The triphenylazulene was obtained in 20% overall yield and was shown to be identical with the product of Assony and Kharasch by its melting point, mixture melting point, and infrared spectrum.

EXPERIMENTAL

1,2,3-Triphenylcyclopentadiene (III) was prepared in 55% yield from 1,2,3-triphenylcyclopentadiol, by the method of Paulson.[7]

1,2,3-Triphenylazulene. To 1,2,3-triphenylcyclopentadiene (2 g., 0.007 mol.) was added 20 ml. diphenyl ether and sodium methoxide (0.3 g., 0.007 mol.). The mixture was heated to 70° under nitrogen. Generation of the triphenylcyclopentadienyl anion was indicated by the intense red color of the reaction mixture. Pyridium methiodide (2.0 g., 0.01 mol.) was added to the solution, causing a distinct darkening of the reaction mixture. The solution was refluxed 1 hr., when evolution of methylamine was noted. The reaction mixture was chromatographed on a column of alumina (20 × 2.5 cm.) using low boiling mixed alkanes as solvent and eluting with a 50%, by volume, mixture of benzene and mixed alkanes. A blue band developed, which, after elution and aspiration of the eluate to dryness, yielded a blue solid (0.5 g., 20%). Recrystallization from nitromethane gave the characteristic blue compound melting at 215.5°.

A mixture-melting point of the product and that prepared *via* the sulfenyl chloride–diphenylacetylene route showed no depression and the infrared spectra of the two samples, run consecutively, also exhibited no observable differences.

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A New Route to 2,5-Dimethoxyphenylacetic Acid

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The mechanism of the amination of various halobenzenes in the presence of sodium amide and liquid ammonia has been elucidated by Roberts and co-workers.[1] Such aminations of halobenzenes which are nonactivated for nucleophilic substitution appear to involve a "benzyne" intermediate. With an explanation of the course of these reactions came a renewed interest in the further characterization of similar reactions and in the synthetic possibilities of such reactions. Thus Bunnett and Brotherton prepared a number of dialkylanilines by the reaction of bromobenzene with sodium amide and dialkylamines[2] and studied some reactions of "benzyne" and "α-naphthalyne";[3] Hrutfiord and Bunnett recognized the utility of such reactions in the synthesis of heterocyclic and homocyclic compounds.[4] Scardiglia and Roberts have extended earlier studies from their laboratory to include reactions of nonactivated aryl halides with various nucleophilic agents induced by alkali amides in liquid ammonia.[5] Additionally extensive characterization of similar reactions has been carried out by Huisgen and co-workers.[6] Recently Leake and Levine have reported the phenylation of ketones by reaction with phenyl halides and alkali amides.[7]

It seemed that an improved synthesis of 2,5-dimethoxyphenylacetic acid might be achieved by reactions presumably involving a "benzyne" intermediate. 2,5-Dimethoxyphenylacetic acid may be readily converted to homogentisic acid (2,5-dihydroxyphenylacetic acid), a compound of considerable biochemical interest. Studies of the nature and mode of formation of homogentisic acid in animals have provided many of the fundamental data on the intermediary metabolism of tyrosine and phenylalanine. A strong indication that homogentisic acid is an intermediate in the oxidative degradation of phenylalanine and tyrosine was first obtained from isotopic experiments.[8-11]

An improved synthesis of homogentisic acid was desirable. In the best published synthesis of this compound the synthesis of the intermediate 2,5-dimethoxyphenylacetic acid presents serious limitations to the synthesis of homogentisic acid itself since the over-all yield of the intermediate is 30–40% and reactions and work-up procedures are lengthy.[12] It seemed of considerable interest to attempt the synthesis of this intermediate using 2,5-dimethoxybromobenzene with appropriate nucleophiles under conditions where formation of a "benzyne" intermediate might be expected, *i.e.*, in the presence of a metal amide and liquid ammonia. Attempts to use diethyl malonate as a potential nucleophile with potassium amide and liquid ammonia were unsuccessful. However the

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isolation of 2,5-dimethoxyaniline in 12% yield indicated that a "benzyne" intermediate had indeed formed. To minimize the competing reaction, sodium amide in liquid ammonia[13] was used in subsequent experiments in slight molar excess to the bromo compound plus nucleophile.

An attempt to use ethyl acetate as a potential nucleophile was also unsuccessful. Examination of Fisher-Hirschfelder-Taylor models suggested that the formation of the products expected from reaction with diethyl malonate or ethyl acetate would be unlikely for steric reasons.

α-Sodio sodium acetate[14] was also tried as a nucleophile at the boiling points of the inert solvents *p*-xylene and tetrahydrofuran as well as at room temperature with 2,5-dimethoxybromobenzene itself as a suspending medium. The α-sodio sodium acetate appeared to be partially soluble in each of these reaction media but in no case could the product of interest be isolated.

When acetonitrile was tested as a potential nucleophile, the reaction mixture after work-up yielded 2,5-dimethoxyphenylacetic acid. While synthesis of this compound *via* the nitrile results in yields of approximately 10%, the reaction takes little time and work-up procedures are short. Thus the synthesis appears to hold promise for the synthesis of homogentisic acid labeled in the side chain for metabolic studies. In addition the reactions constitute a novel route to 2,5-dimethoxyphenylacetic acid.

EXPERIMENTAL

Materials. 2,5-Dimethoxybromobenzene (I) was prepared in approximately 60% yield by the methylation of bromohydroquinone employing conventional reaction conditions with dimethyl sulfate and sodium hydroxide. The product was obtained as a colorless oil which was identified by boiling point, analysis for C, H, and Br, and infrared analysis.[15]

Attempted reaction of I with diethyl malonate. Isolation of 2,5-dimethoxyaniline (II). To approximately 300 ml. of liquid ammonia (−77°) and 0.28 g. of ferric nitrate·9 H_2O, approximately 2 g. of potassium was added and the mixture stirred for 15 min. to form the catalyst (metallic iron) for the preparation of potassium amide. Additional potassium (43.4 g., 1.14 mol.) was then added with stirring. After evolution of hydrogen was complete, 19.2 g. of diethyl malonate (0.12 mol.) was added dropwise with stirring, followed by 21.7 g. of 2,5-dimethoxybromobenzene (0.1 mol.) and the temperature of the reaction mixture raised to approximately −30° for 1 hr. Enough 10% ammonium chloride was then carefully added to convert amide ion to ammonia and the ammonia was then distilled out of the reaction mixture at reduced pressure. The reaction mixture was extracted with diethyl ether, and the ether removed by distillation to leave a dark brown oil. The oil was fractionated by distillation under reduced pressure and partial characterization of minor fractions gave no indication that diethyl(2,5-dimethoxyphenyl)malonate had been formed. The major fraction which distilled at about 1 mm. from 80–90° and crystallized in the condenser was collected. This solid was further purified by sublimation to yield 1.8 g. (12%) of white, crystalline II, which melted at 74–76° (literature m.p. 80°[16]) and behaved as a typical amine.

Anal. Calcd. for $C_8H_{11}NO_2$: C, 62.72; H, 7.24; N, 9.15. Found: C, 62.59; H, 7.23; N, 9.27.

The infrared spectrum supported the structure of the product.

Reaction of I with acetonitrile. Preparation of 2,5-dimethoxyphenylacetic acid (III). Reaction conditions were similar to those described above except that to one flask (−30°) containing 150 ml. of ammonia and 3.84 g. of sodium (0.17 mol.), 6.93 g. of acetonitrile (0.17 mol.) was added followed by the addition of 17.8 g. of 2,5-dimethoxybromobenzene (0.083 mol.). The contents of a second flask (−30°) containing initially 250 ml. of ammonia, 3.84 g. of sodium (0.17 mol.), and a catalytic amount of ferric nitrate·9 H_2O were then slowly flushed into the first flask. After complete transfer, which took approximately 30 min., the reaction mixture was covered with anhydrous diethyl ether and ammonium chloride added to liberate ammonia. To the reaction mixture more diethyl ether was added, and the ether was then removed from the ether extract by distillation, leaving a brown oil. This oil was then submitted to hydrolysis in twice its volume of concentrated hydrochloric acid for 4 hr. During hydrolysis a viscous oil separated, and after hydrolysis this oil was dissolved in 10% sodium carbonate. Acidification of the bicarbonate solution to *p*H 2 yielded a tan crystalline compound which was isolated in 15% yield (2.38 g). Purification of the tan product by sublimation and recrystallization resulted in 50–70% recovery of the tan product as a white, crystalline compound (III). III melted at 121.0–121.5° (literature m.p., 122–123°[12]) and the infrared spectrum supported the proposed structure.

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.19; H, 6.13.

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(13) Sodium amide is less soluble in ammonia at −30° than is potassium amide.

(14) We wish to thank Ethyl Corp., New York, for a generous gift of this compound.

(15) Elemental analyses were performed by Weiler and Strauss, Microanalytical Laboratory; infrared analyses were made by the Division of Industrial Research, Washington State University.

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Epoxidation of Cinnamaldehyde by Alkaline *tert*-Butyl Hydroperoxide

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An attempt was made to form an epoxide of cinnamaldehyde with alkaline hydrogen peroxide using the technique recently described for the epoxidation of acrolein and α-methylacrolein.[1] As the

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