calculated from certain assumptions and spectroscopic data; the rate constant k_5 for reaction (d-5) also has been calculated.

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[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

The Synthesis of Disubstituted Acetylenes

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In pursuing an investigation of the reactions of certain acetylenic systems, a number of disubstituted propynes of the type R—C≡C—CH_2—R′ were required. The present paper reports a study of synthetic methods for the preparation of pure individuals of known structure.

The alkylation of monosubstituted acetylenes was investigated as a promising preparative method. Nef[1] reported the methylation of phenylacetylene by heating it with methyl iodide and potassium hydroxide, and Morgan[2] effected ethylation of phenylacetylene by heating the sodium derivative with ethyl iodide. Both reactions were carried out in sealed tubes at relatively high temperature (140°) and the yields were low. Preliminary studies of these methods indicated that neither would be satisfactory for preparative purposes. In attempting to employ the method of Morgan, it was found that the sodium derivatives of typical alkyl- and arylacetylenes were surprisingly inert toward alkyl halides. At temperatures sufficiently high to bring about a reaction, vigorous deep-seated decomposition occurred. The substituted acetylides are evidently much less reactive than the monosodium derivative of acetylene itself, which reacts smoothly with alkyl halides at low temperatures.[3] Attempts to effect metathetical reactions between alkyl halides and other metallic derivatives of monosubstituted acetylenes (such as the bromomagnesium, cuprous, silver, and mercuric compounds), in a variety of solvent media, were also unsuccessful.[4]

In an investigation of the action of alkyl *p*-toluenesulfonates on organomagnesium halides, Gilman and Beaber[5] reported the synthesis of β-chloroethylphenylacetylene from the bromomagnesium derivative of phenylacetylene and β-chloroethyl *p*-toluenesulfonate. We have employed their method with excellent results for the preparation of several alkyl derivatives of phenylacetylene. However, the modification of Truchet,[6] in which the sodium derivatives of the acetylenes are used, is advantageous in one respect. When the organomagnesium halide is used, two moles of the sulfonic ester is consumed in producing one equivalent of the alkylated acetylene, since one mole of the ester is converted to the corresponding alkyl bromide (reaction I);[7] but with the sodium acetylides only one equivalent of the sulfonic ester is required (reaction II).

$$\text{R—C≡C—MgBr} + 2\text{R}'\text{—OSO}_2\text{—C}_7\text{H}_7 \longrightarrow \text{R—C≡C—R}' + \text{R}'\text{—Br} + \text{Mg(OSO}_2\text{—C}_7\text{H}_7)_2 \quad \text{(I)}$$

$$\text{R—C≡C—Na} + \text{R}'\text{—OSO}_2\text{—C}_7\text{H}_7 \longrightarrow \text{R—C≡C—R}' + \text{NaOSO}_2\text{C}_7\text{H}_7 \quad \text{(II)}$$

The sodium derivatives were used with satisfactory results for the alkylation of phenylacetylene and *n*-octylacetylene, to obtain the following disubstituted acetylenes: ethyl-, *n*-butyl-, and γ-chloropropylphenylacetylene; ethyl- and γ-chloropropyl-*n*-octylacetylene. The sodium derivatives appeared to be particularly advantageous in the aliphatic series, but there are certain limitations. Attempts to effect syntheses using phenylethynylsodium and benzyl or β-chloroethyl *p*-toluenesulfonate were unsuccessful. In these instances, however, the desired compounds were obtained by the use of phenylethynylmagnesium bromide.

The structures of the disubstituted acetylenes were checked by several methods. In some instances oxidation with aqueous potassium permanganate was employed and the resulting acids

(1) Nef, *Ann.*, **310**, 333 (1900).

(2) Morgan, *J. Chem. Soc.*, **29**, 162 (1876).

(3) Picon, *Compt. rend.*, **169**, 32 (1919).

(4) A few exceptionally active halides do react with phenylethynylmagnesium bromide to give substituted phenylacetylenes; *e. g.*, allyl bromide [Grignard and Lapayre, *ibid.*, **192**, 250 (1931)], benzohydryl bromide [Wieland and Kloss, *Ann.*, **470**, 217 (1928)], α-furfuryl chloride [Gilman, Van Ess and Burtner, THIS JOURNAL, **55**, 3461 (1933)].

(5) Gilman and Beaber, *ibid.*, **45**, 839 (1923).

(6) Truchet, *Compt. rend.*, **191**, 854 (1930); *Ann. chim.*, [10] **16**, 309 (1931).

(7) Marvel and Rossander, THIS JOURNAL, **50**, 1491 (1928). The correctness of this equation was confirmed in the present work by the isolation of ethylene chlorobromide and benzyl bromide from the reactions in which β-chloroethyl and benzyl *p*-toluenesulfonates were used.

were identified; in others, the hydrocarbons were hydrated with mercuric sulfate and sulfuric acid to the corresponding ketones. The halogenated hydrocarbons were identified by replacement of the halogen atom by carboxyl, by way of the nitrile, and oxidation of the resulting acetylenic acid.

$$\mathrm{R{-}C{\equiv}C{-}(CH_2)_{\mathit{n}}{-}Cl} \longrightarrow$$

$$\mathrm{R{-}C{\equiv}C{-}(CH_2)_{\mathit{n}}{-}C{\equiv}N} \longrightarrow \mathrm{R{-}C{\equiv}C{-}(CH_2)_{\mathit{n}}{-}CO_2H}$$

$$\mathrm{R{-}C{\equiv}C{-}(CH_2)_{\mathit{n}}{-}COOH + H_2O + 3[O]} \longrightarrow$$

$$\mathrm{R{-}COOH + HOOC{-}(CH_2)_{\mathit{n}}{-}COOH}$$

In all cases the compounds behaved like pure individuals and the structures corresponded with those anticipated.

Experimental

Ethylphenylacetylene (1-Phenylbutyne-1).—In a three-necked flask fitted with a mechanical stirrer, reflux condenser and separatory funnel, were placed 75 cc. of anhydrous ether and 4.6 g. (0.2 mole) of clean sodium wire. With vigorous stirring, 21 g. (0.2 mole) of phenylacetylene was added slowly. The reaction started spontaneously and the phenylacetylene was added at such a rate that the ether refluxed gently. The mixture was refluxed for two hours and the ether was then removed completely by warming on a steam-bath. The solid phenylethynylsodium was covered with 75 cc. of anhydrous di-*n*-butyl ether, the mixture was warmed to 60°, and 40 g. (0.2 mole) of freshly distilled ethyl *p*-toluenesulfonate was added dropwise, while stirring vigorously. A spontaneous exothermic reaction occurred and the temperature was maintained below 70° by external cooling. After two hours at 60–70°, the reaction mixture was cooled and treated with a large volume of water. The upper layer was separated, washed with dilute hydrochloric acid and finally with water. After drying, the product was fractionated under reduced pressure. After removal of a small quantity of unreacted phenylacetylene and of di-*n*-butyl ether, the ethylphenylacetylene distilled sharply at 82–83° (5 mm.). After redistillation the product weighed 20 g. (77% yield); b. p. 82° at 5 mm., d^{20}_4 0.9210.

This preparation was also carried out using toluene as the reaction medium; in this modification the phenylethynylsodium was prepared directly in toluene. Using the quantities of reactants given above, about 5 g. of phenylacetylene was recovered and 18–20 g. of ethylphenylacetylene was obtained.

The structure of this compound was checked by hydration to *n*-butyrophenone. Five grams of the hydrocarbon in 15 cc. of ethyl alcohol was treated with 2 g. of mercuric oxide, and 15 g. (8 cc.) of concd. sulfuric acid was added dropwise with shaking. After cooling to 20°, the mixture was poured into water and the product extracted with ether. The resulting ketone distilled at 220–223° (740 mm.), and was identified as *n*-butyrophenone through the oxime, m. p. 47°, and the semicarbazone, m. p. 187–188°.

β-Chloroethylphenylacetylene (1-Phenyl-4-chlorobutyne-1).[5]—An ethereal solution of phenylethynylmagnesium bromide was prepared by refluxing 21 g. (0.2 mole) of phenylacetylene with slightly more than the calculated quantity of ethylmagnesium bromide (in approximately molar solution). The resulting solution was added dropwise, with vigorous stirring, to 94 g. (0.4 mole) of β-chloroethyl *p*-toluenesulfonate. The mixture was refluxed gently for eight hours and after cooling was decomposed by iced hydrochloric acid. The ethereal layer was separated and washed successively with water, sodium bicarbonate solution, and water. After drying over calcium chloride the ether was removed and the residue was fractionated under reduced pressure. A large fraction which distilled below 50° at 25 mm., was refractionated at atmospheric pressure and gave 5 g. of phenylacetylene and 25 g. of ethylene chlorobromide (86% of the calculated amount). The remainder gave 15 g. (46% yield) of β-chloroethylphenylacetylene: colorless liquid, b. p. 95° (3 mm.); d^{20}_4 1.0763, n^{20}_D 1.5724, n^{20}_C 1.5657, n^{20}_F 1.5882; MR_D calcd., 47.6, obsd. 50.52.

Anal. Calcd. for $C_{10}H_9Cl$:Cl, 21.58. Found: Cl, 21.52, 21.56.

This compound was not obtained when phenylethynylsodium was used in place of phenylethynylmagnesium bromide. In this case the phenylacetylene was recovered unchanged after the reaction mixture was hydrolyzed, but none of the sulfonic ester was recovered.

γ-Chloropropylphenylacetylene (1-Phenyl-5-chloropentyne-1).—This substance was prepared according to the procedure given under ethylphenylacetylene, using 50 g. (0.2 mole) of γ-chloropropyl *p*-toluenesulfonate instead of the ethyl ester. The yield of purified product was 27 g. (75% yield). When toluene was used as the reaction medium, a large quantity of phenylacetylene was recovered and only 9 g. (25% yield) of the disubstituted acetylene was obtained.

A redistilled specimen of γ-chloropropylphenylacetylene had the following constants: b. p. 125–127° (4 mm.); d^{20}_4 1.0576, n^{20}_D 1.5615, n^{20}_C 1.5555, n^{20}_F 1.5761; MR_D calcd., 52.2, obsd. 54.70.

Anal. Calcd. for $C_{11}H_{11}Cl$: Cl, 19.88. Found: Cl, 19.76, 19.84.

The structure of this compound was checked by conversion to 6-phenyl-5-hexynoic acid, and oxidation of the latter to benzoic and glutaric acids. A solution of 5 g. of the chloropropylphenylacetylene in 50 cc. of 90% alcohol was refluxed with 10 g. of pulverized potassium cyanide for thirty hours. After cooling, the mixture was poured into a large volume of water and the oily layer of nitrile was separated. This was refluxed with an excess of 10% potassium hydroxide solution until no oily drops remained. After cooling, the solution was poured into an excess of iced hydrochloric acid, whereupon the acetylenic acid separated as an oil. The latter was extracted with ether and the solvent was distilled off. No attempt was made to purify the intermediate acid. The crude acid was allowed to stand for twenty-four hours at room temperature with a slight excess of 1% aqueous potassium permanganate, with occasional shaking. Oxidation occurred readily and a clear colorless solution was obtained after filtering off the manganese dioxide. The solution was concentrated to a small volume and poured into an excess of iced acid. An oily mixture of acids was precipitated, from which benzoic and glutaric acids were isolated by repeated partition between ether and water. Benzoic acid was identified by a mixed melting point with an authentic specimen. The glutaric acid melted at 97–98°; neutralization equivalent, 68 (calcd., 66); anilide, m. p. 218–219°.

***n*-Butylphenylacetylene (1-Phenylhexyne-1)**.—Phenylethynylsodium was prepared by adding slowly 51 g. (0.5 mole) of phenylacetylene to 11.5 g. (0.5 gram atom) of sodium wire in toluene at 35–40°. Higher temperatures must be avoided or the sodium derivative is converted to a gelatinous mass in the presence of toluene. To the suspension of the sodium derivative, 114 g. (0.5 mole) of *n*-butyl *p*-toluenesulfonate was added slowly, with stirring, while the temperature was maintained at 70°. The reaction mixture was treated in the usual way and the product was fractionated through a 30-cm. heated Vigreux column under reduced pressure. A small amount of phenylacetylene was recovered and 51–55 g. (65–70% yield) of *n*-butylphenylacetylene was obtained. The redistilled product had the following constants: b. p. 94–95° at 4 mm. (bath 110–115°), 109–110° at 12 mm. (bath 129–133°); d^{20}_4 0.9024; n^{20}_{C} 1.5292, n^{20}_{D} 1.5347, n^{20}_{F} 1.5485, n^{20}_{G} 1.561; MR_{D} calcd., 52.0, obsd. 54.8.

On hydration in the usual way there was obtained *n*-amyl phenyl ketone (*n*-caprophenone), m. p. 24°, b. p. 137–139° (15 mm.); the semicarbazone of the ketone, after one crystallization from 50% alcohol, melted at 131.5–132° (reported, 127–128° and 131–132°).[8]

Ethyl-*n*-octylacetylene (Dodecyne-3).—Twenty-eight grams (0.2 mole) of pure *n*-octylacetylene[9] in 80 cc. of di-*n*-butyl ether was treated with 8 g. (0.2 mole) of sodamide, previously pulverized under di-*n*-butyl ether. The mixture was heated at 100° for two hours, with stirring, to complete the formation of the sodium derivative, and after cooling to 60° was treated dropwise with 40 g. (0.2 mole) of ethyl *p*-toluenesulfonate. The reaction mixture was heated at 70° for three hours, cooled and treated with cold water. The product was isolated by fractionation under reduced pressure. There was obtained 21 g. (63% yield) of ethyl-*n*-octylacetylene, b. p. 95° (12 mm.); d^{20}_4 0.7871, n^{20}_{D} 1.44415, n^{20}_{C} 1.44236, n^{20}_{F} 1.45162; MR_{D} calcd., 55.6, obsd. 55.65.

Anal. Calcd. for $C_{12}H_{22}$: C, 86.65; H, 13.35. Found: C, 86.59, 86.63; H, 13.33, 13.35.

The structure of this hydrocarbon was checked by oxidation with 1% aqueous potassium permanganate, as described above, which gave propionic and pelargonic acids. The former boiled at 138°, and gave propionanilide, m. p. 105°; this anilide showed no depression of the m. p. when mixed with an authentic sample of propionanilide. Pelargonic acid was identified by formation of the amide, m. p. 90°, which showed no depression when mixed with the amide obtained from a sample of synthetic pelargonic acid.

3-Chloropropyl-*n*-octylacetylene (1-Chlorotridecyne-4).—This compound was prepared according to the directions given for ethyl-*n*-octylacetylene, using 50 g. (0.2 mole) of γ-chloropropyl *p*-toluenesulfonate in place of the ethyl ester. The yield of purified product was 65% of the theoretical. A redistilled sample of 3-chloropropyl-*n*-octylacetylene had the following constants: b. p. 123–124° (3 mm.), d^{20}_4 0.9275, n^{20}_{D} 1.47073, n^{20}_{C} 1.46810, n^{20}_{F} 1.47749; MR_{D} calcd., 65.1, obsd. 65.0.

Anal. Calcd. for $C_{13}H_{28}Cl$: Cl, 16.54. Found: Cl, 16.40, 16.48.

The structure of this compound was checked by conversion to 4-tetradecynoic acid, and oxidation of the latter with 1% aqueous permanganate, following the procedure given under γ-chloropropylphenylacetylene. There were obtained pelargonic and glutaric acids, which were identified as described above.

Summary

A study has been made of the alkylation of metallic derivatives of monosubstituted acetylenes. The action of alkyl *p*-toluenesulfonates on the sodium or bromomagnesium derivatives of alkyl or arylacetylenes has been found to be a satisfactory procedure for the preparation of a variety of disubstituted acetylenes.

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[8] Truchet (ref. 6b, p. 400) reported that the semicarbazone of the ketone obtained by hydration of *n*-butylphenylacetylene melted at 164–165°, in agreement with the reported value for the semicarbazone of *n-amylacetophenone*. This is evidently an error since the acetylene in question should yield the lower homolog, *n*-butylacetophenone, as we have found.

[9] Johnson and McEwen, THIS JOURNAL, **48**, 473 (1926).