A mixture of the phenol **16** (132 mg) and sodium bicarbonate (100 mg) in MeOH (6 mL), THF (3 mL), and trimethyl orthoformate (3 mL) was stirred at 0 °C. Thallium(III) nitrate trihydrate (215 mg) was added and the mixture stirred at 0 °C for 0.5 h. The reaction mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed successively with water (3 × 20 mL) and brine (20 mL) and dried, and the solvent was evaporated. Flash column chromatography of the residue (15% EtOAc in hexane) afforded the *title dienone* as a colorless syrup (128 mg, 88%): $[\alpha]_D$ −43.0° (*c* 1.12); IR (film) 2880, 2840, 2775, 1672, 1645, 1620, 1450, 1380, 1371, 1290, 1160, 1090, 1070, 1005, 971 cm^{-1}; ^1H NMR δ 6.77 (d, 1 H, H7′, *J* = 10.2 Hz), 6.40 (d, 1 H, H6′, *J* = 10.2 Hz), 4.05 (q, 1 H, H5, *J* = 6.3 Hz), 3.22 (s, 6 H, OCH_3), 2.29–2.80 (m, 4 H, H1′,4′), 2.00 (m, 1 H, H3′), 1.82 (m, 1 H, H3′), 1.41 (s, 3 H, $C2CH_3$), 1.33 (s, 3 H, $C2CH_3$), 1.23 (d, 3 H, $C5CH_3$, *J* = 6.3 Hz).

Anal. (accurate mass) calcd for $C_{17}H_{24}O_5$: 308.1624. Found: 308.1628.

(4*R*,5*R*)-(−)-1′,11′-Dimethoxy-6′-hydroxy-2,2,5-trimethyl-9′,10′-dihydrospiro[1,3-dioxolane-4,8′(7′*H*)-naphthacene]-5′,12′-dione (26). A solution of diisopropylamine (173 μL) in THF (5 mL) under an argon atmosphere was stirred at 0 °C with *n*-BuLi (780 μL, 1.58 M) for 5 min. The solution was cooled to −78 °C and a solution of the phthalide **25** (400 mg) in THF (15 mL) added dropwise over 5 min. After the mixture was stirred for 0.25 h at −78 °C a solution of the dienone **17** (115 mg) in THF (3 mL) was added. The vessel was removed from the cold bath and the reaction mixture stirred until ambient temperature (18 °C) was attained (0.5 h). The reaction mixture was poured into water (70 mL) and extracted with EtOAc (2 × 20 mL), and the combined extracts were washed successively with water (20 mL) and brine (20 mL) and dried, and the solvent evaporated. The residue was dissolved in CH_2Cl_2 (1 mL), Et_2O added (5 mL), and the solution allowed to stand until precipitation of unreacted **25** was complete. The solid material was removed by filtration, the filtrant washed well with Et_2O, and the combined filtrate concentrated and flash column chromatographed (20% EtOAc in petrol) to give unreacted **17** (93 mg, 81%) and the *title compound* (19 mg, 12%). Crystallization from MeOH afforded orange plates: mp 236–238 °C (sweats at 230 °C); $[\alpha]_D$ −62.0° (*c* 0.18, 1:1 MeOH/$CHCl_3$); IR 3520, 2990, 2945, 2850, 1779, 1725, 1670, 1630, 1588, 1450, 1409, 1385, 1368, 1278, 1166, 1121, 1098, 1085, 1070, 1020, 1005, 989, 948, 875 cm^{-1}; ^1H NMR δ 13.34 (s, 1 H, OH), 7.90 (dd, 1 H, H4′, *J* = 8.2 Hz, *J* = 0.8 Hz), 7.67 (dd, 1 H, H3′, *J* = 8.4 Hz, *J* = 8.2 Hz), 7.32 (dd, 1 H, H2′, *J* = 8.4 Hz, *J* = 0.8 Hz), 4.03 (s, 3 H, C1′OCH_3), 3.93 (s, 3 H, C11′OCH_3), 3.20 (ddd, 1 H, H10′, *J* = 17.9 Hz, *J* = 4.2 Hz, *J* = 1.4 Hz), 2.65–2.97 (m, 3 H, H7′,10′), 2.04 (m, 1 H, H9′), 1.99 (m, 1 H, H9′), 1.48 (s, 3 H, $C2CH_3$), 1.41 (s, 3 H, $C2CH_3$), 1.30 (d, 3 H, $C5CH_3$, *J* = 6.4 Hz).

Anal. (accurate mass) calcd for $C_{25}H_{26}O_7$: 438.1679. Found: 438.1673.

(8*R*,1′*R*)-(−)-8-(1′-Hydroxyethyl)-1-methoxy-6,8,11-trihydroxy-7,8,9,10-tetrahydro-5,12-naphthacenedione [(9*R*,13*R*)-7-Deoxy-13-dihydrodaunomycinone] (28). A solution of the ketal **26** (30 mg) in dry CH_2Cl_2 (20 mL) was stirred at −42 °C under an argon atmosphere. Boron trichloride (1.02 M in CH_2Cl_2, 805 μL, 12 equiv) was added and stirring maintained at −42 °C for 2 h. MeOH (2 mL) was added and the mixture stirred for 3 min at −42 °C and then poured into water (50 mL) containing saturated sodium bicarbonate solution (1 mL). The aqueous phase was extracted with $CHCl_3$ (2 × 20 mL), the combined organic phase washed successively with water (2 × 20 mL) and brine (30 mL) and dried, and the solvent evaporated. Column chromatography of the residue (acid washed silica; 10% MeOH in CH_2Cl_2) afforded diol **27** (8 mg, 29%) and the *title diol* (17.3 mg, 66%). Recrystallization from a mixture of CH_2Cl_2 and hexane gave red prisms: mp 245–247 °C; $[\alpha]_D$ −61° (*c* 0.14, 1:1 MeOH/$CHCl_3$); IR 3580, 2920, 1615, 1587, 1580, 1450, 1408, 1284, 1268, 1067, 988 cm^{-1}; ^1H NMR δ (Me_2SO-d_6) 13.89 (s, 1 H, C11OH), 13.38 (s, 1 H, C6OH), 7.82–7.89 (m, 2 H, H3,4), 7.58 (dd, 1 H, H2, *J* = 5.9 Hz, *J* = 3.7 Hz), 4.68 (d, 1 H, C1′OH, *J* = 5.2 Hz), 4.28 (s, 1 H, C8OH), 3.96 (s, 3 H, OCH_3), 3.48 (dq, 1 H, H1′, *J* = 6.3 Hz, *J* = 5.2 Hz), 2.51–2.79 (m, 4 H, H7,10), 1.69 (m, 2 H, H9), 1.17 (d, 3 H, H2′, *J* = 6.3 Hz).

Anal. (accurate mass) Calcd for $C_{21}H_{20}O_7$: 384.1209. Found: 384.1248.

Registry No. (−)-**6**, 100939-58-0; (−)-**7**, 90744-27-7; (−)-**8**, 100939-59-1; (+)-**10**, 100939-60-4; (+)-**11**, 100939-61-5; (−)-**13**, 100992-84-5; (−)-**15**, 101052-85-1; (−)-**16**, 100992-85-6; (−)-**17**, 100939-63-7; **19**, 81504-96-3; **21**, 65131-09-1; (−)-**22**, 95496-08-5; (−)-**23**, 100939-62-6; (−)-**24**, 40940-87-2; **25**, 74724-81-5; (−)-**26**, 100939-64-8; (−)-**27**, 100939-65-9; (−)-**28**, 100992-86-7.

Oxidative Cleavage of 1,2-Diols to Carboxylic Acids by Hydrogen Peroxide

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While a number of oxidants have been described in combination with a metal catalyst for oxidative cleavage of 1,2-diols to carboxylic acids,[1] almost no attention has been devoted to the employment of hydrogen peroxide for this reaction, and the few results that have appeared so far[2] are fragmentary and of little preparative value.

We now report that aqueous hydrogen peroxide in conjunction with catalytic amounts of tungstate and phosphate (or arsenate) ions,[3] under acidic conditions, provides a synthetically useful procedure for the highly selective oxidative cleavage of water-soluble 1,2-diols to carboxylic acids. The method, which utilizes a rather inexpensive catalyst and a cheap nonpolluting oxidant, is particularly suitable when large-scale reactions are considered. Primary–secondary and secondary–secondary as well as secondary–tertiary 1,2-diols (open chain and cyclic) can satisfactorily be oxidized.

The reaction is conveniently conducted by simply stirring at 90 °C an acidic (pH 2) aqueous solution containing the diol, hydrogen peroxide (in a 10% molar excess over the stoichiometric amount required[4]), and the catalyst until the charged oxidant has almost completely disappeared (usually 5 h). A molar ratio for diol/WO_4^{2-}/PO_4^{3-}(AsO_4^{3-}) of 50:2:1 is commonly used. Conventional workup of the reaction mixture affords monobasic, dibasic, and keto acids of satisfactory purity in good to excellent yields (Table I).

The efficiency of the oxidation is dependent upon the pH of the reaction solution. The best results were obtained at pH 2. An increase in pH considerably reduces the activity of the catalytic system. The use of tungstate ions alone as well as replacement of tungsten by molybdenum in the above system also leads to a significant decrease of the yield. It should be pointed out that in the absence of the catalyst oxidation proceeds to only a negligible extent.

Some aspects of the present method are worth mentioning. The reaction appears to be relatively insensitive to geometric constraints. Indeed, *cis*- and *trans*-1,2-cyclohexanediol were both oxidized to adipic acid at nearly similar rates. By contrast, the presence of electron-with-

(1) Sheldon, R. A.; Kochi, J. K. "Metal-Catalyzed Oxidation of Organic Compounds"; Academic Press: New York, 1981.

(2) (a) Choe, S.; Tsutsumi, S. *Nippon Kagaku Zasshi* **1960**, *81*, 785; *Chem. Abstr.* **1962**, *56*, 9987*b*. (b) Trost, B. M.; Masuyama, Y. *Isr. J. Chem.* **1984**, *24*, 134.

(3) Such a catalytic association has successfully been applied to the epoxidation of unactivated olefins by H_2O_2 under phase-transfer conditions: Venturello, C.; Alneri, E.; Ricci, M. *J. Org. Chem.* **1983**, *48*, 3831.

(4) Oxidation of secondary–tertiary and secondary–secondary 1,2-diols to acids obeys a 1:2 and 1:3 stoichiometry of substrate to H_2O_2, respectively. With primary–secondary 1,2-diols, a 1:4 molar ratio is required as the coproduced formic acid is further oxidized to carbon dioxide under the reaction conditions.

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Table I. Oxidative Cleavage of 1,2-Diols to Carboxylic Acids with H_2O_2 Catalyzed by the WO_4^{2-}/PO_4^{3-} Association[a]

entry	substrate	product	yield,[b] %	purity,[c] %
1	*trans*-1,2-cyclopentanediol	glutaric acid	96	>98
2	*cis*-1,2-cyclohexanediol	adipic acid	92	>98
3	*trans*-1,2-cyclohexanediol	adipic acid	94	>98
4	*cis*- + *trans*-1,2-cyclohexanediol[d]	adipic acid	94	>98
5	*trans*-1,2-cycloheptanediol	pimelic acid	87	93[e]
6	*trans*-1-methyl-1,2-cyclohexanediol	6-oxoheptanoic acid	93	96[f]
7	1-phenyl-1,2-ethanediol	benzoic acid	87	>98
8	1,2-hexanediol	valeric acid	92	96[g]
9	2,3-butanediol	acetic acid	87[h]	
10	1,2-propanediol[i]	acetic acid	90[h]	
11	3-methyl-2,3-pentanediol	acetic acid 2-butanone	90[h,j] 64[h]	

[a] Reaction conditions: substrate (50 mmol); 40% w/v aqueous H_2O_2 (100, 150, or 200 mmol + 10% molar excess, depending on the substrate;[4] catalyst, $Na_2WO_4 \cdot 2H_2O$ (2 mmol) and 40% w/v H_3PO_4 (1 mmol); pH 2 (adjusted by concentrated HCl); 90 °C; 5 h. [b] Yield (based on substrate) of isolated product, unless otherwise stated. [c] Determined by GLC (column B, see Experimental Section) after methylation with CH_2N_2. [d] Arsenate (as $Na_2HAsO_4 \cdot 7H_2O$) instead of phosphate ions were used. [e] 5.3% contamination by adipic acid. [f] 1.4% contamination by glutaric acid and less than 0.5% by 5-oxohexanoic acid. [g] 1.2% contamination by butyric acid. The starting diol (1.6%) was also present. [h] Yield determined by GLC on the reaction solution (external standard; column A, see Experimental Section). [i] Reaction time: 9 h. [j] About 20% of the intermediate α-ketol was still present. The different yield of acetic acid and 2-butanone is ascribable partly to additional formation of acetic acid by oxidative cleavage of 2-butanone and partly to peroxidation of the latter. Control experiments confirmed the occurrence of these reactions. H_2O_2 consumption for them would account for the incomplete conversion of the α-ketol.

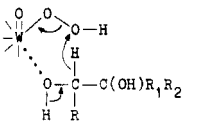
drawing groups adjacent or attached to the carbon atoms carrying the hydroxy groups dramatically reduces the reactivity of the substrate. Thus, oxidation of 3-chloro-1,2-propanediol and tartaric acid gave only poor to negligible yields of chloroacetic (24%) and oxalic (4%) acid, respectively. Most of the starting diol was recovered unchanged. Finally, the rate of diol oxidation is not affected by radical scavengers (e.g., 2,6-di-*tert*-butyl-4-methylphenol).

The reaction appears to proceed via an initial C–H bond fission of the secondary carbinol of the 1,2-diol unit to form the related α-hydroxy ketone (α-ketol), followed by oxidative cleavage of the latter to yield a carboxylic acid and an aldehyde or a ketone, with acyclic compounds, and an aldehydic or keto acid, with cyclic compounds. The aldehyde or semialdehyde are further oxidized to acid.

The intermediacy of the α-ketol is supported by the fact that, in all cases examined, it has been identified in the reaction mixture at low conversion and, when prepared apart, it could easily be converted to the desired acid under the reaction conditions.

It should be noted that in the oxidation of secondary α-hydroxy ketones no α-diketones could be detected.[5] On the contrary, acetaldehyde was found together with acetic acid in the oxidation of acetoin, and 7-oxoheptanoic acid (pimelic semialdehyde) was identified among the oxidation products of 2-hydroxycycloheptanone. Likewise, formaldehyde was found in the oxidation of primary α-hydroxy ketones, while in no case could the α-keto aldehyde be detected. These findings, along with the observed reactivity of tertiary α-hydroxy ketones, suggest that direct C–C bond cleavage between the carbonyl and the carbinol carbon atoms is a general feature of the oxidation of α-ketols to acids by hydrogen peroxide.

The α-ketol presumably arises from the decomposition of an adduct such as **1**, formed from the interaction of the diol with an anionic tungsten peroxo species present in the acidic solution.[6] Involvement of complex **1** rather than the related ester **2** seems more consistent with the observation that, in our system, 1,2-dimethoxypropane is oxidized to acetic acid to an appreciable extent (9% after 9 h at 90 °C).[7,8] This suggests that ester formation between



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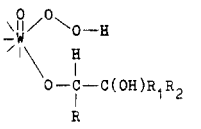
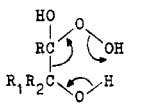


2

diol and the metal peroxo species present in solution probably does not play an important role. A mechanism similar to the suggested one has been proposed for oxidation of monohydric alcohols with hydrogen peroxide catalyzed by oxodiperoxo(picolinate)tungstate(VI).[9]

Unlike their formation, oxidative cleavage of α-ketols does not appear to be significantly affected by the presence of the metal catalyst under the reaction conditions. Indeed, acidic aqueous hydrogen peroxide alone at 90 °C under N_2 has been found to be an effective oxidant for the cleavage of these substrates.[10] A plausible pathway for α-ketol to acid oxidation would involve formation of adduct **3**[11] by nucleophilic attack of hydrogen peroxide upon the protonated carbonyl group of the α-ketol. Concerted or stepwise fragmentation of **3** would lead to the above-mentioned cleavage products.[12]



3

As can be seen from Table I (entries 5, 6, 8), in some cases the expected acid is accompanied by small amounts of the overoxidation product of one less carbon. Moreover, in the oxidation of 1-methyl-1,2-cyclohexanediol (entry 6), glutaric acid is also formed as byproduct. The formation

(5) Under the reaction conditions, 1,2-cyclohexanedione gave a complex mixture containing only small amounts of adipic acid.

(6) A peroxo tungstophosphate has recently been isolated from an aqueous solution of H_2O_2, H_2WO_4, and H_3PO_4 in the presence of a quaternary ammonium salt: Venturello, C.; D'Aloisio, R.; Bart, J. C. J.; Ricci, M. *J. Mol. Catal.* **1985**, *32*, 107.

(7) Under the reaction conditions, no hydrolysis of 1,2-dimethoxypropane took place.

(8) Oxidation of secondary alcohols by oxides of Cr(VI) or V(V), which is well-known to proceed via the ester mechanism, is about 10^4 faster than oxidation of the corresponding methyl ethers: (a) Brownell, R.; Leo, A.; Chang, Y. W.; Westeimer, F. H. *J. Am. Chem. Soc.* **1960**, *82*, 406. (b) Roček, J.; Aylward, D. E. *Ibid.* **1975**, *97*, 5452.

(9) Jacobson, S. E.; Muccigrosso, D. A.; Mares, F. *J. Org. Chem.* **1979**, *44*, 921.

(10) In a typical example, oxidation of phenacyl alcohol (0.68 g, 5 mmol) with 11% w/v acidic (pH 2, HCl) aqueous H_2O_2 (5.1 mL, 16.5 mmol) at 90 °C for 1 h gave 0.52 g (85% yield) of benzoic acid.

(11) Intermediacy of the oxy anion of **3** has been proposed for the cleavage of α-ketols by alkaline H_2O_2: Ogata, Y.; Sawaki, Y.; Shiroyama, M. *J. Org. Chem.* **1977**, *42*, 4061.

(12) A radical fragmentation of **3** can be ruled out on the basis of the absence of byproducts of hydrogen abstraction from alkyl chain.

of the lower carboxylic acids has not been clarified. However, it has been proved that these byproducts result from oxidation of the intermediate α-ketol or, in the case of glutaric acid, from oxidation of 6-oxoheptanoic acid. In the former case, the presence of the metal catalyst appears to be essential, while in the latter it is not necessary.[13]

In the oxidation of primary–secondary 1,2-diols at low conversion, besides the α-ketol the corresponding aldehyde of one less carbon was also found to be present in a small amount (2–5%).[14] It likely arises from cleavage of the α-hydroxy aldehyde formed by C–H bond fission of the less reactive[9] primary carbinol of the starting diol.[15] In no case could the α-hydroxy aldehyde be detected. Under the reaction conditions, however, α-hydroxyphenylacetaldehyde gave benzaldehyde easily.

In our system, aldehydes are oxidized to the respective carboxylic acids more slowly than the corresponding α-ketols. This makes the alternative route to acids via aldehydes occurring with primary–secondary 1,2-diols scarcely operative.

The present method has also been applied to water-insoluble 1,2-diols by the use of a phase-transfer agent [e.g., methyltrioctylammonium chloride (0.4 mol/mol of tungstate); tetrachloroethylene as solvent]. Under these conditions, 1,2-octanediol gave 78% yield of heptanoic acid.

Experimental Section

IR and ^{1}H NMR spectra were recorded on a Perkin-Elmer spectrophotometer and a Bruker WH-90 spectrometer. Mass spectra were recorded on a Varian MAT 112 S instrument. GLC analyses were performed on a Varian 3700 instrument, using a glass column (2 m × 2 mm i.d.) packed with one of the following: A, 5% FFAP on 20-40 Fluoropak 80 (65–180 °C at 10 °C/min); B, 5% UCC-W 982 on 60-80 Chromosorb G (75–250 °C at 10 °C/min). TLC of carboxylic acids were performed on Merck precoated silica gel 60F-254 plates, and spots were detected by spraying with a bromophenol blue solution. Products were identified by combustion analysis and spectral data (when isolated) or by GLC analysis (column A) in comparison with authentic samples. Overoxidation byproducts (accompanying the main product; Table I, entries 5, 6, 8) were identified and determined by GLC–MS and GLC analysis (column B), respectively, of the crude acid after esterification with diazomethane.

Materials. Sodium tungstate dihydrate (Carlo Erba), disodium hydrogen arsenate heptahydrate (Merck), and hydrogen peroxide (40% w/v, Fluka) were used as purchased. Phosphoric acid (85%, Carlo Erba) was used after dilution to 40% w/v. 1,2-Propanediol, 1,2-cyclohexanediol (cis + trans), 1-phenyl-1,2-ethanediol, 2,3-butanediol, 3-chloro-1,2-propanediol, and tartaric acid as well as acetol and acetoin were obtained from Aldrich and distilled or recrystallized before use, as appropriate. Noncommercial 1,2-diols[16] and α-ketols[17] used in this work, 1,2-dimethoxypropane,[18] mandelic aldehyde,[19] and samples for comparison of 7-oxoheptanoic[20] and 5-oxohexanoic[21] acid were prepared according to the literature procedures.

6-Oxoheptanoic Acid. A 100-mL round-bottomed flask equipped with a magnetic stirring bar, thermometer, and reflux condenser was charged with 40% w/v aqueous H_2O_2 (9.35 mL, 110 mmol), 40% w/v H_3PO_4 (0.25 mL, 1 mmol), $Na_2WO_4 \cdot 2H_2O$ (0.66 g, 2 mmol), and *trans*-1-methyl-1,2-cyclohexanediol (6.5 g, 50 mmol). The resultant solution was adjusted to pH 2 by concentrated HCl and then stirred at 90 °C for 5 h. After cooling and the addition of Na_2SO_3 until the KI–starch test was negative, the solution was evaporated in vacuo to dryness, the residue eluted on a column (50 cm × 45 mm) of silica gel (200 g, 70–230 mesh; Et_2O as the eluant), and the fraction with $R_f = 0.64$ was collected. Removal of the solvent gave 6.70 g (46.5 mmol, 93%) of 6-oxoheptanoic acid (96.4% pure by GLC of methyl ester) as a low-melting solid, mp 32–33 °C (C_6H_6/*n*-hexane) (lit.[22] mp 33–34 °C).

Glutaric, pimelic, benzoic, and valeric acids were similarly prepared, except that for the former two $CHCl_3/CH_3COOH$ (9/1) was used as the eluant (R_f = 0.47 and 0.70, respectively) and the isolated product was additionally kept suspended in *n*-hexane with stirring (30 min) to remove acetic acid, then filtered, and dried, whereas for the remaining acids the reaction mixture was extracted with Et_2O (4 × 20 mL), the combined extracts were evaporated, and the residue was chromatographed on a column (1/1 Et_2O/*n*-hexane; R_f = 0.54 and 0.67, respectively).

Adipic Acid. *trans*-1,2-Cyclohexanediol (5.8 g, 50 mmol) was treated as above, except 14 mL of 40% w/v aqueous H_2O_2 (165 mmol) was used. At the end, the solution was stored in a refrigerator (5 °C) overnight. The formed crystals were filtered, washed with ice-cold water (2 mL), and dried to give 6.65 g (45.5 mmol, 91%) of adipic acid (98.7% pure by GLC of methyl ester), mp 153–154 °C (acetone) (lit.[23] mp 154–154.5 °C). After Na_2SO_3 was added until the KI–starch test was negative, the mother liquor was made basic (pH 8) with 10% NaOH and then evaporated in vacuo to dryness. The residue was triturated with boiling acetone with stirring (40 min), filtered, and dissolved in water and the resultant solution acidified with concentrated HCl. Concentration of the solution on a rotary evaporator followed by cooling (5 °C) gave an additional 0.21 g of adipic acid of 96.5% purity.

The same procedure was used starting from *cis*-1,2-cyclohexanediol.

Notice: For 1-mol scale reactions a somewhat modified procedure was followed. Due to the exothermic reaction, the diol was added gradually, with stirring, to the acidic (pH 2) aqueous solution of H_2O_2 and of the catalyst heated to 90 °C, taking care of keeping the temperature of the mixture around this value. In the workup, column chromatography was avoided. A sufficiently pure product could be obtained in 80–85% yield simply by distillation or crystallization of the residue from evaporation of the reaction solution or its ethereal extract. Furthermore, in order to prevent a little decomposition of the oxidant during dissolution of $Na_2WO_4 \cdot 2H_2O$, the salt was added in portions, with stirring, to the H_2O_2–H_3PO_4 solution.

Identification of Reaction Intermediates. Intermediate aldehydes and α-ketols as well as cleavage products of the latter (e.g., pimelic semialdehyde) were identified as follows. 1,2-Diols or α-ketols were oxidized according to the standard procedure, with the reaction being stopped (by rapid cooling) after 1 h (2 h in the case of 1,2-propanediol) or 30 min, respectively. The aqueous solution was salted out (NaCl) and extracted with Et_2O (4 × 10 mL), and the ethereal extract, after treatment with diazomethane, was analyzed by GLC–MS coupling (column B). In the case of highly water-soluble products (e.g., acetaldehyde), identification was achieved by GLC analysis (column A) of the reaction solution, after cautious reduction of excess H_2O_2 by Na_2SO_3, in comparison with authentic samples.

Registry No. H_2O_2, 7722-84-1; Na_2WO_4, 13472-45-2; H_3PO_4, 7664-38-2; Na_2HAsO_4, 7778-43-0; *trans*-1,2-cyclopentanediol, 5057-99-8; *cis*-1,2-cyclohexanediol, 1792-81-0; *trans*-1,2-cyclohexanediol, 1460-57-7; *trans*-1,2-cycloheptanediol, 13553-19-0;

(13) 2-Butanone (entry 11, Table I) showed a behavior similar to that of 6-oxoheptanoic acid, giving acetic acid even in the absence of the metal catalyst.

(14) Oxidation of 1-phenyl-1,2-ethanediol at 30% conversion of H_2O_2 (1 h; 90 °C) gave 25.4% of phenacyl alcohol, 2.2% of benzaldehyde, and 35.2% of benzoic acid. Of the starting diol, 33.8% was recovered. Products were determined by GLC analysis using an internal standard (for details, see Epxerimental Section).

(15) An alternative pathway to aldehyde involving direct C–C bond cleavage of the starting diol seems very unlikely, since pinacol was found to give only a trace amount of acetone. On the other hand, 2-phenyl-1,2-propanediol gave acetophenone in 20% yield. This result offers further support to the mechanism via α-hydroxy aldehyde.

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(18) Brettle, R.; Khan, M. A.; Rowbottom, J. D. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2927.

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The Half-Wave Potentials of 8-Substituted 5-Deazaflavins. Polarographic Determination of the Dissociation Constants of Some 8-Substituted 5-Deazaflavosemiquinones

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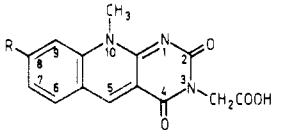
5-Deazaflavin has been applied as a photocatalyst in the reduction of a wide variety of biological redox systems.[1,2] Its application, however, has serious drawbacks since continuous UV irradiation is required to drive the process and the energy of the required wavelength (300–400 nm) destroys the protein with time. To avoid photodestruction of the protein we have synthesized a number of 5-deazaflavins **1a–g**, which feature a chromophoric group at



1	R
a	Cl
b	NO_2
c	p-NO_2-C_6H_4
d	$(CH_3)_2N$
e	NH_2
f	p-NH_2-C_6H_4
g	p-$(CH_3)_2N$-C_6H_4-N=N

the C(8) position of the 5-deazaisoalloxazine skeleton, causing the absorption maximum to undergo a red shift, and a carboxymethyl group at the N(3) position increasing the solubility of 5-deazaflavins in aqueous media, in which photoreduction of redox enzymes is carried out.[3,4]

Because 8-hydroxy-5-deazaflavin has been found in nature as part of F-420, i.e., the coenzyme of methane-producing bacteria,[5,6] several 8-substituted 5-deazaflavins have been synthesized as model compounds. Their UV spectroscopic data and redox potentials have been examined and found to be very sensitive to the electronic influence of the substituents.[7,8]

Table I. Comparison of Half-Wave Potentials of 5-Deazaflavins 1b and 1e at Different pH Values (in mV vs. NHE)

	pH		
compd	1.90	7.00	9.00
1b	160	−165	−260
	−435	−835	−840
	−710	−1005	−1070
1e	−715	−1000	−1060

Table II. Half-Wave Potentials ($E_{1/2}$) at Different pH Values, Standard Potentials (E_0), and pK_1 and pK_2 Values of 5-Deazaflavins

compd	pH	$E_{1/2}$,[a] mV vs. NHE	E_0,[a] mV vs. NHE	pK_1	pK_2
1a	1.90	−510	−395	1.0 ± 0.2	5.9 ± 0.2
	7.00	−740			
	9.00	−745			
1d	1.90	−775	−615	2.7 ± 0.3	9.3 ± 0.8
	7.00	−1030			
	9.00	−1135			
1e	1.90	−715	−581	2.2 ± 0.2	8.2 ± 0.3
	7.00	−1000			
	9.00	−1060			
1f	1.34	−635	−513	2.0 ± 0.2	7.5 ± 0.2
	6.22	−880			
	7.00	−915			
	8.14	−950			
	9.65	−960			

[a] ±10 mV.

The present report is concerned with the redox properties of a new set of 8-substituted 5-deazaflavins, i.e., 8-chloro- (**1a**), 8-nitro- (**1b**), 8-*p*-(nitrophenyl)- (**1c**), 8-(dimethylamino)- (**1d**), 8-amino- (**1e**), 8-(*p*-aminophenyl)- (**1f**), and 8-[(*p*-(dimethylamino)phenyl)azo]-5-deazaflavin (**1g**). The mechanism proposed[2,9,10] for the photoreduction of enzymes with 5-deazaflavin acting as a photocatalyst, implies the formation of the 5-deazaflavosemiquinone radical. Because of the high reactivity and very low redox potential of the radical, it is possible to reduce a wide variety of enzymes with catalytic quantities of 5-deazaflavin. To investigate the effect of the substituent at the C(8) position on the reducing power of the radical, we wanted to determine the half-wave potentials ($E_{1/2}$) of our 5-deazaflavins by differential pulse polarography.

In addition, the substituent effects on the dissociation constants of the 5-deazaflavosemiquinones have been determined from these polarographic data.

Results and Discussion

Determination of $E_{1/2}$ for the radical formation step of 5-deazaflavins containing a reducible group at C(8) as in **1b,c,g** is not possible because reduction of the group at C(8) takes place at a less negative potential than reduction of the 5-deazaisoalloxazine skeleton. This is exemplified by comparison of the electrochemical reduction of **1b** and **1e** at different pH values (Table I). As can be seen from Table I, the polarogram of **1b** shows two peaks at less negative potential corresponding to the reduction of the nitro group in two steps, followed by a peak at the same potential as obtained for **1e**. The same reduction sequence

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