloride. The crude product was dissolved in methylene chloride and chromatographed on alumina. The eluent was evaporated and the resulting residue was crystallized from ethanol to yield a black powder (23 mg, 14%), mp 119–121°.

Anal. Calcd for $C_{18}H_{16}N_2$: C, 83.07; H, 6.15; N, 10.76. Found: C, 83.12; H, 6.03; N, 10.91.

4,10-Dimethyl-5,6,7,8-tetrahydrobenz[*f*]azulene (II).—To a solution prepared under a nitrogen atmosphere by addition of 8 ml (0.088 mole) of cyclopentadiene to 2.0 g (0.088 g-atom) of sodium in 100 ml of tetrahydrofuran was added with stirring 11.5 g (0.044 mole) of 2,8-dimethyl-3,4,5,6-tetrahydrobenzo[c]pyrylium perchlorate.[12] The mixture was stirred for 1 hr and then refluxed for 15 min. The tetrahydrofuran was evaporated and the residue was diluted with 100 ml of diethylene glycol. The mixture was heated on a steam bath for 1 hr and then steam distilled (200–235°) until no more blue oil or solid distilled. The distillate was extracted with hexane. The hexane solution was concentrated, and the concentrate was chromatographed on alumina. A mixture of hexane and benzene was the developer. A yellow band was eluted before a blue band was eluted. Evaporation of the eluent from the blue band yielded a blue solid

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(8) K. Hafner, *Ann.*, **606**, 79 (1957).

(9) (a) P. A. Pattner, *Helv. Chim. Acta*, **24**, 283 E (1941). (b) E. Heilbronner, "Non-benzenoid Aromatic Compounds," D. Ginsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p 222.

(10) All melting points are uncorrected, all elemental analyses by Galbraith Laboratories, Knoxville, Tenn., all ε values determined from measurements with Beckman DU spectrophotometer, and all chromatographic separations made with neutral alumina.

(11) E. Kloster-Jensen, E. Kovaits, A. Eschenmoser and E. H. Heilbronner, *Helv. Chim. Acta*, **39**, 1051 (1956).

(12) P. Praill and A. Whitear, *J. Chem. Soc.*, 3573 (1961).

which gave 304 mg (3.3%) of blue crystals, mp 56–58°, after crystallization from ethanol.

Rechromatography followed by recrystallization of material similar to the foregoing yielded blue crystals of II: mp 60–61°; λ_{max}, mμ (log ϵ), 249 (4.45), 292 (4.66), 557 (2.65), 597 (2.59), 654 (2.17).

Anal. Calcd for $C_{16}H_{18}$: C, 91.43; H, 8.57. Found: C, 91.22; H, 8.65.

The 1,3,5-trinitrobenzene adduct of II prepared in and recrystallized from ethanol consisted of brown crystals, mp 126–27°.

Anal. Calcd for $C_{22}H_{21}N_3O_6$: C, 62.41; H, 4.96; O, 22.69. Found: C, 62.24; H, 5.09; N, 9.86; O, 22.50.

1-(2′,4′-Dinitrophenyl)quinolinium Fluoride.—Quinoline (6.5 g, 0.05 mole) was dissolved in 30 ml of benzene and 11.0 g (0.06 mole) of 2,4-dinitrofluorobenzene was added. The mixture was heated under reflux for 1 hr during which time the mixture turned dark orange. As the mixture was cooled overnight at ice temperature a precipitate formed. The product after four recrystallizations from hexane consisted of very pale yellow crystals, mp 78–79° (lit.[13] mp 78–79°).

Anal. Calcd for $C_9H_7N \cdot C_6H_3FN_2O_4$: C, 57.15; H, 3.20; N, 13.33. Found: C, 56.98; H, 3.26; N, 13.43.

Reaction of 1-(2′,4′-Dinitrophenyl)quinolinium Fluoride with N-Methylaniline.—As N-methylaniline (3.3 g, 0.035 mole) was added to a solution of 1-(2′,4′-dinitrophenyl)quinolinium fluoride (5.0 g, 0.016 mole) in 30 ml of methanol, a deep red coloration developed. The mixture was heated under reflux for 4 hr and allowed to stand overnight. Orange-red crystals formed in the reaction mixture; these were collected and recrystallized from acetone. A mixture melting point with N-methyl-N-phenyl-2,4-dinitroaniline gave no depression.

4-(γ-Hydroxypropyl)-6,8-dimethylazulene (IV).—To a solution of 17.3 g (0.10 mole) of 4,6,8-trimethylazulene in 800 ml of anhydrous ether, cooled to −20° and under a nitrogen atmosphere, was added dropwise 150 ml of a 15.17% solution of *n*-butyllithium in hexane. During the addition, the reaction mixture turned from violet to clear gold, indicating formation of the lithium salt of 4,6,8-trimethylazulene.[14] After stirring 0.5 hr a solution of 20 ml (0.42 mole) of ethylene oxide in 20 ml of anhydrous ether was added dropwise. The reaction mixture turned purple and formed a fine brown precipitate. After 45 min of stirring 5 ml (0.11 mole) of ethylene oxide was added. The reaction mixture was stirred for 6 hr, warmed to room temperature, washed with 2 *N* hydrochloric acid, washed with water until neutral, dried, and concentrated. Chromatography of the residue on alumina with ether as the eluent led to a purple oil. The oil was rechromatographed. Elution with hexane caused separation of two bands. The first band, eluted with hexane, yielded 4,6,8-trimethylazulene. The second band was eluted with ether and yielded a blue oil. Vacuum distillation of the oil gave 3.81 g (19%) of viscous blue oil: bp 193–97° (0–1 mm); λ_{max} in cyclohexane 550 and 590 mμ; ν 3400 cm^{-1}.

The adduct of IV and 1,3,5-trinitrobenzene was prepared in ethanol and recrystallized successively from ethanol–water, cyclohexanol, and hexane. The adduct was brown and melted at 85.5–87°.

Anal. Calcd for $C_{21}H_{21}N_3O_7$: C, 59.01; H, 4.97; N, 9.83; O, 26.20. Found: C, 59.23; H, 5.09; N, 9.73; O, 26.02.

4-(γ-Bromopropyl)-6,8-dimethylazulene.—A mixture of 4.0 g (0.018 mole) of 4-(γ-hydroxypropyl)-6,8-dimethylazulene (IV), 9 ml (0.053 mole) of 48% hydrobromic acid, 1.2 ml of concentrated sulfuric acid, and 5 ml of hexane was refluxed for 1 hr. After 16 hr at room temperature, the reaction mixture was diluted with water, neutralized with sodium carbonate, and extracted with ether. The ether layer was washed with water, dried, concentrated, and chromatographed on alumina. Three fractions were obtained utilizing 25, 50, and 75% mixtures of acetone to hexane or acetone to ether as eluents. Repeated chromatography was necessary to bring about good separation of the fractions. The first fraction was 0.38 g (15%) of a blue oil identified as starting material IV. The second fraction yielded 0.32 g (7%) of crude 4-(γ-bromopropyl)-6,8-dimethylazulene as a blue oil, λ_{max} in cyclohexane 552 and 572 mμ.

A brown crystalline adduct of 6-(γ-bromopropyl)azulene and 1,3,5-trinitrobenzene was prepared in and recrystallized from ethanol.

Anal. Calcd for $C_{21}H_{20}N_3O_6Br$: C, 51.44; H, 4.11; N, 8.57; Br, 16.30; O, 19.58. Found: C, 51.61; H, 4.19; N, 8.34; Br, 16.44; O, 19.66.

A third fraction, a blue solid (mp 110–111°), was not identified.

Acknowledgment.—We express our gratitude to Messrs. John Engel and Herbert Petty, who as National Science Foundation Undergraduate Research Participants during the summer of 1963 and during 1963–1964, respectively, contributed to the synthetic and spectral studies.

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[13] F. Kröhnke, private communication; mp 174–175° reported in *Chem. Ber.*, **91**, 1300 (1958), has been found to be in error.

[14] K. Hafner, K. Pelster, and H. Palzelt, *Ann.*, **650**, 80 (1961).

The Effect of Nucleophiles on the Stoichiometric Hydroformylation Reaction[1]

LEO ROOS[2] AND MILTON ORCHIN

Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221

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The yield of aldehydes obtained from the stoichiometric hydroformylation of 1-pentene with $HCo(CO)_4$ is greatly enhanced by adding nucleophiles such as benzonitrile in appropriate concentrations. The ratio of straight-chain to branched-chain aldehyde is thereby increased and the extent of olefin isomerization is greatly reduced. Stabilization of the acylcobalt complex at the tricarbonyl level and avoidance of tetracarbonyl formation appear to account for the remarkable effects.

The rate of the high-pressure catalytic hydroformylation of olefins is increased by the addition of organic bases such as pyridine, quinoline, and triethylamine[3–6] or of oxygenated compounds such as ketones and alcohols.[7] No detailed mechanism has been suggested to explain the observed results, although it is thought that these compounds somehow enhance the cleavage of dicobalt octacarbonyl by hydrogen to form cobalt hydrocarbonyl.[4,5]

A similar effect was observed when catalytic amounts of benzonitrile were added to the stoichiometric hydroformylation reaction of 1-pentene.[8]

$$\begin{aligned}xs\ CH_3CH_2CH_2CH{=}CH_2 + 2HCo(CO)_4 + CO \longrightarrow \\ CH_3(CH_2)_4CHO + CH_3(CH_2)_2CH(CH_3)CHO + \\ Co_2(CO)_8 + CH_3{-}CH_2{-}CH{=}CH{-}CH_3\end{aligned}$$

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[2] Public Health Service Predoctoral Fellow, 1962–1965.

[3] T. Yoshida, R. Iwanaga, and H. Mori, U. S. Patent 2,848,304 (1958).

[4] R. Iwanaga, *Bull. Chem. Soc. Japan*, **35**, 865 (1962).

[5] R. Iwanaga, *ibid.*, **35**, 869 (1962).

[6] H. Uchida and A. Matsuda, *ibid.*, **36**, 1351 (1963).

[7] Y. Takegami, C. Yokokawa, and Y. Watanabe, *ibid.*, **37**, 935 (1964).

[8] G. L. Karapinka, Ph.D. Dissertation, University of Cincinnati, 1962.