less product thus obtained was crystallized several times from dilute methanol (Norit) as colorless prisms, m.p. 214–215°; yield 50%.

Anal. Calcd. for $C_{20}H_{23}NO_3.HCl·H_2O$: C, 63.24; H, 6.85; N, 3.68. Found: C, 63.21; H, 6.95; N, 3.65.

2,3,9,10-Bismethylenedioxybenz[a]acridizinium chloride (*dehydrocoptisine chloride*, II, X = Cl). A mixture of the oxime of 6,7-methylenedioxyisoquinoline 1-carboxaldehyde[3] (0.9 g.) 2,3-methylenedioxybenzylbromide[4] (1 g.) and dimethylformamide (15 ml.) was allowed to react in the usual way and the quaternary salt was cyclized with concentrated hydrochloric acid. The red precipitate was collected and crystallized from a mixture of ethanol and methanol as red needles, decomposing above 300° (sealed tube); yield 1.5 g. (85%); λ_{max} 248, 317, 356, 490; min. 264, 294, 337, and 418 mμ.

The analytical sample was recrystallized from excess methanol, without change in melting point.

Anal. Calcd. for $C_{19}H_{12}ClNO_4·3/2\ H_2O$: C, 60.00; H, 3.94. Found: C, 59.69; H, 4.05.

The perchlorate was obtained as red needles from dimethylformamide and methanol, decomposing from 350°.

Anal. Calcd. for $C_{19}H_{12}ClNO_8$: C, 54.61; H, 2.87; N, 3.35. Found: C, 54.50; H, 3.21; N, 3.75.

2,3,9,10-Bismethylenedioxydibenzo[a,g]quinolizidine (*tetrahydrocoptisine*, *±-stylopine*, IV). The above salt (II. X = Cl) was hydrogenated in the usual way and the free base was crystallized twice from methanol. The tetrahydrocoptisine (XIV) was obtained as colorless needles, m.p. 217–218° dec. (lit.,[9,15,16] m.p. 219°, 227–228°, 215–216°); yield 50%. It was found that a solution of the base in glacial acetic acid slowly turned green on addition of a drop of concentrated sulfuric acid, while the further addition of a drop of dilute nitric acid produced a red color. Tetrahydrocoptisine was reported to behave similarly.[9]

Anal.[24] Calcd. for $C_{19}H_{17}NO_4$: C, 70.57; H, 5.30; N, 4.33. Found: C, 70.64; H, 5.14; N, 4.56.

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[CONTRIBUTION NO. 656 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DENEMOURS AND CO.]

Trimerization of Acetylenes

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The trimerization of monovinylacetylene and the cotrimerization of divinylacetylene with acetylene and with methylacetylene have been effected under mild conditions using triisobutylaluminum/titanium tetrachloride catalyst to give trivinylbenzenes and *o*-divinylbenzenes, respectively.

The thermal trimerization of acetylene to benzene was reported almost one hundred years ago by Berthelot.[1] Since then, such catalysts as metal carbonyls,[2] triphenylphosphinenickel carbonyl,[3] trialkylchromium,[4] diborane-activated silicaalumina,[5] and triisobutylaluminum–titanium tetrachloride[6] have been shown to facilitate the trimerization of acetylenes. Trialkylaluminum–titanium tetrachloride catalysts are well known for their ability to catalyze the polymerization of olefins,[7] and have been used to polymerize 1-hexyne to linear conjugated structures.[8]

Although vinylacetylenes might thus be expected to give complex products with trialkylaluminum–titanium tetrachloride catalysts, we have found that these catalysts promote trimerization of monovinylacetylene and cotrimerization of divinylacetylene with acetylene readily at −10 to 50° to give vinylbenzenes in modest to good yields.

At −10°, monovinylacetylene gave a mixture of 1,2,4- and 1,3,5-trivinylbenzenes in 74% yield. The yield at 50° was only 10%. The composition of this mixture as determined by ultraviolet analysis of the hydrogenated products was 90% 1,2,4-trivinylbenzene and 10% 1,3,5-trivinylbenzene. Statistically, one would expect a product containing 75% of 1,2,4-trivinylbenzene. 1,3,5-Trivinylbenzene has been prepared by another method,[9] but apparently the 1,2,4-isomer has not been reported.

The 1,2,4- and 1,3,5-trivinylbenzenes were separated by gas chromatography although considerable polymerization occurred on the column. The retention time of the 1,2,4-isomer was slightly shorter than that of the 1,3,5-isomer.

The infrared spectra of 1,3,5-trivinylbenzene and of the mixture of trivinylbenzenes were in general those expected for vinylbenzenes. The spectrum of 1,2,4-trivinylbenzene showed a strong band at 11.98 μ which was absent in the spectrum of 1,3,5-trivinylbenzene. As would be expected, the trivinylbenzenes absorb strongly in the ultraviolet, $\lambda_{max}^{C_2H_5OH}$ 246 mμ ($\epsilon = 31{,}000$).

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o-Divinylbenzene and dimethyl-*o*-divinylbenzene isomers are readily obtained by cotrimerization of divinylacetylene with acetylene and with methylacetylene, respectively. With acetylene in large excess, *o*-divinylbenzene was obtained in about 30% yield based on divinylacetylene. In limited process studies, the yields were increased to about 60% *o*-divinylbenzene when nearly stoichiometric proportions of acetylene were used.[10] The cotrimerization of divinylacetylene and acetylene has also been effected with triphenylphosphinenickel tricarbonyl and with bis(triphenylphosphine)nickel dicarbonyl. With these catalysts the yields were somewhat lower and the products were more difficult to purify.

Gas chromatographic analysis of the mixture of dimethyl-1,2-divinylbenzenes obtained from methyl acetylene and divinylacetylene showed three components representing approximately 5%, 85%, and 10% of the total. The identity of these isomers was not established. As 3,5-dimethyl-1,2-divinylbenzene is favored statistically, it would be expected to predominate, particularly because it was shown that the statistically favorable isomer was the main product in the case of the trivinylbenzene synthesis.

EXPERIMENTAL

Trimerization of vinylacetylene. Vinylacetylene (120 g.), scrubbed with 30% aqueous sodium bisulfite and with 20% aqueous sodium hydroxide, and dried with calcium chloride and anhydrous calcium sulfate, was added to a mixture of 1000 ml. of toluene, 6.4 g. of triisobutylaluminum, and 2.0 g. of titanium tetrachloride over a period of 75 min. (scrupulously dried equipment was used). The temperature was maintained at −10° by cooling. Methanol (400 ml.) was added to destroy the catalyst and to precipitate methanol-insoluble products. Distillation of the filtrate gave 15 g. of recovered monovinylacetylene and 78 g. of trivinylbenzenes,[11] b.p. 90° at 5 mm., n_D^{25} 1.6050, corresponding to a conversion of 65% and yield of 74%. In a similar run at 29–52°, the yield was only 10%.

Anal. Calcd. for $C_{12}H_{12}$: C, 92.25; H, 7.75; Hydrogenation No. 0.0385; mol. wt. 156. Found: C, 91.72; H, 8.07; Hydrogenation No. 0.0400, 0.0408; mol. wt. 156 (by mass spectrometry).

Hydrogenation of the trivinylbenzene fraction was carried out in ethanol at 33° under atmospheric pressure using a platinum oxide catalyst. Ultraviolet analysis of the hydrogenated product indicated that it contained 90% 1,2,4-triethylbenzene and 10% 1,3,5-triethylbenzene.

Gas chromatographic analysis of the trivinylbenzene isomers was carried out using a 1-m. stainless steel column (O.D.—0.25 in.) containing polypropylene glycol (20%) on Columnpak at 160° with a preheater temperature of 220° and a helium flow of 75 ml./min. The chromatogram showed a large peak (about 75% of total) at a retention time of 35 min. and a smaller peak (25%) at 38 min. The 38-min. peak was shown to be due to 1,3,5-trivinylbenzene by comparison with the chromatogram of an authentic sample.[9] Attempts to use preparative-scale gas chromatography resulted in nearly complete polymerization of the trivinylbenzenes on the column. As polymerization does occur on the column, the quantitative interpretations of the gas chromatographic analysis may be subject to considerable error.

The ultraviolet spectrum of the trivinylbenzene fraction showed strong absorption in the ultraviolet region, $\lambda_{\max}^{C_2H_5OH}$ 246 mμ (ε 31,000). The infrared absorption spectrum showed bands at 3.25 μ, 3.35 μ (unsaturated carbon-hydrogen bonds), 6.15 μ (conjugated olefinic —C═C—), 6.30 μ (aromatic —C═C—), 10.15 μ and 11.02 μ (CH deformations, —CH═CH$_2$), 11.37 μ (out-of-plane C—H deformation vibration in 1,3,5-trivinylbenzene), and 11.98 μ (out-of-plane CH deformation vibration in 1,2,4-trivinylbenzene).

The infrared spectrum of an authentic sample[9] of 1,3,5-trivinylbenzene was very similar except it did not show the strong band at 11.98 μ.

o-Divinylbenzene. A. *Catalyst: Triisobutylaluminum/titanium tetrachloride.* To a dry, 1-l. reaction flask equipped with a mechanical stirrer, condenser, dropping funnel for addition of divinylacetylene (DVA),[12] gas addition tube, and a thermometer there was added 150 ml. of toluene dried over sodium. The reaction system was flushed with nitrogen and 10 ml. of triisobutylaluminum and 1 ml. of titanium tetrachloride were added in turn by means of a hypodermic syringe. The catalyst solution was cooled in ice water and acetylene was passed into the system at the rate of 0.8 mole per hr. A solution of 16 g. of divinylacetylene in 30 ml. of toluene was added over the course of 2 hr. The temperature of the reaction solution was maintained at 15–20° by means of a water bath. Methanol (50 ml.) containing a trace of *N*-phenyl-β-naphthylamine to inhibit polymerization was added. The solution was filtered and the filtrate was distilled. *o*-Divinylbenzene,[13] 8 g., 30% yield, n_D^{25} 1.5740, b.p. 52°/3 mm., $3_{\max}^{C_2H_5OH}$ 229 mμ (ε 20,400), was collected. The infrared spectrum of this product was identical with that of a sample prepared with triphenylphosphinenickel tricarbonyl as catalyst.

B. *Catalyst: Triphenylphosphinenickel tricarbonyl.* A 1-l., creased, five-necked flask was equipped with a mechanical stirrer, condenser, two 500-ml. addition funnels, and a gas addition tube. The reaction system was flushed with dry oxygen-free nitrogen. *N,N*-Dimethylacetamide, 200 ml., and 4 g. of calcium carbide were placed in the reaction flask. A solution of 30 g. of triphenylphosphinenickel tricarbonyl in 150 ml. of dimethylacetamide was placed in one additional funnel. A solution of 95 g. of divinylacetylene in 100 ml. of *N,N*-dimethylacetamide (inhibited with 0.5 g. of phenothiazine) was placed in the other addition funnel. A portion of the catalyst solution was added to the reaction vessel and acetylene passed into the mixture at approximately 0.5 mole per hr. The temperature of the catalyst solution was gradually raised to 95°. At this temperature, the acetylene flow rate was increased to 2 moles per hr. The divinylacetylene solution was added dropwise over the course of 5 hr. The temperature was maintained at 100–110° by means of a cooling bath. Catalyst solution was added as necessary to maintain acetylene absorption. The product was distilled and the fraction, b.p. 25–60°/5 mm., was collected, diluted with pentane, and washed with water. The product was then dried and distilled through a two-foot spinning-band column. Two major fractions were obtained: 1) styrene, 8 g., b.p. 25°/5 mm., n_D^{25} 1.5432, characterized by its infrared spectrum; 2) *o*-divinylbenzene, 34.5 g., 22% yield, b.p. 59–60°/4.5 mm., n_D^{25} 1.5740, (lit.[14] b.p. 73.5°/11 mm., n_D^{21} 1.5760, b.p. 73–74°/12 mm., n_D^{22} 1.5759). The infrared spectrum of the product showed absorption at 3.23, 3.25, 3.30 (hydrogen attached to unsaturated carbon), 6.14 (conjugated carbon-carbon double bond), 6.75, 6.88, 7.05 (aromatic ring vibrations), 10.14,

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(10) We are indebted to Dr. R. W. Keown of E. I. du Pont de Nemours & Co. for this information.

(11) F. W. Hoover, U. S. patent **2,951,884**, September 6, 1960.

(12) As divinylacetylene readily forms explosive peroxides when exposed to air, all reactions with this substance should be conducted in an inert atmosphere.

(13) F. W. Hoover, U. S. patent **2,933,541**, April 19, 1960.

(14) R. Deluchat, *Ann. Chim.* (11), **1**, 181 (1934); K. Fries, H. Bestian, and W. Klauditz, *Ber.*, **69B**, 715 (1936).

10.95 (vinyl hydrogen), and 13.20 μ (four adjacent hydrogens on an aromatic ring). The NMR spectrum was in agreement with the assigned structure, *o*-divinylbenzene.

Cotrimerization of divinylacetylene and methylacetylene. To a dry 500-ml. reactor equipped with a mechanical stirrer, condenser, dropping funnel, gas addition tube (open-end type extended below liquid level) and a thermometer, there was added 200 ml. of toluene dried with calcium hydride. Triisobutylaluminum (5 ml.) was added to the reactor under nitrogen by means of a hypodermic syringe, followed by titanium tetrachloride (1.5 ml.). Methylacetylene, dried by passing it through a tower containing Drierite, was added at the rate of 1.2 moles per hour. Concurrently, a solution of 15.6 g. (0.2 mole) of divinylacetylene in 50 ml. of toluene was added dropwise over a period of 80 min. Throughout the reaction, the temperature was maintained between 9° and 16° by means of an ice bath. Ten minutes after completion of the addition of the divinylacetylene, the catalyst was deactivated by addition of 50 ml. of methanol. On distillation there was obtained 40 g. of a trimethylbenzene isomer mixture, b.p. 32°/2 mm., and 9 g. (28% yield) of dimethyl-*o*-divinylbenzene[12] isomer mixture, b.p. 50–51°/0.2 mm., n_D^{25} 1.5598 and $\lambda_{max}^{C_2H_5OH}$ 228 mμ (ε 23,200).

Anal. Calcd. for $C_{14}H_{16}$: C, 91.14; H, 8.86; mol. wt., 158. Found: C, 90.73; H, 9.13; mol. wt., 158 (by mass spectrometry).

Gas chromatographic analysis of the product using a 1-m. Perkin Elmer Column R at 168° (preheat 220°) with a helium flow of 75 ml./min. showed three components with retention times of 11.7 min., 14.2 min., and 17.2 min., representing approximately 5%, 85%, and 10%, respectively, of the total. The three isomers were not identified.

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[CONTRIBUTION FROM THE LABORATORY OF BIOCHEMISTRY, NATIONAL CANCER INSTITUTE[1]]

Replacement and Elimination of Bromine in Bromonitrofluorenones. The Preparation of 2,3- and 1,2,3-Substituted Fluorenes and Fluorenones

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The oxidation by peracetic acid of 2-amino-3-bromofluorene and 2-amino-3-bromofluorenone, and of 1,3-dibromo-2-fluorenamine furnished the corresponding nitro derivatives. In the nitrobromofluorenones the bromine was readily replaced by amino groups in ethanolic ammonia. Ethanolic potassium hydroxide introduced a hydroxyl group into these compounds, but in one case elimination of bromine in the 1-position with substitution by hydrogen occurred. Potassium hydroxide in pyridine substituted a hydroxyl for a bromine at the 3-, but not at the 1-position in 1,3-dibromo-2-nitrofluorenone. These replacement reactions led to the facile preparation of a number of new 2,3- and 1,2,3-substituted fluorenones, and fluorenes.

The recent description[3] of a procedure for the oxidation of a primary aromatic amine by peracetic acid to the corresponding nitro derivative has suggested its use for the purpose of activating halogens *ortho* to the nitro group, thereby permitting the selective replacement of the halogen by other functional groups. The present paper deals with the application of this method to the convenient preparation of a number of otherwise difficultly available 2,3- and 1,2,3-substituted fluorene and fluorenone derivatives.

Bromination of 2-aminofluorenone by bromine afforded the 3-bromo derivative. The use of *tert*-butyl bromide in dimethyl sulfoxide[4] in addition produced 2-amino-3-bromo-9-fluorenol. Reduction of 2-amino-3-bromofluorenone by the Wolff-Kishner reaction resulted in good yields of 3-bromo-2-fluorenamine, provided that the reaction was performed in the absence of alkali. If alkali was added, halogen elimination ensued so that the product was 2-fluorenamine.

The action of peracetic acid on the 2-amino-3-bromofluorene and 2-amino-3-bromofluorenone readily gave the nitro derivatives. In the resulting nitrobromofluorenone bromine was easily replaced by amino, or by hydroxyl to yield the corresponding 2-nitro-3-amino-9-fluorenone or 2-nitro-3-hydroxy-9-fluorenone. This latter material served as a good source for the otherwise difficultly prepared 2-amino-3-fluorenol.[5] In fact, this aminohydroxyfluorene could be made in a single sequence of operations directly from 2-nitro-3-bromo-9-fluorenone by first treating with alkali under mild conditions, followed by addition of hydrazine and raising the temperature, thus effecting the Wolff-Kishner reaction. This new, short sequence of steps would appear to be the procedure of choice for the preparation of 2-amino-3-fluorenol.

Attempts to replace the bromine by fluorine in 2-nitro-3-bromo-9-fluorenone in acetamide as solvent gave the expected elimination of bromine, but under these conditions fluorine did not enter

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