prepared in a dry, bottle-cap type pressure tube under argon. Anhydrous $ZnBr_2$ (0.356 g, 1.6 mmol) was then added, the reaction vessel capped, and the slurry heated to 90 °C for 3 h. The contents of the flask were then transferred to a small, round-bottomed flask via a double-ended needle and distilled, bp 110 °C (0.4 mm).

Reaction of (Silylamino)phosphine 3 with Propylene Sulfide. **3** (3.03 g, 25.6 mmol) was added to propylene sulfide (2.0 g, 27.0 mmol) in a chilled (0 °C) sublimation device under argon. The reaction vessel was then allowed to stir at room temperature for 24 h. The excess propylene sulfide was then removed in vacuo and the product sublimed (90 °C (0.1 mm)) to produce a quantitative yield of a low-melting (25–30 °C) white solid.

Hydrolysis of Dimethyl[2-(trimethylsiloxy)cyclohexyl]-phosphine (Trimethylsilyl)imide (5). A solution of the phosphine imide (30 mmol) in acetic acid/H_2O/THF (10 mL/10 mL /10 mL) was allowed to stir at room temperature for 2–3 h and worked up by removing the solvent in vacuo and purifying the β-hydroxy phosphine oxide by flash chromatography (silica gel, 10% MeOH/CH_2Cl_2). The yield of white solid thus obtained was quantitative. The material could be recrystallized from ethyl acetate to yield plates with mp 155–156 °C.

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Registry No. **3**, 63744-11-6; **4**, 89618-64-4; **5**, 89618-65-5; **6**, 89618-66-6; **7a**, 89618-67-7; **7b**, 89618-68-8; **9**, 68437-96-7; **10**, 89618-69-9; **11**, 63744-10-5; $ZnBr_2$, 7699-45-8; *trans*-1-(dimethylphosphoryl)-2-hydroxy cyclohexane, 89618-70-2; propene, 115-07-1; methylthiirane, 1072-43-1; methyloxirane, 75-56-9; 7-oxabicyclo[4.1.0]heptane, 286-20-4; phenyloxirane, 96-09-3; 2-methyl-2-phenyloxirane, 2085-88-3.

Electrochemical Procedure for a Practical Preparation of Piperonal from Isosafrole

Sigeru Torii,* Kenji Uneyama, and Kyoji Ueda

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama 700, Japan

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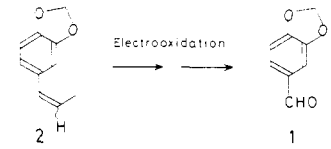
Piperonal (3,4-(methylenedioxy)benzaldehyde) (**1**), an important fragrance used as a soap additive and a synthetic precursor of Dopa, has been industrially prepared by ozonolysis[1] or chromic acid oxidation[2] of isosafrole **2**. Because of the environmental pollution associated with chromium species and the requirement of a large quantity of electricity and a carefully controlled reaction temperature (0–5 °C) for ozonolysis, these demerits have prompted us to develop a nonpolluting and more economical process. Recently, several attempts employing ruthenium tetroxide oxidation combined with m-periodate[3] and air-oxidation under γ-ray irradiation[4] have appeared.

On the other hand, an electrochemical oxidation would be a promising method for a piperonal synthesis from isosafrole because an electrooxidative bond cleavage of carbon–carbon double bonds is possible in principle. For example, an electrochemical conversion of cyclic enol acetates to keto esters in a MeOH–AcOH–$LiClO_4$ system has been achieved in satisfactory yield.[5] However, the direct bond cleavage method leads in some cases to overoxidation of the product aldehyde to give the corresponding carboxylic acid, as observed in the conversion of methyl eugenol to 3,4-dimethoxybenzoic acid.[6] A plausible reaction pathway for the electrochemical carbon–carbon bond cleavage would be initial oxygenation of the double bond to the corresponding glycol or a derivative followed by C–C bond cleavage. We describe a two-step electrochemical procedure that leads to a highly selective preparation of **1** from **2** via **3a**.



Epoxidation of olefins is efficiently achieved by the halide ion mediated electrochemical oxidation in which bromide ion is found to be the most useful.[7] Thus, **2** was subjected to the electrooxidation in MeCN–H_2O (7:2) containing 1.5–2.0 equiv of sodium bromide at room temperature. Platinum foils were employed as electrodes, and a constant current was passed (20 mA, 2.83 F/mol) in an undivided cell. The products were epoxide **4** (71%) and glycol **3a** (23%) after chromatography. Unlike the electrochemical epoxidation of isoprenoids, where the use of 0.1–1.0 equiv of sodium bromide was suitable to suppress the formation of the corresponding dibromide,[7] the use of more than 1 equiv of sodium bromide was required to provide **3a** and **4** in good yield. Dibromide **3c** was found to be spontaneously hydrolyzed to give **3b**, which collapsed to the epoxide **4** under the electrolysis conditions. Epoxide **4** is unstable under the reaction conditions and suffers partial hydrolysis resulting in the formation of **3a**.[8] After electrolysis, 1% aqueous sulfuric acid was added to the reaction mixture, which was stirred for 1 h to give **3a** (98%) as a diastereomeric mixture (25:75 by NMR). The glycol **3a** was subjected to acid-catalyzed dehydration (*p*-TsOH–benzene), affording ketone **5** (84%), which is a precursor of methyl Dopa.[8,9]

The efficiency of the epoxidation is dependent upon the pH of the reaction solution. In a MeCN–H_2O–NaBr system, the solution at the end of electrolysis was alkaline. On addition of a small amount of an acid, a mixture of **4**, **3a**, and the corresponding bromohydrin **3b** was obtained. Under more acidic conditions such as MeCN–H_2O–NaBr–H_2SO_4, **3b** was obtained quantitatively. The nature of the halide ion is also important in the product selectivity. In contrast to the successful results obtained with

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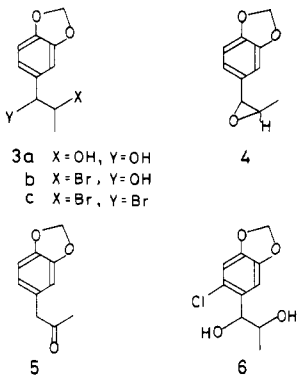

bromide ion, the use of chloride or iodide ions resulted in a poor yield of **3a** (39% for NaCl and 43% for NaI).

The electrochemical carbon–carbon bond cleavage of glycols has been examined in MeOH–Et_4NOTs for cyclic glycols[10] and glycol monomethyl ethers[11] and in MeOH–NaOH for tetraphenylethylene glycol.[12] The related α-hydroxy ketones can be cleaved in MeOH–$LiClO_4$.[13] At first, **3a** was subjected to electrooxidation both in MeOH–Et_4NOTs and MeOH–$LiClO_4$, affording **1** in 66% and 44% yields, respectively. When the halide ion promoted electrooxidation was examined, sodium bromide in MeCN–H_2O (9:1) provided a satisfactory yield (86%) of **1**, while chloride ion gave good to moderate yields in aqueous acetonitrile [$Ca(ClO)_2$ (0.1 equiv) 85%; $CaCl_2$ (0.2 equiv) 71%; NaCl (0.3 equiv) 61%]. Interestingly, a two-layer system consisting benzene and water (6:4) including $NaHCO_3$ or NaOH greatly enhanced the desired bond cleavage. In aqueous $NaHCO_3$ (0.5 equiv to **3a**)–benzene the yield of **1** was 62%, and 15% of the starting material was recovered after 6 F/mol when the reaction solution was found to be acidic. Also the yield increased with an increase of the $NaHCO_3$ concentration [% of **1** with $NaHCO_3$ (equiv): 62% (0.5), 88% (1.9), 90% 3.7)]. Meanwhile, the use of an appropriate concentration of NaOH led to the quantitative formation of **1** [quantitative (1.0 equiv), 96% (2.0 equiv), 91% (4.0 equiv)]. In contrast, upon electrolysis with NaBr or $LiClO_4$ instead of the base, the desired reaction proceeded very slowly (about 50% of **3a** was recovered) and the yield of **1** was poor (16–19%) after 6 F/mol. In a benzene–water system **3a** dissolves in the aqueous phase and the product **1** exclusively in the organic phase. Hence, the product **1** migrates into the benzene layer so that overoxidation of **1** can be avoided.

A comparison of the electrochemical and the conventional chemical oxidation of **3a** is summarized in Table I. Among the oxidants employed, sodium periodate, ceric ammonium nitrate (CAN), and calcium hypochlorite provided satisfactory yields. However, the use of an excess of expensive reagents such as sodium periodate and CAN is disadvantageous for manufacturing piperonal. On oxidizing **3a** with calcium hypochlorite in MeCN–H_2O–AcOH, as reported by Nwaukwa and Keehn[14] for several simple glycols, chlorination on the aromatic ring of **3a** took place predominantly, leading to **6**. In contrast, oxidation of **3a** in a two-layer system of benzene–water provided **1** quantitatively when 2 equiv of hypochlorite were used. Electrooxidation of **3a** in a benzene–water system including a small amount of sodium hydroxide also afforded **1** quantitatively. The electrolysis procedure is simple in operation and economical with respect to the reagents employed, and furthermore it requires no disposal of by-products (e.g., waste Ca compounds).

Table I. Electrochemical and Chemical Oxidations of Isosafrole Glycol 3a

entry	oxidant[a] (equiv)	solvent	temp, °C	time, h	yield of 1, %
1	electrolysis	C_6H_6-H_2O[b]	65		99
2	$NaIO_4$ (1.5)	MeOH-H_2O[c]	0-5	0.5	94
3	CAN (2)	AcOH-H_2O[d]	rt	0.5	93
4	$Ca(OCl)_2$	C_6H_6-H_2O[e]	65	3	quant

[a] Molar equivalent to **3a**. [b] C_6H_6-H_2O = 6:4. [c] MeOH-H_2O = 4:3. [d] AcOH-H_2O = 1:2. [e] C_6H_6-H_2O = 2:1. rt = room temperature; quant = quantitative.

Experimental Section

The ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ with Me_4Si as an internal standard on a JEOL FX-90Q spectrometer. The IR spectra were obtained with a JASCO IRA-1 spectrometer.

Electrolysis of Isosafrole (2). Preparation of 1-[3,4-(Methylenedioxy)phenyl]propane-1,2-diol (3a). A mixture of **2** (100 mg, 0.62 mmol) and NaBr (192 mg, 1.9 mmol) dissolved in MeCN (7 mL) and H_2O (3 mL) was electrolyzed in a beaker-type undivided cell (3 cm in diameter and 10 cm in height). A constant current (20 mA, 2.83 F/mol) was passed for 140 min by using platinum foils (2 × 1.5 cm^2) as electrodes and a Metronix Model 543B DC power supply. After the electrolysis at room temperature, 0.5 mL of 1% aqueous H_2SO_4 was added to the mixture, which was stirred for 1 h and neutralized with aqueous $NaHCO_3$. After evaporation of solvents under reduced pressure, the organic substances were extracted with ethyl acetate. The extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo to give a colorless oil, which was chromatographed (Mallinckrodt Silica CC-7 Special), affording **3a** (116 mg, 98%) as colorless crystals[8] whose spectral data were identical with those reported. In an another experiment, after the electrolysis as mentioned above, the mixture was concentrated in vacuo and the organic substances were extracted with ethyl acetate. The usual workup and chromatography provided **3a** (28 mg, 23%) and **4** (78 mg, 71%). The structure of **4** was identified spectroscopically by comparison with IR and ^1H NMR spectra of the authentic sample prepared by mCPBA oxidation of **2**.[9]

2-Bromo-1-[3,4-(methylenedioxy)phenyl]-1-propanol (3b). A mixture of **2** (100 mg) and NaBr (96 mg) dissolved in MeCN (7 mL)–1% aqueous H_2SO_4 (3 mL) was electrolyzed (20 mA for 125 min, 2.5 F/mol) in a similar manner as described above, affording **3b**[9a] (160 mg, quantitative yield) as a colorless oil: bp 110–112 °C (0.02 mmHg); IR (neat) 3520, 3400 (OH), 1490, 1440, 1240, 1040, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.85 (br s, 1 H, Ar H), 6.77 (br s, 2 H, Ar H), 5.92 (s, 2 H, CH_2), 4.87 (d, J = 4 Hz, 1 H, CHOH), 4.32 (dq, J_1 = 7 Hz, J_2 = 4 Hz, 1 H, CHBr), 2.54 (br s, 1 H, OH), 1.56 (d, J = 7 Hz, 3 H, CH_3). Anal. Calcd for $C_{10}H_{11}O_3Br$: C, 46.35; H, 4.28. Found: C, 46.10; H, 4.20.

Electrolysis of 3a. Preparation of Piperonal (1). Glycol **3a** (100 mg, 0.51 mmol) dissolved in benzene (6 mL) and 0.5% aqueous NaOH (4 mL) was electrolyzed at 65 °C (18 mA for 3 h, 4 F/mol) in a similar manner as described above, affording **1** (76 mg, 99%) as colorless crystals whose spectral and TLC data were consistent with those of an authentic sample.

Oxidation of 3a with $NaIO_4$. A solution of $NaIO_4$ (82 mg, 0.38 mmol) was added to **3a** (50 mg, 0.26 mmol) dissolved in MeOH (8 mL) at 0–5 °C. The mixture was stirred at the temperature for 30 min. The usual workup provided **1** (36 mg, 94%).

Oxidation of 3a with CAN. Into a solution of **3a** (100 mg, 0.51 mmol) dissolved in AcOH–H_2O (1:2, 3 mL) was added CAN (587 mg, 1.07 mmol) dissolved in AcOH–H_2O (1:2, 12 mL). The mixture was stirred at room temperature for 30 min. The usual workup provided **1** (71 mg, 93%).

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Oxidation of 3a with $Ca(ClO)_2$. A suspension of $Ca(ClO)_2$ (61 mg, 0.26 mmol) in benzene (2 mL)–H_2O (1 mL) was added to a solution of **3a** (100 mg, 0.51 mmol) dissolved in benzene (4 mL)–H_2O (2 mL). After vigorous stirring at 65 °C for 1 h, $Ca(ClO)_2$ (183 mg, 0.77 mmol) suspended in benzene (2 mL)–H_2O (1 mL) was added again and the mixture was stirred for additional 2 h. After adding AcOEt and centrifuging a precipitate, the organic substances were extracted with AcOEt and the usual workup provided **1** (75 mg, 98%).

1-[2-Chloro-4,5-(methylenedioxy)phenyl]propane-1,2-diol (6). A suspension of $Ca(ClO)_2$ (60% purity, 92 mg, 0.39 mmol) in AcOH (0.12 mL)–H_2O (1.2 mL) was added dropwise to a solution of **3a** (50 mg, 0.26 mmol) dissolved in MeCN (2 mL)–CH_2Cl_2 (1 mL). The reaction mixture was stirred at room temperature for 1 h. Ether extraction followed by usual workup and chromatography provided **6** (50 mg, 85%) as colorless crystals: mp 85–86 °C; IR ($CHCl_3$) 3560 (OH), 3380 (OH), 1475, 1220, 1120, 1035, 935, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.96 (s, 1 H, Ar H), 6.80 (s, 1 H, Ar H), 5.97 (s, 2 H, CH_2), 4.86 (d, J = 7 Hz, 1 H, CH), 3.84 (quint, J = 7 Hz, 1 H, CH), 3.04 (br s, 1 H, OH), 2.64 (br s, 1 H, OH), 1.14 (d, J = 7 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 147.6 (s), 147.1 (s), 132.4 (s), 124.5 (s), 109.6 (d), 107.7 (d), 101.8 (t), 74.4 (d), 71.8 (d), 18.8 (q). Anal. Calcd for $C_{10}H_{11}O_4Cl$: C, 52.07; H, 4.81. Found: C, 52.26; H, 4.99.

1-[3,4-(Methylenedioxy)phenyl]-2-propanone (5). A solution of **3a** (100 mg, 0.5 mmol) and *p*-TsOH (200 mg) dissolved in a distilled benzene (20 mL) was refluxed for 20 min. The usual workup gave **5** (75 mg, 84%).[8,9]

Registry No. **1**, 120-57-0; **2**, 120-58-1; **3a**, 62512-79-2; **3b**, 57961-85-0; **5**, 4676-39-5; **6**, 89321-20-0; CAN, 16774-21-3; $NaIO_4$, 7790-28-5; $Ca(ClO)_2$, 7778-54-3.

Reaction of the Anion of Meldrum's Acid with an *N*-Alkylpyridinium Salt

Ernest Wenkert,* Enrique L. Michelotti, and Jan St. Pyrek

Departments of Chemistry, Rice University, Houston, Texas 77001, and University of California—San Diego, La Jolla, California 92093

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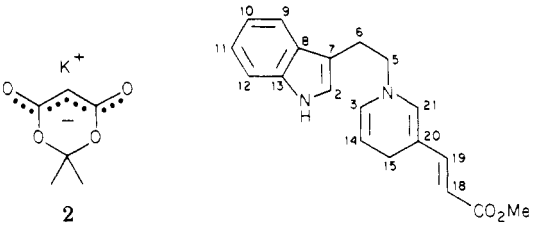
A two-step reaction scheme emanating from 1-[β-(β-indolyl)ethyl]-3-acylpyridinium salts or their vinylogues (carbon nucleophile addition, followed by acid-induced cyclization) has formed the basis for some time for synthesis of a variety of indole alkaloids.[1] Thus the reactions in Scheme I constituted early steps in the synthesis of the yohimbines.[2,3] An attempt to modify the first of these reactions by the replacement of the dimethyl malonate anion by the salt of Meldrum's acid led to a dramatic change in the reaction outcome—the subject of the present report.

Exposure of the pyridinium salt 1 to the potassium salt 2 of 2,2-dimethyl-4,6-dioxo-1,3-dioxane (Meldrum's acid) in refluxing tetrahydrofuran for 3 days and treatment of the reaction mixture with methanolic hydrochloric acid for 3 days led to two isolable products. The minor constituent could be recognized to be tetracycle 4, i.e., the product of the acid-induced ring closure of the product 3 of 1,4-reduction of the pyridinium salt 1. The structurally more complex major constituent could be assumed to be a product of oxidation of the adduct of the two salts by



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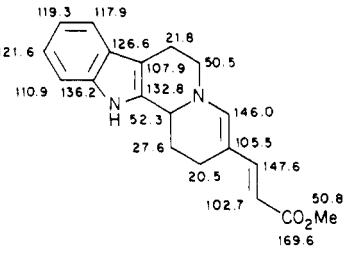

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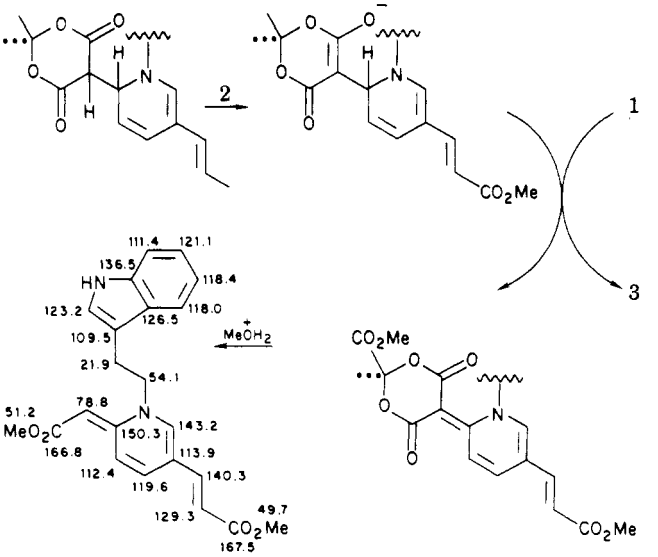
analogy with the unusual chemistry experienced recently in the reaction of methyl sodioacetoacetate with 1-[β-(β-indolyl)ethyl]-3-formylpyridinium bromide.[4]

The molecular formula of $C_{22}H_{22}O_4N_2$ of the major product appeared to justify the aforementioned surmise. Its yellow color and ultraviolet spectra [λ_{max}^{EtOH} 221 nm (log ϵ 4.57), 253 (4.10), 275 (4.04), 290 (3.88), 3.92 (4.57); $\lambda_{max}^{EtOH/HCl}$ 220 nm (log ϵ 4.62), 270 (4.27), 290 (4.10)] showed the presence of an extended chromophore and hence a complex system of conjugated multiple bonds. Its infrared spectrum [ν_{max}^{KBr} NH 3250 (m), C=O, C=C 1700 (s), 1660 (s), 1610 (s), 1570 (s) cm^{-1}] exhibited indole N–H, ester carbonyl, and vinylogous amide carbonyl absorption bands. Its low-resolution mass spectrum revealed intense m/e 144 and 143 fragments, characteristic of the β-ethylindole cation, indicating that the β-indolylethyl unit of the starting compound had remained unmodified in the product. In the face of these spectral data, the ^1H and ^{13}C NMR spectra, and the following mechanism for the formation of the substance as well as dihydropyridine 3 the new substance could be assigned structure 5.



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Structure 5 could be confirmed by ^1H and ^{13}C NMR spectral analyses of the compound's protic salt 6 and by

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