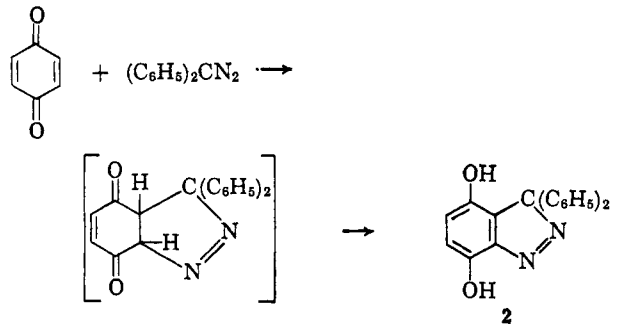
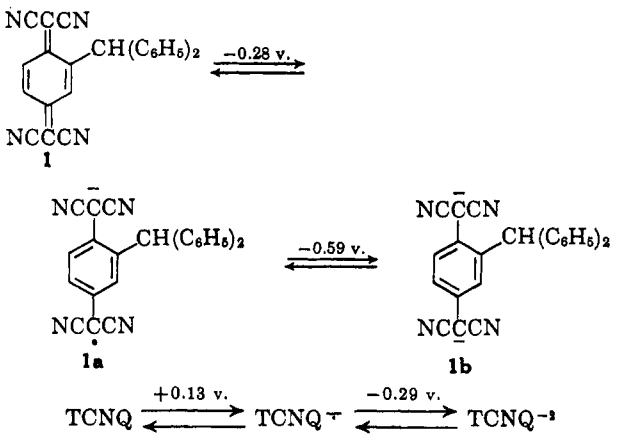


TCNQ formed a solid π complex with 9-diazofluorene at room temperature. In acetone at reflux the complex decomposed with nitrogen evolution. The reaction product, however, was not soluble enough to allow purification and characterization. Ethyl diazoacetate underwent thermal decomposition with no attack on TCNQ.

The quinodimethan system of **1** cannot be planar because of the bulky benzhydryl substituent. This is reflected in the absorption spectrum of **1**: λ_{max} 361 mμ (ϵ 25,600), 258 (6650), 221 (17,700). This differs greatly from that of TCNQ: λ_{max} 395 mμ (ϵ 63,600). A marked change in the ease of reduction was also observed. Compound **1** undergoes polarographic reduction in acetonitrile solution with 0.1 *M* lithium perchlorate as supporting electrolyte. Two well-defined one-electron waves occurred at −0.28 and −0.59 v. *vs.* the standard calomel electrode. Both reductions were reversible and are assumed to be indicative of formation of radical anion **1a** and dianion **1b**. The corresponding one-electron reductions of



TCNQ occur at +0.13 and −0.29 v.[3] The greater difficulty of reduction of **1** *vs.* TCNQ is evidence that the lack of planarity destabilizes the anion radical and dianion more than the parent quinodimethan, which is certainly in accord with expectation.

The anion radical **1a** can be prepared by controlled electrochemical reduction of **1**. Air immediately oxidized **1a**. Solutions of **1a** in acetonitrile gave a strong, but broad electron spin resonance signal. Fine structure has not been resolved. Upon standing at room temperature under nitrogen the electron spin resonance signal of **1a** slowly changed to that of TCNQ anion radical. A similar transformation occurred in an attempt to form a salt of **1a**. The reaction of an acetonitrile solution of **1** with metallic copper yielded the copper(I) salt of TCNQ anion radical. This reaction may also proceed by way of **1a**. The remarkable elimination of the benzhydryl group (probably as a radical) is additional evidence of the instability due to nonplanarity of the anion radical **1a**.

Experimental

2-Benzhydryl-7,7,8,8-tetracyanoquinodimethan (1).—A solution of 19 g. (0.09 mole) of diphenyldiazomethane in 25 ml. of acetone was added to a stirred slurry of 17.3 g. (0.085 mole) of tetracyanoquinodimethan in 300 ml. of acetone. The system was connected to a wet-test meter through a reflux condenser. The mixture was heated at reflux, and gas (2.12 l., 100%) was evolved. The mixture was filtered, and the solid was rinsed with acetone. A yellow, crystalline solid (18.3 g., 58%, m.p. 343–348°) was obtained. Recrystallization from acetonitrile (very slightly soluble) gave **1**, m.p. 350–353° dec.

Anal. Calcd. for $C_{25}H_{14}N_4$: C, 81.06; H, 3.81; N, 15.13. Found: C, 81.03; H, 3.83; N, 15.14.

The infrared spectrum of **1** showed absorption at 3.29 (saturated CH), 4.50 (conjugated nitrile), 6.27, 6.35, 6.45, 6.57, and 6.71 (conjugated C=C), and 13.25 and 14.06 μ (monosubstituted aromatic). The insolubility of **1** precluded an n.m.r. spectrum.

Anion Radical of 1.—Compound **1** was reduced by applying a voltage of from −0.31 to −0.33 v. *vs.* the standard calomel electrode to a slurry of **1** in acetonitrile containing 0.1 *M* lithium perchlorate. The solution of the anion radical was a deep violet, and it decolorized immediately upon exposure to air.

Reaction of 1 with Copper.—A strip of copper was suspended in a stirred slurry of 0.74 g. of **1** in 300 ml. of acetonitrile. A purple solid formed on the copper surface and was periodically removed by scraping. The solid was identical in infrared and ultraviolet spectra with the cuprous salt of TCNQ anion radical.

Anal. Calcd. for $C_{12}H_4CuN_4$: C, 53.9; H, 1.50; N, 20.9. Found: C, 53.7; H, 1.84; N, 21.2.

TCNA with Ethyl Diazoacetate.—A mixture of 20.4 g. of TCNQ and 14 g. of ethyl diazoacetate in 500 ml. of acetone was heated at reflux for 17 hr. at which time 2.7 l. of nitrogen had been evolved. From the reaction mixture there was recovered 19.5 g. (95%) of TCNQ, m.p. 290–295°.

The Structure of 2-(D-*arabino*-Tetrahydroxybutyl)quinoxaline

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The oxidative condensation of 2-amino-2-deoxy-D-glucose hydrochloride with *o*-phenylene diamine in the presence of cupric acetate yields a crystalline quinoxaline derivative[1] identical with the product formed in the reaction of *o*-phenylene diamine with D-glucose,[2] D-fructose,[3] and D-*arabino*-hexosulose.[4] This derivative has long been formulated[5] as 2-(D-*arabino*-tetrahydroxybutyl)quinoxaline (I), with the sugar residue in the acyclic form, and this structure is supported by glycol cleavage[6] and ultraviolet spectroscopic[7] studies. An alternative cyclic formulation (II) has, however, been

(1) R. Lohmar and K. P. Link, *J. Biol. Chem.*, **150**, 351 (1943).
(2) P. Griess and G. Harrow, *Ber.*, **20**, 281, 2205 (1887).
(3) H. Ohle, *ibid.*, **67**, 155 (1934).
(4) E. Fischer, *ibid.*, **22**, 87 (1889).
(5) For a review see N. K. Richtmyer, *Advan. Carbohydrate Chem.*, **6**, 175 (1951).
(6) A. Müller and I. Varga, *Ber.*, **72**, 1993 (1939); G. Henseke and K.-J. Bähner, *ibid.*, **91**, 1605 (1958).
(7) R. Kuhn and F. Bär, *ibid.*, **67**, 898 (1934).

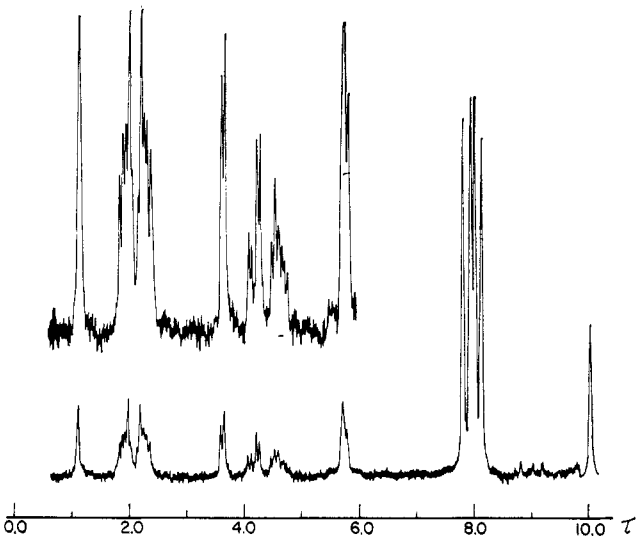
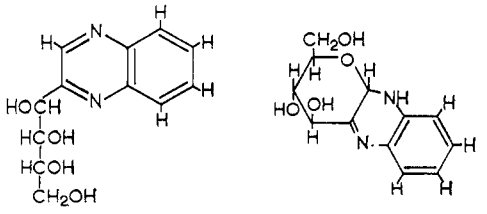


Figure 1.—N.m.r. spectrum of 2-(D-*arabino*-tetraacetoxybutyl)-quinoxaline (III).

advanced by Kent and Whitehouse[8] for the quinoxaline prepared by Lohmar and Link[1] from 2-amino-2-deoxy-D-glucose hydrochloride.

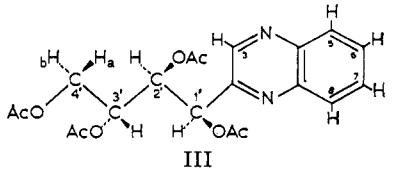
We have prepared the quinoxaline and its tetraacetate according to the conditions of Lohmar and Link.[1] Analysis of the n.m.r. spectra of these two derivatives leaves no doubt that the original formulation I is the correct one, and indicates that the acyclic sugar chain is in the extended, planar zig-zag conformation.

The spectrum of the quinoxaline in dimethyl sulfoxide shows a sharp low-field unit-proton singlet at τ 0.80, which may be assigned[9] to the C-3 proton of the quinoxaline system (C-1 hydrogen of the parent sugar). An almost-symmetrical four-proton multiplet of the A_2B_2 type,[10] centered at τ 2.00, may be assigned[9] to the protons on the benzene ring. No other signals are observed below τ 4.5. These facts prove that structure I is correct, since in the formulation II the proton at C-1 of the sugar would appear in the nonexchanging solvent as a doublet through coupling with the proton on nitrogen, and the latter proton would also be observed at low field as a doublet, probably broadened by nitrogen quadrupole coupling.



I

II



III

Analysis of the spectrum of the quinoxaline tetraacetate (Figure 1 and Table I) confirms the formulation (III). The C-3 proton of the quinoxaline system[9] appears as a low-field singlet, τ 1.10. A symmetrical A_2B_2 system,[10] centered at τ 2.05, is observed for the four protons on the benzene ring. The four acetoxy groups are observed as separate three-proton singlets.

TABLE I

N.M.R. SPECTRAL DATA ON 2-(D-*arabino*-TETRAACETOXYBUTYL)QUINOXALINE (III)

Protons	Chemical shift, τ	Integral, protons	Multiplicity[a]	Coupling constant,[b] c.p.s.
C-3	1.10	1	s	
C-5,8	1.90	2	m	
C-6,7	2.20	2	m	
C-1′	3.58	1	d	$J_{1',2'}$ = 3.0
C-2′	4.14	1	q	$J_{1',2'}$ = 3.0
				$J_{2',3'}$ = 8.5
C-3′	4.50	1	m	
C-4′	5.66	2	m	$J_{4a',4b'}$ = 12.0
				$J_{3',4a'}$ = 3.0[c]
				$J_{3',4b'}$ = 5.5[c]
1′-OAc	7.78	3	s	
2′-OAc	7.91	3	s	
3′-OAc	7.98	3	s	
4′-OAc	8.10	3	s	

[a] d, doublet; m, multiplet; q, quartet; s, singlet, [b] See ref. 11. [c] The absolute magnitudes may be larger, owing to second-order effects.

The methine protons and the methylene protons of the sugar residue show a spin–spin coupling pattern which excludes the possibility of formulation of the tetraacetate as an acetylated analog of II and fully supports the structure III. The C-1′ proton of the D-*arabino*-tetraacetoxybutyl group appears at τ 3.58, as a doublet by coupling with the C-2′ proton, $J_{1',2'}$ = 3.0 c.p.s.[11] Coupling of this magnitude is indicative[12] of a projected angle between the C–H bonds on C-1′ and C-2′ of approximately 60° in the favored rotamer state. The C-2′ proton appears as a quartet, τ 4.14, $J_{1',2'}$ = 3.0 and $J_{2',3'}$ = 8.5 c.p.s. The $J_{2',3'}$ value indicates[12] a projected angle of approximately 180° between the C–H bonds on C-2′ and C-3′ in the favored rotamer state. The C-3′ proton appears as a multiplet, τ 4.50, split by the C-2′ proton and by the methylene group at C-4′. The two protons of the methylene group are slightly nonequivalent on account of the adjacent asymmetric center[13] and give rise to a multiplet, the AB part of an ABX system, centered at τ 5.66. Similar nonequivalence of the methylene protons in a terminal acetoxymethyl group has been observed in a number of acetylated sugar phenylhydrazine derivatives.[14] The

(8) P. W. Kent and M. W. Whitehouse, "Biochemistry of the Aminosugars," Butterworth and Co. (Publishers) Ltd., London, 1955, p. 225.

(9) N. S. Bhacca, D. P. Hollis, L. F. Johnson, E. A. Pier, and J. N. Shoolery, "NMR Spectral Catalog," National Press, Palo Alto, Calif., 1963, Spectrum No. 494.

(10) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp. 142–151.

(11) The spectra have been analyzed on a first-order basis, and the recorded coupling constants are the observed splittings. The relative chemical shifts of the methine protons in III are sufficiently different that the recorded τ and J parameters should be close to the theoretical values.

(12) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Am. Chem. Soc.*, **85**, 2871 (1963); L. D. Hall, *Advan. Carbohydrate Chem.*, **19**, 51 (1964).

(13) G. M. Whitesides, F. Kaplan, K. Nagarajan, and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S.*, **48**, 1112 (1962).

(14) M. L. Wolfrom, G. Fraenkel, D. R. Lineback, and F. Komitsky, Jr., *J. Org. Chem.*, **29**, 457 (1964).

extended conformation in which the terminal acetoxy group is coplanar with the carbon chain may be regarded as the favored rotamer state.

While rotation about the C–C bonds in the side chain undoubtedly occurs at room temperature, the resolution of the spectrum indicates a high degree of conformational purity, and is in agreement with an extended, planar zig-zag arrangement as the favored conformation. This conformation corresponds to attainment of the minimum nonbonded interactions between the small–medium–large sets of groups at the ends of each carbon–carbon bond.

Experimental

N.m.r. Spectra.—Spectra were measured at approximately 30° with a Varian A-60 60-Mc.p.s. n.m.r. spectrometer. Tetramethylsilane (τ 10.00) was used as the internal reference standard. The spectrum for substance I was measured in dimethyl sulfoxide solution; that for III was measured in deuteriochloroform.

2-(D-*arabino*-Tetrahydroxybutyl)quinoxaline (I).—This compound was prepared by the method of Lohmar and Link[1]: m.p. 190–191°; n.m.r. data, τ 0.80 (singlet, 1 proton, H-3 of quinoxaline), 1.89 (multiplet, 2 protons, H-5 and H-8 of quinoxaline), 2.17 (multiplet, 2 protons, H-6 and H-7 of quinoxaline), and no other resonances below 4.6.

2-(D-*arabino*-Tetraacetoxybutyl)quinoxaline (III).—This compound was prepared[1] by acetylation of I with pyridine and acetic anhydride: m.p. 119–120°; λ_{max}^{EtOH} 211.1 mμ (ε 24,000), 236.9 (ε 32,000), 317.4 (ε 7600); for n.m.r. data, see Table I.

Acknowledgment.—The authors thank Mr. W. N. Turner for measurement of the n.m.r. spectra.

Synthesis of Isoquinolines. IV.[1] 4-Benzylisoquinolines

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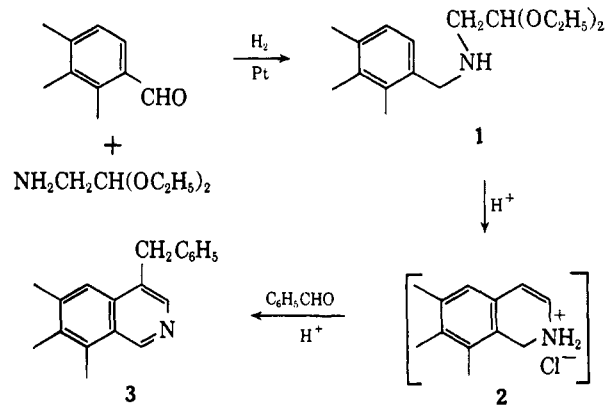
Recent work in this laboratory has yielded a new synthesis of 1,2,3,4-tetrahydroisoquinolines[1,3] based upon the Fischer modification of the Pomeranz–Fritsch synthesis.[4] In that case, the unstable 1,2-dihydroisoquinolines (**2**) formed by dilute acid treatment of the reduced Schiff bases (**1**) were catalytically hydrogenated to 1,2,3,4-tetrahydroisoquinolines. It now appears that, when such intermediates (**2**) are treated with benzaldehyde, 4-benzylisoquinolines (**3**) are formed in good yield and with a minimum of experimental difficulty.

During the course of this work, a similar reaction was reported by Grewe, Krüger, and Vangermain.[5] They obtained a separable mixture of 4-benzyl-1,2,3,4-tetrahydroisoquinoline and 4-benzylisoquinoline by catalytic hydrogenation of isoquinoline in the presence of acetic acid and benzaldehyde. Furthermore, they proposed a 1,2-dihydroisoquinoline intermediate. This is, in turn, quite similar to work reported by Burrows and Burrows[6] who proposed an enamine or 1,2-dihydroisoquinoline intermediate for the condensation of 1,2,3,4-tetrahydroisoquinoline and benzaldehyde. This latter reaction led to 4-benzylisoquinoline in 34% yield. The work reported in this paper, is, in a sense, complementary to previous papers in that properly substituted benzaldehydes can be used as starting materials in place of the more difficultly obtainable heterocyclic molecules.



The reduced Schiff bases (**1**), derived from vanillin (4-hydroxy-3-methoxybenzaldehyde), isovanillin (3-hydroxy-4-methoxybenzaldehyde), and *o*-vanillin (2-hydroxy-3-methoxybenzaldehyde), were prepared by atmospheric pressure hydrogenation of the appropriate aldehyde and aminoacetaldehyde diethylacetal in the presence of a platinum catalyst. The bases were not isolated as such, but were treated with acidic, ethanolic solutions of benzaldehyde to yield the desired 4-benzylisoquinolines. The yields were calculated from the initial aldehydes and were as follows: 4-benzyl-6-hydroxy-7-methoxyisoquinoline (**4**, from vanillin), 63%; 4-benzyl-7-hydroxy-6-methoxyisoquinoline (**5**, from isovanillin), 54%; and 4-benzyl-8-hydroxy-7-methoxyisoquinoline (**6**, from *o*-vanillin, isolated as the hydrochloride), 61%. The three bases were characterized as picrates. In the case of **6**, the free base as obtained by basification of an aqueous solution of hydrochloride was not amenable to further purification. However, when this neutralization was carried out by passing a solution of hydrochloride over a column of basic alumina, the free base was obtained. A similar difficulty was observed[1,3] with 8-hydroxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline.

The structures of the products were established by their elemental analyses and by their unique n.m.r. spectra. Each of the three showed two single protons, on C-1 and C-3, with τ values corresponding to the α hydrogens on an aromatic nitrogen ring. The C-1 protons of **4**, **5**, and **6** were at τ 1.1, 1.1, and 0.5 (hydrochloride), respectively, and the C-3 protons were at τ 1.78, 1.78, and 1.8. The recorded values for isoquinoline itself are τ 1.4 for C-1, 2.0 for C-3, and 3.3 for C-4.[7] There was no evidence in the n.m.r. spectra which would indicate ring closure *ortho* to oxygen functions rather

(1) J. M. Bobbitt, J. M. Kiely, K. L. Khanna, and R. Ebermann, *J. Org. Chem.*, in press.

(2) Abstracted in part from the M.S. Theses of D. P. W., University of Connecticut, 1964, and J. M. K., University of Connecticut, 1963.

(3) J. M. Bobbitt, K. L. Khanna, and J. M. Kiely, *Chem. Ind.* (London), 1950 (1964).

(4) For discussion and references, see W. J. Gensler, *Org. Reactions*, **6**, 19 (1951).

(5) R. Grewe, W. Krüger, and E. Vangermain, *Ber.*, **97**, 119 (1964).

(6) W. D. Burrows and E. P. Burrows, *J. Org. Chem.*, **28**, 1180 (1963). This paper also contains a literature survey of a number of similar reactions.

(7) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 268.