[Contribution from the Department of Chemistry,
University of Washington]

AN ATTEMPTED SYNTHESIS OF 1,10-CYCLOPENTENOHEPTALENE. 1,8-TETRAMETHYLENEAZULENE

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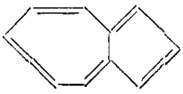
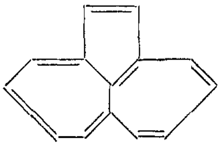
Interest in the theoretical aspects of the structural features reponsible for, or necessary to, aromatic character has resulted in recent years in a number of attempts to synthesize new aromatic systems. Thus far, however, azulene (I) remains the only example of a non-benzenoid hydrocarbon which has sufficient (*ca.* 46 kcal./mole) resonance stability to be classed as aromatic (1) and which also has been shown to undergo characteristic electrophilic substitution reactions (2).

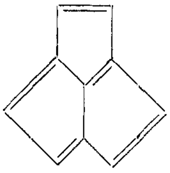
Azulene has ten 2pπ-electrons and thus affords support for the molecular orbital theory wherein stabilization is attributed to the presence of 4n + 2π-electrons filling a closed shell of cyclic molecular orbitals (3). Azulene is also a non-alternant hydrocarbon. It occurred to us that a tricyclic system related structurally to azulene, 1,10-cyclopentenoheptalene (II), would have the requisite 4n + 2 π-electrons and also be non-alternant.



I



II



III

No tricyclic fused ring systems containing only five- or seven-membered carbocyclic rings had been reported previously and only one, 1,6-cyclopentenopentalene (III),[2] had been mentioned (4) in the voluminous literature concerned with the theoretical aspects of aromaticity. Craig (4) concluded from certain theoretical considerations that III would be an "abnormal" compound and thus not aromatic in the usual sense.

Application by us of Craig's symmetry operation to II gave contradictory results for the two ways in which the structure could be lettered and thus afforded no indication of the probable character of the molecule. Application of the "starring" rule showed that there would be "like pairs" of atoms (between which there theoretically would be no π-bond formation) in the periphery of the molecule. This result is in contrast to that obtained with azulene and suggests that a stable peripheral orbital shell would not exist.

Several different syntheses were considered and after some preliminary investigation, a route *via* 6,7,8,9-tetrahydro-*5H*-cycloheptabenzene-5-one (VII) was

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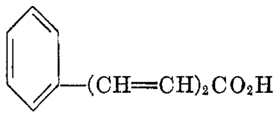
* Dedicated to the late Professor W. E. Bachmann.

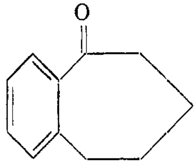
[1] From the Ph.D. thesis of Shih Yi Wang.

[2] A study directed toward the synthesis of III is in progress in this laboratory.

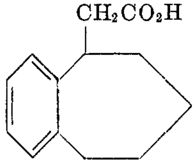
chosen. Yields of 80% or better were realized in all but the last steps. Condensation of cinnamaldehyde with malonic acid in a Doebner reaction gave 2-styrylacrylic acid (VI) in excellent yield. Reduction of VI by the method of Papa, *et al.*, (5) afforded phenylvaleric acid. Cyclization of the corresponding acid chloride in the pressure of aluminum chloride gave VII. A Reformatsky reaction of VII with ethyl bromoacetate followed by dehydration yielded the unsaturated Reformatsky ester. This product displayed an absorption maximum at 243 mμ. The double bond is therefore probably in the *endo*cyclic position as styrenes characteristically absorb in this region (6) while compounds of the cinnamate type usually show absorption maxima at 255–280 mμ (7).



VI

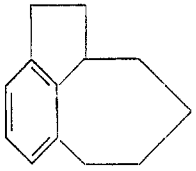


VII

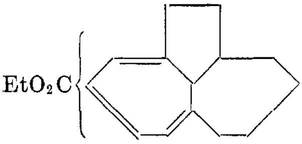


VIII

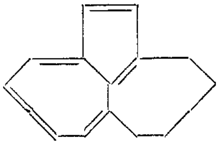
The unsaturated ester was converted to the corresponding acid which was readily reduced (5) to 6,7,8,9-tetrahydro-*5H*-cycloheptabenzene-5-acetic acid (VIII). An inverse Friedel-Crafts reaction on the acid chloride of VIII gave the desired tricyclic ketone in high yield and a modified Wolff-Kishner reduction (8) of this product afforded 1,7-tetramethyleneindan (IX).



IX



X



XI

The diazoacetic ester method was used to enlarge the benzenoid portion of IX to a seven-membered ring. That the resulting ester (probably X) contained three double bonds was shown by a measured uptake of 2.9 mole-equivalents of hydrogen. The unsaturated ester was saponified and the acid obtained was decarboxylated and dehydrogenated by treatment with 10% palladium-charcoal at 320–350°. The yields of products in the last step were low but other methods tried (vapor phase reactions over various palladium catalysts and liquid phase reactions with sulfur or selenium) were less successful.

Considerable difficulty was experienced in the isolation and purification of the products from the dehydrogenation reaction. A pure sample of 1,8-tetramethyleneazulene (XI) was ultimately obtained by a lengthy procedure involving chromatography, extraction with phosphoric acid, steam-distillation, formation, and subsequent decomposition of the trinitrobenzene complex and, finally, sublimation. Omission of any step in this process resulted in a considerably

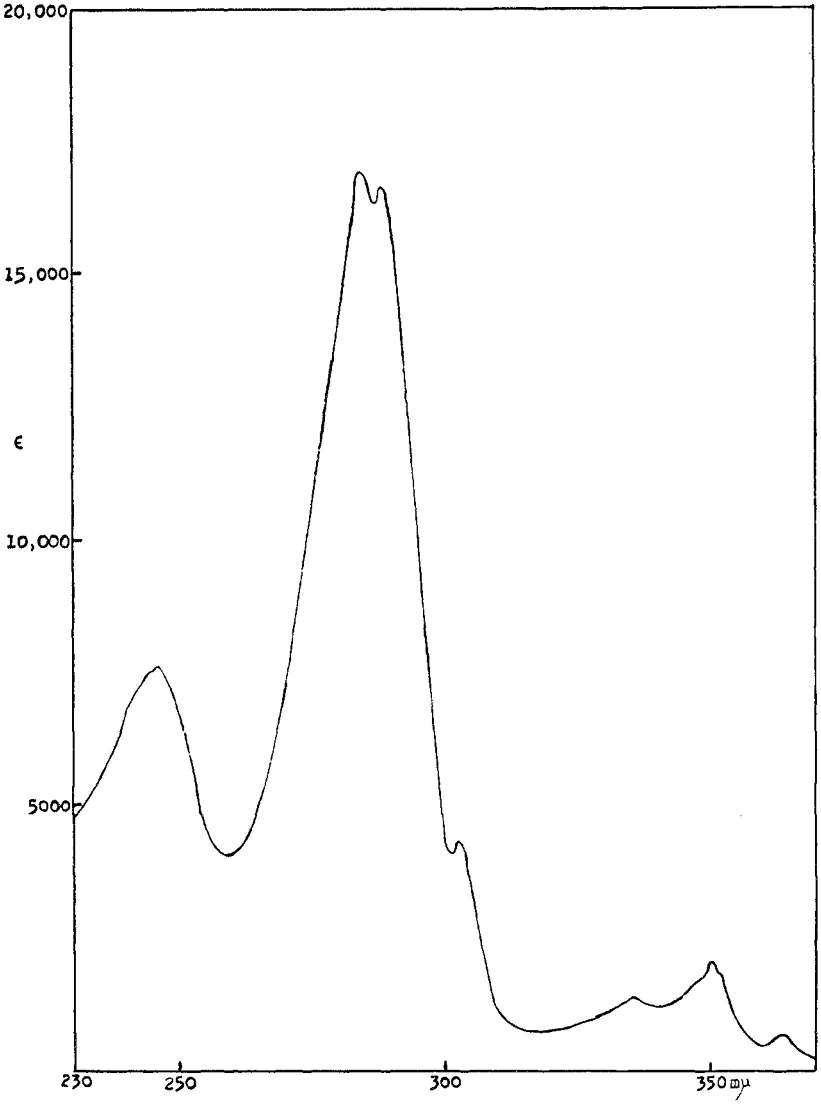


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA OF 1,8-TETRAMETHYLENEAZULENE IN CYCLOHEXANE

less pure product. The ultraviolet and visible absorption spectra of this new azulene derivative are shown in Figs. 1 and 2.

During the chromatography of the crude dehydrogenation product on alumina a greenish band was observed. The eluate fractions containing the green bands from a number of runs were combined and an attempt was made to purify the green component of the crude material. A minute quantity of an unstable green

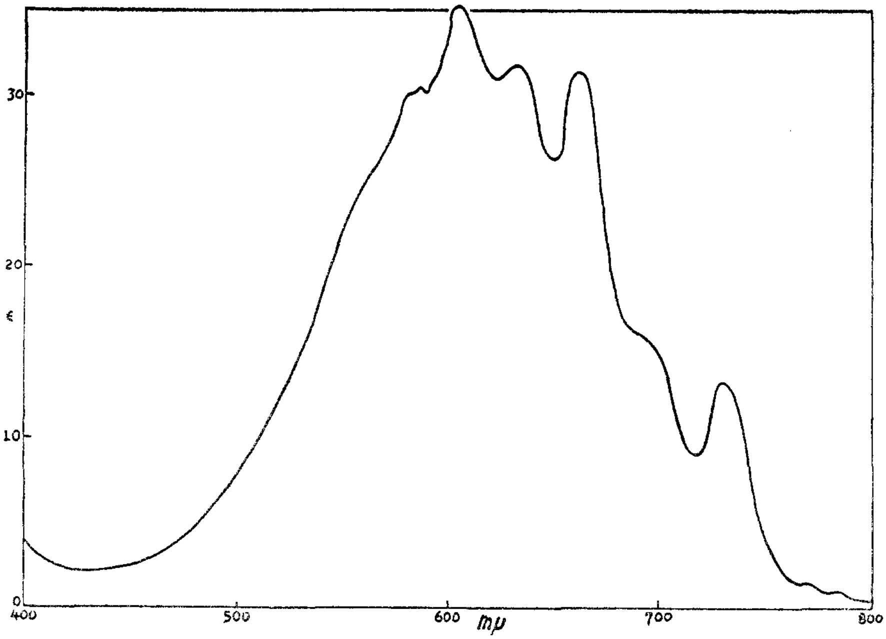


FIG. 2. VISIBLE ABSORPTION SPECTRUM OF 1,8-TETRAMETHYLENEAZULENE IN CYCLOHEXANE

solid was obtained but it was not possible to show that the green substance represented a heptalene derivative or any other such structure having the tricyclic fused ring system.

EXPERIMENTAL

2-Styrylacrylic acid (VI). To a mixture of 132 g. of cinnamaldehyde, 125 g. of malonic acid, and 120 ml. of dry pyridine was added 15 ml. of piperidine. The mixture became orange in color and the ensuing exothermic reaction caused vigorous boiling. Dissolution of the malonic acid was aided by frequent shaking and, after the heat of reaction had lessened, the mixture was heated on a steam-bath until no more carbon dioxide was evolved (six hours). The yellow crystalline precipitate obtained on acidification of the cooled reaction mixture with 6 *N* hydrochloric acid was filtered and washed carefully with 6 *N* hydrochloric acid and then water. The dried product (175 g., quantitative yield), which melted at 161–165°, was used in the next step without further purification. The reported melting point for the pure acid is 165–166° (9).

Phenylvaleric acid. A solution of 174 g. of the crude 2-styrylacrylic acid and 300 g. of sodium hydroxide in 2 l. of water was treated with a total of 200 g. of Raney nickel alloy as described by Papa, Schwenk, and Whiteman (5) except that the temperature of the mixture was kept at 65–75° during the reduction period (four hours). Then an additional 10 g. of alloy was added and the mixture was heated at 90° for two hours. The hot solution was filtered, the residue washed with four 100-ml. portions of hot 2% sodium hydroxide, and the combined filtrate and washings were added immediately, with stirring, to 2 l. of hot concentrated hydrochloric acid. The resulting mixture was digested at the boiling point for 20 minutes to dissolve aluminum salts, then cooled and the crystalline material which separated was collected. Recrystallization from alcohol gave 169 g. (95%) of product which melted at 54–56°. A second recrystallization of a sample from ligroin raised the melting point to 57–58° in agreement with the reported value of 58–59° (10) and a mixture melting point with an authentic sample gave no depression.

6,7,8,9-Tetrahydro-5H-cycloheptabenzene-5-one (VII). Treatment of 89 g. of the aforementioned phenylvaleric acid with thionyl chloride as described by Martin and Fieser (11) followed by removal of the excess thionyl chloride and distillation *in vacuo* gave 79.5 g. (81%) of the corresponding acid chloride as the fraction boiling at 140–144° at 16 mm.

In accordance with the procedure of Plattner (12) as modified by Aspinall and Baker (13), from 196.5 g. of the phenylvaleryl chloride there was obtained 144 g. (90%) of the cyclic ketone as the fraction boiling at 82–84° at 0.3 mm.; n_D^{20} 1.5638. The reported constants are: b.p. 99–102° at 1 mm.; n_D^{20} 1.5636 (10).

Ethyl 8,9-dihydro-7H-cycloheptabenzene-5-acetate. A mixture of 80 g. of 6,7,8,9-tetrahydro-*5H*-cycloheptabenzene-5-one, 100 g. of amalgamated zinc, 40 ml. of ethyl bromoacetate, and 400 ml. of dry benzene were heated to boiling under a nitrogen atmosphere. Iodine (0.3 g.) was added and when the reaction began (five minutes) the heat source was removed. An additional 130 ml. of ethyl bromoacetate was added dropwise with stirring over a period of three hours. At the same time three further additions of zinc and iodine were made at hourly intervals and with the last of these were added an additional 20 ml. of the halo ester. Heat was then reapplied and the stirring was continued for another four hours. After hydrolysis of the addition product by the dropwise addition of 1 l. of ice cold 6 *N* sulfuric acid to the cooled reaction mixture, the organic layer was separated and the aqueous layer was extracted four times with 60-ml. portions of benzene. The combined organic layers were washed with 100 ml. of 6 *N* sulfuric acid (three times), four times with 50-ml. portions of 2% ammonium hydroxide, and four times with water. The crude hydroxy ester obtained after drying the solution and removing the solvent was heated under reflux with 200 ml. of formic acid for 15 minutes and then allowed to stand overnight. Benzene and water were added to the dark liquid and the separated aqueous layer was extracted several times with benzene. The combined organic solutions were washed with three 100-ml. portions of 5% sodium carbonate, then with water, and dried. After removal of the solvent the residue was distilled and the product (92.8 g., 85%) was obtained as a colorless liquid; b.p. 152–153° at 4 mm. This unsaturated ester crystallized from dry ether and was recrystallized from alcohol; m.p. 49.5–50.5°. The ultraviolet absorption spectrum of an ethanol solution showed a single maximum at 243 mμ (ε 10,480).

Anal. Calc'd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88.
Found: C, 78.13; H, 7.83.

6,7,8,9-Tetrahydro-7H-cycloheptabenzene-5-acetic acid (VIII). The above unsaturated ester (115 g.) was heated under reflux with 1200 ml. of water and 150 g. of sodium hydroxide until a clear solution resulted (ten hours). The alkaline solution [the acid may be isolated; m.p. 96–97°; Neut. equiv. 202 (Calc'd: 202); absorption maximum (alcohol) at 243 mμ (ε 10,000)] was transferred to a 3-l. beaker, treated with a total of 110 g. of Raney nickel alloy, and the crude acid was isolated as previously described for the preparation of phenylvaleric acid. Recrystallization from alcohol (cooling in a refrigerator for several days was necessary to obtain complete precipitation) followed by washing with 6 *N* hydrochloric acid and drying in a desiccator gave 93.8 g. (92%) of product melting at 98.5–99.5°. It had a neutral equivalent of 204 (Calc'd: 204).

Anal. Cal'd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89.
Found: C, 76.16; H, 7.85.

3,4-Tetramethyleneindanone-1. A solution of 6,7,8,9-tetrahydro-*5H*-cycloheptabenzene-5-acetyl chloride (44.5 g.), prepared from the corresponding acid by treatment with two moles of thionyl chloride and subsequent distillation (b.p. 117–121° at 0.3–0.4 mm.; yield, 86%), in 250 ml. of dry benzene was added dropwise to a stirred suspension of 33 g. of anhydrous aluminum chloride in 400 ml. of dry benzene at 5–10°. The mixture was then stirred overnight during which time it was allowed to come to room temperature. The mixture was cooled again, 100 ml. of ether was introduced, and then 600 ml. of ice cold 1:1 hydrochloric acid was added, with stirring, at such a rate that the temperature remained below 10°.

The separated water layer was extracted several times with 50-ml. portions of benzene-ether, the extracts were combined with the original organic layer and the whole was washed with dilute hydrochloric acid, 5% sodium carbonate (unreacted acid was recovered on neutralization of this wash solution), water, and saturated sodium chloride. The residue obtained after removal of the solvent from the dried organic solution solidified in rod-like crystals which recrystallized readily from alcohol to give 33 g. (89%) of the desired ketone: m.p. 121–121.5°.

Anal. Calc'd for $C_{13}H_{14}O$: C, 83.83; H, 7.58.
Found: C, 83.99; H, 7.78.

1,7-Tetramethyleneindan (IX). In a modified Wolff-Kishner reduction (8), a mixture of 18.6 g. of 3,4-tetramethyleneindanone-1, 49 ml. of 85% hydrazine hydrate, and 35 ml. of ethanol was heated under reflux for three hours. The condenser was removed, 75 ml. of diethylene glycol was added, and the mixture was heated to 170°. Potassium hydroxide (15 g.) was added to the cooled contents of the flask and the mixture was heated under reflux until the evolution of nitrogen ceased (five to six hours). To the cooled, dark mixture was added 300 ml. of water and the whole was extracted with ether. The ether solution was washed with water and saturated calcium chloride, then dried, and the solvent was removed. Distillation of the residual liquid under reduced pressure gave 16.4 g. (95%) of colorless liquid; b.p. 120–122° at 10 mm. The reported boiling point is 127–128° at 12 mm. (14).

1,8-Tetramethyleneazulene (XI). Ethyl diazoacetate (11 ml.) was added dropwise with stirring over a period of 30 minutes to 17.2 g. of 1,7-tetramethyleneindan heated to 135–140° in a small three-necked flask equipped with a condenser and dropping-funnel. The temperature (oil-bath) was then raised gradually to 165–170° and, after two hours, the mixture was distilled *in vacuo*. After a small forerun, unreacted tetramethyleneindan was collected (13.7 g., b.p. 120–122° at 10 mm.). The pressure was then reduced to 0.1 mm. and the material (4.1 g.) boiling at 90–140° was collected. The first portions were light red in color and the majority of the material (b.p. 130–140°) was dark red. A sample of the latter fraction took up 2.9 mole-equivalents of hydrogen in the presence of a platinum oxide catalyst. After heating a solution of the red product in 80 ml. of alcohol and 20 ml. of water with 6 g. of potassium hydroxide under reflux for four hours, 60 ml. of water was added, and the alcohol was removed by distillation and the aqueous solution was extracted with ether and then acidified. The green oil which separated was extracted into ether and the ether solution was washed twice with water and dried by filtering through a layer of anhydrous magnesium sulfate. Removal of the solvent left 3.3. g. of crude product as a dark green semisolid.

The crude product (2.3 g.) was mixed with 230 mg. of 10% palladium-charcoal in a small (5-ml. bulb) one-piece distilling flask and heated in a salt bath at 300–350° until the foaming subsided somewhat and the appearance of a dark blue material was observed (about one minute). The pressure was then reduced and the dark blue distillate was collected. This material was dissolved in *n*-hexane and the solution was washed with 2% sodium hydroxide (acidification of the alkaline solution gave a green acidic material which could be subjected again to the dehydrogenation process). The neutral residue from the *n*-hexane solution was chromatographed on an alumina column with *n*-hexane as the eluent. Two zones (blue and green) developed and were collected. The material from the blue fraction was rechromatographed and the eluate solution was extracted with 85% phosphoric acid. Ice was added carefully to the red acid solution to decompose the complex and the blue substance was extracted with *n*-hexane. The solvent was evaporated, the residue was taken up in ethanol, and this solution was subjected to steam-distillation. An alcoholic solution of the blue solid which appeared in the distillate was treated with trinitrobenzene and the dark crystalline complex was dissolved in *n*-hexane and decomposed on an alumina column. The blue eluate fraction was evaporated to dryness (with the addition of 1 ml. of alcohol to remove last traces of the hexane) and the crystalline residue was sublimed to give 34 mg. (0.2%) of shiny blue plates; m.p. 47–48°. A cyclohexane solution displayed maxima in mμ at 246, ϵ 7600; 284, ϵ 16900; 288, ϵ 16600; 302, ϵ 4300; 336, ϵ 1360; 350, ϵ 2110; 364, ϵ 67; 586, ϵ 30; 605, ϵ 35; 630, ϵ 32; 660, ϵ 31; and 730, ϵ 13 (Figs. 1 and 2).

Anal. Calc'd for $C_{14}H_{14}$: C, 92.26; H, 7.74.
Found: C, 92.05; H, 7.93.

A *trinitrobenzene derivative* crystallized from alcohol as slender black needles; m.p. 133–134°.

Anal. Calc'd for $C_{20}H_{17}N_3O_6$: C, 60.75; H, 4.34; N, 10.63.
Found: C, 60.86; H, 4.46; N, 10.33.

Green compound. The green eluate fractions obtained during the isolation of 1,8-tetramethyleneazulene from several dehydrogenations were combined and rechromatographed four additional times. The solvent was then removed and a few ml. of dry ether was added. Evaporation of the ether in an air steam left a few milligrams of a green solid which melted at 140–145° with decomposition. This substance formed no complex with 85% phosphoric acid, gave a brown solution (but no solid derivative) with trinitrobenzene in alcohol, and on attempted recrystallization from organic solvents gave a white solid which gradually became polymeric in nature. Attempted sublimation, distillation etc. resulted in decomposition of the green product. The absorption spectrum of the green material in cyclohexane (λ_{max} in mμ at 246, 288, 355, 490, 625 and 760) was somewhat similar to that of the 1,8-tetramethyleneazulene.

SUMMARY

An attempted synthesis of 1,10-cyclopentenoheptalene is described. Catalytic dehydrogenation of the saponified product from the reaction of 1,7-tetramethyleneindan and diazoacetic ester yielded 1,8-tetramethyleneazulene as the only product which could be characterized.

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