slowly with stirring. The reaction flask was heated for 1 hr. at 60°; 1 ml. of water was added to the cooled contents and 10 min. later it was poured into 200 ml. of ice water. After 1 hr. the water was decanted and the oil was washed with cold water, then with water at 60° and finally with saturated sodium bicarbonate solution and again with water. After this treatment the product became friable. There resulted 8.0 g. (96%) of material $(\alpha)^{16}D$ +58.6° (c 2.1, chloroform). This optical rotation corresponds to a mixture containing 3.14 g. (39.2%) of the β anomer. The separation was effected by flowing chromatography on Woelm acid alumina (activity I). Three grams of the mixture dissolved in 10 ml. of benzene was placed on a column (400 × 20 mm.) of alumina previously wetted with benzene. Elution was first carried out with benzene collecting thirty-five fractions of 40 ml. of eluate each; evaporation of fractions 1 to 30 afforded 1.400 g. of hexa-*O*-benzoyl-D-*glycero*-α-D-*galacto*-heptose, $[\alpha]^{16}D$ +79.8° (c 1.0, chloroform). Purification from isopropyl alcohol gave the pure α anomer; $(\alpha)^{16}D$ +82.2° (c, 1.0; chloroform). Eluting with a mixture of ethyl ether and benzene 1:9 gave twenty fractions of 40 ml. each; evaporation to dryness yielded 0.900 g. of hexa-*O*-benzyol-D-*glycero*-β-D-*galacto*-heptose, needles, m.p. 115–116° $(\alpha)^{21}D$ +21.1° (c 0.9, chloroform); further recrystallization failed to change these values.

Anal. Calcd. for $C_{49}H_{38}O_{13}$: C, 70.48; H, 4.60; Found: C, 70.83; H, 5.00.

Anomerization of Hexa-*O*-benzoyl-D-*glycero*-α-D-*galacto*-heptose.—Anhydrous zinc chloride (0.200 g.) was fused in a lightly corked glass tube and at a temperature of 130°, hexa-*O*-benzoyl-D-*glycero*-α-D-*galacto*-heptose (1 g.) and benzoic acid (1 g.) were added. After 30 min. of heating in an oil bath at 130–140°, the reaction flask was cooled and the mixture was dissolved in pyridine, filtered, and the dark solution was poured into water. The oil obtained solidified after washing with water and finally with cold methanol. The solid material was filtered, dissolved in methanol–acetone (5:1), decolorized by filtration through Norit and the filtrate, evaporated to dryness yielded 0.850 g. of material, $[\alpha]^{20}D$ +76.09° (c 1.2, chloroform). This optical rotation corresponds to a mixture containing 0.093 g. (10.9 %) of the β anomer. The identification of both of the anomers in the mixture was effected by thin-layer chromatography on silicic acid–starch with benzene as eluent. The crude product of anomerization was chromatographed simultaneously with the pure α and β anomers. The mixture was resolved into two spots with R_f values of 0.26 and 0.0, coincident with those for the α and β anomers, respectively. The spots were visible after spraying with the silver nitrate–ammonia-sodium methylate reagent, recommended by Cadenas and Deferrari,[12] and heating the plates for 10 min. at 105°

Penta-*O*-benzoyl-β-D-galactopyranose.—D-Galactose (2 g.) in dry pyridine (30 ml.) was heated on a boiling water bath for 1 hr. and on cooling, benzoyl chloride (8 ml.) was added slowly with stirring. The reaction flask was heated for 90 min. at 60°; after cooling 1 ml. of water was added and 10 min. later an additional 10 ml. of water; the mixture was then poured into 200 ml. of ice water. After standing overnight, the water was decanted and the resulting gum washed several times with water, and finally it was covered with methanol, wherein it crystallized after standing overnight. There resulted 7.030 g. (91.3%) of crude product $[\alpha]^{20}D$ + 103.8° (c 1.0, chloroform). This optical rotation corresponds to a mixture containing 4.38 g. (62.3%) β anomer and 2.650 g. (37.7 %) α anomer. After three fractional recrystallizations of this material from methanol–acetone 5:1 pure penta-*O*-benzoyl-β-D-galactopyranose resulted, as needles of m.p. 169–170° $[\alpha]^{20}D$ + 53.5° (c 0.8, chloroform).

Anal. Calcd. for $C_{41}H_{32}O_{11}$: C, 70.28; H, 4.57; Found: C, 70.37; H, 4.66.

Anomerization of Penta-*O*-benzoyl-α-D-galactopyranose.—Penta-*O*-benzoyl-α-D-galactose[6] (5 g.) was added to a mixture of anhydrous zinc chloride (0.500 g.) and benzoic acid (5 g.) heated at 130° in an oil bath. After 1 hr. at this temperature the mixture was cooled and dissolved in pyridine (20 ml.), filtered, and the filtrate poured into 100 ml. of ice water. The oil was extracted with chloroform and the extract was washed with 2 *N* sulfuric acid, water, cold sodium bicarbonate solution, again with water, and finally dried over anhydrous sodium sulfate. Solvent removal yielded 4.200 g. of material $(\alpha)^{20}D$ + 176.8° (c 1.55, chloroform). This optical rotation corresponds to a mixture with 0.320 g. (7.6 %) of the β anomer. The identification of both of the anomers in the mixture was effected by thin-layer chromatography as described for the anomerization mixture of hexa-*O*-benzoyl-D-*glycero*-α-D-galacto-heptose. The α and β anomers showed R_f values of 0.52 and 0.0, respectively.

(12) R. Cadenas and J. O. Deferrari, *The Analyst*, **86**, 132 (1961).

Olefinic Structures from Acetylated Phenylhydrazones of Sugars

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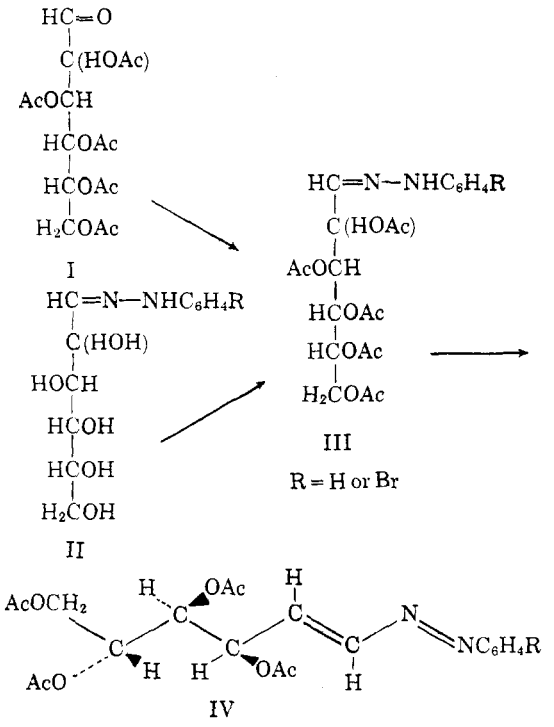
The acetylated forms of the acyclic phenylhydrazones of D-glucose, D-mannose, and D-galactose readily eliminate acetic acid to yield a tetraacetoxy-1-phenylazo-*trans*-1-hexene (IV) whose structure was established by NMR spectra data and by chemical evidence. The optical rotatory dispersion of IV exhibits a complex Cotton effect.

Attempts in this laboratory some years ago to prepare penta-*O*-acetyl-*aldehydo*-D-glucose phenylhydrazone (III) by treating *aldehydo*-D-glucose pentaacetate (I) with phenylhydrazine resulted in a crystalline reaction product (IV) in which a molecule of acetic acid had been lost. The compound was isomeric with a substance described by Wolfrom and Blair[2] and obtained by the acetylation of D-mannose phenylhydrazone but was at first thought to be different from it. The difference was resolved when the crystals were found to be dimorphous but indeed identical in chemical composition. The same substance was also obtained by the mild acetylation of D-glucose "β"-phenyl-

(1) Research Associate (A. T.) and Fellow (D. R. L.) of the Corn Industries Research Foundation.

(2) M. L. Wolfrom and M. Grace Blair, *J. Am. Chem. Soc.*, **68**, 2110 (1946).

hydrazone[3,4] (II, the acyclic form[5]) and by treatment of penta-*O*-acetyl-*aldehydo*-D-mannose ethyl hemiacetal with phenylhydrazine.



In each of the above procedures amorphous intermediate products were formed which upon boiling with dilute ethanol eliminated acetic acid to produce the crystalline product (IV). As the phenylhydrazine residue is basic, this procedure is effectually a basic treatment. The intermediate products (III) are shown by synthesis from the *aldehydo*-hexose acetates and other evidence to be acetylated acyclic phenylhydrazones of D-glucose and D-mannose. An amorphous penta-*O*-acetyl-D-glucose phenylhydrazone obtained by Behrend and Reinsberg[6] by the mild acetylation of D-glucose "β"-phenylhydrazone showed no evidence of an *N*-acetyl group and they proposed the acyclic structure (III) for it. An amorphous acetylated D-mannose phenylhydrazone was reported by Hofmann[7] and by Stepanenko and co-worker,[8] which appears to be a mixture of partially acetylated phenylhydrazones wherein the presence of the *aldehydo* form can be demonstrated by the formazan reaction.[4,9]

The *p*-bromophenylhydrazine derivative was also prepared in this work in the same manner through the acetylation of D-mannose *p*-bromophenylhydrazone and by the reaction of *aldehydo*-D-glucose pentaacetate and *p*-bromophenylhydrazine.

An analogous product was obtained in the D-galactose structure and here the intermediate acetylated phenylhydrazone had been obtained crystalline by Wolfrom and Christman.[10] It was found that adding pyridine to the reaction mixture from D-galactose resulted in an enhanced yield predictable since an acid elimination is involved; on the other hand, too high an alkalinity would remove the acetate groups which undoubtedly stabilize the product toward further reactions.

The fact that IV can be made from either D-glucose or D-mannose phenylhydrazone acetates is evidence that the acetic acid which is lost involves elimination of the acetate group from C-2. Mester and Major[5] report that the substance does not undergo the formazan reaction, the structural requirement for which is the presence of an imino hydrogen and a Schiff base linkage. This would eliminate an acyclic phenylhydrazone structure. The product (IV) gives a negative Knorr[11] test for 1-phenylpyrazolines. The absence of absorption in the infrared at 6.2 μ (N = C—) is further evidence against a Schiff base linkage in an acyclic phenylhydrazone or in a pyrazoline structure.

The key to the structure of IV was obtained from its NMR spectrum (Fig. 1). The spectrum can be

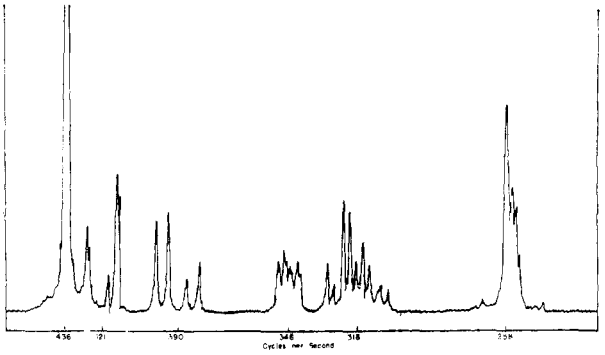


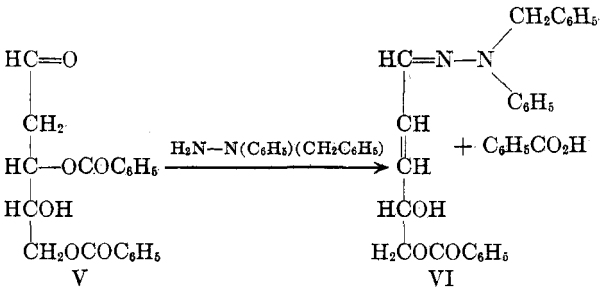
Fig. 1.—NMR spectrum (Varian Associates) of D-*arabino*-3,4,5,6-tetraacetoxy-1-(*p*-bromophenyl)azo-*trans*-1-hexene in deuterochloroform solution with tetramethylsilane as an internal reference standard.

broken into four regions beginning at the left (low field) side of the spectrum. The tall signal at 436 c.p.s. (cycles per second) is from the four aromatic hydrogens in the *p*-bromophenyl function. Just to the right of this tall signal are two peaks spaced 12 c.p.s. apart. The total area from these two signals corresponds to about one-fourth of that produced by the phenyl hydrogens and hence the 12 c.p.s. spacing must be due to spin coupling of one proton with another three bonds away. The group of four lines centered around 390 also contains two spacings of 12 c.p.s. The situation is most typical of hydrogen on adjacent doubly bonded carbons in a *trans*-

(3) H. Jacobi, *Ann.*, **272**, 170 (1893).
(4) R. Behrend and F. Lohr, *ibid.*, **362**, 78 (1908).
(5) L. Mester and A. Major, *J. Am. Chem. Soc.*, **77**, 4297 (1955).
(6) R. Behrend and W. Reinsberg, *Ann.*, **377**, 189 (1910).
(7) A. Hofmann, *ibid.*, **366**, 277 (1909).
(8) B. N. Stepanenko and V. A. Ignatyuk-Maistrenko, *Dokl. Akad. Nauk. SSSR*, **73**, 1251 (1950); *Chem. Abstr.*, **45**, 2877 (1951).
(9) L. Mester, *Advan. Carbohydrate Chem.*, **13**, 105 (1958).
(10) M. L. Wolfrom and C. C. Christman, *J. Am. Chem. Soc.*, **53**, 3413 (1931).
(11) L. Knorr, *Ber.*, **26**, 100 (1893).

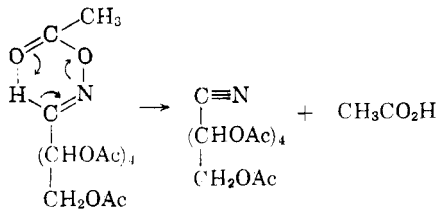
configuration. The smaller spacing of about 1 c.p.s. in the group of lines centered about 421 and 5 c.p.s. in the group centered around 390 must be due to spin coupling to a proton on an adjacent carbon. The group of lines centered around 346 and 318 total three hydrogens in area and are characteristic of hydrogens on carbons containing acetate functions. The signals centered around 258 are characteristic of a methylene group which holds an acetate function. Finally the group of lines centered around 125 (not shown in Fig. 1) can be assigned to the four acetate methyl groups. These data indicate that formula (IV) portrays the correct structure for the substance, designative as D-*arabino*-3,4,5,6-tetraacetoxy-1-phenylazo-*trans*-1-hexene.

Other similar acid eliminations from sugar esters have been noted. 3,5-Di-*O*-benzoyl-2-deoxy-D-ribose (V), reacts with 1-benzyl-1-phenylhydrazine[12] to form 5-*O*-benzoyl-D-*glycero*-4,5-dihydroxy-2-pentenal benzylphenylhydrazone (VI) probably formed



V VI

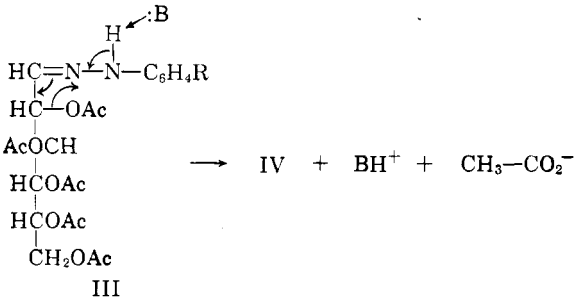
through an intermediate six-membered transition state. In this case there is no hydrogen available on nitrogen and the double bond formed is in conjugation with the HC=N of the hydrazone function. Sowden and co-workers[12] offered a valid chemical proof for VI. Hexa-*O*-acetyl D-glucose oxime[13] (VII) eliminates one mole of acetic acid on heating above its fusion point and produces penta-*O*-acetyl-D-glucononitrile (VIII).



VII VIII

Hurd and Blunck[14] suggested that esters which possess a β-hydrogen in the alkyl group may undergo a chelate type six-atom ring closure by way of a hydrogen bridge. Readjustment of the electrons would give rise to an acid and an olefin. The mechanism still appears to be accepted,[15] and would adequately explain the elimination of acids from V and VII. Application of similar reasoning to the elimination of acetic acid from the hydrazone (III) is weakened because it would involve an eight-membered ring.

An alternative explanation for the observed results involves a simple base-catalyzed[16] elimination.

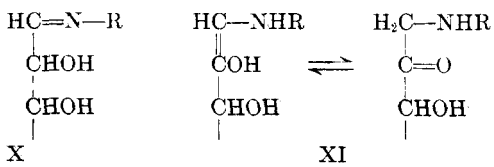


III

The acetate ion can then function as a base for further reaction. A study of a scale model reveals that if the protons on C-1 and C-2 are placed in a *cis*-position the oxygen atom of the C-2 acetate group would be in such proximity to the nitrogen atoms that a strong repulsive interaction would be set up which would tend to rotate the linkage between C-1 and C-2 so that the hydrogens on these positions would be in the *trans*-conformation. This conformation of the transition state would favor the formation of a *trans*-olefin. The fact that the presence of pyridine provides an increase in yield is in harmony with this proposed mechanism.

The rotatory optical dispersions (Fig. 2) of IV (R = H and Br) show a complex Cotton effect not referable to a single Drude factor. This phenomenon, rarely observed in a sugar derivative, is worthy of note.

It is possible that a reaction similar to that leading to IV may represent one of the early stages of the browning or Maillard reaction[17,18] in which sugars and amino acids (or amines) undergo changes to produce dark-colored nitrogenous polymers.[19] The first step in this reaction is established as an amino-carbonyl condensation in which a Schiff base structure (X) is a tautomer; X may then enolize wholly



X XI

or in part to XI, a reaction which has come to be known as the Amadori[20] "rearrangement." The

(12) M. Grace Blair, D. Lipkin, J. C. Sowden, and D. R. Strobach, *J. Org. Chem.*, **25**, 1679 (1960).

(13) M. L. Wolfrom and A. Thompson, *J. Am. Chem. Soc.*, **53**, 622 (1931).

(14) C. D. Hurd and F. H. Blunck, *ibid.*, **60**, 2419 (1938).

(15) W. J. Bailey and R. Barclay, Jr., *J. Org. Chem.*, **21**, 328 (1956).

(16) R. D. Guthrie and L. F. Johnson, *J. Chem. Soc.*, 4166 (1961).

(17) L.-C. Maillard, *Compt. rend.*, **154**, 66 (1912); *Ann. chim.* (Paris), [9] **5**, 258 (1916).

(18) G. P. Ellis, *Advan. Carbohydrate Chem.*, **14**, 63 (1959).

(19) M. L. Wolfrom, R. C. Schlicht, A. W. Langer, Jr., and C. S. Rooney, *J. Am. Chem. Soc.*, **75**, 1013 (1953).

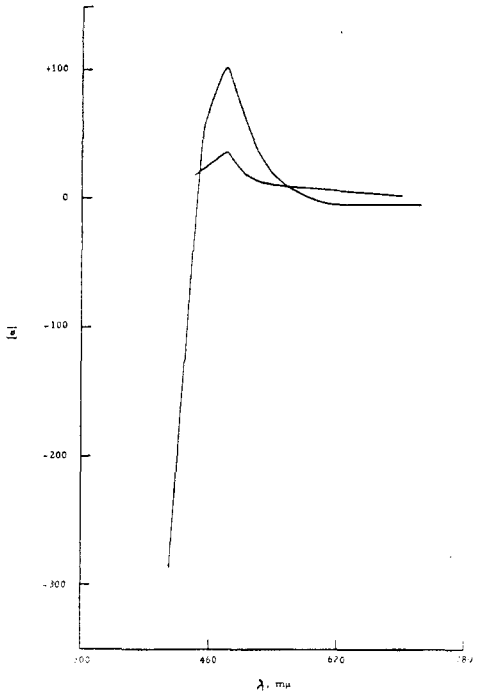


Fig. 2.—Optical rotatory dispersion at 25° of D-*arabino*-3,4,5,6-tetraacetoxy-1-phenylazo-*trans*-1-hexene (lower curve) in acetonitrile solution (*c* 0.5) and D-*arabino*-3,4,5,6-tetraacetoxy-1-(*p*-bromophenyl)azo-*trans*-1-hexene (upper curve) in acetonitrile solution (*c* 0.5); Rudolph Automatic Recording Spectropolarimeter, Model #260/655/850/810-614, Rudolph Instruments Engineering Co., Little Falls, New Jersey.

unsaturated structures (X) or (XI) would then initiate β-eliminations, such as that leading to IV, resulting in doubly unsaturated derivatives now believed to play a significant role in the Maillard reaction.[21]

Experimental

D-*arabino*-3,4,5,6-Tetraacetoxy-1-phenylazo-*trans*-1-hexene (IV, R = H).—The substance was first prepared by Wolfrom and Blair[2] by the acetylation of D-mannose phenylhydrazone[22] with pyridine and acetic anhydride. It could be prepared from several other sources as outlined below; the various preparations had the same properties and gave no melting point depressions on admixture. The compound crystallized as orange needles from ethanol and exhibited dimorphism indistinguishable by melting point; m.p. 122–124°, $[\alpha]^{26}D$ +3° (*c* 2, CH_3CN, optical rotatory dispersion shown in Fig. 2), +14° (*c* 4, pyridine), $\lambda_{max}^{C_2H_5OH}$ 302.5 mμ, ϵ_{max} 2.42 × 10⁴, λ_{max}^{KBr} none at 6.2 μ (N=C), NMR spectrum essentially identical with that of Fig. 1 (save for the benzene band), X-ray powder diffraction data[23]: (unstable dimorph) 10.43 m, 9.67 w, 8.89 w, 8.12 w, 6.78 w, 5.57 m, 5.41 w, 5.28 w, 5.07 vs(1), 4.93 w, 4.79 w, 4.28 m, 4.11 w, 3.95 w, 3.74 s (3), 3.61 w, 3.51 w, 3.38 s (2); (stable dimorph) 14.6 w, 10.1 s (3), 8.13 w, 6.67 vw, 5.55 vs (2), 4.92 vs (1), 4.31 m, 4.10 w, 3.75 vw, 3.60 m, 3.33 vw.

The product gave a negative Knorr[11] test for 1-phenylpyrazolines.

(a) **From *aldehydo*-D-glucose Pentaacetate.**—A cooled solution of 2.0 g of potassium acetate and 1.2 g. of phenylhydrazine hydrochloride in 25 ml. of water (decolorized with carbon) was added to a cooled solution of 2.0 g. of *aldehydo*-D-glucose pentaacetate[24] in 25 ml. of ethanol and diluted to 125 ml. with water. Upon vigorous stirring a yellow gum separated which was washed with water, dissolved in ethanol, water added to incipient cloudiness, and the solution boiled 3–5 min.; yield 0.7 g., m.p. 123–124°.

(b) **From 2,3,4,5,6-penta-O-acetyl-*aldehydo*-D-mannose ethyl Hemiacetal.**—The same product was obtained by treatment of 2,3,4,5,6-penta-*O*-acetyl *aldehydo*-D-mannose ethyl hemiacetyl[25] in the manner described above; m.p. 122–124°.

(c) **From *aldehydo*-D-glucose Phenylhydrazone.**—The same compound was obtained by mild acetylation of 4.0 g. of the crystalline *aldehydo*-D-glucose phenylhydrazone[2-5] as described by Wolfrom and Blair[2] for the acetylation of D-mannose phenylhydrazone; yield 1.3 g., m.p. 122–124°.

D-*arabino*-3,4,5,6-Tetraacetoxy-1-(*p*-bromophenyl)azo-*trans*-1-hexene (IV, R = Br).—This substance was prepared by the acetylation of *D*-mannose *p*-bromophenylhydrazone[26] (4 g.) as described by Wolfrom and Blair[2] for the corresponding reaction with D-mannose phenylhydrazone; yield 3.6 g., m.p. 141–142°.

It was also prepared from *aldehydo*-D-glucose pentaacetate (2.0 g.) as described above for the corresponding reaction with phenylhydrazine hydrochloride except that 12.5 ml. of ethanol was added to the reaction mixture and dilution was effected with 250 ml. of water; yield 0.6 g., orange needles, m.p. 142–143°, $[\alpha]^{23}D$ +1.0° (*c* 2, CH_3CN, optical rotatory dispersion shown in Fig. 2), +9.5 → +20.7° (*c* 4, pyridine), $\lambda_{max}^{C_2H_5OH}$ 315 mμ, ϵ_{max} 3.38 × 10⁴, λ_{max}^{KBr} none at 6.2 μ (N=C), NMR spectrum shown in Fig. 1, X-ray powder diffraction data[23]: 14.49 vw, 10.28 m, 8.56 m, 6.97 w, 5.54 s (2), 5.20 w, 4.91 vs (1), 4.72 w, 4.41 w, 4.26 vw, 4.08 m, 3.74 m, 3.61 s (3), 3.53 w, 3.42 vw, 3.32 m, 3.20 w, 3.06 m, 2.87 w, 2.76 vw, 2.69 vw, 2.59 m.

Anal. Calcd. for $C_{12}H_{11}BrN_2O_4(CH_3CO)_4$: C, 48.10; H, 4.64; N, 5.61; Br, 16.01; *O*-CH_3CO, 8.01 ml. of 0.1 *N* NaOH for 100 mg. Found: C, 48.63; H, 4.59; N, 5.39; Br, 15.87; *O*-CH_3CO, 8.10 ml.

D-*lyxo*-3,4,5,6-Tetraacetoxy-1-phenylazo-*trans*-1-hexene.—An amount of 3.00 g. of 2,3,4,5,6-penta-*O*-acetyl-D-galactose phenylhydrazone[10] was dissolved in 25 ml. of absolute ethanol, water added to opalescence, and the solution boiled gently under reflux for 5 min. A red oil separated during this process. The mixture was maintained overnight in the cold, diluted with water, and the sirup which separated was removed by decantation and crystallized as orange needles from absolute ethanol; yield 425 mg., m.p. 80.5–82°, $[\alpha]^{25}D$ −8.5° (*c* 2, CH_3CN), −63° (*c* 4, pyridine), $\lambda_{max}^{C_2H_5OH}$ 303 mμ, ε 2.28 × 10⁴, infrared spectrum (KBr pellet) comparable, with minor variations, to that of D-*arabino*-3,4,5,6-tetraacetoxy-1-phenylazo-*trans*-1-hexene, X-ray powder diffraction data[23]: 9.33 m (2), 8.63 m, 7.85 w, 6.82 w, 6.00 w, 5.35 m, 5.14 m (3), 4.87 m, 4.63 s (1), 4.23 w, 4.01 w, 3.87 w, 3.71 m, 3.57 vw, 3.44 w, 3.32 w.

Anal. Calcd. for $C_{12}H_{12}N_2O_4(CH_3CO)_4$: C, 57.11; H, 5.75; N, 6.66; CH_3CO, 40.95. Found: C, 57.12; H, 5.65; N, 6.06; CH_3CO, 40.41.

When the above procedure was repeated with the addition

(20) M. Amadori, *Atti accad. nazl. Lincei*, [6] 2, 337 (1925); R. Kuhn and F. Weygand, *Ber.*, **70**, 769 (1937); J. E. Hodge, *Advan. Carbohydrate Chem.*, **10**, 169 (1955).

(21) E. F. L. J. Anet, *Australian J. Chem.*, **13**, 396 (1960); M. L. Wolfrom, E. G. Wallace, and E. A. Metcalf, *J. Am. Chem. Soc.*, **64**, 265 (1942).

(22) E. Fischer and J. Hirschberger, *Ber.*, **21**, 1805 (1888).

(23) Interplanar spacing, Å., CuKα radiation. Relative intensities, estimated visually: s, strong; m, medium; w, weak; v, very. Strongest lines numbered, 1 strongest.

(24) M. L. Wolfrom, *J. Am. Chem. Soc.*, **52**, 2464 (1930); M. L. Wolfrom, M. Konigsberg, and D. I. Weisblat, *ibid.*, **61**, 574 (1936).

(25) M. L. Wolfrom, M. Konigsberg, and F. B. Moody, *ibid.*, **62**, 2343 (1940).

(26) M. Kölle, *Z. physiol. Chem.*, **29**, 429 (1900).

of 2.5 ml. of pyridine to the mixture, the yield was increased to 611 mg. and the product crystallized more readily.

Acknowledgment.—It is a pleasure to acknowledge the assistance of Dr. LeRoy F. Johnson of Varian Associates, Palo Alto, California, and of Dr. Gideon Fraenkel of this department, in the interpretation of the NMR spectra. Mr. Neal Franks carried out the optical rotatory dispersion measurements.

Synthetic Furocoumarins. VI.[1] Analogs of Psoralene Derived from Hydroquinone

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Angular furocoumarins have been obtained from 6-hydroxy-4-methylcoumarin *via* substitution in the 5-position, despite any steric hindrance by the 4-methyl group as previously reported. Linear isomers have been synthesized by blocking the reactive 5-position and from 5-hydroxy-2-methylcoumarin, which eliminates the need for a blocking group. NMR studies have provided corroboration of the structures assigned.

The synthesis of furocoumarins theoretically derived from resorcinol, such as psoralene and isopsoralene, has been extensively investigated because of the photosensitizing activity associated with many of those compounds.[2] In contrast, very little has been published concerning the synthesis or natural occurrence of furocoumarins derived from hydroquinone and nothing is reported about their biological activity. Three triphenylfurocoumarins have been obtained by a three step process involving condensation of hydroquinone[3] with benzoin followed by oxidation and treatment with sodium acetate and acetic anhydride. These compounds are not of very much interest as potential photosensitizing agents because Musajo, *et al.*,[4] have reported that the introduction of a phenyl substituent on the furan ring of psoralene eliminates its photosensitizing activity. Although the structure of the naturally occurring compound Halfordin[5] is still in doubt, it may be another example of a furocoumarin theoretically derived from hydroquinone. No other furocoumarins of this type have been reported up to the present time.

This paper describes the syntheses of several hydroquinone type furocoumarins, including examples of both angular and linear ring arrangements. The photosensitizing activity of these compounds is currently being evaluated and will be reported elsewhere. An angular furocoumarin (IIa) was obtained readily from 5-formyl-6-hydroxy-4-methylcoumarin (Ib), which has been described by Sastri, *et al.*,[6] and also by Naik and Thakor.[7] Their disagreement about the melting point of this compound was resolved when it was found that their procedures give a mixture of compounds, from which pure Ib, m.p. 208°, can be extracted by aqueous potassium carbonate. In contrast to the observation of Naik and Thakor,[7] the 5-formyl compound is very soluble in 5% aqueous sodium hydroxide, although the solution rapidly becomes an intense orange color and the compound cannot then be reprecipitated by acidification. The identity of our sample was established by Dakin oxidation[6,7] to 5,6-dihydroxy-4-methylcoumarin (Ic), from which a dimethyl ether and a diacetate were obtained. The melting points of all three compounds agreed closely with the reported values.[6,8]

Condensation of 5-formyl-6-hydroxy-4-methylcoumarin with methyl bromoacetate gave methyl 5 - formyl - 4 - methylcoumarin - 6 - oxyacetate (Id), which was hydrolyzed to the corresponding acid (Ie) by hot 10% aq. sulfuric acid. Heating (Ie) with acetic anhydride and sodium acetate gave 9-methyl-7*H*-furo[3,2-*f*][1]benzopyran-7-one

(1) Part V. K. D. Kaufman, W. E. Russey, and L. R. Worden, *J. Org. Chem.*, **27**, 875 (1962).

(2) K. D. Kaufman, *J. Org. Chem.*, **26**, 117 (1961), gives a brief review of the synthetic methods employed and of some of the biological studies, particularly on the enhancement of human skin pigmentation.

(3) O. Dischendorfer and W. Limonstchew, *Monatsh.*, **80**, 58 (1949), and **81**, 737 (1950). *Chem. Abstr.*, **43**, 7016g (1949), erroneously gives the formula of benzoquinone instead of hydroquinone.

(4) L. Musajo, G. Rodighiero, G. Caporale, and C. Antonello, *Farmaco (Pavia) Ed. Sci.*, **13**, 355 (1958).

(5) M. P. Hegarty and F. N. Lahey, *Australian J. Chem.*, **9**, 120 (1956).

(6) V. D. N. Sastri, N. Narasimhachari, P. Rajagoplan, T. R. Seshadri, and T. R. Thiruvengadam, *Proc. Indian Acad. Sci.*, **37A**, 681 (1953).

(7) R. M. Naik and V. M. Thakor, *J. Org. Chem.*, **22**, 1626 (1957).

(8) V. J. Dalvi, R. B. Desai, and S. Sethna, *J. Indian Chem. Soc.*, **28**, 366 (1951). It should perhaps be mentioned that they obtained these compounds from the Elbs persulfate oxidation of 5-methoxy-4-methylcoumarin, which was assumed to occur in the 6-position. If their oxidation occurred at the 8-position, demethylation would give the unknown 5,8-dihydroxy-4-methylcoumarin. Dakin oxidation of 5-formyl-6-hydroxy-4-methylcoumarin could also give the 5,8 isomer because, in the alkaline medium, the pyrone ring might be opened and upon acidification could close in either of two directions. The 5,6-dihydroxy structure seems much more probable, particularly because the compound gives a green color with ferric chloride in alcohol. In either case, the structure of 5-formyl-6-hydroxy-4-methylcoumarin is definitely established.