droxide to give 6 g. of a tan amorphous solid. Hygroscopicity was too great for melting point determination. The yield was 17%.

Anal. Calcd. for $C_{21}H_{20}O_2NCl$: N, 3.96; Cl, 10.02. Found: N, 4.40; Cl, 10.93.

Summary

A series of twenty pyridyl and N-methylpiperidyl alkanol esters of diphenylacetic and fluorene-9-carboxylic acids was prepared and studied *in vitro* for spasmolytic action. The diphenylacetic acid esters appears generally more active than the corresponding fluorene-9-carboxylic acid esters, particularly against spasm induced by acetylcholine and barium chloride; the latter are, however, less toxic. Reduction and N-methylation of the pyridine ring usually increases both the activity and toxicity. The most promising spasmolytic of the series is 1-(α-pyridyl)-2-ethyl diphenylacetate hydrochloride.

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[CONTRIBUTION FROM THE APPLIED SCIENCE RESEARCH LABORATORY OF THE UNIVERSITY OF CINCINNATI]

Aliphatic Trienes—A Synthesis from Acetylene-diols

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Aliphatic acetylene-diols of the type R—CH(OH)—C≡C—CH(OH)—R, which can be prepared readily either by treating the acetylene di-Grignard reagent with two moles of aliphatic aldehyde or by treating aldehyde with acetylene under the catalytic influence of copper acetylide, can be conveniently semi-hydrogenated to the corresponding olefin-diols.[2] During the course of a study of synthetic drying oils in this Laboratory it became desirable to synthesize certain aliphatic trienes. The acetylene-diols were chosen as convenient starting materials for these syntheses.

Several attempts have been made to dehydrate the olefin-1,4-diols produced by semi-hydrogenation of products obtained when acetylene dimagnesium bromide is caused to react with aliphatic carbonyl compounds. In every instance reported, however, the product has been a substituted dihydrofuran.[3] Bourguel and Rambaud[4] reported the synthesis of 2,5-dimethylhexatriene through the dehydration of 2,5-dimethyl-2,5-dihydroxy-3-hexene. However, it was later shown by Zalkind and Bukhovets[5] that the product thought by those investigators to be the olefin-diol was, in reality, the acetylene-diol. Consequently, the product they believed to be the triene was actually a divinylacetylene derivative. The true 2,5-dimethylhexatriene has recently been synthesized by Kharasch, Nudenberg and Sternfeld[6] through the condensation of β-methylallyl chloride with sodamide in liquid ammonia.

We have found that the difficulties attending the dehydration of the olefin-1,4-glycols are avoided by replacing the hydroxyl groups by chlorine through the action of anhydrous hydrogen chloride in petroleum ether solution, and dehydrohalogenation by means of pyridine. 3,5,7-Decatriene, for example, was prepared by the following series of reactions

$$2H_3C{-}CH_2{-}CH_2CHO + BrMg{-}C{\equiv}C{-}MgBr \longrightarrow C_3H_7{-}CH(OH){-}C{\equiv}C{-}CH(OH){-}C_3H_7 \quad (1)$$

$$C_3H_7{-}CH(OH){-}C{\equiv}C{-}CH(OH){-}C_3H_7 + H_2 \xrightarrow{Ni} C_3H_7{-}CH(OH){-}CH{=}CH{-}CH(OH){-}C_3H_7 \quad (2)$$

$$C_3H_7{-}CH(OH){-}CH{=}CH{-}CH(OH){-}C_3H_7 \xrightarrow{HCl} C_3H_7{-}CHCl{-}CH{=}CH{-}CHCl{-}C_3H_7 \quad (3)$$

$$C_3H_7{-}CHCl{-}CH{=}CH{-}CHCl{-}C_3H_7 \xrightarrow{\text{pyridine}} C_2H_5{-}CH{=}CH{-}CH{=}CH{-}CH{=}CH{-}C_2H_5 \quad (4)$$

2,5-Dimethyl-1,3,5-hexatriene was prepared by the same series of reactions starting with acetone and the acetylene di-Grignard. This product formed a crystalline adduct with maleic anhydride which melted at 114–115°, confirming the value reported for the same product by Kharasch, Nudenberg and Sternfeld.[6]

Experimental

Acetylene Dimagnesium Bromide.—This was prepared according to the method of Jozitsch[7] by passing acetylene for five hours at 150 ml./min. through a well-stirred solution of 3 moles of ethylmagnesium bromide in 1500 ml. of absolute ether contained in a 3-liter, 3-necked flask equipped with a mercury-sealed stirrer, reflux condenser, dropping funnel and gas inlet tube.

4,7-Dihydroxy-5-decyne.[8]—After the acetylene di-Grignard had stood overnight, 265 ml. (217 g., 3 moles) of freshly distilled butyraldehyde was added, with good agitation, over the course of one and one-half hours. Stirring was continued for another hour and the mixture

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(2) Zalkind and Bezsonova, *J. Phys. Chem.*, U. S. S. R., **53**, I. 284 (1921); *C. A.*, **18**, 2327 (1923); Zalkind, *Ber.*, **56B**, 187 (1923); *ibid.*, **60B**, 1125 (1927).

(3) Blomquist and Marvel, THIS JOURNAL, **55**, 1658 (1933).

(4) Bourguel and Rambaud, *Bull. soc. chim.*, [4] **47**, 173 (1930).

(5) Zalkind and Bukhovets, *J. Gen. Chem.*, U. S. S. R., **7**, 2417 (1937); *C. A.*, **32**, 2086 (1938); *cf.* Zalkind, THIS JOURNAL, **63**, 2282 (1941); Johnson and Johnson, *ibid.*, **62**, 2615 (1940); **63**, 2282 (1941).

(6) Kharasch, Nudenberg and Sternfeld, THIS JOURNAL, **62**, 2034 (1940).

(7) Jozitsch, *Bull. soc. chim.*, [3] **32**, 552 (1904); *cf.* Dupont, *Ann. chim. phys.*, [8] **30**, 485 (1913).

(8) Marvel and Williams, THIS JOURNAL, **61**, 2714 (1939).

allowed to stand twenty-four hours before hydrolyzing. The reaction mixture was poured into cracked ice and sulfuric acid, the organic layer separated and the aqueous layer extracted with one 200-ml. portion of ether, which was added to the organic layer. After washing with bicarbonate solution the ether solution was dried over sodium sulfate and the ether removed. Distillation through a glass helices-packed column (20 mm. × 150 cm.) gave 130 g. (51%) of 4,7-dihydroxy-5-decyne, b. p. 116–119° at 1.5 mm. pressure (lit.[8] b. p. 113–114° at 1 mm., n^{20}_{D} 1.4678, d^{20}_{4} 0.946.) Yields of 65% were obtained from larger-scale preparations.

4,7-Dihydroxy-5,6-dibromo-5-decene.—Bromination of 4,7-dihydroxy-5-decyne in carbon tetrachloride solution gave the dibromide, which after two recrystallizations from carbon tetrachloride and one from alcohol–water, gave white plates, m. p. 118.4–118.9°.

Anal. Calcd. for $C_{10}H_{18}O_2Br_2$: Br, 48.5. Found: Br, 48.3.

4,7-Dihydroxy-5-decene.—4,7-Dihydroxy-5-decyne was semi-hydrogenated in 0.2 mole batches at room temperature and 15 p.s.i. hydrogen pressure with Raney nickel as catalyst. The batches were composed of 34 g. (0.2 mole) of the acetylene compound, 6 ml. of a Raney nickel catalyst suspended in alcohol (corresponding to 1.6 g. of dry nickel powder) and 150 ml. of 95% ethyl alcohol. This was shaken under hydrogen until 0.2 mole of hydrogen was absorbed (twenty-five minutes). A total of 329 g. of 4,7-dihydroxy-5-decyne gave 253 g. (76%) of 4,7-dihydroxy-5-decene (b. p. 126–128° at 3 mm. pressure, n^{20}_{D} 1.4640, d^{20}_{20} 0.935).

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.8; H, 11.7. Found: C, 69.6; H, 11.3.

Seventeen and two-tenths grams of the olefin (0.1 mole) absorbed exactly 0.1 mole of hydrogen when dissolved in 150 ml. of alcohol and treated with an additional 6 ml. of Raney nickel suspension under 45 psi of hydrogen. The saturated glycol, 4,7-dihydroxydecane, m. p. 79–79.5°, previously prepared by Marvel and Williams,[8] was isolated as the reaction product.

2,5-Dipropyl-2,5-dihydrofuran.—Anhydrous hydrogen chloride (50–75 ml./min.) was passed into a stirred solution of 106 g. of 4,7-dihydroxy-5-decene in 150 ml. of anhydrous ether at 0–5° for thirteen hours. After storing in a refrigerator overnight, the reaction mixture was poured onto ice, the organic layer separated and washed, dried over sodium sulfate and, finally, the ether removed. Fractionation through a small column at 3 mm. pressure gave 49 ml. of material boiling below 90° (with copious evolution of hydrogen chloride) and 35 g. of unreacted starting material. The low-boiling fraction was twice fractionated through a 10 mm. × 50 cm. Vigreux column. A pure fraction, boiling at 67.7–69°, analyzed as 2,5-dipropyl-2,5-dihydrofuran (n^{20}_{D} 1.4412, d^{20}_{20} 0.882).

Anal. Calcd. for $C_{10}H_{18}O$: C, 78.0; H, 11.7. Found: C, 78.3; H, 12.0.

Apparently, in this experiment, the bulk of the diol was converted to the monochloro compound, which decomposed during the initial distillation to yield the dihydrofuran derivative.

4,7-Dichloro-5-decene.—The desired dichloro compound was obtained in 40% yield by passing anhydrous hydrogen chloride into a petroleum ether solution of 4,7-dihydroxy-5-decene at 15° for sixty hours. After two fractionations through a 10 mm. × 50 cm. Vigreux column, a pure fraction of the dichloro compound was obtained (b. p. 64–66° at 1 mm. pressure, n^{20}_{D} 1.4704, d^{20}_{20} 0.999).

Anal. Calcd. for $C_{10}H_{18}Cl_2$: C, 57.4; H, 8.7; Cl, 33.9. Found: C, 57.6; H, 8.6; Cl, 33.8.

3,5,7-Decatriene.—Fifty-two grams (0.25 mole) of 4,7-dichloro-5-decene was refluxed for fifteen hours with 200 ml. of pyridine containing 0.1 g. of hydroquinone. The reaction mixture was poured into an excess of dilute sulfuric acid. The oil separating was washed once with distilled water, dried and immediately distilled through a 10 mm. × 50 cm. Vigreux column, under nitrogen and in the presence of 0.1 g. of hydroquinone. Thirteen ml. (11.9 g., 35% yield) of the triene distilled from 78.1–79.6° at 15 mm. pressure (n^{20}_{D} 1.5274, d^{20}_{20} 0.794).

Anal. Calcd. for $C_{10}H_{16}$: C, 88.3; H, 11.8. Found: C, 88.1; H, 11.5.

The triene oxidized rapidly in the presence of air and catalytic drier to form a non-tacky, crinkly film, which later became tacky again as further oxidation occurred.

2,5-Dimethyl-1,3,5-hexatriene.—2,5-Dihydroxy-2,5-dimethyl-3-hexyne, a compound first prepared by du Pont,[9] was prepared from acetone and the acetylene di-Grignard reagent (m. p. 94.5–95.3°, lit. 94.5–95°[9]). The acetylene compound was semi-hydrogenated to *cis*-2,5-dihydroxy-2,5-dimethyl-3-hexene, a compound first prepared by Zalkind[10] (m. p. 69.5–70.3°, lit.[10] 69–69.5°). Ninety-two grams of the olefin-diol was suspended in one liter of petroleum ether and stirred well at 18° while hydrogen chloride gas was passed into the solution at the rate of 75 ml. per min. The solid phase disappeared within one hour. After five hours, the aqueous layer was separated and the petroleum ether layer washed with saturated bicarbonate solution and dried. The solvent was removed and the remaining oil refluxed in pyridine solution overnight. After the pyridine was removed through solution in dilute sulfuric acid, the oil was fractionated through a 10 mm. × 50 cm. Vigreux column at 110 mm. pressure (0.1 g. of hydroquinone was added to the still-pot). A fraction distilling from 45–45.5° proved to be 2,2,5,5-tetramethyl-2,5-dihydrofuran[10] (yield 15%). A fraction distilling at 70–74°, representing 10% of the theoretical amount, was crude triene. It readily formed a crystalline adduct with maleic anhydride, which melted at 114–115°, confirming the value reported by Kharasch, Nudenberg and Sternfeld.[6] The low yield of the triene in this experiment was due largely to the formation of polymer in the column and in the still-pot. Also the formation of the dihydrofuran derivative indicated that a longer reaction time with hydrogen chloride would lead to improved yields of the triene.

Summary

3,5,7-Decatriene has been prepared by treating acetylene dimagnesium bromide with two moles of butyraldehyde, semi-hydrogenating the resulting 4,7-dihydroxy-5-decyne, converting the resulting olefin-diol into 4,7-dichloro-5-decene through reaction with anhydrous hydrogen chloride and, finally, dehydrohalogenating to the triene by treating with pyridine.

2,5-Dimethyl-1,3,5-hexatriene, a compound previously prepared by Kharasch, Nudenberg and Sternfeld by another method, was prepared from acetylenedimagnesium bromide and acetone by the above route, thus establishing the generality of the synthesis.

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[9] du Pont, *Ann. chim.*, [8] **30**, 485 (1913); *cf.* ref. (2).

[10] Zalkind, *Chem. Zentr.*, **85**, I. 1813 (1914); **94**, III. 1390 (1923); *Ber.*, **56B**, 187 (1923).