Electrochemical Dimerization of 3-Methylcrotonaldehyde[1]

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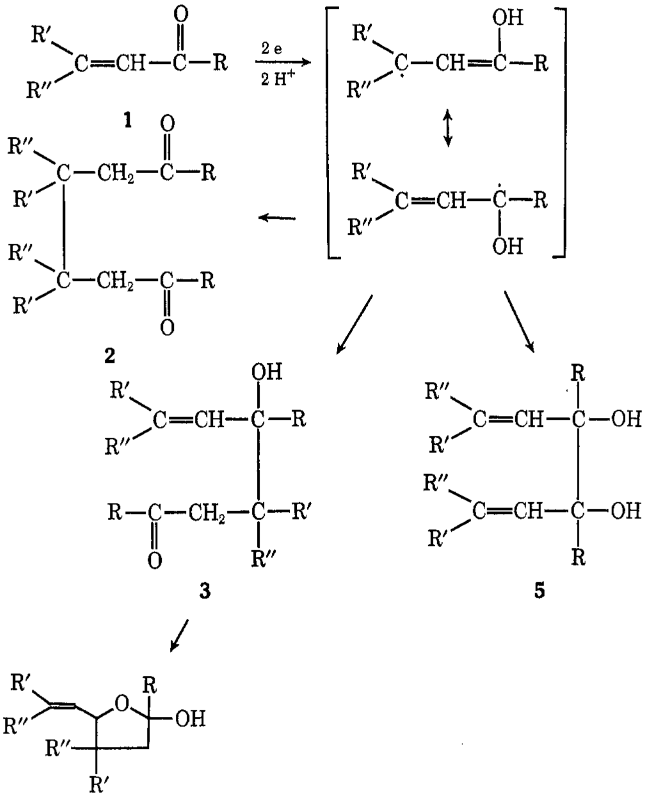
Received November 3, 1970

The electrochemical reduction of 3-methylcrotonaldehyde (**8**) was carried out at the controlled potential of -1.30 V in 0.25 *M* acetate buffer at pH 5.00 for the purpose of investigating this type of reduction as a possible synthetic tool for the preparation of dimeric glycols **5**. A 42% conversion to dimeric material was realized, which material consisted of three products. One was identified as the hydroxytetrahydrofuran **9** (67%), a second as the desired glycol **10** (24%), and the third product was tentatively assigned the structure **11** (9%).

The electrochemical reduction of α,β-unsaturated compounds (**1**) in aqueous media can yield, *a priori*, three different types of dimeric products (Scheme I):

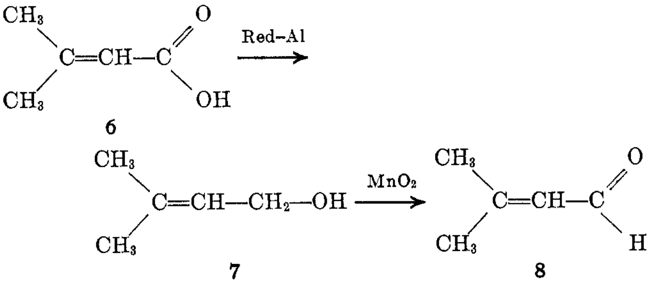
SCHEME I



a dicarbonyl compound (**2**), resulting from the coupling of two β radicals; a hydroxycarbonyl compound (**3**) [usually isolated as the hemiketal or hemiacetal (**4**)] from the "head to tail" coupling of a β radical and a carbonyl radical; and a glycol (**5**) from the coupling of two carbonyl radicals.

In most cases studied, the electrochemical reduction of α,β-unsaturated carbonyl compounds was found to lead to mixtures of dimeric products in which the diketone (**2**) was the major or only identifiable product.[2-4] However, there are several reports in the literature where electrochemical reduction affords dimeric glycols (**5**) as the major products. In these instances, the "R" attached to the carbonyl position is very small compared to the vinyl R′ and R″. The controlled potential reductions of crotonaldehyde,[4] prednisone, and cortisone[5] are excellent examples of such findings. This evidence appeared to point to the participation, at least in part, of steric control in determining the course of dimerization. If steric considerations were determined to be a prime controlling factor in these reactions, so that glycols could be produced exclusively in the reduction of β,β-disubstituted α,β-unsaturated aldehydes, then this could be a method of great synthetic utility, applicable to syntheses of many terpenes. For this reason, and the fact that no β,β-disubstituted α,β-unsaturated aldehydes had been investigated, we chose 3-methylcrotonaldehyde (**8**) as a model compound for this work.

Although 3-methylcrotonaldehyde (**8**) had been previously prepared by several different routes,[6] we deemed it more convenient to synthesize this aldehyde from the readily available carboxylic acid, 3-methylcrotonic acid (**6**), *via* the allylic alcohol (**7**). The carboxylic acid (**6**)



was therefore reduced with $NaAlH_2(OCH_2CH_2OCH_3)_2$ to 3-methyl-2-buten-1-ol, which was in turn oxidized to the desired aldehyde with activated manganese dioxide.[7]

The reduction potentials for this compound were determined by standard polarographic technique in acetate and phosphate buffers over the pH range 4–8. These values were normal (Table I), giving a roughly linear relationship of $E_{1/2}$ to pH.

The controlled potential reduction of the aldehyde was carried out under a nitrogen atmosphere in an electrolysis cell employing a stirred mercury pool cathode and a silver/silver chloride anode. Acetate buffer solution (0.25 *M*, pH 5.00) was used as the supporting electrolyte solvent system. Using a working potential of -1.30 V (at pH 5.00 $E_{1/2} = -1.27$ V) the reduction of 500 mg of the aldehyde was complete within 2 hr.

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[1] Taken from a portion of the Ph.D. dissertation of D. T. Miller, 1970.

[2] J. J. Lingane, "Electroanalytical Chemistry," 2nd ed, Interscience, New York, N. Y., 1958.

[3] R. Pasternak, *Helv. Chim. Acta*, **31**, 753 (1948).

[4] J. Wiemann and M. Paget, *Bull. Soc. Chim. Fr.*, 285 (1955).

[5] P. Kabasakalian and J. McGlotten, *J. Amer. Chem. Soc.*, **78**, 5032 (1956).

[6] (a) H. Normant, *Bull. Soc. Chim. Fr.*, 728 (1958); (b) K. Suga and Watanabe, *Hiroshima Daigaku Chigaku Kenkyu Hokoku*, **9**, 67 (1958); (c) J. R. Pollock, Ed., "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1965.

[7] I. M. Goldman, *J. Org. Chem.*, **34**, 1979 (1969).

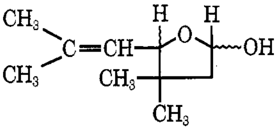
TABLE I

POLAROGRAPHY OF 3-METHYLCROTONALDEHYDE[a]

pH	$E_{1/2}$,[b] V	Buffer
4.00	−1.19	0.25 *M* acetate
5.00	−1.27	0.25 *M* acetate
6.00	−1.32	0.25 *M* acetate
7.00	−1.48	0.25 *M* phosphate
8.00	−1.49	0.25 *M* phosphate

[a] Aldehyde concentration 4.0×10^{-4} *M*. [b] Wave height was approximately 0.8 μA at all pH values.

Extraction of the reaction mixture with ether yielded a pale yellow oil which was chromatographed on neutral silica gel, giving separation into three major chromatographic components totaling 211 mg, 42%. Positive structural assignments were made for two of these components and a tentative assignment was given to the third. The largest component, representing 67% of the total weight was identified on the basis of its ir, nmr, and mass spectral data as a mixture of the cis–trans isomers of the hydroxytetrahydrofuran derivative **9**. It exhibited a moderate hydroxyl absorption and a weak double bond absorption at 1700 cm^{-1}. Its nmr spectrum was most revealing. A six-proton doublet at 0.95 ppm (J = 7 Hz), and a six-proton doublet centered at 1.75 ppm (J = 4 Hz) were attributed to saturated gem methyls and gem vinyl methyls, respectively.



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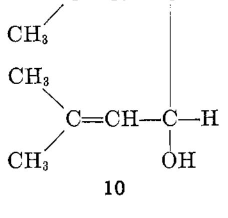
A broad one-proton singlet at 3.4 ppm was assigned to the hydroxyl proton. Two doublets (J = 9 Hz for both) integrating for one proton between them were centered at 4.4 and 4.7 ppm and were assigned to the proton on the carbon bearing the isobutene moiety, having slightly shifted resonances in the cis and trans isomers. These resonances appear as doublets because of coupling with the vinyl proton which shows up as a one-proton doublet centered at 5.15 ppm (J = 9 Hz). Finally, a broad one-proton triplet at 5.55 ppm (J = 6 Hz) was assigned to the proton on the carbon of the hemiacetal group.

The next largest component was shown to be the desired glycol **10**, representing 24% of the total weight. Its ir spectrum showed the presence of strong hydroxyl absorption and moderate double bond absorption at 1700 cm^{-1}. The two sets of gem vinyl methyls appeared as a 12-proton singlet in the nmr at 1.7 ppm.



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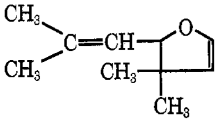
Both the vinyl protons and the protons on the carbons bearing oxygen appeared as two broad triplets integrating for two protons each. However, examination of early and late fractions of this chromatographic component revealed that these actually resulted from superimposed resonances attributable to the presence of both the *dl* and meso forms. Thus, one "apparent triplet" was actually two superimposed doublets centered at 5.1 and 5.25 ppm (J = 7 Hz) and was assigned to the vinyl protons. The other "apparent triplet" was shown to be two superimposed doublets of doublets centered at 4.15 and 4.3 ppm (J_1 = 7 Hz, J_2 = 2 Hz), and assigned to the protons on carbon bearing hydroxyl.

The smallest component represented only 9% of the reduction product. Its nmr spectrum (very dilute) was similar in many respects to that of **9**, and its ir spectrum was notable in that it lacked either hydroxyl or carbonyl absorption but did exhibit double bond absorption at 1720 cm^{-1}. It was tentatively assigned the dihydrofuran structure **11** based on this evidence.



11

On the basis of this work we must conclude that even in a very favorable case the carbonyl to carbonyl coupling is still only a secondary mode of reaction. This process then, would not seem to be of great synthetic promise for terpene synthesis.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a Varian Model T-60 spectrometer in $CDCl_3$ solution using TMS as the internal standard. Ir spectra were taken on a Perkin-Elmer Infracord Model 137B in $CHCl_3$ solution. Mass spectra were obtained with a Varian Model M-66 mass spectrometer equipped with a peak matching device for precise mass measurements. Melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected. A Leeds and Northrup 4701 pH meter was employed for pH measurements. The controlled potential electrolysis experiment was carried out using a Lingane–Jones potentiostat[8] in conjunction with an electrolysis cell having a stirred mercury pool cathode, a silver/silver chloride anode and a sce reference.

3-Methyl-2-buten-1-ol (7).—Under an atmosphere of N_2, 3-methylcrotonic acid (6) (50 g, 0.5 mol) was dissolved in 1 l. of dry benzene in a 3-l., three-neck round-bottom flask, fitted with a mechanical stirrer, reflux condenser, and a 500-ml constant-pressure addition funnel. The addition funnel was charged with 235 g (0.80 mol) of "Red-Al"[9] [$NaAlH_2(OCH_2CH_2\text{-}OCH_3)_2$] which was diluted with an additional amount of 200 ml of dry benzene. Stirring was begun and the metal hydride solution was added in a thin stream, while cooling with an ice bath, at such a rate as to maintain gentle reflux and moderate liberation of H_2. During the addition, which lasted about 1 hr, the solution became cloudy and finally set to a thick gel which resisted stirring but gradually became liquified. The solution was heated to reflux for an additional 30 min and then left stirring overnight at room temperature, after which time the solution was a clear bright gold color. The complex was decomposed by the dropwise addition of saturated NH_4Cl solution (about 200 ml) with cooling. The benzene solution was decanted and the aluminum salt residue was washed two times with 400 ml of ethyl ether. The organic extracts were combined, washed twice with H_2O, once with saturated NaCl, and dried over Na_2SO_4. Evaporation of the solvent gave 28 g crude alcohol containing some benzene. Distillation [52–55° (19 mm)] gave 16 g, 38% yield: nmr δ2.0 (d, 6 H) (J = 4 Hz), 2.9 (s, 1 H), 4.1 (d, 2 H) (J = 7 Hz),

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[8] J. J. Lingane and S. L. Jones, *Anal. Chem.*, **22**, 1169 (1950).

[9] Red-Al is a trade name of the Aldrich Chemical Co. for a 70% solution of bis(2-methoxyethoxy)aluminum hydride in benzene.

5.4 (t, 1 H) (J = 7 Hz); ir (liquid film) 3300 (s), 2950 (s), 1690–1700 (w), 1450 (m), 1360 (m), 1100 (s), 1000 (s), 780 (w), 675 cm^{-1} (w).

3-Methylcrotonaldehyde (8).—Dry active MnO_2 (20 g) was prepared and activated in 200 ml of distilled benzene as reported by Goldman.[7] The alcohol **7** (2.0 g) was dissolved in 5 ml of benzene and added under N_2 with stirring to the activated MnO_2. The reaction was stirred at room temperature overnight. The suspension was filtered through Celite on a Büchner funnel and washed with ethyl ether, and the filtrate was evaporated to 1.0 g of a yellow oil showing nearly pure aldehyde by nmr, yield 50%: nmr δ 2.1 (d, 6 H) (J = 11.5 Hz), 5.9 (d, 1 H) (J = 8 Hz), 10.1 (d, 1 H) (J = 8 Hz); ir (liquid film) 2750 (m), 1680 (s), 1450 (m), 1360 (m), 1200 (m), 1120 (m), 1050 (m), 830 (m), 680 cm^{-1} (m). A semicarbazone derivative melted at 221–223° (lit.[6c] mp 221–222°).

Polarography of 3-Methylcrotonaldehyde (8).—The polarographic measurements were made on a L & N, Model 62200, Type E, recording polarograph using a standard dme and sce in a 10-ml polarographic cell. The solutions were purged with N_2 for 15–20 min prior to each run. The polarographic solutions, which were 4×10^{-4} M in aldehyde, were prepared by diluting to 25 ml, 2 ml of a 0.005 M stock solution of the aldehyde with the desired 0.25 M buffer solution, resulting in pH 4.00, $E_{1/2} = -1.19$ V; pH 5.00, $E_{1/2} = -1.27$ V; pH 6.00, $E_{1/2} = -1.32$ V; pH 7.00, $E_{1/2} = -1.48$ V; pH 8.00, $E_{1/2} = -1.49$ V. The wave height was approximately 0.8 μamp at all pH values.

Controlled Potential Electrolysis of 3-Methylcrotonaldehyde (8).—The electrolysis was carried out with a Lingane-Jones[8] potentiostat in the electrolysis cell previously described. About 150 ml of pH 5.00, 0.25 M acetate buffer was placed in the cell over the pool of instrument grade mercury and purged with N_2 for 20 min. The cell was connected to the potentiostat and an initial background current was measured of 2 mA with an applied voltage of about 4 V and a reference to working electrode potential of −1.30 V. 3-Methylcrotonaldehyde (**8**), 0.50 g, in 10 cc of EtOH was then added dropwise at a rate such that the current limitations of the instrument were not exceeded (about 10 A). The electrolysis was complete within 2 hr as indicated by the return of the current to near the initial background value. The aqueous solution was extracted three times with ethyl ether, washed with saturated NaCl, and dried over Na_2SO_4. Evaporation of the solvent gave 0.53 g of a clear yellow oil, having a slight odor of acetic acid. Tlc analysis of this crude oil showed at least two mobile components when eluted with 50% ether–hexane (Eastman silica gel chromatograms). The entirec rude was chromatographed on 12 g of Silicar cc-7, eluting successively with hexane, benzene–hexane, benzene, ether–benzene, ether, ethanol, methylene chloride. Three major peaks were discernible, totaling 211 mg, 42%. The first peak, 18 mg, was eluted in 15% ether–benzene and was tentatively identified as the dihydrofuran derivative **11**. The second peak, 141 mg, eluted in 20% ether–benzene was identified as the hydroxytetrahydrofuran derivative **9**. The last significant peak, 52 mg, was eluted in 40% ether–benzene and was identified as the desired glycol (**10**). The evidence for these compounds is given below.

Component 1 (18 mg), 4,4-dimethyl-5-(2-methyl-1-propenyl)-dihydrofuran (11) (tentative): nmr δ 1.2 (d, 6 H) (J = 8 Hz), 1.7 (d, 6 H) (J = 4 Hz), 4.2 (d, 1 H), (J = 8 Hz), 5.15 (broad s, 1 H); ir 2900 (s), 1720 (w), 1690 (w), 1450 (m), 1370 (m), 1200–1050 (m), 1000 (s), 910 cm^{-1} (m).

Since **11** would obviously derive from the hydroxytetrahydrofuran derivative (**9**) by elimination of H_2O, an attempt at producing **11** from **9** by acid catalysis was made. Twenty milligrams of **9** (sublimed) was dissolved in 10 ml of dry benzene, a tiny crystal of p-toluenesulfonic acid was added, and the mixture was stirred at 45° for 12 hr under N_2. The benzene solution was then washed with H_2O, dried and evaporated, leaving a small amount of oil having a very sweet odor. Ir showed the loss of hydroxyl, and the presence of a double bond and carbonyl group. The nmr was weak and complex. The product may have been a mixture of **11** and a new aldehyde, produced by acid-catalyzed opening of the dihydrofuran system.

Component 2 (141 mg), 4,4-dimethyl-1-hydroxy-5-(2-methyl-1-propenyl)tetrahydrofuran (9): nmr δ 0.95 (d, 6 H) (J = 7 Hz), 1.75 (d, 6 H) (J = 4 Hz), 3.4 (s, 1 H), 4.4 (d, 0.25 H) (J = 9 Hz), 4.7 (d, 0.75 H) (J = 9 Hz), 5.15 (d, 1 H) (J = 9 Hz), 5.55 (t, 1 H) (J = 6 Hz); ir 3300 (w–m), 2900 (s), 1690 (w), 1450 (m), 1370 (m), 1140 (m), 1050 (m), 1005 (s), 950 (m), 910 cm^{-1} (m); mass spectrum, molecular ion at 170, intense peak at 85; precise mass 170.1313, corresponding to $C_{10}H_{18}O_2$.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.69; H, 10.62.

Component 3 (52 mg), 2,7-dimethyl-2,6-octadiene-4,5-diol (10): nmr δ 1.7 (s, 12 H), 4.15 (doublet of doublets) and 4.3 (doublet of doublets) both totaling 2 protons, (J_1 = 7 Hz, J_2 = 2 Hz for both), 5.1 and 5.25 (d, broad, 2 H total) (J = 7 Hz); ir 3500 (s), 3400 (s), 1660 (m), 1450 (s), 1380 (s), 1320 (m), 1230 (s), 1110 (s), 1040 (s), 1000 (s), 900 (w), 850 (m), 820 (m); mass spectrum, intense peak at 85 amu, no molecular ion.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.50; H, 10.56.

Registry No.—**7**, 556-82-1; **8**, 107-86-8; **9**, 28405-68-7; **10**, 28405-69-8.

Acknowledgment.—The authors wish to express their appreciation to the National Science Foundation for financial support throughout this study (NSF Grant GP-8073).

Condensation of Phenylhydroxylamine with Hydroxymethylenedesoxybenzoin

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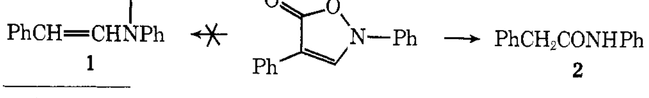
Received September 18, 1970

The reaction of phenylhydroxylamine with hydroxymethylenedesoxybenzoin has been shown to give derivatives of benzoylphenylacetanilide rather than the previously reported vinylhydroxylamines.

The recent finding that the postulated N-phenyl-N-styrylhydroxylamine (**1**) from the reaction of a 3-isoxazolin-5-one with aqueous base[1] is actually phenylacetanilide (**2**)[2,3] led us to reexamine the structure of other reported[4] vinylhydroxylamines from the condensation of phenylhydroxylamine with hydroxymethylenedesoxybenzoin. The reported[4] series of transformations summarized in Scheme I was of interest since the hydrolysis of the compound assigned the structure of the trans isomer of **3** had been cited in support of the incorrect structure **1**. When the hydrolysis product had been shown instead to be **2**, DeSarlo and Renzi proposed[2] that the precursor was benzoylphenylacetanilide (**5**) rather than **3** and suggested that a rearrangement might be responsible for the formation of **5**.



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(1) H. Rupe and J. Grünholz, *Helv. Chim. Acta*, **6**, 102 (1923).

(2) F. DeSarlo and G. Renzi, *Tetrahedron*, **22**, 2995 (1966).

(3) D. J. Woodman, C. H. Borman, N. Tontapanish, and P. M. Stonebraker, *J. Org. Chem.*, **34**, 2981 (1969).

(4) H. Rupe and W. Wittwer, *Helv. Chim. Acta*, **5**, 205 (1922).