in the table, indicate that in passing from CH_3NO_2 to DMF the yield in geranial is raised from 68 to 95%.

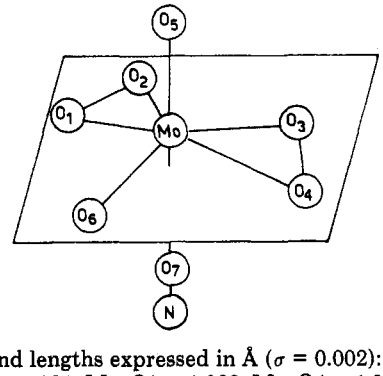
While mechanistic studies are in progress to elucidate the peculiar features shown by **1a**, our efforts are also directed toward the development of a catalytic process based on picolinate *N*-oxido-molybdenum complexes.

Experimental Section

Materials. All alcohols are high-purity materials further purified by distillation or crystallization. 1,2 Dichloroethane, nitromethane, and *N,N*-dimethylformamide were also purified by standard procedures. All other chemicals are commercially available products used as received. The products of oxidation were identified on the basis of their spectral properties and by comparison with authentic samples.

Preparation of $[MoO(O_2)_2C_5H_4N(O)COO]^-R_4N^+\cdot H_2O$ (R = Me, Bu). $Na_2MoO_4\cdot 2H_2O$ (3.36 g, 14 mmol) was dissolved in 10 mL of water, and the acidity of the solution was adjusted at pH 2 with H_2SO_4 (50%). Then 7 mL of H_2O_2 (36%, w/v) was added, and the resultant solution was diluted to 20 mL with water (solution A). Picolinic acid *N*-oxide (2.14 g, 15 mmol) was dissolved in 10 mL of an aqueous solution of tetramethylammonium hydroxide (1.5 M), and the resultant mixture was diluted to 20 mL with water (solution B). In an ice-cold bath, under vigorous stirring, 20 mL of solution A was added to 18 mL of solution B, maintaining the acidity of the media at pH 2 by adding 50% H_2SO_4. After 30 min, the formation of a bright yellow precipitate (4.06 g, 10 mmol, 71%) was complete. The solid was filtered off and washed several times with ether. The product was recrystallized from DCE. The water molecule may be removed by keeping the complex overnight in the dark at 0.1 mmHg in the presence of P_2O_5. The dehydrated complex is a very stable material, which may be stored for several weeks: iodometric titration, [active oxygen] ≡ 2[**1a**] = 98%; mp 183-184 °C dec (uncorrected); IR (KBr) ν(Mo=O) 950, ν(O—Mo—O) 586, 524, ν(C=O), 1660, ν(N→O) 1240 cm^{-1}. Anal. Calcd for $C_{10}H_{18}MoN_2O_9$: C, 29.50, H, 4.01; N, 6.89. Found: C, 29,48; H, 3.97; N, 6.82.

Suitable crystals for X-ray analysis were obtained by slow crystallization at -3 °C in DCE. The crystal system was obtained with an automatic Phillips PW 1100/16 with standard software: cell parameters a = 10.290, b = 21.476, c = 6.982 Å; β = 94.65°; Z = 4; space group $P2_1/a$. The structure was solved with the Patterson method and refined to factor R = 0.023 by using 2319 reflections with $I \geq 3\sigma(I)$. See the paragraph at the end of paper about supplementary material.



Selected bond lengths expressed in Å (σ = 0.002): Mo-O1 = 1.967, Mo-O2 = 1.931, Mo-O3 = 1.923, Mo-O4 = 1.947, Mo-O5 = 1.675, Mo-O6 = 2.256, Mo-O7 = 2.075, N-O7 = 1.329. Selected bond angles in degrees (σ = 0.1): O1-Mo-O^2 = 44.6, O3-Mo-O4 = 44.4, O5-Mo-O1 = 100.6, O5-Mo-O4 = 101.2, O7-Mo-O1 = 89.3, O7-Mo-O4 = 87.9, O7-Mo-O5 = 92.1, O5-Mo-O6 = 168.1.

The complex with R = Bu has been obtained according to the same procedure by using tetrabutylammonium hydroxide: active oxygen 98%; mp 144-145 °C dec (uncorrected); IR (KBr), ν(Mo=O) 947, ν(O—Mo—O) 582, 528, ν(C=O) 1663 ν(N→O) 1238 cm^{-1}. Anal. Calcd for $C_{22}H_{40}MoN_2O_8$: C, 47.48; H, 7.25; N, 5.03. Found: C, 47.71; H, 7.37; N, 5.01.

Due to its higher solubility in DCE, it has been used in all the oxidations described in this paper.

Procedures. In a typical run, 5 mL of DCE containing 0.3 mmol of substrate was added to a DCE solution (10 mL) containing the complex (0.15 mmol) and an internal GC standard in a glass reactor maintained at 50 °C. After complete consumption of active oxygen (absence of iodometric titer), the yield was calculated by GLC analysis on a FFAP 3% (0.5-m) or on a Carbowax 20 M 10% (1.5-m) column, both on Chromosorb WAW-DMCS, with a Varian 3700 or a Varian 6000 instrument equipped with a Varian CDS 401 or a Shimatzu C-R3A.

Registry No. **1a**, 105194-63-6; $[MoO(O_2)_2C_5H_4N(O)COO]^-Me_4N^+$, 110316-47-7; Na_2MoO_4, 7631-95-0; $H_3C(CH_2)_7OH$, 111-87-5; $H_3C(CH_2)_6CHO$, 124-13-0; $PhCH_2OH$, 100-51-6; PhCHO, 100-52-7; $H_3C(CH_2)_5CH(OH)CH_3$, 123-96-6; $H_3C(CH_2)_5COCH_3$, 111-13-7; $PhCH(OH)CH_3$, 98-85-1; $PhCOCH_3$, 98-86-2; $H_2C{=}CH(CH_2)_8OH$, 13019-22-2; $H_2C{=}CH(CH_2)_7CHO$, 39770-05-3; $(H_3C)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2OH$, 624-15-7; $(H_3C)_2C{=}CH(CH_2)_2C(CH_3){=}CHCHO$, 5392-40-5; picolinic acid *N*-oxide, 824-40-8; cyclopentanol, 96-41-3; cyclopentanone, 120-92-3; cyclohexanol, 108-93-0; cyclohexanone, 108-94-1; 5-methyl-2-(1-methylethyl)cyclohexanol, 1490-04-6; 5-methyl-2-(1-methylethyl)cyclohexanone, 10458-14-7; cyclohexen-3-ol, 822-67-3; cyclohexen-3-one, 930-68-7; 3-methyl-3-(4-methyl-3-pentyl)oxiranemethanol, 50727-94-1; 3-hydroxypregn-5-en-20-one, 38372-24-6; pregn-5-ene-3,20-dione, 1236-09-5.

Supplementary Material Available: Tables of atomic coordinates, bond distances, and bond angles and the full structure of compound 1 (R = Me) (4 pages). Ordering information is given on any current masthead page.

A Simple Transformation of Carminic Acid into Kermesic Acid

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Carminic acid (**1a**) is the principal component of the food dye cochineal, obtained from the insect *Dactylopius coccus*, possessing a significant inhibitory activity against ascites tumors in Jensen rats[1,2] due to its structural similarity to the antitumor agent shikonin and the anthracyclines[3] with the merit that it is not toxic and does not bind to DNA.[4] In a previous paper we reported chemical and spectroscopic evidence that the C-glycosyl bond of carminic acid possesses the β-configuration.[5,6] This result was more recently confirmed by a complete ^1H and ^{13}C NMR study.[7]

The aglycon moiety of carminic acid is represented by kermesic acid (**1b**), the coloring matter of kermes,[8] the most ancient dyestuff on record. Kermesic acid is at present not commercially available and has been syn-

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(2) Mihail, N.; Cracium, C. *Naturwissenschaften* **1970**, *57*, 500.
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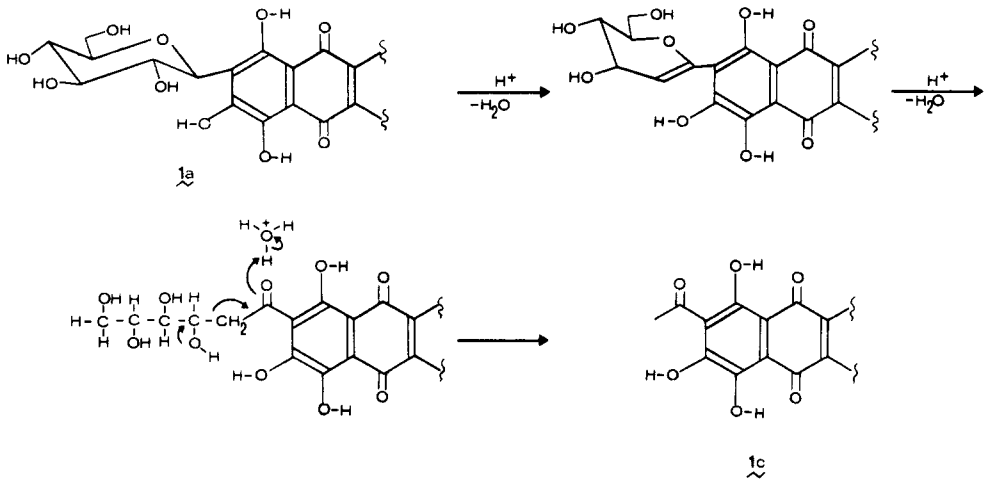
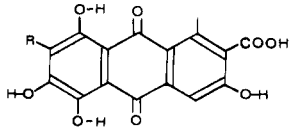
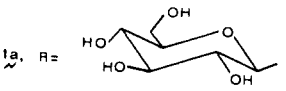
Scheme I



thesized by nonconventional procedures that require a Diels–Alder cycloaddition of a suitable trimethylsilyl enol ether of acylketene acetals.[9-11] Our interest in the study of the biological properties of kermesic acid prompted us to search for a simple transformation of the commercially available carminic acid into kermesic acid. In particular, we reexamined the old reaction of carminic acid with sulfuric acid[12] in the light of more recent knowledge on the acid-catalyzed aldol condensation[13,14] with the hope that the product of the reaction would be the methyl ketone **1c** (see Scheme I). The latter is obtainable by an initial sulfuric acid dehydration of the hydroxy group at the α position of the glucosidic carbon, formation of an easily hydrolizable enol ether which, after hydrolysis, could suffer a retroaldolic condensation to afford compound **1c**. Subsequent manipulation of this ketone should permit the preparation of kermesic acid (**1b**).





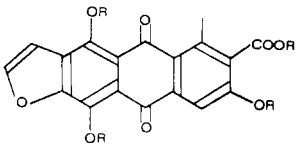
1a, R=

b, R=H

c, R=CH_3CO

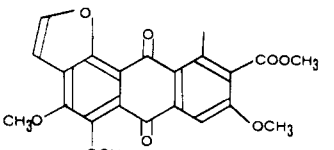
With this in mind we treated carminic acid with 60% sulfuric acid and isolated a water-insoluble mixture containing the anthrafurandione **2a** which was characterized after methylation with methyl iodide and potassium carbonate in dimethylformamide as the methyl ether methyl ester **2b**. The compound was obtained in 18% yield and was accompained by more polar compounds resulting from excessive decomposition of carminic acid.

The structure of **2b** was deduced from the spectroscopic data and was confirmed unequivocally by subsequent evidence. In particular elemental analysis and the mass spectrum showed the correct molecular formula and IR and UV spectra confirmed that the compound preserved the anthraquinone structure and the ester group. Full assignement of all protons in the ^1H NMR spectrum of **2b** indicated the presence of a α,β-substituted furan ring fused with the A ring of the anthraquinone since the only aromatic proton in the spectrum resonated as a singlet at 7.6 ppm as expected for the C-4 proton at the peri position of the carminic acid.[7,15] Moreover, two resonances over 3.95 pm (4.08 and 4.25) suggested the presence of two peri-positioned methoxy groups, thus supporting the structure **2b**, with the furan ring fused at carbons 6 and 7 of the anthraquinone structure, rather than the isomeric structure **3**.[15] ^{13}C NMR spectral analysis supported this assignement: three methoxy signals (apart from that of the ester) were observed, one at usual position (56.3 ppm),[15] while the others were shifted downfield (62.3 and 61.8 ppm), thus indicating that they were in the peri position (4 and 11) and had an adjacent substituent (at positions 3a and 11a) responsible for the downfield shift from the usually observed resonance.[15,16]

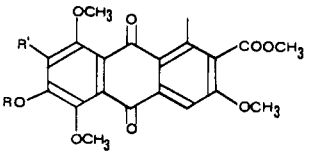


2a, R=H

b, R=CH_3



3



4a, R=H ; R'=CHO

b, R=R'=H

c, R=CH_3 ; R'=H

Subsequent unequivocal confirmation of the assignment was obtained by degradation of the furan ring of **2b** to the

(9) Cameron, D. W.; Deutscher, D. J.; Fuetrill, I. G.; Griffiths, P. G. *Aust. J. Chem.* **1981**, *34*, 2401.
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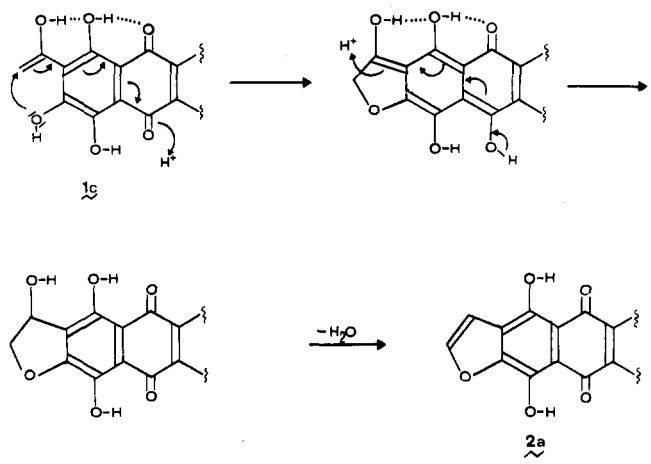
Scheme II



hydroxy aldehyde **4a** with chromic acid or with osmium tetraoxide in the presence of sodium periodate. Moreover the same compound was obtained in better yields under controlled ozonolysis conditions.

Physicochemical properties of **4a** were in agreement with the assigned structure. In particular its absorption in the UV spectrum in alkaline ethanol (λ_{max} 478 nm) and in the IR spectrum (1660 cm^{-1}) indicated that the free hydroxy group was located in such a position that no hydrogen bond was possible with the anthraquinone carbonyls. On the contrary a hydrogen bond was possible between the hydroxy group and the aldehydic carbonyl as shown by its absorption frequency (1640 cm^{-1}). A major support to the structure **4a** for the compound derived from its ^{13}C NMR spectrum showing resonances typical for carbonyls of anthraquinones (182.7 and 182.2 ppm) free from hydrogen bonds. Decarbonylation of the aldehyde **4a** with tris(triphenylphosphine)chlororhodium afforded the trimethoxyanthraquinone **4b**, which was dealkylated by an aluminum chloride–sodium chloride melt to kermesic acid identical (mp, mmp) with that obtained by synthesis.[9] This compound by methylation afforded the tetramethoxyanthraquinone **4c** which showed a physicochemical profile identical with that of the compound obtained according to Cameron et al.[9] A simple rationalization of the formation of the anthrafurandione **2a** (Scheme II) could involve the protonation of the C-10 anthraquinone carbonyl. The latter, by a conjugative effect (facilited by a hydrogen bond which stabilizes the enolic form of the methyl ketone **1c**) causes a charge affinity inversion process of the aliphatic α–carbon to the carbonyl group at C-7. The latter process results in an intramolecular nucleophilic attack by the hydroxy group at C-6 with formation, after a proton addition, of the immediate furan ring precursor. The fact that the glucose residue at carbon 7 reacts only with the hydroxy group at carbon 6 affording only the anthrafurandione **2a** without trace of isomer **3** may be reasonably explained by considering that the hydroxy group at carbon 6 is less acidic than that at carbon 8 which is hydrogen-bonded to the 9-carbonyl.[17] The transformation of the carminic acid into kermesic acid offers the possibility of obtaining kermesic acid in a simple way from a readily available compound.

Experimental Section

All melting points are uncorrected. ^1H NMR spectra were recorded on a Varian XL-200 spectrometer as chloroform-*d* solutions and are reported in δ (ppm) units relative to Me_4Si. Mass spectra were determined on a Varian MAT 112 S spectrometer by direct inlet methods. The progress of all reactions and column chromatography (silica gel, 230–400 mesh) were monitored by TLC on silica gel (HF_{254}) plates. Dichloromethane–acetone mixtures were used as developing solvents and spots were detected visually or by spraying with 70% sulfuric acid followed by heating.

Products were purified by rapid chromatography.

Treatment of Carminic Acid with Sulfuric Acid. To carminic acid (**1a**) (15 g), dissolved in water (90 mL), was added sulfuric acid (90 mL), and the solution was refluxed for 13 min at which time a brown precipitate formed. After cooling at room temperature, hot water was added and the mixture was cooled. The precipitate (10.2 g) containing **2a** and brown decomposition products was collected, dried, and then allowed to react with methyl iodide (10 mL) and potassium carbonate (4 g) in dimethylformamide (30 mL) at reflux for 2 h. Usual workup and extraction with ethyl acetate afforded a crude product (14.5 g) which after chromatography afforded 6-methyl-4,8,11-trimethoxyanthra[2,3-*b*]furan-5,10-dione (**2b**) (2.25 g, 18% yield from **1a**) as yellow crystals: mp 171–172 °C (from dichloromethane–diisopropyl ether); IR 1720, 1660 cm^{-1}; UV λ_{max} 386, 276, 224 nm (log ϵ 3.87, 4.70, 4.40); ^1H NMR 7.74 (1 H, d, J = 2 Hz), 7.60 (1 H, s), 7.02 (1 H, d, J = 2 Hz), 4.25 (3 H, s), 4.08 (3 H, s), 3.95 (6 H, 2 × s), 2.62 (3 H, s); ^{13}C NMR 18.5 (q, Me at C-6), 52.5 (q, COOMe), 56.3 (q, OMe at C-8), 61.8 and 62.3 (interchangeable q, OMe at C-4 and C-11), 106.2 (2 × d, overlapping, C-3 and C-9), 147.9 (d, C-2), 182.8 and 184.4 (2 × s, quinone carbonyls), 121.1, 123.3, 127.5, 129.0, 129.1, 138.4 (6 × s, C-3a, -4a, -9a, -10a, -5a, and -11a), 130.2, 138.7, 142.8, 149.8, 158.7 (5 × s, C-7, -11, -6, -4, and -8), 167.7 (s, COO); mass spectrum, m/z 410 (M^+).

Anal. Calcd for $C_{22}H_{18}O_8$: C, 64.39; H, 4.42. Found: C 64.4; H, 4.5.

Ozonolysis of 6-Methyl-4,8,11-trimethoxyanthra[2,3-*b*]furan-5,10-dione (2b). Compound **2b** (1 g) dissolved in dichloromethane (900 mL) was ozonized for 5 min at −78 °C. Excess ozone was removed by bubbling argon through the solution for 1 h at −78 °C. Triphenylphosphine (polymer-bound) (800 mg) was added at −78 °C and the cooling bath was then removed. After 30 min usual workup and rapid chromatography afforded 9,10-dioxo-7-formyl-6-hydroxy-1-methyl-3,5,8-trimethoxyanthracene-2-carboxylic acid methyl ester (**4a**) (690 mg): mp 156–157 °C (from dichloromethane–diisopropyl ether); IR 1720, 1660, 1640 cm^{-1}; UV λ_{max} 380, 276 nm (log ϵ 3.60, 4.46); λ_{max} (EtOH containing 1% aqueous KOH) 478, 380, 326, 272 (log ϵ 3.38, 3.84, 4.17, 4.46); ^1H NMR δ 12.48 (1 H, s, 6-OH, exchangeable with D_2O), 10.44 (1 H, s, CHO), 7.56 (1 H, s, 4-H), 4.05 (3 H, s, OMe at C-5 or at C-8), 4.03 (3 H, s, OMe at C-5 or at C-8), 3.95 (6 H, 2 × s, overlapping, OMe at C-7 and COOMe), 2.60 (3 H, s, Me at C-1); ^{13}C NMR δ 18.5 (q, Me at C-1), 52.4 (q, COOMe), 56.3 (q, OMe at C-3), 6.15 and 6.50 (2 × q, interchangeable, OMe at C-5 and C-8), 106.4 (d, C-4), 182.2 and 182.7 (2 × s, quinone carbonyls), 118.1, 127.2, 132.3, 137.8 (4 × s, C-4a, -8a, -9a, and -10a), 119.1, 131.0, 139.3, 144.6, 159.0, 159.8, 161.1, (7 × s, C-1, -2, -3, -5, -6, -7, and -8), 167.3 (s, COO), 195.5 (s, CHO); mass spectrum, m/z 414 (M^+).

Anal. Calcd for $C_{21}H_{18}O_9$: C, 60.87; H, 4.38. Found: C, 60.7; H, 4.5.

Decarbonylation of 7-Formyl-9,10-dioxo-6-hydroxy-1-methyl-3,5,8-trimethoxyanthracene-2-carboxylic Acid Methyl Ester (4a). The compound **4a** (500 mg) was dissolved in degassed toluene (15 mL) and was refluxed under nitrogen in the presence of tris(triphenylphosphine) chlororhodium (500 mg) for 1 h. The mixture was filtered through a pad of Celite and the solvent was removed under pressure. The residue was chromatographed to afford 9,10-dioxo-6-hydroxy-1-methyl-3,5,8-trimethoxyanthracene-2-carboxylic acid methyl ester (**4b**): mp 265–266 °C (from methanol); IR 1720, 1660 cm^{-1}; UV λ_{max} 422, 265 (log ϵ 3.6, 4.5, 4.4); ^1H NMR ($CDCl_3$–DMSO-d_6) δ 7.65 (1 H, s, 4-H), 7.02 (1 H, s, 7-H), 4.00 (6 H, 2 × s, overlapping, OMe at C-5 and C-8), 3.96 (6 H, 2 × s, overlapping, OMe at C-3 and COOMe), 2.65 (3 H, s, Me at C-1); mass spectrum, m/e 386 (M^+).

Anal. Calcd for $C_{20}H_{18}O_8$: C, 62.18; H, 4.69. Found: C, 62.2; H, 4.69.

9,10-Dioxo-1-methyl-3,5,6,8-tetrahydroxyanthracene-2-carboxylic Acid (Kermesic Acid) (1b). The compound **4b** (400 mg) was added to a melt of anhydrous aluminium chloride (37.5 g) and sodium chloride (7.5 g) at 180 °C under argon. After 5

(17) Schwing-Weill, M. J.; Wechsler, S. *Analysis* **1986**, 14, 290.

min the mixture was kept at room temperature for further 1 min and then was quenched in ice (1.5 kg) containing hydrochloric acid (150 mL, 37%). The suspension was warmed to 50 °C for 5 min, cooled, and extracted with ethyl acetate. The crude product (250 mg) was recrystallized from acetic acid as dark red needles: mp >320 °C dec; IR (KBr) 3400, 1675, 1620, 1570 cm^{-1}; UV λ_{max} 276, 312, 350, 466, 498, 538 (log ϵ 4.52, 4.12, 3.72, 3.90, 3.96, 3.76); ^1H NMR (DMSO-d_6) δ 13.7 (s, 1 H, OH, exchangeable with D_2O), 11.4 and 13.0 (2 H, 2 × br s, 2 OH, exchangeable with D_2O), 7.7 (1 H, s, H-4), 6.7 (1 H, s, H-7), 2.70 (3 H, s, CH_3); mass spectrum, m/e 330 (M^+). All these properties were in agreement with the literature.[9] Mixture melting point with a sample obtained according to Cameron et al.[9] was >320 °C.

9,10-Dioxo-3,5,6,8-tetramethoxyanthracene-2-carboxylic Acid Methyl Ester (4c). The trimethoxyanthraquinone **4b** (500 mg) dissolved in diethyl ether–methanol (250 mL) was treated with excess diazomethane. The solvent was removed under reduced pressure and the residue was recrystallized from methanol to afford the tetramethoxyanthraquinone **4c** (480 mg): mp 196–198 °C (from methanol); IR 1720, 1660 cm^{-1}; UV λ_{max} 415, 280, 269 (log ϵ 4.47, 4.45, 3.79); ^1H NMR δ 7.55 (1 H, s, 4-H), 6.81 (1 H, s, 7-H), 4.01 (6 H, 2 × s, overlapping, OMe at C-5, and C-8), 3.96 (9 H, 3 × s, overlapping, OMe at C-3, -6, and COOMe), 2.65 (3 H, s, CH_3); ^{13}C NMR δ 18.6 (q, Me at C-1), 56.3 (q, COOMe), 56.3, 56.3, 57.3 (3 × q, OMe at C-3, -6 and -8), 61.6 (q, OMe at C-5), 103.7 (d, C-7), 106.3 (d, C-4), 183.1 and 183.6 (2 × s, quinone carbonyls), 127.7, 128.0, 137.2 (4 × s, C-4a, -8a, -9a, and -10a), 130.8, 143.5, 157.5, 157.5, 158.6, 158.6 (6 × s, C-1, -2, -3, -5, -6, and -8), 167.7 (s, COO); mass spectrum, m/e 400 (M^+).

Anal. Calcd for $C_{21}H_{20}O_8$: C, 63.0; H, 5.0. Found: C, 63.2; H, 4.9. All these physicochemical properties and mmp show that the compound was identical with that obtained by the reported route.[9,10]

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Registry No. **1a**, 1260-17-9; **1b**, 18499-92-8; **2a**, 110551-54-7; **2b**, 110551-55-8; **4a**, 110551-56-9; **4b**, 110551-57-0; **4c**, 69119-28-4.

Lactone Formation in the Oxidation of Diols with *N*-Iodosuccinimide and Silver Acetate

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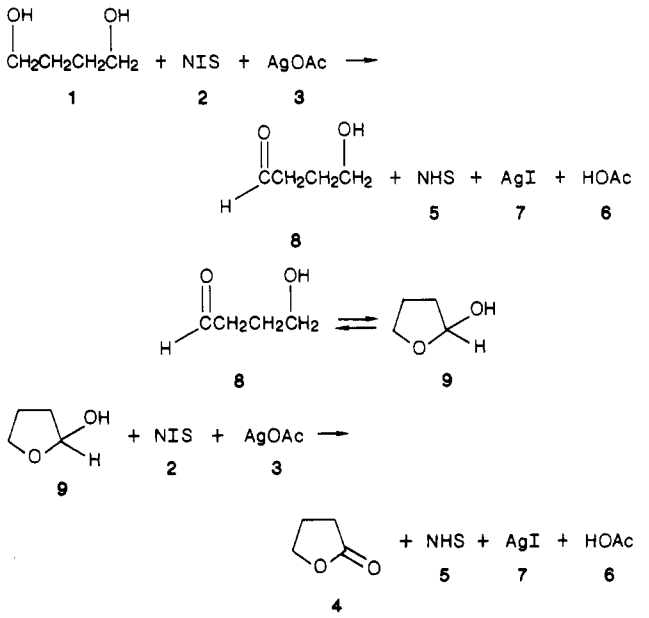
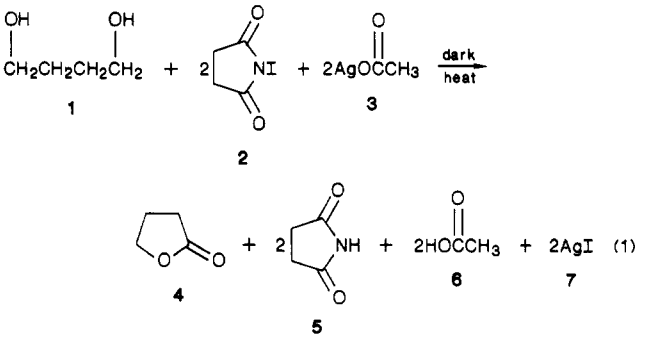
Recently,[1] we found that primary and secondary alcohols were oxidized to aldehydes and ketones when treated in the dark with *N*-iodosuccinimide (NIS), silver acetate, and heat. Tertiary alcohols were unaffected when subjected to these same reaction conditions. In this new study we have oxidized four symmetrical diprimary diols (1,4-butanediol, 1,5-pentanediol, 1,6-hexanediol, and 1,2-benzenedimethanol) and one unsymmetrical primary, tertiary diol (α,α-dimethyl-1,2-benzenedimethanol) with NIS in the presence of silver acetate with heat in the absence of light. Lactones were found to be the products of the diol oxidations. The proposed last chemical step in the formation of the lactones from the primary diols is the oxidation of cyclic hemiacetals with NIS and silver acetate, a new reaction for *N*-iodosuccinimide and hemiacetals. Under light-catalyzed radical conditions the hypoiodite of the cyclic hemiacetal **9** undergoes carbon–carbon bond cleavage to produce γ-iodopropyl formate.[2] The pathway of the decomposition of the cyclic hemiacetal hypoiodites depends on whether it is irradiated or heated with silver acetate in the absence of light. Lactone preparation[3] from diols has been reported by previous authors using a variety of oxidizing agents although none has formed hypoiodites of hemiacetals in their procedures.

Scheme I



The formation of the lactone products can be illustrated by a discussion of the oxidation of 1,4-butanediol (**1**) with NIS (**2**) and silver acetate (**3**). When the diol **1** is mixed with the solvent benzene, **2**, and **3** and heated, the products found on the gas chromatograph are γ-butyrolactone (**4**) (80–85%) and acetic acid (**6**) (85–89%) as shown in eq 1.



The stoichiometry in eq 1 also is supported by good yields of succinimide (**5**) and silver iodide (**7**). The formation of the γ-butyrolactone in good yield indicates a probable nonradical pathway for the NIS/silver acetate oxidation of diols to lactones.

We believe that the diol-to-lactone conversion occurs in two steps as shown in Scheme I. Here 1,4-butanediol (**1**) is first oxidized to the hydroxy aldehyde **8** which is in

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