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THE MIGRATORY APTITUDE IN THE ANODIC OXIDATION OF β-HYDROXYCARBOXYLIC ACIDS, AND A NEW SYNTHESIS OF dl-MUSCONE[1)]

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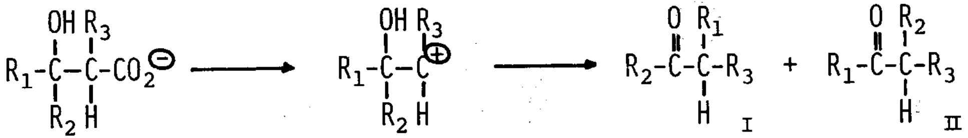
It has well been known that the electrochemical decarboxylation of β-hydroxycarboxylic acids gives ketones (I and II in eq (1)) by the rearrangement involving the migration of β-alkyl substituent to the developing cationinc center. Although this reaction has been used in some organic syntheses,[2),3)] the lack of the systematic study on the migratory aptitude of alkyl substituent (R_1 or R_2) in the rearrangement has hindered markedly the development of this reaction as a promising method in organic syntheses.



$$R_1\text{-}\overset{OH}{\underset{R_2}{C}}\text{-}\overset{R_3}{\underset{H}{C}}\text{-}CO_2^{\ominus} \longrightarrow R_1\text{-}\overset{OH}{\underset{R_2}{C}}\text{-}\overset{R_3}{\underset{H}{C}}{}^{\oplus} \longrightarrow R_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{R_1}{\underset{H}{C}}\text{-}R_3 + R_1\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{R_2}{\underset{H}{C}}\text{-}R_3 \quad \cdots (1)$$

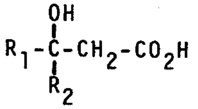
1 **2** I II

Type A $R_3 = H$

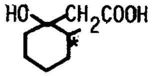
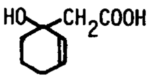
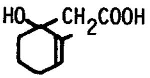
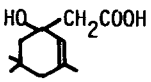
Type B $R_3 = CH_3$

As one of our basic studies on the electroorganic syntheses, we investigated the migratory aptitude of alkyl group R_1 or R_2 in the anodic oxidation of β-hydroxycarboxylic acids **3-15**, and exploited a new route of the synthesis of dl-muscone from cyclododecanone on the basis of the findings as to the relative preference for migration. The acids **3-8** (0.02 mole) prepared from the corresponding ketones by Reformatsky reaction[4)] were anodically oxidized with carbon rod electrode in the mixed solvent of acetonitrile (18 ml) and triethylamine (1 ml) until the current became negregible.[5)] The anodic oxidation of the potassium salts[6)] of olefinic acids **9-15**, which were obtained by the alkaline hydrolysis of the corresponding β-hydroxy esters,[7)] was carried out in pyridine-water (9:1). The anode potential was about 2.4 V vs SCE.. The products were identified by spectroscopic analysis and/or by comparison with the authentic samples. The ratio of II to I, which was determined by nmr and/or glc methods, was constant throughout the reaction.

The results in which the substituent R_3 is hydrogen (Type A) are shown in Table I, and Table II gives the results obtained from the starting compounds where R_3 is methyl (Type B).

Table I. Anodic Oxidation of 

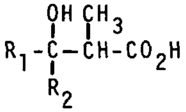
$R_1-\overset{OH}{\underset{R_2}{C}}-CH_2-CO_2H$ (Type A) a)

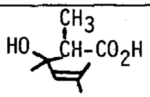
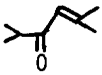
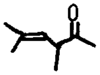
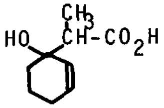
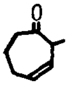
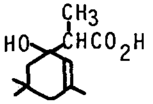
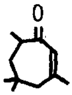
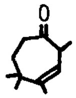
	Starting Carboxylic Acids R_1	R_2	Product's Ratio a) II/I
3	Me	-Et	1.5
4	Me	-i-Pr	1.8
5	Me	-t-Bu	2.2
6	Me	$-CH_2\phi$	4.5
7	Me		5.3
8	 b)		1.0
9	Me		only II
10	 c)		5.6
11	 c)		5.0
12	 c)		17.0

a) The migrations of R_1 and R_2 give the products I and II, respectively.
b) The migration of the carbon asterisked yields the product II.
c) R_2 corresponds to the olefinic side.

It is clearly shown in Table I that the migratory aptitudes of simple alkyl groups are in the similar magnitude, while olefinic, cyclopropyl and benzylic substituents migrate predominantly. The migratory aptitudes of the simple alkyl groups are comparable to those observed in the reaction of ketones with diazomethane.9)

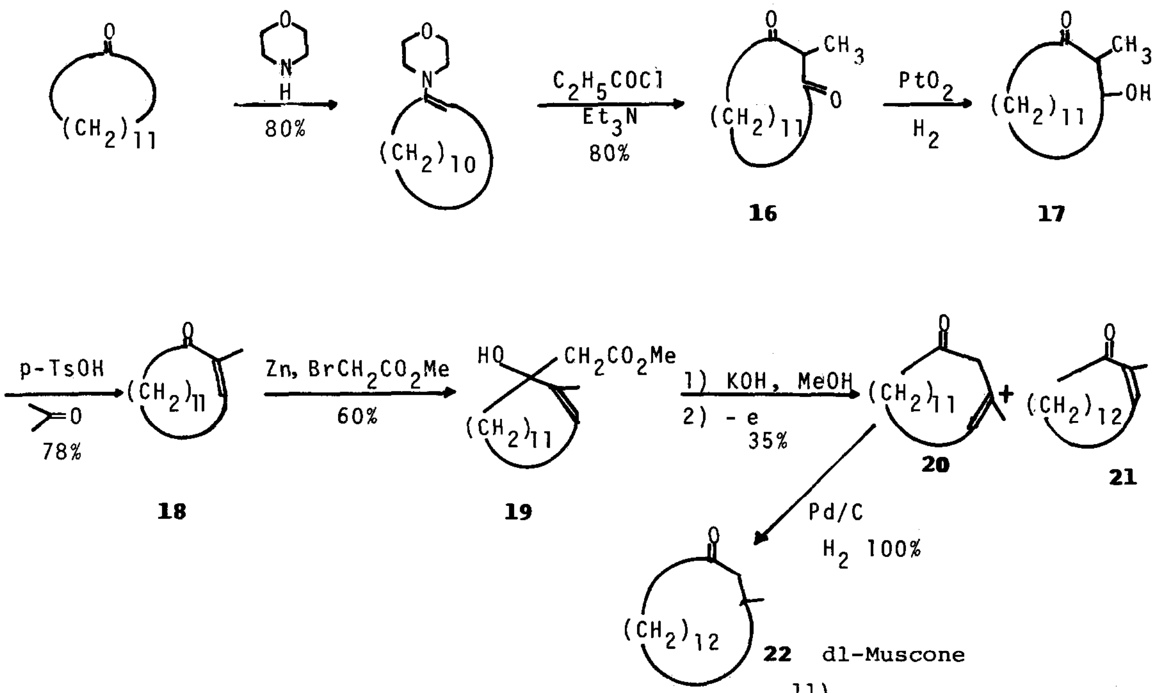
As it is shown in Table II, however, the selectivity was markedly diminished in the rearrangement of type B. This results may suggest that the conformation

Table II. Anodic Oxidation of  $R_1\text{-}\overset{\displaystyle OH}{\underset{\displaystyle R_2}{C}}\text{-}\overset{\displaystyle CH_3}{CH}\text{-}CO_2H$ (Type B).

	Starting Carboxylic Acids	Products I	 II	Product's Ratio II/I
13				1.9
14				1.2
15				1.0

of the intermediate cation **2** plays an important role in the controle of the migratory aptitude.[10)]

The finding that the olefinic group showed some predominance in the rearrangement prompted us to exploit a new process of the synthesis of dl-muscone from cyclododecanone. The reaction scheme is shown below.



1,3-Diketone (**16**) prepared by the reported method [11)] was reduced to **17** with a catalytic amount of platinum oxide under the atmospheric pressure of hydrogen.

The dehydration of **17** by heating with p-toluenesulfonic acid in acetone gave **18**, the yield being 78% from **16**.

The Reformatsky reaction of **18** gave the key intermediate **19**: mp 52-53°, ir; 3500, 1710 cm^{-1}, nmr (δ_{TMS} ppm, in CCl_4); 1.0-1.7 (m., 22H), 1.55 (s., 3H), 1.8-2.3 (m., 2H), 2.5 (d., 2H), 3.5 (s., 1H), 3.6 (s., 3H), 5.3 (t., 1H), m/e (%): 296 (p).

The anodic oxidation of the potassium carboxylate prepared by the alkaline hydrolysis of **19** under the similar condition to that shown above yielded a rearranged ketone **20** (the yield, 30%) contaminated with a small amount of the isomer **21** (the yield, 5%). The ketone **20** was isolated by tlc (silica gel, ethyl acetate - hexane (1:10)): **20**; ir; 1705 cm^{-1}, nmr (δ_{TMS} ppm, in CCl_4); 1.00-1.70 (broad s., 18H), 1.60 (s., 3H), 1.70-2.55 (m., 4H), 2.90 (s., 2H), 5.25 (t., 1H). **21**; ir; 1655 cm^{-1}, nmr (δ_{TMS} ppm, in CCl_4); 1.00-1.70 (broad s., 20H), 1.70-2.70 (m., 4H), 1.73 (s., 3H), 6.53 (t., 1H).

The hydrogenation of **20** gave dl-muscone (**22**) quantitatively, which was identified by spectroscopic comparison with the authentic sample.12) **22**; ir; 1715 cm^{-1}, nmr (δ_{TMS} ppm, in CCl_4); 0.93 (d., 3H), 1.0-1.8 (broad s., 23H), 2.0-2.6 (m., 4H).

As the exploitation of the new route in the synthesis of dl-muscone clearly demonstrates, the systematic study on the migratory aptitude in the anodic oxidation of β-hydroxycarboxylic acids brings about a promising tool in organic syntheses.

References and Notes

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