Tetrahedron Vol. 47, No. 4/5, pp. 851-857, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00

SELECTIVITY IN CATALYTIC DIOL ELECTROOXIDATION USING A POLYPYRIDINE Ru(IV) COMPLEX

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(*Received in USA* 24 *August* 1990)

Abstract: 1,2-, 1,3-, and 1,4-Butanediols and phthalic alcohol were oxidized electrocatalytically using the polypyridine $[(bpy)(trpy)RuO]^{2+}$ complex (1) as oxidant under different conditions: concentration of 1, pH, and temperature. By controlling the number of coulombs passed through the electrolytic cell, it was possible to obtain selective reactions. 1-Hydroxy-2-butanone, 1-hydroxy-3-butanone, γ-butyrolactone, phthalide, phthalic aldehyde, and phthalic acid were the products obtained by controlled potential electrolysis from these substrates, with yields ranging from 41 to 89%.

Introduction

Many transition metal compounds with a high oxidation state are strong oxidants and are frequently used in synthetic organic chemistry. Although several of these compounds, such as NH_4VO_3, CrO_3, MnO_2, $Mn(AcO)_3$, RuO_4, and OsO_4, are used as oxidants and are extremely useful in the laboratory,[1] there are some limitations as to their selectivity and the possibility of using them catalytically. The use of metal complexes in catalytic reactions has significantly progressed over the last thirty years because of the theoretical understanding of the process occurring with the substrate in the coordination sphere of metal complexes. This is especially true for homogeneous catalysis, in which it is possible in a number of cases to determine the sequence of elementary reactions, to identify the intermediate compounds, to follow the changes in metal oxidation state during the catalytic process, and to give a quantum-chemical description of substrate coupling with the metal.

Catalysis with metal complexes has several practical advantages such as comparatively mild conditions under which the reaction can be conducted in solution (low temperature and pressure), low sensitivity to impurities, high availability of active centers for interaction with the substrate, and the possibility of controlling the catalytic system by changing ligand environment and medium composition. These principles of catalysis with metal complexes can be easily transferred to the catalysis of electrochemical reactions. In principle, the use of electrolytic techniques for organic redox reactions has many advantages. In a direct electroorganic reaction, the electrode may replace the oxidants or reductants, and the organic substance exchanges electrons directly with the electrode. Characteristic reactivities originate from the properties of the electrode-solution interface. Complications may arise in practice because of overvoltage and absence of selectivity. In an indirect electroorganic reaction, the organic substance does not exchange electrons directly with the electrode but through the intermediate action of some electroactive substance (homogeneous catalysts or catalysts immobilized on the electrode surface), with redox chemistry occurring in the catalyst and with the electrode functioning as a source of reducing or oxidant equivalents under conditions of controlled potential. An advantage of this procedure is that the reactivity characteristics of the electrocatalytic system are controlled by individual chemical sites whose reactivity properties may be studied separately and modified according to the demands of the reaction. It is very important to know how to select an appropriate redox system for indirect electrooxidation of particular substrates. Oxidant mediators include a variety of metals, non-metals, and redox organic systems.[2,3]

Among the metal complexes utilized in indirect electrooxidation of organic compounds,[4,5] ruthenium complexes with a high oxidation state have attracted special attention, and ruthenium(IV) oxo complexes with polypyridine ligands in particular.[6] The presence of an oxo group is important in the stabilization of the higher oxidation state and also mechanistically by providing an oxygen atom transfer pathway, an initial lead-in site for attack on a substrate, or by representing an acceptor site for a transferred proton in a mechanism of hydride transfer. The $[(bpy)(trpy)RuO]^{2+}$ (**1**) (bpy = 2,2′-bipyridine; trpy = 2,2′:6′,2″-terpyridine) complex, in particular, is capable of oxidizing C-H bonds adjacent to unsaturated bonds to yield alcohols, ketones, and aldehydes or carboxylic acids, depending on whether the carbon is tertiary, secondary, or primary.[7,8] As an oxidant, the complex is coordinatively well-defined and chemically stable. Coordinative stability is essential for catalysis, and the primary coordination geometry of the complex remains intact in the different oxidation states. A structural change occurs only in the oxo *active site*, contrary to what occurs with oxidants such as CrO_3 or MnO_4^-, in which the reduction provokes changes in composition and coordination number [e.g., $CrO_3/Cr(H_2O)_6{}^{3+}$] that create difficulties for the systems to become catalytic.

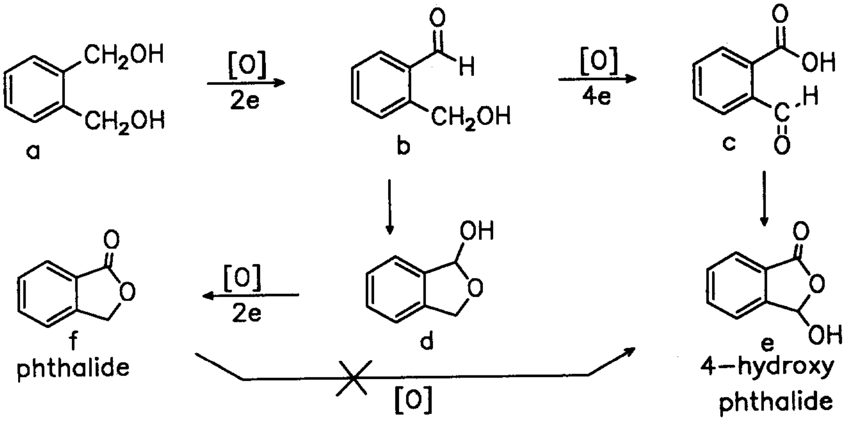
Complex (**1**) oxidizes the substrate and is reduced to the $[(bpy)(trpy)Ru(OH_2)]^{2+}$ (**2**) aqua complex; the ruthenium(IV) complex (**1**) is regenerated anodically on a platinum electrode at +0.8 V vs. a saturated calomel electrode (SCE). Thus, complex (**1**) can be used in catalytic quantities and can be recovered at the end of the process. We have conducted a systematic study to explore the oxidizing ability of this complex by establishing experimental conditions that would achieve selectivity in important preparations. Thus, by controlling the number of coulombs passed through the solution and the catalyst/substrate concentration ratio, it was possible to determine the relative reactivities of several classes of substrates and, based on the reactivities, to obtain selective oxidations. In a study of olefin and ketone oxidation,[9] cyclohexene gave origin to 2-cyclohexene-1-one exclusively. In allylic ether oxidation, the methylene localized between the double bond and the oxygen was selectively oxidized. On vinyl ether oxidation, the methylene adjacent to the double bond was oxidized, and oxidation of the phenol resulted exclusively in *o*-benzoquinone.[10] 2-, 3-, and 4-Picoline were oxidized to their corresponding picolinic acids.[11] In recent studies conducted on several alcohol classes,[12] primary aliphatic alcohols proved to be the least reactive, giving origin to their respective aldehydes, while primary benzyl alcohols were the most reactive and could give origin to their aldehydes or acids when the relative concentration of **1** and the number of coulombs were controlled. The secondary alcohol cyclohexanol and allyl alcohol were also quite reactive, giving origin to cyclohexanone and acrylic acid, respectively.[12]

Due to observed selectivity on alcohol oxidation, we studied electrocatalytic oxidation of dihydroxylated substrates using **1** under controlled potential, and we established experimental conditions which allowed us to obtain products by selective oxidations.

Results and Discussion

1,2-Butanediol, a substrate with adjacent primary and secondary hydroxyl groups, was oxidized at room temperature and neutral pH to produce 1-hydroxy-2-butanone after passage of a number of coulombs corresponding to a two-electron reaction. The most reactive hydroxyl group was oxidized selectively, and no other oxidation product was observed. The secondary hydroxyl group of this substrate, however, was less reactive than that of cyclohexanol.[12] Oxidation of 1,3-butanediol, a diol with non-adjacent primary and secondary hydroxyl groups, under the same experimental conditions produced only 1-hydroxy-3-butanone. The number of coulombs involved in this process was higher than that equivalent to a two-electron reaction since electrolysis was exhaustive. A number of coulombs equivalent to a two-electron reaction leads to the same product but with a very low yield. As expected, the secondary hydroxyl group was oxidized within a longer reaction time than needed for the oxidation of the adjacent diol, 1,2-butanediol. Oxidation of 1,4-butanediol, a diol with non-adjacent primary hydroxyl groups, was oxidized under the same experimental conditions as above and produced γ-butyrolactone as the only product. The number of coulombs involved in this process was equivalent to a four-electron reaction. The aldehyde formed by oxidation involving a two-electron reaction forms a ring with the hydroxyl group on C-4, producing a hemi-acetal product which in turn is rapidly oxidized electrocatalytically to γ-lactone also in a two-electron reaction. In an attempt to increase the γ-butyrolactone yield, oxidation was performed at 50 °C, and a mixture of 18% γ-lactone and 12% succinic acid was obtained.

When submitted to the same expeimental conditions, phthalic alcohol [1,2-bis(hydroxymethyl)-benzene], a substrate with two benzyl hydroxyl groups yielded a mixture of the following products: phthalic aldehyde, phthalic acid, phthalide (the corresponding lactone), and 4-hydroxy-phthalide. Phthalide must be formed through a reaction pathway similar to that which led to the production of γ-lactone from 1,4-butanediol. To understand the reaction pathway for the formation of 4-hydroxy-phthalide, it is necessary to consider the absence of phthalic anhydride, even in other preparations in which more energetic reaction conditions were used. Thus, it is unlikely that 4-hydroxy-phthalide was formed from phthalide because methylene oxidation should be more difficult than oxidation of carbinol to anhydride. It is more probable that 4-hydroxy-phthalide was formed by the chemical reaction between the formyl and carboxyl groups of 2-formyl-benzoic acid, a reaction intermediate, since phthalic acid was always one of the products detected. Scheme 1 shows these cyclization reactions.



Scheme 1. Reaction Sequence Scheme for Phthalic Alcohol[a] Oxidation and Cyclization

Since in benzylic alcohol oxidation, the proportion of the products benzaldehyde and benzoic acid varies according to the oxidant concentration,[12] experiments were performed in which temperature, pH, and concentration of **1** varied. The most significant results are presented in Table 1 which lists the products obtained and their proportions in the mixture.

Table 1. Percentage Distribution of Phthalic Alcohol Oxidation Products As a Function of Variation in pH, Complex Concentration, and Temperature

			Reaction product composition (%)			
Experiment	pH	[Complex] mM	phthalic acid	phthalide	phthalic aldehyde	4-hydroxy-phthalide
A	6.8[b]	3.12	31.5	30.3	26.9	11.3
B	8.0[b]	3.12	24.5	35.7	5.1	34.7
C	6.8[c]	0.78	5.2	56.2	31.2	7.3
D	8.0[c]	0.78	6.4	53.8	21.8	17.9
E	5.7[c]	0.78	8.1	30.2	53.5	8.1
F	6.8[d]	3.12	89.8	5.1	--	5.1

[a] 207.3 mg (1.5 mmoles). [b] 26 °C. [c] 10 °C. [d] 50 °C.

Under the same conditions used for the other oxidations, the proportion of the products was approximately homogeneous, with no selectivity (Exp. A). Under the same conditions of pH and concentration of **1** but at 50 °C, phthalic acid was obtained at the proportion of 89.8% (Exp. F: 219.1 mg, 88% yield). When the oxidant concentration was reduced fourfold and the reaction performed at 10 °C at neutral pH, the main product was phthalide at a proportion of 56.2% (Exp. C: 108.0 mg, 54% yield) and 31.2% of phthalic aldehyde (60.3 mg, 30% yield). A good proportion of phthalide (Exp. D: 53.8%, 84.4 mg, 42%

yield) with a lower proportion of phthalic aldehyde (21.8%, 33.6 mg, 17% yield) could be obtained under the same conditions of oxidant concentration and temperature but at slightly basic pH. The proportion of phthalic aldehyde could be increased to 53.5% (Exp. E: 92.5 mg, 46% yield) accompanied by 30.2% phthalide (52.3 mg, 26% yield) when the reaction was conducted at 10 °C, [**1**] = 0.78 mM and slightly acidic pH. 4-Hydroxy-phthalide was always a minor product except when oxidation was performed at pH 8.0, room temperature, and [**1**] = 3.12 mM, when it reached a proportion of 34.7% (78.1 mg) together with phthalide (Exp. B). Thus, under more vigorous conditions, the most oxidized product was obtained (phthalic acid); under milder conditions, the least oxidized products were obtained (phthalide or phthalic aldehyde). When Exp. A and B of Table 1 are compared, it can be seen that when the pH was changed from neutral to basic at the same concentration and temperature, there was an increase in the cyclization product, i.e., phthalide. When Exp. C and D are compared, with a change in pH from neutral to basic, with fourfold lower concentration of **1** at 10 °C, the proportion of phthalide was maintained and the proportion of the other cyclization product, 4-hydroxy-phthalide, was increased. When Exp. C and E are compared, with a change in pH from neutral to acid, with low concentrations of **1** and low temperature, a greater proportion of phthalic aldehyde was obtained with a consequent decrease in the proportion of the cyclization product: phthalide. It can be seen that the cyclization reaction involving the formyl group and methylcarbinol and producing phthalide is sensitive to slight variations in pH, being clearly favored at basic pH and impaired at acidic pH, the latter favoring the formation of phthalic aldehyde. If at basic pH, the oxidation of the second hydroxyl group to dialdehyde (b → c, Scheme 1) is slower than at acidic pH, cyclization reaction is favored (b → d, Scheme 1), and the hydroxyl group is rapidly oxidized (d → f, Scheme 1).

Experimental Section

Phthalic alcohol was prepared using a literature procedure[13] and characterized by ^{1}H NMR and IR spectra. 1,2-, 1,3- and 1,4-Butanediol were purchased from EM Reagents and were used without further purification. All other solvents and chemicals were reagent grade or better and were used as received. GC chromatograms were recorded with Intralab 300 gas chromatograph using OV 80 column. ^{1}H NMR spectra were recorded on a Bruker 80-MHz spectrometer, and IR spectra were recorded on a Perkin-Elmer 1480IR spectrophotometer. Ruthenium complex **2** was prepared by using literature procedures.[14]

General Procedure for the Electrooxidation. The coulometric experiments were conducted using a two-compartment cylindrical cell containing a platinum gauze working electrode and a platinum plate auxiliary electrode. The reference electrode was a saturated calomel electrode (SCE). The electrolyses were performed at a fixed applied potential of +0.8 V using a PAR 273 potentiostat/galvanostat. This was sufficient to generate the Ru(IV) oxidant **1** from Ru(II) aqua complex **2**. The pH was maintained by using a phosphate buffer. The substrates were unreactive under the experimental conditions, i.e., under a potential of +0.8 V vs. SCE; the currents are in the microampere range. The number of coulombs passed in each experiment was obtained by using the coulometer of the potentiostat or by calculating by integration of the i x t curve registered on an Y-T recorder. The electrolyses were continued until the current fell to about "background" values or upon reaching the desired number of coulombs.

Phthalic Alcohol Oxidation. **2** (0.0707 g, 0.1 mmol or 0.0177 g, 0.025 mmol) was dissolved in a buffer solution (29 mL, 3.12 mM or 0.78 mM respectively; pH 5.7, 6.8, or 8.0) in a thermostated electrochemical cell. The solution was maintained under vigorous stirring and a potential of +0.8 V was applied. The current quickly reached values near 150 mA (higher concentration of **1**) or 40 mA (lower concentration of **1**), falling within a few minutes to values below 1 mA (residual current), corresponding to the passage of 19.3 or 4.8 coulombs. The dark color of **2** turned light yellow. Phthalic alcohol (0.2073 g, 1.5 mmol) was dissolved using an ultrasonic cleaner in a buffer solution (3 mL) and was added all at once to the electrolytic cell. The solution turned dark again, the current was increased to 320 mA (50 °C and [**1**] - 3.12 mM) or 16 mA (10 °C and [**1**] - 0.78 mM), and hydrogen evolution was observed in the auxiliary electrode compartment. The current fell exponentially as a function of time. The maximum time for this process was 23 hours at 10 °C, and the minimum time was 4 hours at 50 °C. The mixture was extracted with ethyl ether (which does not extract the metal complex), and the phthalide and phthalic aldehyde were obtained. The latter was separated from phthalide by the formation of a bisulfite derivative: a saturated solution of sodium bisulfite was added to the mixture, the phthalide was extracted with CH_2Cl_2, the solution was dried, and the solvent was evaporated. The turbid aqueous solution of the bisulfite derivative was treated with a saturated Na_2CO_3 solution until it became clear. After extraction with CH_2Cl_2 the solution was dried, and the solvent was evaporated. Gas liquid chromatography indicated that the degree of purity of these products required no further purification. Phthalide[15a,16a] and phthalic aldehyde[15b,16b] were identified by comparison of their IR and ^1H NMR spectra with those reported in the literature. The yields indicated in the Results and Discussion section are those corresponding to the masses of the products obtained after isolation. The aqueous phase resulting from the ether extraction described above was acidified with concentrated HCl to pH 2, saturated with NaCl, and extracted with a 8:2 mixture of ether/methylene chloride (which also does not dissolve the metal complex). After solvent evaporation, the white crystalline product consisted of a mixture of phthalic acid and 4-hydroxy-phthalide. Since the acid is insoluble in ethyl ether, 4-hydroxy-phthalide was extracted with this solvent. Phthalic acid was identified on the basis of melting point (205-208 °C, lit. mp 210-211 °C)[17] and also by comparison of the ^1H NMR and IR spectra with those in the literature.[15c,16c] The ethyl ether was dried and evaporated, giving a crystalline solid with a melting point of 83-85 °C and showing IR and ^1H NMR spectra, permitting its assignment as 4-hydroxy-phthalide.[18] Here again the yields indicated in the previous section are those corresponding to the masses of the products obtained after separation.

1,2-, 1,3-, and 1,4-Butanediol Oxidation. The diol (0.1350 g, 1.54 mmol) was dissolved in a buffer solution (1 mL) and added all at once to a vigorously stirred buffer solution (31 mL) containing **2** (0.0707 g, 0.1 mmol, 3.12 mM) previously oxidized at 26 °C. The current was increased to 42.5 mA for 1,2-butanediol, 28 mA for 1,3-butanediol, and to 56 mA for 1,4-butanediol. After the current fell to approximately 3 mA (19 hours for 1,2-butanediol, 48 hours for 1,3-butanediol, and 20 hours for 1,4-butanediol), the mixture was extracted with ether. The solvent was dried and evaporated, and the remaining liquid was purified by preparative TLC on a silica gel plate (3:2 ethyl ether/petroleum ether). γ-Butyrolactone (56.8 mg, 44%) was identified by comparison of its IR and ^{1}H NMR spectra with those in the literature.[15d,16d] 1-Hydroxy-2-butanone[19] (62 mg, 47%) and 1-hydroxy-3-butanone[20] (54.1 mg, 41%) were identified on the basis of their spectra.

Conclusion

Selectivity can be obtained at various stages of diol oxidation. The quantity of coulombs passed through the electrolysis cell, catalyst concentration, pH, and reaction temperature influence the formation of product. In some cases, this procedure results in interesting cyclization reactions which yield lactones.

Acknowledgments: The authors thank FAPESP, CNPq, and CAPES for financial support.

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(18) IR (KBr, cm^{-1}) 3300, 1735, 1600, 1460, 1070; ^{1}H NMR (80 MHz, $CDCl_3$, TMS) δ 7.70 (m, 4 H), 6.65 (s, 1 H), 5.00 (s, 1 H).

(19) IR (KBr, cm^{-1}) 3420, 1725, 1100; ^{1}H NMR (80 MHz, $CDCl_3$, TMS) δ 4.20 (d, 2 H), 2.32 (t, J = 6.7 Hz, 1 H), 1.65 (q, J = 6.7 Hz, 2 H), 0.95 (t, J = 6.7 Hz, 3 H).

(20) IR (KBr, cm^{-1}) 3380, 1710; ^{1}H NMR (80 MHz, $CDCl_3$, TMS) δ 5.32 (br, 1 H), 3.90 (t, J = 5.0 Hz, 2 H), 2.70 (t, J = 5.0 Hz, 2 H), 2.20 (s, 3 H).