The Self-Addition of Methyl 3-Deoxy-3-nitrohexopyranoside Derivatives to Tricyclic Diels–Alder Products and Their Aromatization to the 7-Nitroisochromene System[1,2]

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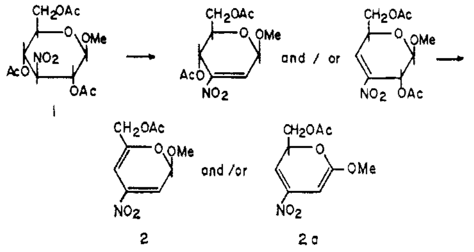
Received December 19, 1967

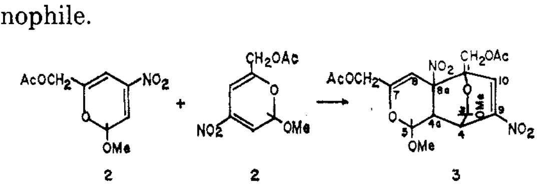
The dehydroacetylation of methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-nitro-β-D-glucopyranoside (**1**) and of its D-*manno* (**21**) and D-*galacto* (**22**) isomers resulted in the loss of two molecules of acetic acid and gave, as a reaction intermediate, a derivative (**2**) of 2*H*-pyran which dimerized spontaneously in a Diels–Alder reaction to an optically inactive, tricyclic product, 3,4,4a,8a-tetrahydro-3,5-dimethoxy-8a,9-dinitro-1,4-ethenopyrano[4,3-*c*]pyran-1,7-(5*H*)-dimethanol diacetate (**3**). At lower temperatures an optically active diastereoisomer (**3a**) of **3** was isolated in addition. The stereochemistry of the products is discussed, and their structure follows from spectroscopic data and from a facile, thermal conversion into an isochromene, 1-hydroxy-7-nitro-1*H*-2-benzopyran-3,5-dimethanol 3,5-diacetate (**5**). Acid-catalyzed acetalization of **5** furnished the corresponding 1-alkoxy derivatives, **7**, **8**, and **9**, whereas phenylhydrazine gave a monophenylhydrazone (**6**) of the ring-open tautomer. Mild oxidation of **5** led to the corresponding isocoumarin (**10**) and more drastic oxidation, to nitrobenzene-3,4,5-tricarboxylic acid (**11**) which was characterized also as trimethyl ester (**12**). Sodium borohydride reduction of **5** furnished a tetraol (**13**) that was degraded by periodate to 3,4-dihydro-3-hydroxy-7-nitro-1*H*-2-benzopyran-5-methanol (**14**). With semicarbazide, **14** yielded 2,6-bishydroxymethyl-4-nitrophenylacetaldehyde semicarbazone (**15**), and with sodium borohydride it was reduced to 4-(2-hydroxyethyl)-3,5-bishydroxymethylnitrobenzene (**16**).

The dehydroacetylation of β-acyloxynitroalkanes to α-nitroalkenes (Schmidt–Rutz reaction) is widely employed in general aliphatic[3,4] as well as in carbohydrate[5] chemistry. Recently it has been demonstrated that methyl 3-deoxy-3-nitro-hexopyranosides which are acetylated in position 2 but suitably blocked in position 4 give rise to the expected, 2,3-unsaturated derivatives. Thus, methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-glucopyranoside furnished methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*erythro*-hex-2-enopyranoside,[6] and several diastereoisomers of this nitroolefinic glycoside were later obtained analogously.[7] In continuation of these studies it was decided to examine the dehydroacetylation of the methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-nitro-β-D-hexopyranosides, of which the *gluco* (**1**), *manno* (**21**), and *galacto* (**22**) isomers are available.[1b] These compounds contain a nitro group flanked on both sides by acetoxy functions. One might therefore have expected the formation of either the 2,3- or the 3,4-unsaturated derivatives or both; as an additional possibility the elimination of two molecules of acetic acid, resulting in the formation of dienes,[8] had to be considered. This is exemplified for **1** in eq 1. Variations in the product composition, if such were observed, would have been interesting to correlate mechanistically with the configurations of the initial triacetates.



(1)

When methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-nitro-β-D-glucopyranoside (**1**) was heated under reflux in dry benzene in the presence of sodium hydrogen carbonate, a colorless crystalline product of mp 131° was isolated in 43% yield. Elemental analysis and molecular weight determination established the formula $C_{18}H_{22}N_2O_{12}$ which obviously does not correspond to any of the structures in eq 1. The composition fits, however, a dimer of the diene **2** (or of **2a**, or a combination of both), and it was therefore considered that the dehydroacetylation of **1** had in fact led to **2** (and/or **2a**) which then immediately underwent an intermolecular Diels–Alder addition. One of the sixteen structural possibilities[9] for such a dimerization is expressed in eq 2, where one molecule of **2** serves as the diene and the 2,3 double bond of a second molecule of **2** serves as the dienophile.



(2)

The reaction product of mp 131° will be shown in the following discussion to possess indeed the structure **3**. It is to be designated as 3,4,4a,8a-tetrahydro-3,5-dimethoxy-8a,9-dinitro-1,4-ethenopyrano[4,3-*c*]pyran-1,7(5*H*)-dimethanol diacetate.

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[1] (a) Paper VIII in the series on reactions of nitro sugars. (b) For paper VII, see H. H. Baer, F. Kienzle, and F. Rajabalee, *Can. J. Chem.*, **46**, 80 (1968).

[2] This work was undertaken in partial fulfillment of the requirements for a Ph.D. degree and will be incorporated in a thesis to be submitted by F. K. at the University of Ottawa. The essential aspects have been presented before the 4th International Conference on Carbohydrate Chemistry, Kingston, Ontario, July 1967.

[3] A. Schmidt and G. Rutz, *Ber.*, **61**, 2142 (1928); B. M. Vanderbilt and H. B. Hass, *Ind. Eng. Chem.*, **32**, 34 (1940); H. B. Hass, A. G. Susie, and R. L. Heider, *J. Org. Chem.*, **15**, 8 (1950).

[4] For a review, see V. V. Perekalin, "Unsaturated Nitro Compounds," translated by L. Mandel, Israel Service of Scientific Translations, Jerusalem, 1964.

[5] For a review, see J. C. Sowden, *Advan. Carbohyd. Chem.*, **6**, 291 (1951).

[6] H. H. Baer and T. Neilson, *Can. J. Chem.*, **43**, 840 (1965).

[7] H. H. Baer, F. Kienzle, and T. Neilson, *ibid.*, **43**, 1829 (1965); H. H. Baer and F. Kienzle, *ibid.*, **45**, 983 (1967).

[8] 3-Nitro-1,3-pentadiene has been reported to arise upon heating of 2,4-diacetoxy-3-nitropentane with sodium acetate: G. D. Buckley and J. L. Charlish, *J. Chem. Soc.*, 1472 (1947).

[9] This figure is arrived at entirely on a formalistic basis assuming all the double bonds in the hypothetical intermediates **2** and **2a** to have dienophilic character; it accounts for different orientations in the diene additions, but the stereochemistry is not being considered at this point.

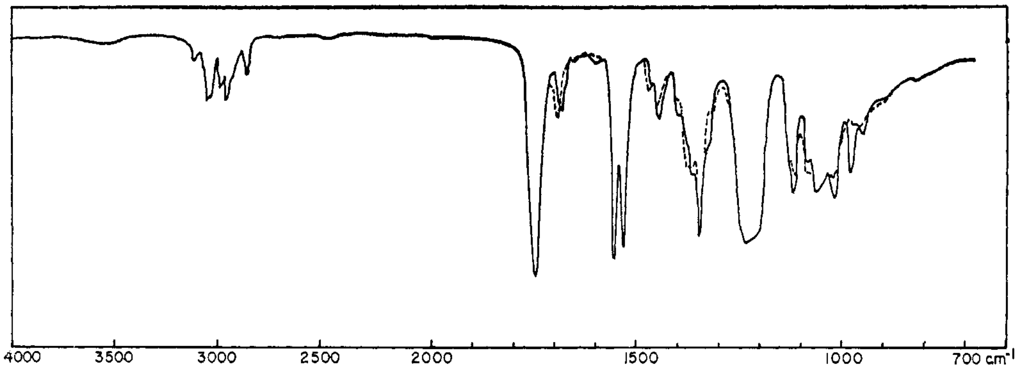


Figure 1.—Infrared spectra of compounds **3** (solid line) and **3a** (broken line where it deviates from **3**) in chloroform.

TABLE I

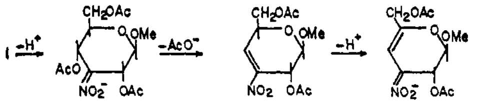
INFRARED FREQUENCIES IN NUJOL[a]

Compd	OH	—C=CH	C=O	C=C	NO_2	Other prominent peaks
3		3120 w 3100 m	1735 s	1690 m	1550 s 1530 s	1400 w, 1368 ms, 1350 ms, 1330 w, 1250 s, 1210 w, 1123 m, 1090 w, 1070 m, 1025 ms, 980–700 w[b]
3a		3120 w	1740 s	1680 m	1550 s 1525 s	1405 w, 1368 ms, 1350 ms, 1320 w, 1270 m, 1240 s (sh 1220), 1125 m, 1093 m, 1030 m, 980–700 w[b]
5	3300 s, bd	3100 w	1735 s 1710 s	1658 ms 1600 ms	1515 s	1410 w, 1365 m, 1340 s, 1300 ms, 1260 s, 1240 s, 1210 m, 1100 w, 1080 m, 1055 ms, 1035 ms, 990 m, 918 m, 870–700 w[b]
6			1760 s 1740 s 1727 s	1600 m 1550 ms	1518 s	3320 w, 1535 w, 1498 w, 1415 w, 1350 s, 1310 w, 1290 w, 1260 w, 1225 s, 1160–670 w, m[b]
7		3100 w	1740 s	1658 m 1600 m	1520 s	1405 w, 1360 ms, 1340 s, 1315 w, 1230 s, bd, 1100–900 ms, bd
8		3100 w	1738 s	1650 m 1600 m	1525 s	1408 w, 1340 s (sh 1330, 1315), 1275 m, 1250 m, 1225 s, 1080 ms, 1025 ms, 1000–700 w, m[b]
9		3100 w	1735 s	1650 m 1595 m	1525 s	1405 w, 1338 s (sh 1325), 1280 m, 1250 m, 1225 s, 1075 ms, 1030–700 w, m[b]
10		3115 w	1750 s 1730 s	1665 m 1603 m	1530 s	1438 ms, 1370 ms, 1350 s, 1330 ms, 1245 s, 1225 s, 1100 m, 1050–700 w, m[b]
11	3300 s, bd 2700–2500 w[b]		1715 s	1605 m	1530 ms	1420 w, 1363 ms, 1300 m, 1245 m, 1215 m, 1170 m, 1133 w, 1080 w, 820–650 w[b]
12		3125 w	1735 s	1610 m	1540 ms	1440 s, 1420 w, 1365 m, 1310 m, 1275 s, 1240 s, 1115 w, 1070 w, 1000 m, 950–700 w[b]
13	3250 s, bd			1610 w 1595 w	1510 s	1345 s, 1250 w, 1090 ms, 1020 s
14	3350, 3250 s, bd	3100 w		1610 w 1595 w	1533 s (sh 1520)	1415 w, 1350 s, 1320 w, 1260 w, 1130 s, 1085 s, 1025 ms, 1000–670 w[b]
15	3600–3200 s[b,c]	3100 w	1665 s, bd	1590 ms, bd[d]	1515 ms	1350 s, 1263 w, 1175 w, 1145 w, 1075 s, 1000–700 w[b]
16	3300 s, bd	3100 w		1600 w	1515 s	1340 s, 1290–1170 w,[b] 1080 s, 1025 s, 900–700 w[b]

[a] In cm^{-1}. Designations are s (strong), ms (medium strong), m (medium), w (weak), bd (broad), sh (shoulder). [b] Several bands. [c] OH and NH stretching vibrations. [d] C=C stretching and NH bending vibrations.

Deduction of the Structure of Compound 3 by Spectroscopy.[10]—Infrared spectra (Figure 1 and Table I) of compound **3** exhibited olefinic C—H and C=C stretching vibrations as well as strong bands for ester carbonyl and for an unconjugated and a conjugated nitro group. There was no hydroxyl absorption.

The ultraviolet spectrum of an ethanolic solution revealed no high-intensity, long-wavelength absorption, but addition of alkali produced a nitronate chromophore absorbing strongly at λ_{max} 255 mμ. This behavior is in conformity with an α-nitroalkene that can readily add base to form a β-substituted alkanenitronate, although it would of course likewise agree with the presence, in **3**, of a secondary nitroalkane grouping. However, the triacetate **1** under the same conditions gave rise to an absorption of λ_{max} 302 mμ (ε 19,000) ascribed to an *unsaturated* nitronate (**4**, eq 3),[1b] and the failure to



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(3)

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[10] Unless otherwise specified, infrared data refer to Nujol mull spectra taken on a Beckman IR-8 instrument, ultraviolet and visible absorptions were recorded on a Perkin-Elmer 202 spectrophotometer using 1-cm cells, and nmr spectra were obtained on a Varian HA-60 instrument using deuteriochloroform solutions and tetramethylsilane as an internal standard.

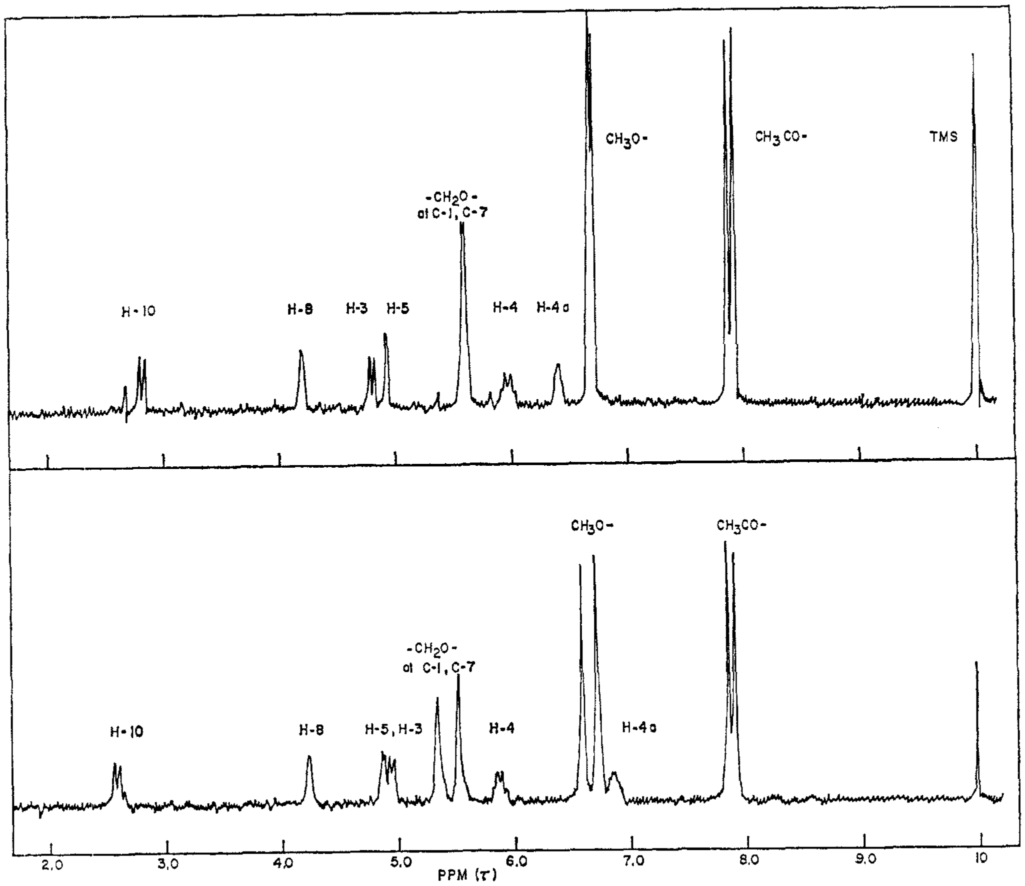

Figure 2.—Nmr spectra in deuteriochloroform of compound **3** (upper curve) and compound **3a** (lower curve).

produce that particular absorption can be taken as evidence for the absence of the moieties shown.

$$—O—CH(CH_2OAc)—CH(OAc)—CH(NO_2)—$$

$$—O—CH(CH_2OAc)—CH{=}C(NO_2)—$$

The nmr spectrum of **3** is shown in Figure 2. Sharp singlets, each of three-proton intensity, are seen for two acetoxy groups (τ 7.93, 7.87) and for two methoxy groups (τ 6.70, 6.67). The signal centered at τ 5.59, with an intensity of four protons, is ascribed to the methylene parts of the two acetoxymethyl groups. The signal has the appearance of a triplet but, as will be seen below, it really consists of two virtually coinciding AB quartets with geminal couplings of 13 cps, a feature that rules out the presence of vicinal hydrogen. The remaining signals in the spectrum, all of one-proton intensity and well separated, are a narrow multiplet at τ 6.40 (H-4a), a quartet at 5.97 (H-4), a doublet with a splitting of 0.7 cps at 4.92 (H-5), a doublet with a splitting of 2.5 cps at 4.80 (H-3), a singlet at 4.18 (H-8), and a doublet with a splitting of 2.6 cps at 2.81 (H-10). The assignments given in parentheses could be made, in a tentative way, after chemical degradation had pointed to formula **3** as the most probable structure. One discrepancy, however, seemed to exist in the doublet character of the signal at lowest field. This signal, because of its chemical shift (τ 2.81), doubtless was due to a nitro-olefinic proton (H-10), but formula **3** contains no proton vicinal to H-10, and for allylic coupling with H-4 the splitting of 2.6 cps appeared to be rather too large considering the possible geometry of the molecule.[11] No alternative formula could be written that would have satisfied the apparent structural requirement $>CH—CH{=}C(NO_2)—$ without at the same time causing other serious inconsistencies, both spectroscopic and chemical. The problem was resolved by spin decoupling data obtained from a 100-Mc spectrum,[12] which verified the assignments made above and, in particular, proved that allylic coupling actually existed between H-10 and H-4.

Irradiation of H-4 caused the H-10 doublet to collapse to a singlet; at the same time, the H-3 doublet became a singlet also, and the signal for H-4a narrowed to a doublet with a splitting of 0.7 cps. Irradiation of H-4a removed the splitting (0.7 cps) of H-5 and changed the H-4 quartet into a triplet. The H-4 quartet was likewise converted into a triplet by irradiation of either H-3 or H-10. In the 100-Mc spectrum, the coinciding signals for the two acetoxymethylene groups (τ 5.6) appeared as an AB quartet with clearly separated center lines. Spin decoupling showed that there was a weak allylic coupling between the protons of the methylene group at C-7 and the olefinic proton H-8 (whose signal, described above as a singlet, did have fine structure).

Chemical Degradation of Compound 3.[10]—In a previous communication[1b] it was reported that in the preparation of the triacetate **1**, by acetylating its parent deoxynitro glycoside in the presence of pyridine

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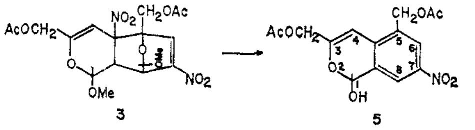
[11] A molecular model indicates that the H-4 bond must lie nearly in the plane of the nitroolefinic double bond; allylic coupling would therefore be expected to be at a minimum.

[12] We are greatly obliged to Professor R. U. Lemieux and Dr. G. Bigam, Edmonton, Alta., for their kindness in performing these measurements.

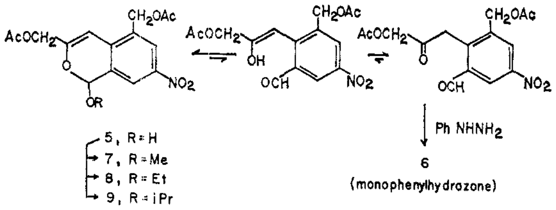
and recrystallizing the crude acetate from ethanol, small amounts of three crystalline by-products were encountered. One of them was colorless and proved to be identical with **3**. The other two were yellow and were identical with transformation products of **3** now to be described.[13]

When **3** was heated in the dry state above its melting point, or when it was boiled in benzene or dioxane in the presence of a small amount of pyridine, a yellow coloration developed. Lemon-yellow crystals could be isolated with difficulty, but the same substance was obtained in a facile manner (yield, 50%) by fusion of **3** in acetamide for 3 min on a steam bath. Elemental analysis of the optically inactive product, mp 151–152°, indicated the composition $C_{15}H_{15}NO_8$, and the structure was firmly established by spectroscopic and chemical evidence as that of the isochromene derivative **5**, 1-hydroxy-7-nitro-1*H*-2-benzopyran-3,5-dimethanol 3,5-diacetate. This compound, so unexpectedly engendered from a carbohydrate under mild reaction conditions, furnished chemical proof for the structure of its precursor (**3**). It is seen (eq 4) that **5** can arise from **3** by a fragmentation involving the loss of the —O—CH(OCH_3)— bridge, elimination of nitrous acid, and hydrolysis of the remaining methyl acetal. The latter hydrolysis is presumably linked with the production of nitrous acid for which there is direct evidence in an evolution of oxides of nitrogen during the reaction.



(4)

The solid-state infrared spectrum of compound **5** (Table I) exhibited a broad peak in the 3300-cm^{-1} region indicating hydrogen-bonded hydroxyl. Bands attributable to ester carbonyl and to an aromatic nitro group were at 1735 and 1515 cm^{-1}, respectively, and C=C vibrations occurred at 1658 and 1600 cm^{-1}. At 1710 cm^{-1} an additional carbonyl peak appeared, which was presumed to be due to an aldehyde group stemming from a partial tautomerization of **5** according to eq 5.

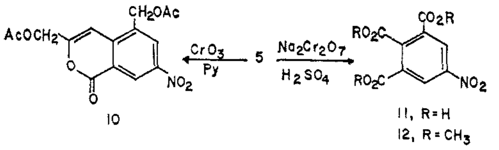


(5)

In chloroform solution, the infrared spectrum showed a sharp hydroxyl band at 3590 cm^{-1} and the carbonyl peak at 1710 cm^{-1} was absent, which suggested that in solution the enolic lactol (**5**) is the prevalent tautomeric form. This view was supported by the strong ultraviolet absorption showing a maximum at 346 mμ (ε 11,000 in ethanol) and extending into the visible region. Although no spectral data for comparably substituted isochromenes could be found in the literature, this spectrum is believed to be consistent with a substituted *p*-nitrostyrene system[14] such as **5** rather than with the dicarbonyl tautomer that bears structural resemblance to colorless *m*-nitrobenzaldehyde (λ_{max} 262 mμ in methanol) and *p*-nitrophenylacetone.[15] Addition of sodium hydroxide caused a deep, orange red coloration (λ_{max} 490 mμ).[16] The nmr spectrum of **5** (Table II) was in full agreement with the isochromene structure.

Both the cyclic hemiacetal and the potential carbonyl character of **5** were also revealed by chemical reactions. Phenylhydrazine gave a monophenylhydrazone (**6**) of the dicarbonyl tautomer, the second carbonyl function remaining free despite the use of excess reagent.[17] Treatment of **5** with cold alcohols containing hydrogen chloride resulted in facile acetalization giving crystalline methyl (**7**), ethyl (**8**), and isopropyl (**9**) derivatives. Their nmr data (Table II) could be interpreted readily on the basis of the assigned structures.

Oxidation with chromium trioxide in pyridine converted the isochromene (**5**) into the isocoumarin derivative **10**, 7-nitro-1*H*-2-benzopyran-1-one-3,5-dimethanol diacetate. This product exhibited ultraviolet maxima at 264 mμ (ε 7400) and 326 mμ (ε 13,500) in methanolic solution.[18] Its infrared spectrum lacked hydroxyl absorption and showed carbonyl bands[19] at 1747 and 1730 cm^{-1}. All hydrogen atoms of **10** were readily accounted for in the nmr spectrum (Table II). With ethanolic sodium hydroxide, **10** gave an intense, purple coloration (λ_{max} 540 mμ).[16]



A more drastic, chromic acid oxidation of **5** led to nitrobenzene-3,4,5-tricarboxylic acid (**11**, 5-nitrohemimellitic acid). This acid has been reported to melt "above 190° " and to yield upon sublimation an internal anhydride of mp 182–183°.[20] The trimethyl

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[13] The by-product[1b] of mp 147–148° was identical with **5**, and that of mp 119° was identical with **8**.

[14] *p*-Nitrostyrene itself shows λ_{max} 303 mμ (ε 14,400) in methanol: M. Pestemer, T. Langer, and F. Manchen, *Monatsh. Chem.*, **68**, 362 (1936). The substituents present in **5**, especially the enolic ether bridge, are thought to cause the observed bathochromic shift.

[15] This compound is described as forming "almost colorless crystals:" F. Arndt, B. Eistert, and W. Ender, *Ber.*, **62**, 44 (1929).

[16] According to A. Rose, N. P. Buu-Hoï, and P. Jacquignon [*J. Chem. Soc.*, 6100 (1965)], 7-nitroisocoumarins that are substituted in position 3 with *o*- or *p*-hydroxyaryl residues develop a dark violet color with alkali. It is noteworthy that **10**, even though it lacks a hydroxyaryl substituent, gives a similar reaction. We believe that the lactone ring hydrolyzes rapidly to form a resonance-stabilized, purple enolate. Analogously, the color produced by **5** in alkaline medium is believed to be due to the enolate of the open-chain tautomer. In agreement with this assumption, the alkylated derivatives **7–9** do not give the color reaction.

[17] The location of the phenylhydrazone grouping has not yet been determined with certainty. The carbonyl band at lowest wave number (1727 cm^{-1}, Table I) would suggest a free keto rather than an aromatic aldehyde group (*m*-nitrobenzaldehyde absorbs at 1707 cm^{-1}). Unfortunately, nmr spectra of **6** were of poor quality owing to insufficient solubility, and they did not yield reliable information to confirm this assignment.

[18] The band at longest wavelength of various isocoumarins has been reported to occur in the region between 318 and 340 mμ: G. Benz, *Ark. Kemi Min. Geol.*, **14**, 511 (1959); J. E. Hay and L. J. Haynes, *J. Chem. Soc.*, 2231 (1958).

[19] Carbonyl absorption in several isocoumarins has been found in the range of 1725–1745 cm^{-1}; see, *e.g.*, 4-methyl-5,6,7-trimethoxyisocoumarin, tetramethylellagic acid, and hexamethylflavogallol (Sadtler Standard Spectra No. 10067, 10064, and 10060, respectively).

[20] V. Prelog and R. Schneider, *Helv. Chim. Acta*, **32**, 1632 (1949). No analysis was recorded for the free acid; whether it was an anhydrous product or a hydrate is therefore not known. The melting point of the internal anhydride refers to a product that was sublimed twice.

TABLE II

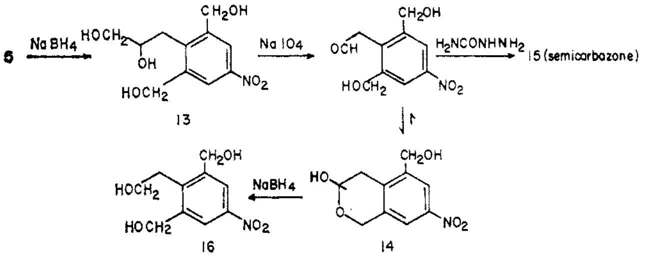
60-MC NMR DATA[a]

Compd	Solvent	Aromatic protons	H-4[b]	H-1[b]	–CH_2–O	CH_3–O	Others
5	$CDCl_3$	q 1.74 (2)[c]	s 3.50 (1)	s 3.72 (1)	s 4.72 (2), s 5.21 (2)	s 7.85 (3), s 7.87 (3)	s 6.88 (1)[d]
7	$CDCl_3$	q 1.78 (2)[c]	s 3.74 (1)	s 3.96 (1)	s 4.80 (2), s 5.25 (2)	s 7.87 (3) s 7.89 (3)	s 6.43 (3)[e]
8	$CDCl_3$	q 1.80 (2)[f]	s 3.68 (1)	s 3.81 (1)	s 4.75 (2), s 5.21 (2)	s 7.85 (6)	q 6.10 (2),[g] t 8.73 (3)[h]
9	$CDCl_3$	q 1.80 (2)[f]	s 3.72 (2)[i]		s 4.75 (2), s 5.23 (2)	s 7.86 (6)	m 5.70 (1),[j] m 8.73 (6)[k]
10	$CDCl_3$	q 1.20 (2)[c]	s 3.15 (1)		s 4.60 (2), s 4.99 (2)	s 7.80 (3), s 7.85 (3)	
11	DMSO-d_6	s 1.5 (2)					s 1.2 (3)[l]
12	$CDCl_3$	s 0.96 (2)					s 5.98 s 6.02 } (9)[m]
13	D_2O	s 1.8 (2)			5.3–6.5[n]		m 7.0 (2)[o]
14	DMSO-d_6	q 2.2 (2)			s 5.35 (2), s 5.65 (2)		m 7.4 (2),[o] s 4.9 (1),[p] s 4.7 (1),[d] s 3.4 (1)[d]
16	DMSO-d_6–D_2O	s 1.9 (2)			s 5.45 (4), m 6.6 (2)		m 7.25 (2)[o]

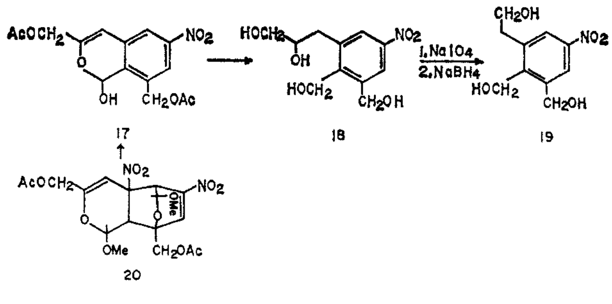
[a] Designations are s for singlet, t for triplet, q for quartet, and m for multiplet. Figures in parentheses are proton intensities obtained by integration. Chemical shifts are given as τ values, relative to TMS = 10 for compounds measured in $CDCl_3$ solution and relative to DOH = 5.25 for **13**. Chemical shifts for **11, 14,** and **16** are without standardization and therefore approximate only. [b] In compounds **5–10**. [c] J_{meta} = *ca.* 2 cps. [d] Hydroxyl signal, disappearing on deuterium exchange. [e] Methoxyl. [f] J_{meta} = 2.3–2.5 cps. [g] –CH_2– in ethoxyl. [h] CH_3– in ethoxyl. [i] Signals for H-4 and H-1 coincide. [j] –CH– in isopropoxyl. [k] CH_3– in isopropoxyl. [l] Broad peak due to carboxyl. [m] Estimated ratio of signals, 1:2. [n] Poorly resolved signals, partially obscured by DOH peak. [o] Unsymmetrical multiplet presumably due to benzylic CH_2. [p] Anomeric proton on C-3.

ester melts at 144°.[20] Our acid **11** was obtained as a monohydrate of mp 208–210°; it gave an anhydride that melted at 178° after one sublimation, and with diazomethane it formed a trimethyl ester (**12**) of mp 144°. The nmr spectrum of **11** in deuterium oxide consisted of only one signal, a sharp singlet in the aromatic resonance region, as expected for this symmetrically substituted benzene derivative. Similarly, the ester (**12**) in deuteriochloroform solution produced only one signal, a sharp singlet corresponding in intensity to two protons, in the aromatic resonance region (τ 0.96); the signals for the three methyl ester groups were two singlets at τ 5.98 and 6.02 (total intensity, 9 H). The only positional isomers of **11** and **12**, respectively, that would also be compatible with these spectral features are nitrobenzene-2,4,6-tricarboxylic acid (nitrotrimesic acid) and its trimethyl ester. Their melting points[21] are 290° and 107–108°, respectively, and the acid is incapable of internal anhydride formation. Therefore, no doubt exists about the identity of **11**. The degradation of **5** to **11** proved that carbon was attached to the benzene ring of **5** in the three positions *meta* and *para* to the nitro group.

Treatment of compound **5** with sodium borohydride resulted in reduction with concurrent loss of the acetyl groups and gave a tetraol (**13**). The tetraol was subjected to glycol cleavage with periodate, which afforded an aldehyde that existed in the tautomeric, cyclic hemiacetal form (**14**), both in solution and in the crystalline state. This was evident from the absence, in its infrared spectrum, of a carbonyl peak and the presence of a sharp peak at 1130 cm^{-1} that is probably associated with the cyclic C–O–C bond; furthermore, the nmr spectrum (Table II) did not show a low-field signal attributable to an aldehydic proton but possessed a one-proton triplet near τ 5.0 due to the anomeric H-3. The nature of **14** as a potential aldehyde was ascertaine, by the preparation of a semicarbazone (**15**). Finally borohydride reduction of **14** yielded a triol, 4-(2-hydroxyethyl)-3,5-bishydroxymethylnitrobenzene (**16**).



The chemical degradation of **5** discussed so far constitutes unambiguous proof of the structure depicted if one alternative isomer, namely **17**, which also is compatible with the results, can be ruled out. This may indeed be done on spectroscopic grounds. Let us compare the tetraol **13** and the triol **16** with their positional isomers **18** and **19** that would arise from hypothetical **17**.



The tetraol that was actually obtained produced in its nmr spectrum a single sharp peak (τ 1.8, in D_2O) for its aromatic protons, indicating equality of chemical shifts and therefore suggesting a symmetrical substitution pattern. The same was true for the triol whose

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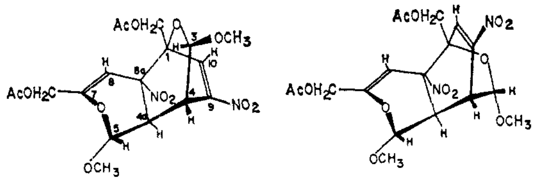
(21) F. Piozzi, *Gazz. Chim. Ital.*, **83**, 673 (1953).

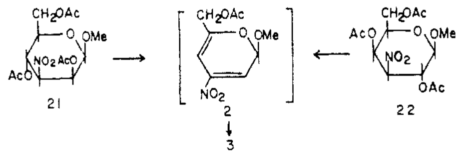


endo *exo*

Figure 3.—Possible configurations of compound **3**.

signal for its two aromatic protons was a singlet near τ 1.9. Formulas **13** and **16** were consequently preferred over the alternative structures **18** and **19** where the unsymmetrical substitution patterns would be expected to cause chemical shift differences for the aromatic protons, and, therefore, pairs of doublets due to *meta* coupling. It is recognized that this argument could be disputed, namely if the magnetic differences in the structurally rather similar side chains of **18** (and **19**) were insufficient to affect the aromatic protons noticeably. At any rate, all the unsymmetrically substituted nitrobenzenes encountered in this study did show, without exception, the expected multiplicity (see compounds **5**, **7**, **8**, **9**, **10**, **14** in Table II). A compelling reason, however, for discarding the structure **17** in favor of **5** is that **17** would require its precursor, the Diels–Alder adduct, to be formulated as **20**, and this would be entirely inconsistent with the nmr spectrum of the adduct (**3**) discussed above.

Stereochemistry.—When methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-nitro-β-D-mannopyranoside (**21**) and the corresponding *galacto* isomer **22** were dehydroacetylated with sodium hydrogen carbonate in refluxing benzene, the products were identical with compound **3** obtained from **1**. Formation of the diene **2** as a common intermediate in all three cases readily explains this fact.



There was, however, another stereochemical feature requiring special discussion. Compound **3**, surprisingly enough, proved optically inactive[22] although the reaction sequence **1** → **2** → **3** did not affect the anomeric center structurally and was not at first sight expected to involve it mechanistically. The observed optical inactivity imposed the conclusion that racemization at the anomeric carbon had nonetheless occurred at some stage during the reaction, perhaps in the intermediates **2**.[23] It was therefore of interest to examine whether changes in the reaction conditions might have some stereochemical influence at that point.

When, for the dehydroacetylation of **1**, potassium carbonate was substituted for sodium bicarbonate, the reaction went to completion within 5 hr, even at the lower temperature of 25–30°. The crystalline product was very similar to **3** in its infrared spectrum, but it showed a lower, usually unsharp melting point which was difficult to bring to constancy by recrystallization. Nmr spectroscopy revealed that the crude product contained besides **3** approximately 10–20% of another, similar substance (**3a**) which could be enriched to some extent by repeated recrystallizations. Mixtures of **3** and **3a** were readily converted into the isochromene, no product other than **5** being thereby encountered. A mixture in which **3a** predominated over **3** was obtained by dehydroacetylation of **1** with potassium carbonate in tetrahydrofuran at −70°, and from it, pure **3a** (mp 115°) was finally isolated. In contrast to **3**, **3a** was optically active, $[\alpha]_D$ −4.5°. Analytical and spectral data indicated that **3a** was a diastereoisomer of **3**. Thus, the infrared spectra of the two pure isomers virtually coincided in some spectral regions and showed but slight divergencies in others (Figure 1 and Table I). Acetamide fusion of both compounds produced the same ultraviolet band at 346 mμ. The nmr spectrum of **3a** exhibited all the general features of the spectrum of **3**, with slight variations in the values of certain chemical shifts and coupling constants (Figure 2). Although spin decoupling experiments have not yet been done with **3a**, the close kinship of the two spectra leaves little doubt in the validity of the proton assignments that correspond to those established for **3**.

As for a stereochemical representation of **3**, one has to take into account its optical inactivity and must proceed from the assumption that **2**, the intermediate diene, is capable of racemization. When a molecule of **2** acts as dienophile to combine with a molecule of its enantiomer acting as diene and if Alder's rule of preferential *endo* addition is obeyed,[24] the configuration depicted in Figure 3 arises.[25] This picture is in accord with the magnitude of the splittings observed in the nmr signals for H-3, H-4, H-4a, and H-5. Inspection of a Dreiding model shows that the dihedral angles between H-3 and H-4, and between H-4 and H-4a, in the rigid, bridged system approximate 60°, consistent with the splittings of about 2.5 cps. The ring comprising C-5, C-6, C-7, and C-8 is constrained in a twist boat conformation in which the dihedral angle between H-5 and H-4a is about 75°, causing these protons to be coupled by less than 1 cps.[26]

While we favor the *endo* configuration for **3** in view of Alder's rule and in the absence of contradictory evidence, it is recognized that the *exo* configuration (Figure 3), if more stable, might have arisen by thermodynamic control of the reaction. Since this also satisfies the nmr data just discussed, a decision cannot be made on this basis.

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(22) Zero rotation was determined in several samples at 589, 578, 546, 436, and 365 mμ using a Perkin-Elmer Model 141 automatic polarimeter.

(23) Abstraction of the anomeric proton in **2** would give a resonance-stabilized anion which on protonation could furnish the enantiomer of **2**. An attempt to prove this proposition by using sodium deuterium carbonate in a dehydroacetylation of **1** failed inasmuch as no deuterium was incorporated in **3**. A possible explanation might be dissociation of **2** into an ion pair.

(24) Although there are many exceptions [see, for instance, J. A. Berson, Z. Hamlet, and W. A. Mueller, *J. Amer. Chem. Soc.*, **84**, 297 (1962), and literature cited therein], the rule has been stated in a review by R. Huisgen, R. Grashey, and J. Sauer ("The Chemistry of Alkenes," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1964) to be "quite closely obeyed in the additions of cyclic dienes to cyclic dienophiles." The additions to cyclopentadiene of nitroethylene, 1-nitropropene, 1-nitro-1-butene, and various 2-aryl-1-nitroethylenes have been shown to follow predominantly the *endo* path, with *endo/exo* ratios 9 : 1 (one case), 6 : 1 (three cases), 4 : 1 and 3 : 1 (one case each): W. E. Noland, B. A. Langager, J. W. Manthey, A. G. Zacchei, D. L. Petrak, and G. L. Eian, *Can. J. Chem.*, **45**, 2969 (1967). See also R. R. Fraser, *ibid.*, **40**, 78 (1962); G. I. Poos, J. Kleis, R. R. Wittekind, and J. D. Rosenau, *J. Org. Chem.*, **26**, 4898 (1961); J. Weinstock, N. Schwartz, and M. F. Kormendy, *ibid.*, **26**, 5247 (1961).

(25) Addition in the reverse order is of course of equal probability and leads to the antipode. Consequently, **3** must be a racemate.

(26) Actually, on the model the twist boat can be flipped so as to make the methoxyl group equatorial and H-5–H-4a *trans* diaxial, but such a conformation would cause a large coupling in the latter protons and is therefore ruled out.

Regarding the stereochemistry of optically active **3a** one may assume that, at low temperatures, the racemization of intermediate **2** is retarded relative to the diene addition, and that consequently an adduct arises in which both anomeric centers (C-3 and C-5) have retained the original absolute configuration. The stereochemical representations for an *endo* and *exo* adduct, respectively, would then be the same as those of **3** except for inverted C-3 configurations.

Experimental Section

Melting points were taken in capillaries in an electrically heated aluminum block using a calibrated thermometer. Unless stated otherwise, evaporations were performed *in vacuo* at 35–40° (bath temperature). The term "petroleum ether" refers to the fraction of bp 30–60°. Spectral data were obtained as noted.[10] The most characteristic infrared frequencies of new compounds are compiled in Table I.

3,4,4a,8a-Tetrahydro-3,5-dimethoxy-8a,9-dinitro-1,4-ethenopyrano[4,3-*c*]pyran-1,7(5*H*)-dimethanol Diacetate (3) and Stereoisomer 3a.—All reactions were performed under exclusion of moisture and with carefully dried solvents and reagents.

A solution of 3.0 g of methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-nitro-β-D-glucopyranoside (**1**)[1b] in benzene (150 ml) was heated under reflux and magnetically stirred with *sodium bicarbonate* (15 g) for 8 hr. The cooled reaction mixture was filtered, and the solution was evaporated to give a syrup which was dissolved in about 10 ml of ethyl acetate. Addition of petroleum ether to incipient turbidity caused crystallization of small, colorless prisms which were collected after 3 hr and washed with ethyl acetate–petroleum ether (1:3). The product (850 mg, mp 124°) was recrystallized once from the same solvents, which raised its mp to 128°. According to an nmr spectrum, the product was **3** (free from **3a**), but it contained an estimated 0.5 mol of ethyl acetate of crystallization. Recrystallization from chloroform–petroleum ether furnished solvent-free **3**, mp 130–131° dec, [α]^{23} 0° (at 365–589 mμ; *c* 2, chloroform).

Anal. Calcd for $C_{18}H_{22}N_2O_{12}$ (458.4): C, 47.17; H, 4.84; N, 6.11; O, 41.86. Found: C, 47.18; H, 5.29; N, 6.22; O, 41.50; mol wt, 448 (by osmometry in benzene).

Crystalline **3** gave a single spot on silica gel G thin layer plates irrigated with butanone–heptane (1:1); the mother liquor gave the same spot and, in addition, contained faster and more slowly traveling material, but it did not yield any more crystals.

In an alternative procedure, a solution of **1** (3.8 g) in benzene (150 ml) and anhydrous *potassium carbonate* (20 g, finely powdered) were vigorously stirred together for 5 hr at 25–30°. Filtration and removal of the solvent gave a syrup which partially crystallized from ethyl acetate–petroleum ether. The crude crystals (1.473 g) melted at 118–119°, and according to their nmr spectrum they consisted mainly of **3** but contained 10–20% of the stereoisomer **3a**. One recrystallization from ethyl acetate–petroleum ether raised the mp to 126°, and the infrared spectrum of the product was identical with that of **3** as obtained by the bicarbonate procedure.

The experiment just described was repeated several times, in some cases with minor modifications regarding the reaction time and temperature. Yields were generally between 45 and 55%, and the crude products melted in the range 116–122°. In one case the crude product (mp 116°) was recrystallized twice from chloroform–petroleum ether, which gave a material melting at 110–111° and showing [α]^{23}D −1.5° (*c* 1, chloroform). According to an nmr spectrum it was a mixture of **3** and **3a** in a ratio of about 2:1.

Attempts to isolate pure **3a** by fractional crystallization proved very laborious. A fractionation that involved 15 recrystallizations afforded pure **3** (mp 131°) and a 1:2 mixture of **3** and **3a**.

The following procedure furnished *pure* **3a**. A solution of **1** (1.0 g) in tetrahydrofuran (60 ml) was stirred with anhydrous potassium carbonate (10 g) for 53 hr at −70°. The mixture was then allowed to stand for another 2 days at −5° before it was worked up by filtration and evaporation. Inspection of the resulting syrup by thin layer chromatography revealed that all **1** had been consumed; a faster moving main spot accompanied by at least three weak spots due to unknown products was seen. Crystallization from ethyl acetate–petroleum ether gave a product (348 mg) melting at 109–110°. Two recrystallizations from the same solvents raised the mp to 113°. An nmr spectrum showed that at this point the product was a 2:1 mixture of **3a** and **3**. Two further recrystallizations from chloroform–carbon tetrachloride–cyclohexane finally gave 67 mg of pure **3a** as colorless platelets of mp 115° dec, [α]^{23}D −4.5° (*c* 0.5, chloroform).

Anal. Calcd for $C_{18}H_{22}N_2O_{12}$ (458.4): C, 47.17; H, 4.84; N, 6.11. Found: C, 47.33; H, 4.91; N, 5.95.

The D-*manno* and D-*galacto* isomers of **1** (**21** and **22**, respectively[1b]) were dehydroacetylated on a 100-mg scale by the use of sodium bicarbonate in refluxing benzene (for **21**) or potassium carbonate in benzene at 25–30° (for **22**). The recrystallized products, which were obtained in yields of 12–14%, proved identical with **3** from **1** showing undepressed mixture melting points and identical infrared spectra.

Catalytic hydrogenation of **3** was attempted using palladium on charcoal, palladium oxyhydrate on barium sulfate, rhodium on charcoal, or platinum dioxide, all in ethyl acetate medium at room temperature and atmospheric pressure. Only starting material could be isolated. A hydrogenation with platinum oxide at 54 psi for 20 hr resulted in a mixture consisting of at least four components, according to thin-layer chromatography.

1-Hydroxy-7-nitro-1*H*-2-benzopyran-3,5-dimethanol 3,5-Diacetate (5). A. Preliminary Experiments.—Small samples (5–10 mg) of **3** and 1 drop of pyridine were dissolved in 2–3 ml of benzene or dioxane and heated on a steam bath for 5 min. The solutions turned yellow and a strong absorption band at λ_{max} 346 mμ was engendered. Evaporation gave a yellow, partly crystalline solid which was difficult to purify. In another experiment, 70 mg of **3** was kept for 3 min in an oil bath at 133°, whereby the substance melted, turned yellow, and evolved fumes of oxides of nitrogen. Crystallization from ethyl acetate and petroleum ether then gave crystals (8 mg) melting at 144–147°. Their infrared and ultraviolet spectra were identical with those of **5** which was prepared as described under B, and also with those of the previously mentioned[1b] yellow by-product, mp 147–148°. A sample (3 mg) of pure **3** was dissolved in molten acetamide (100 mg) on a steam bath. After 2 min the mixture showed the characteristic ultraviolet peak at 346 mμ (in methanol). An identical experiment with pure **3a** gave the same result.

B. Preparation.—Acetamide (6 g) was fused on a steam bath, and crystalline **3** (1.25 g) was introduced into the liquid in which it dissolved rapidly with evolution of nitrous fumes. After 3 min the yellow liquid was cooled to 25° whereby it solidified. The solid was dissolved by boiling in ethyl acetate (50 ml) from which, upon cooling to 0°, acetamide crystallized out. It was removed and washed with ice-cold benzene–petroleum ether (2:1). The combined filtrate and washing solvents were concentrated to about 15 ml and cooled, thereby yielding another crop of acetamide which was removed and washed as above. The filtrate, upon evaporation to dryness, gave a yellow crystalline solid which was triturated for some time with 5 ml of ice-water. Part of the solid dissolved and the remainder became gummy and stuck to the wall of the vessel. The aqueous extract was discarded, and the residue was triturated a few more times with small amounts of ice cold water and then dried by evaporation with several successive portions of benzene. Finally, the residue was dissolved in the minimum amount of hot benzene, and the solution, placed overnight in a refrigerator, deposited 390 mg (42.5%) of **5** as small, yellow prisms of mp 148°, raised to 150–151° by one recrystallization and to 151–152° by a second recrystallization. On thin layer plates of silica gel G the product gave a single spot and moved at lower speed than **3** (with butanone–heptane, 1:1). Ultraviolet bands were at λ_{max} 240 mμ (ε 9800) and 346 mμ (ε 11,000) (in methanol). Fehling solution was reduced on heating. With 0.1 *N* alcoholic potassium hydroxide a bright red, but gradually fading, color was produced. The color was more intense and more stable when 1 drop of aqueous 1 *N* sodium hydroxide was added to the alcoholic solution.

Anal. Calcd for $C_{15}H_{15}NO_8$ (337.3): C, 53.42; H, 4.49; N, 4.15; O, 37.95. Found: C, 53.58; H, 4.70; N, 4.13; O, 38.05.

Performance of the acetamide fusion using mixtures of **3** and **3a** gave the same result; yields of up to 50% were obtained.

C. Phenylhydrazone (6).—A solution of phenylhydrazine hydrochloride (250 mg) and sodium acetate (400 mg) in water (3 ml) was clarified by filtration with a small amount of activated charcoal and added to a solution of **5** (100 mg) in ethanol (40 ml). The mixture was gently refluxed with magnetic stirring for 15 min. After cooling, water (30 ml) was added and the mixture was allowed to stand at 4° for 2 hr. The crystalline product was collected, washed with cold, 50% aqueous ethanol, and dried.

The yield was 140 mg of **6** showing mp 155–156°. Twice recrystallized from aqueous ethanol, the small needles melted sharply at 161°.

Anal. Calcd for $C_{21}H_{21}N_3O_7$ (427.4): C, 59.01; H, 4.96; N, 9.86. Found: C, 59.21; H, 5.05; N, 9.75.

1-Methoxy-7-nitro-1*H*-2-benzopyran-3,5-dimethanol Diacetate (7).—Compound **5** (65 mg) was dissolved by heating in methanol (25 ml), and 1 *N* hydrochloric acid (2 ml) was added to the solution after it had cooled to room temperature. The solution was then stored for 8 hr at 0° and subsequently evaporated to dryness, with several additions of fresh methanol. The yellow residue was dissolved in a small amount of methanol, water was added to incipient turbidity, and the product (**7**), which crystallized at 4° in the course of several days, was washed with water and amounted to 48 mg (70.5%). It melted at 102–104° and, after recrystallization from 50% methanol, it melted at 111–112°.

Anal. Calcd for $C_{16}H_{17}NO_8$ (351.3): C, 54.70; H, 4.88; N, 3.99. Found: C, 54.49; H, 5.01; N, 4.18.

1-Ethoxy-7-nitro-1*H*-2-benzopyran-3,5-dimethanol Diacetate (8).—Compound **5** (95 mg) was dissolved in hot ethanol (15 ml), and after cooling, 1 *N* hydrochloric acid (3 ml) and water (20 ml) were added; the reaction mixture was allowed to stand at 4° for 20 hr. Partial evaporation caused a yellow syrup to separate. The supernatant liquid was discarded and the syrup was washed twice with water. Crystallization from 50% aqueous ethanol gave 60 mg (67%) of **8**; its melting point of 115° was raised to 118–119° by one recrystallization from the same solvent. Ultraviolet bands were at λ_{max} 240 mμ (ε 1050) and 345 mμ (ε 12,500) (in methanol).

Anal. Calcd for $C_{17}H_{19}NO_8$ (365.4): C, 55.89; H, 5.24; N, 3.83. Found: C, 55.29; H, 5.33; N, 4.36.

The infrared spectrum of **8** was identical with that of the previously mentioned[1b] yellow by-product, mp 119°.

1-Isopropoxy-7-nitro-1*H*-2-benzopyran-3,5-dimethanol Diacetate (9).—Compound **5** (74 mg) was dissolved with heating in isopropyl alcohol (25 ml). Hydrogen chloride gas was briefly passed into the cooled solution which was then stored at 0° for 7 hr. Evaporation gave a yellow syrup which crystallized from isopropyl alcohol–water, affording **9** (44 mg, 53%) as fine yellow needles of mp 103°.

Anal. Calcd for $C_{18}H_{21}NO_8$ (379.4): C, 56.99; H, 5.58; N, 3.69. Found: C, 57.21; H, 5.69; N, 3.76.

7-Nitro-1*H*-2-benzopyran-1-one-3,5-dimethanol Diacetate (10).—Chromium trioxide (250 mg) and pyridine (10 ml) were stirred for 2 hr in a nitrogen atmosphere at room temperature; a solution of **5** (190 mg) in pyridine (5 ml) was then added and stirring was continued for 6 hr.[27] The pyridine was evaporated, the last traces having been removed by two evaporations with added toluene. The dark brown residue was extracted with three 30-ml portions of ether; the extract was concentrated, clarified with activated charcoal, and evaporated to a yellowish syrup. The syrup was dissolved in hot water containing a small amount of ethanol and, in the course of 24 hr at 4°, furnished 59 mg of **10** as beautiful, pale yellow plates of mp 110–111°. The ultraviolet spectrum in methanol showed a peak of λ_{max} 326 mμ (ε 13,500) with a shoulder at 264 mμ (ε 7400) and strong end absorption.

Anal. Calcd for $C_{15}H_{13}NO_8$ (335.3): C, 53.78; H, 3.97; N, 4.18. Found: C, 54.01; H, 4.09; N, 4.39.

Nitrobenzene-3,4,5-tricarboxylic Acid (11).—A magnetically stirred suspension of **5** (400 mg) in a solution of sodium dichromate (1.2 g) in water (10 ml) was slowly heated, and a mixture of concentrated sulfuric acid (14 ml) and water (7 ml) was gradually added. After the addition the reaction mixture was gently boiled under reflux with continued stirring for 30 min. The cooled, dark green solution was diluted with water (50 ml) and extracted thrice with 50-ml portions of ether. The combined ether extracts were washed twice with water, dried over anhydrous sodium sulfate and evaporated to give a syrup which was dissolved again in a small amount of ether. Upon addition of benzene and petroleum ether, crystallization of **11** (96 mg, 29%) occurred at 4° in the course of 48 hr. The crude product (mp 196–198°) was recrystallized from ether–benzene to give 54 mg of oblique prisms, mp 208–210° (lit.[20] mp above 190°), which were easily soluble in water but nearly insoluble in benzene or chloroform. The ultraviolet spectrum in water showed strong end absorption with a shoulder at 274 mμ (ε 8000).

Anal. Calcd for $C_9H_5NO_8 \cdot H_2O$ (273.2): C, 39.72; H, 2.59; N, 5.16. Found: C, 40.04; H, 2.75; N, 5.45.

A 5-mg sample of **11** was sublimed once under high vacuum at 210° (bath temperature) to give crystals of mp 178° (reported[20] for the internal anhydride of **11**, mp 182–183° after two sublimations).

Trimethyl Nitrobenzene-3,4,5-tricarboxylate (12).—An ether solution of **11** (20 mg) was treated with ethereal diazomethane until a yellow color persisted. After 15 min the solution was evaporated leaving a white solid residue which was dissolved in deuteriochloroform for nmr spectroscopy and thereafter recovered by evaporation. Crystallization from ethanol–water gave fine, pale yellow needles (9 mg) of mp 144° (for **12**, lit.[20] mp 143–144° and, after sublimation, 144–145°).

Anal. Calcd for $C_{12}H_{11}NO_8$ (297.2): C, 48.50; H, 3.73; OCH_3, 31.32. Found: C, 48.63; H, 3.90; OCH_3, 31.08; mol wt, 297 (by mass spectrometry).

3,5-Bishydroxymethyl-4-(2,3-dihydroxypropyl)nitrobenzene (13).—To a solution of **5** (250 mg) in methanol (50 ml) was added sodium borohydride (500 mg) in water (5 ml), at room temperature. Within 5 min, the 346-mμ absorption band of **5** disappeared, and a new peak arose at 282 mμ. After 15 min the solution was deionized with 20 ml of Rexyn 101(H^+) and evaporated. The residue was evaporated eight times with methanol for removal of boric acid. The resulting syrup crystallized upon trituration with ethyl acetate, and recrystallization from that solvent gave 128 mg (67%) of pointed prisms: mp 135–136°; λ_{max} 282 mμ (ε 10,500, in methanol).

Anal. Calcd for $C_{11}H_{15}NO_6$ (257.3): C, 51.35; H, 5.88; N, 5.46; O, 37.31. Found: C, 51.02; H, 6.07; N, 5.48; O, 37.41.

3,4-Dihydro-3-hydroxy-7-nitro-1*H*-2-benzopyran-5-methanol (14).—The tetraol **13** (100 mg) was dissolved in a solution of sodium metaperiodate (83 mg, 1 molar equiv) in water (10 ml). The reaction mixture was allowed to stand in the dark at room temperature for 18 hr and was then evaporated to dryness with several additions of absolute ethanol. The organic product was extracted from the inorganic salt by trituration with cold absolute ethanol. The extract was clarified with a small amount of charcoal and evaporated to give a residue which was taken up in a small amount of ethyl acetate. The ethyl acetate solution was separated from some brownish, insoluble material and yielded, upon evaporation, a pale yellow solid (**14**, 78 mg, 89%) that melted at 146–147°. Recrystallized from acetone–chloroform–petroleum ether, it had mp 149–149.5°, λ_{max} 283 mμ (ε 6100, in ethyl acetate). It reduced hot Fehling solution.

Anal. Calcd for $C_{10}H_{11}NO_5$ (225.2): C, 53.33; H, 4.92; N, 6.22. Found: C, 53.21; H, 4.93; N, 6.38.

2,6-Bishydroxymethyl-4-nitrophenylacetaldehyde Semicarbazone (15).—A mixture of compound **14** (30 mg) dissolved in ethanol (1 ml) and of semicarbazide hydrochloride (100 mg) and sodium acetate (150 mg) dissolved in water (1 ml) was heated for 10 min on a steam bath. No crystallization took place on storing the reaction mixture at 4° for a prolonged period of time, but, upon allowing it to evaporate slowly in the open air to about half its volume, nearly colorless prisms of **15** were deposited. They were washed with ice-cold water to yield 19 mg, mp 186° dec.

Anal. Calcd for $C_{11}H_{14}N_4O_5$ (282.3): C, 46.80; H, 5.00; N, 19.86. Found: C, 46.63; H, 5.15; N, 19.86.

4-(2-Hydroxyethyl)-3,5-bishydroxymethylnitrobenzene (16).—A mixture of compound **14** (40 mg) in methanol (5 ml) and sodium borohydride (50 mg) in water (2 ml) was allowed to react at room temperature for 2 hr. Deionization with 5 ml of Rexyn 101(H^+) followed by eight coevaporations with methanol furnished a crystalline residue which was dissolved in the minimum amount of hot water. The triol **16** separated as long needles of mp 135° in the course of 3 days at 4°. The yield was 28 mg (69%).

Anal. Calcd for $C_{10}H_{13}NO_5$ (227.2): C, 52.86; H, 5.77; N, 6.17. Found: C, 52.82; H, 5.91; N, 6.38.

Registry No.—**3,** 16134-24-0; **3a,** 16134-12-6; **5,** 16134-13-7; **6,** 16134-25-1; **7,** 16134-14-8; **8,** 16134-15-9; **9,** 16134-16-0; **10,** 16134-17-1; **11,** 3807-81-6; **12,** 16134-19-3; **13,** 16134-20-6; **14,** 16134-21-7; **15,** 16134-22-8; **16,** 16134-23-9.

Acknowledgment.—Generous support by the National Research Council of Canada is gratefully acknowledged. The Ogilvie Flourmills Co. Ltd. is thanked for the award of a postgraduate fellowship to F. K.

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[27] J. Schmidlin, G. Anner, J. R. Billeter, K. Heusler, H. Ueberwasser, P. Wieland, and A. Wettstein, *Helv. Chim. Acta*, **40**, 1034 (1957).