Tetrahedron Letters,Vol.24,No.28,pp 2857-2860,1983 0040-4039/83 $3.00 + .00
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ELECTROGENERATED ACID AS A POWERFUL CATALYST FOR TRANSFORMATION OF EPOXIDES TO KETONES AND ACETONIDES

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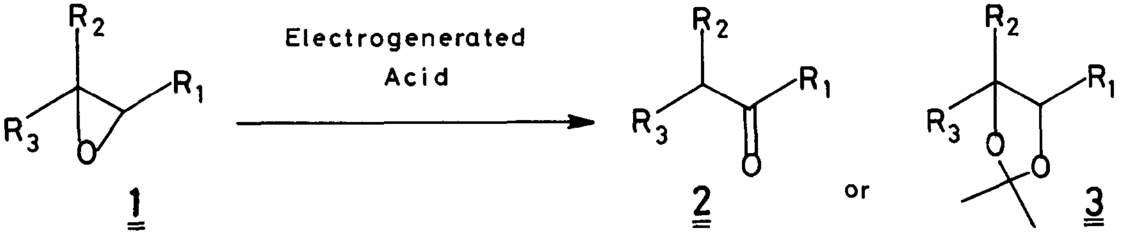
Summary: Electrochemical Transformation of epoxides **1** to ketones **2** and acetonides **3** were achieved by using an electrogenerated acid-catalyst. A combination of $M(ClO_4)_n$ [M; Li, Na, Mg, n = 1, 2] with polar aprotic solvents [CH_2Cl_2, $ClCH_2CH_2Cl$, THF, CH_3COCH_3, AcOEt, $(MeO)_2CO$] is useful for the electrochemical transformation.

Much attention has been paied to the electrochemical techniques as a potential tool in synthetic chemistry. Electrolysis procedure can be frequently employed for oxidation and reduction of organic compounds. However, very little is known about the acid-catalyzed reaction in an anodic process although several electrochemical reactions in MeCN-$LiClO_4$-Pt 1) and MeOH-$LiClO_4$ or Et_4NClO_4-Pt systems 2) have been explained in terms of an acid-catalysis. We describe here a practical method for the transformation of epoxides **1** to ketones **2** and acetonides **3** promoted by a powerful electrogenerated acid. During our study, an electron-transfer chain reaction for an electrochemical ring opening of some epoxides has been proposed. 3) In contrast to this, the present electrochemical transformation of epoxides **1** to ketones **2** is an electrogenerated acid-catalyzed reaction.



A typical electrolysis condition is as follows; A mixture of **1a** (0.2 mmol) and $LiClO_4$ (1.0 mmol) dissolved in CH_2Cl_2 (7.5 ml) - THF (0.5 ml) 4) was electrolyzed under a constant current (10 mA for 1 min, 0.03 F/mol) at room temperature using platinum foils as electrodes in an undivided cell, affording **2a** (91%) and 8-benzyloxy-2,6-dimethyloct-1-en-3-ol (**4a**) (8%). The electrochemical transformation of **1** to **2** is characterized by the following facts; (1) The reaction completes by passing a very small amount of electricity (0.02 - 0.1 F/mol), (2) Without electrolysis no **2a** was detected and **1a** was recovered, (3) By electrolysis in a divided cell **2a** was obtained only from an anolyte and **1a** was completely recovered from a catholyte, (4) Ketone **2a** was obtained in good yield (91%) evenwhen **1a** was allowed to react in a preelectrolyzed solution,[5] (5) Presence of pyridine (1 eq) in the preelectrolyzed solution inhibited the conversion and no **2a** was detected, (6) In the prolonged electrolysis, a dark gray lithium metal deposited on the cathode and a check of pH revealed that the electrolysis solution was acidic, (7) The electrolysis gave higher yield and selectivity than those of the usual acid-catalysis (Table 2). These experimental results strongly suggest that the electrochemical conversion is an electrogenerated acid-catalyzed reaction rather than an electron-transfer chain reaction.[3],[6]

The mechanism on the generation of the electrogenerated acid is not uncovered yet. However, it is plausible that oxidation of a trace amount of water existing in the electrolysis solution would generate a naked acid in an unbuffered condition which is therefore extremely strong in aprotic solvents.[7]

The effect of electrolytes is important. Perchlorates such as $LiClO_4$ (91%, 0.02 F/mol), $NaClO_4$ (90%, 0.04 F/mol), and $Mg(ClO_4)_2$ (79%, 0.04 F/mol in THF) significantly promoted the conversion. Use of Et_4NClO_4 provided **2a** in a good yield (89%) but it required more electricity (0.5 F/mol in CH_2Cl_2). Interestingly, use of Et_4NOTs in CH_2Cl_2 led to the preferential formation of **4a** (57%) although the current efficiency was unsatisfactory (3.1 F/mol). In contrast, both Et_4NBr and CF_3CO_2Li did not give the desired ketones. Use of Et_4NBr in CH_2Cl_2 resulted in a recovery of **1a** even after 3.7 F/mol of electricity was passed. On electrolyzing **1a** with CF_3CO_2Li, debenzylation took place in part, affording benzaldehyde (21%) and 6,7-epoxy-3,7-dimethyloctan-1-ol (19%) along with the recovered **1a** (70%) after 4.5 F/mol.

Aprotic solvents such as CH_2Cl_2 (91%), $ClCH_2CH_2Cl$ (95%), THF (85%), Me_2CO_3 (75%), and AcOEt (76%) are useful for the purpose. However, use of MeCN (simply distilled once over P_2O_5) and MeOH (treated with Mg and distilled) did not promote the electrochemical reaction.

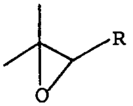
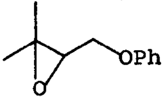
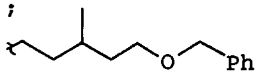
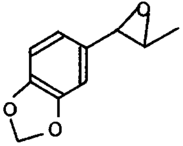
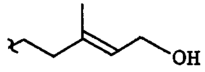
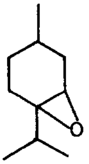
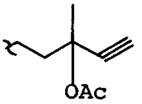
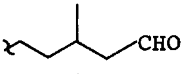
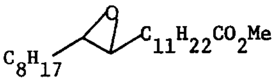
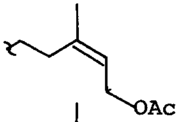
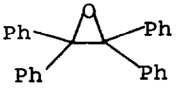
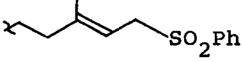
Similarly, the electrochemical conversion of **1** into acetonides **3** was performed by electrolyzing **1** in a distilled acetone containing $LiClO_4$ or $Mg(ClO_4)_2$ at room temperature. Particularly noteworthy is the fact that the electrochemical acetonidation can be performed by use of a trace amount of $LiClO_4$ (1% mol eq to **1c**) and a catalytic amount of electricity (0.1 F/mol). The selectivity of the acetonidation is strictly controlled by the concentration of $LiClO_4$; [Acetonide **3c** (%) : Ketone **2c** (%) ($LiClO_4$ mol eq to **1**), 87:5 (0.01), 76:15 (0.2), 61:28 (2.0), 51:40 (12)]. Ketone **2c** increased with the concentration of $LiClO_4$ presumably because in the high concentration of the salt the intermediate carbenium ion would be significantly associated with $LiClO_4$ as proposed by Pocker,[8] thus retarding nucleophilic attack of acetone. As an electrolyte, $LiClO_4$ (87%, 0.1 F/mol), $NaClO_4$ (84%, 0.16 F/mol), $Mg(ClO_4)_2$ (90% 0.1 F/mol), and $LiBF_4$ (81%, 0.1 F/mol) were effective. However, Et_4NClO_4 gave poor yield and current efficiency (37%, 1.7 F/mol) and the use of Et_4NBr or Et_4NOTs resulted recovery of **1c** even after 2.0 F/mol of electricity was passed.

The electrolysis of the corresponding diol of **1c** in $LiClO_4$ - acetone provided **3c** (85%, 0.3 F/mol) although the current efficiency was lower than that of epoxide **1c** (0.1 F/mol). In contrast to this, cyclohexene oxide gave cyclohexene diol (91%) as a sole product which could not be converted to the corresponding acetonide evenwhen 1 F/mol of electricity was passed. This result suggests that acyclic diols also can be transformed into acetonides by the present electrolytic method.

The results of the electrochemical rearrangement of epoxides 1 to ketones 2 and acetonides 3 are summarized in Table 1. Acyclic ω-epoxyisoprenoids 1a-1f were converted to 2a-2f and 3a-3f in satisfactory yields. Functional groups involved in 1 (OH, OAc, SO_2Ph, CHO, and C=C and C≡C bonds) did not change in the electrolysis conditions. Epoxides 1h derived from isosafrole provided 1-(3,4-methylenedioxyphenyl)propan-2-one (2h) (82%), a synthetic precursor of α-methyldopa.[9] Similarly, menthene oxide 1i gave a mixture of menthone and isomenthone (72%). Although epoxide 1j of a long chain fatty acid (erucic acid) is less reactive, it could be converted to the corresponding ketone 2j (82%) and acetonide 3j (84%). Electrolysis of 1k proceeded very slowly (1.22 F/mol), affording triphenylmethyl phenyl ketone 2k (30%) along with benzophenone (69%). In contrast, the reaction of 1k in a preelectrolyzed solution provided 2k in 97% yield (After 2.53 F/mol, 1k was added to the preelectrolyzed solution and stood for 2.5 h.).

The result of the electrochemical rearrangement (1 → 2) apparently demonstrates usefulness of the electrolysis method (Table 2) in comparison with the conventional chemical acid-catalyzed reaction. On the contrary to the electrolysis, the action of BF_3 etherate in benzene which is one of the most widely employed reagents for the epoxide ring opening induced

TABLE 1. Electrochemical Transformations of Epoxides 1 to Ketones 2 and Acetonides 3

	Epoxide 1	F/mol	Product % 2^{A}, 3^{B}		Epoxide 1	F/mol	Product % 2^{A}, 3^{B}
				g		0.06 0.09	67 (83)*
R ; a		0.09 0.2	91 (86)**	h		0.06 0.09	82 ^{C} (85)*
b		0.06 0.17	74 (70)*	i		0.12	72 ^{C}
c		0.03 0.1	80 (87)*				
d		0.04 0.06	88 (83)**	j		0.23 0.72	82 ^{D} (84)* ^{G}
e		0.01 0.1	87 ^{F} (88)*	k		1.22 2.53	30 97 ^{E}
f		0.03 0.15	88 (85)**				

A) 1 (0.2 mmol), $LiClO_4$ (1 mmol) and Et_4NClO_4 (0.5 mmol) in CH_2Cl_2 (a - g), $ClCH_2CH_2Cl$ (h, i, j), CH_2Cl_2-THF (k) (8 ml) at room temp. Current density (mA/cm^2) 6.7 (a,b,i,k), 3.3 (d,e,g,h,j) and 1.7 (c,f). B) Yield of 3 is indicated by (%): *; $LiClO_4$, **; $Mg(ClO_4)_2$. C) at 75 °C. D) at 65 °C. E) Reaction in a preelectrolyzed solution. F) 1e (2.4 mmol) G) 53°C in part Wagner-Meerwein type rearrangement, affording 7-benzyloxy-2,2,5-trimethylheptan-1-al (16%) as a by-product along with the desired ketone **2a** (77%).

TABLE 2. A Comparison between Electrochemical and Chemical Acid-catalyzed Rearrangements of **1a** to **2a** in CH_2Cl_2.[a]

Acid	Time	Product (%) **2a**	Acid	Time	Product (%) **2a**
Electrolysis	1 min	91			
CH_3COOH	12 hr	0	60% $HClO_4$ aq	1 min	77
HCOOH	12 hr	0	TsOH	1 min	47[e]
CF_3COOH	1 min	49[b]	47% BF_3-etherate[c]	1 min	77[d]

a) Reaction of 1a with 1 eq of acid at room temperature. b) The corresponding diol monotrifluoroacetate (50%) was obtained . c) In benzene. d) 7-Benzyloxy-2,2,5-trimethylheptan-1-al (16%) was isolated as a by-product. e) **4a** (53%) was obtained as a by-product.

Acknowledgement: The authors are grateful to the Ministry of Education, Science, and Culture for a financial support by a Grant-in-Aid (No. 57118002) for the Special Project Research (Innovative Studies on Highly Selective Synthesis).

References and Notes

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4) Methylene chloride was once distilled over P_2O_5 and THF was dried with sodium-benzophenone and distilled.

5) After electrolyzing the solution (CH_2Cl_2-THF-$LiClO_4$, 10 mA for 1 min, 0.03 F/mol), **1a** was added to the solution and allowed to react for 3 min.

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(Received in Japan 3 March 1983)