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SYNTHESES OF CARBONYL COMPOUNDS BY THE ANODIC CLEAVAGE OF GLYCOLS AND RELATED COMPOUNDS 1)

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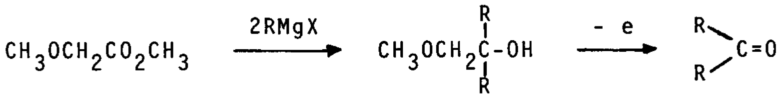
Previously, we have found that the anodic oxidation of glycols brought about a very clean cleavage of a carbon-carbon bond to form carbonyl compounds.2)

We wish to report that this anodic oxidation is a remarkably potential method in the general syntheses of carbonyl compounds such as symmetrical and unsymmetrical ketones, and those hardly prepared by the usual chemical methods.

As shown in the Scheme I, the electrochemical oxidation of dialkylmethoxymethylcarbinol, prepared from the Grignard reaction of methyl methoxyacetate (**1**),3) gave symmetrical ketones in high yields.

Scheme I



$$CH_3OCH_2CO_2CH_3 \xrightarrow{2RMgX} CH_3OCH_2C(R)_2\text{-}OH \xrightarrow{-e} R_2C{=}O$$

1 **2**a - e

Since both of the alkyl groups in the symmetrical ketones are derived from the Grignard reagent, this new method is applicable to the syntheses of a variety of ketones from the single starting compound (**1**), providing that the Grignard reaction is feasible. The results are summarized in the Table I.

The general procedure of the electrooxidation of dialkylmethoxymethylcarbinol.

Into a 50 ml undivided cell fitted with carbon rod electrodes were placed dialkylmethoxymethylcarbinol (0.02 mol), tetraethylammonium p-toluenesulfonate (0.002 mol), and methanol (30 ml). The constant current (0.2 A) (4 - 6 F/mol) was passed through the solution at room temperature. After the almost complete consumption of the starting material was observed by gas chromatography, the reaction mixture was poured into 100 ml of water, and was extracted with three 100 ml. portions of ether. After the combined ethereal layer was dried, the product was obtained by the distillation.

Table I. The isolated yields of α-hydroxy ethers and symmetrical ketones

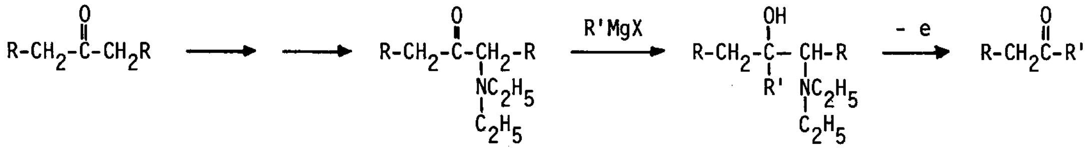
		R	α-hydroxy Ethers (%)*	Symmetrical Ketones (%)**
2	a	n-Pr	85	85
	b	i-Pr	70	88
	c	n-Bu	82	80
	d	i-Bu	83	80
	e	cyclohexyl	48	80

* Methyl methoxyacetate (0.05 mol) was added to the Grignard reagent (0.3 mol) prepared in THF, and the solution was refluxed for one day.

** The isolated yield was calculated when 4 - 6 F/mol of electricity was passed. All of the products were identified by the comparison of NMR and IR with those of authentic samples.

The syntheses of unsymmetrical ketones were also exploited on the basis of the fact that the electrooxidation of 1,2-amino alcohols showed the similar bond cleavage to 1,2-glycols. The process is shown in the Scheme II.

Scheme II



3a - c

α-(N,N-Diethylamino)ketones,[4] which were prepared easily from the corresponding ketones, were alkylated with the Grignard reaction, and the resulting 1,2-amino alcohols were electrooxidized to unsymmetrical ketones in satisfactory yields. For example, the anodic oxidation of 1,2-amino alcohol (**3**a) (0.02 mol) in methanol (30 ml) containing sodium methoxide (0.04 mol) as a supporting electrolyte was carried out until 3 F/mol of electricity was passed. The reaction mixture was poured into aqueous hydrochloric acid and the product was extracted with ether. The results are summarized in the Table II.

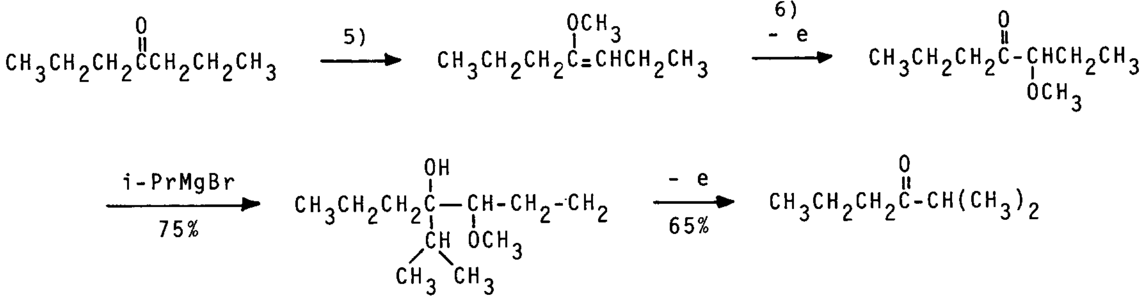
Table II. The isolated yields of amino alcohols and unsymmetrical ketones

		R	R'	Amino Alcohols (%)	Unsymmetrical Ketones (%)
3	a	H	n-Bu	71	72
	b	H	cyclohexyl	49	60
	c	Et	i-Pr	57	52

The reaction depicted in the Scheme II also indicated that the substitution of one of the alkyl groups in the ketones by another group can easily be achieved with this new method. For instance, di-n-propyl ketone was transformed to n-propyl isopropyl ketone in a moderate yield as shown in the Table II.

The similar transformation was also feasible in the oxidative cleavage of 1,2-glycols as shown in the Scheme III.

Scheme III



As shown in the Scheme IV, the alkylation of α-methoxycyclohexanone[7] with lithio acetonitrile,[8] lithio ethyl acetate[9] or alkyl magnesium bromide followed by the anodic oxidation gave the ring opened carbonyl compounds, which were hardly prepared by conventional chemical methods. The results are summarized in the Table III.

Table III. The isolated yields of α-hydroxy ethers (**4**a - d) and carbonyl compounds (**5**a - d)

	R	α-Hydroxy Ethers (%) (**4**)	Carbonyl Compounds (%) (**5**)
a	Me	61	75
b	n-Bu	73	72
c	CH_2CN	50	40*
d	CH_2CO_2Et	60	44*

* The isolated yields were calculated when 2 F/mol of electricity was passed.

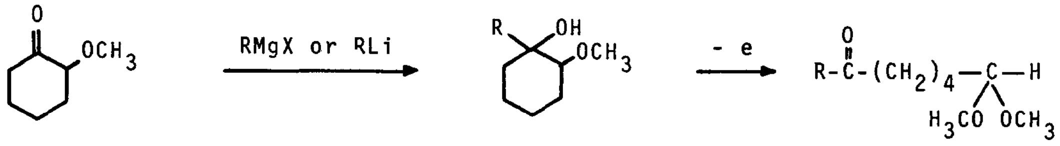
5a: IR (cm^{-1}) 2830 (OCH_3), 1710 (C=O), 1130 (C-O); nmr (CCl_4) δ 4.30 (t., 1H), 3.26 (s., 6H), 2.40 (t., 2H), 2.1 (s., 3H), 1.4 (broad s., 6H).

5b: IR (cm^{-1}) 2830 (OCH_3), 1710 (C=O), 1130 (C-O); nmr (CCl_4) δ 4.23 (t., 1H), 3.20 (s., 6H), 2.30 (t., 4H), 1.3 (broad s., 10H), 0.9 (t., 3H).

5c: IR (cm^{-1}) 2830 (OCH_3), 1730 (C=O), 1120 (C-O); nmr (CCl_4) δ 4.30 (t., 1H), 3.63 (s., 2H), 3.22 (s., 6H), 2.26 (t., 2H), 1.4 (broad s., 6H).

5d: IR (cm^{-1}) 2830 (OCH_3), 1740 ($\overset{O}{\overset{\|}{C}}$-O), 1710 (C=O), 1120 (O-C); nmr (CCl_4) δ 4.10 (q., 2H), 3.27 (s., 2H), 3.18 (s., 6H), 2.47 (t., 2H), 1.4 (broad s., 8H), 1.3 (t., 3H).

Scheme IV



4a - d

5a - d

As it is demonstrated above, the anodic oxidation of 1,2-glycols and related compounds is undoubtedly one of the most promising methods in the syntheses of carbonyl compounds from the viewpoints of its simplicity, non-polluting nature, and wide potentiality.

References amd Notes

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