GENERATION AND REACTIONS OF 3-CARBOXY- AND 3-CARBALKOXYPROPYL RADICALS

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Carboxy- and carbalkoxyalkyl radicals are obtained by either the catalytic or thermal decomposition of peroxyalkanedicarboxylic acids and their esters [1], the peroxides and hydroperoxides of cycloalkanones [2], oxazaridines [3], by the oxidative decarboxylation of ω -carbalkoxyalkanoic acids using Pb(OCOCH₃)₄ [4], and electrochemically [5].

In order to generate the 3-carboxy- and 3-carbalkoxypropyl radicals, and also to ascertain the behavior of these radicals under the conditions of oxidation-reduction reactions, in the present paper we studied the oxidative decarboxylation of glutaric acid (Ia) and its monoesters, and specifically the methyl (Ib), ethyl (Ic), isopropyl (Id), and benzyl (Ie) esters, under the influence of Na₂S₂O₈ in the presence of catalytic amounts of Ag⁺.

 $\begin{array}{c} \operatorname{ROOC}(\operatorname{CH}_2)_3\operatorname{COOH} \xrightarrow{S_2O_4 \leftarrow \operatorname{Ag}^+} \operatorname{ROOC}(\operatorname{CH}_2)_2\operatorname{CH}_2 + \operatorname{CO}_2 + \operatorname{H}^+ \\ (\operatorname{Ia-e}) & (\operatorname{IIa-e}) \end{array}$ Here and subsequently R = H (a), CH₃ (b), C₂H₅ (c), i-C₃H₇ (d) and C₆H₅CH₂ (e).

The decarboxylation of carboxylic acids by the given oxidation system is a simple method for the generation of various radicals that are finding constantly broader use [6]. The reaction mechanism can be depicted by the following series of equations [7]:

> $Ag^+ + S_2O_8^{2-} \rightarrow Ag^{2+} + SO_4^{-} + SO_4^{2-}$ $Ag^+ + SO_4^- \rightarrow Ag^{2+} + SO_4^{2-}$ $\begin{array}{c} Ag^{2+} + \text{RCOOH} \rightarrow Ag^{+} + \text{RCOO}^{\bullet} + \text{H}^{+} \\ \text{RCOO}^{\bullet} \rightarrow \text{R}^{\bullet} + \text{CO}_{2} \end{array}$

We ran the decarboxylation of acids (Ia-e) in either aqueous or 50% aqueous-acetonitrile solution in either a nitrogen or argon atmosphere. Acetonitrile was used to create a homogeneous reaction mixture during the decarboxylation of the difficultly water-soluble ester (Ie), and also in the decarboxylation of (Ia-d) in order to assure standard reaction conditions. The Na₂S₂O₈ was used in an equimolar amount with respect to (I), while the amount of taken $AgNO_3$ was 5-15 mole %.

Employing GLC, butyric acid (IIIa) and γ -butyrolactone (IV) were identified in the reaction products (Table 1), with the exception of Experiment 13. Besides (IIIa) and (IV), methyl butyrate (IIIb) [from Ib)], ethyl butyrate (IIIc) [from (Ic)], isopropyl butyrate (IIId) [from (Id)], benzyl butyrate (IIIe) [from (Ie)], and CO2 are formed (in all of the experiments), and also very small amounts of methane, ethane, and propane (Experiments 2-4). Acid (IIIa) and esters (IIIb-e) are formed from radicals (IIa-e) as the result of cleavage of a hydrogen atom from the hydrogen donor SH, which can be (Ia-e), (IIa-e), (IV), or CH₃CN.

$$(IIa - e) + SH \rightarrow CH_{3}CH_{2}CH_{2}COOR + S'$$

$$(IIIa - e)$$
(1)

Methane, ethane, and propane are obtained in a similar manner from the corresponding hydrocarbon radicals R, which are generated in reaction (3).

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TABLE 1. Oxidative Decarboxylation of $ROOC(CH_2)_3COOH$ (Ia-e) (60°C, 3 h, Na₂S₂O₈ conversion 100%)*

Expt. No.	R	Solvent, ml		Reaction products, mole/mole of $Na_2S_2O_8$				
		H20	CH3CN	CO2	RH	(III)	(IV)	(IV)/(III)
1 2 3 4 5 6 7 8 9 10 11 12 13	H (a) CH ₃ (b) C ₃ H ₅ (c) $i-C_3H_7 (d)$ C ₆ H ₅ CH ₂ (e) H (a) CH ₃ (b) CH ₃ (b) CH ₃ (b) CH ₃ (b) CH ₃ (b) CH ₃ (c) $i-C_3H_7 (d)$ C ₆ H ₅ CH ₂ (e)	43 43 43 23 23 40 23 23 40 23 23 23 23		0,60 0,53 0,50 0,48 0,52 q.i. "	q.i.† 0,013 q.i. — — — —	0,24 q.i. 0,27 q.i. 0,42 q.i. " " " "	0,24 q.i. 0,1 q.i. 0,07 q.i. " "	$\left \begin{array}{c}1\\0,17\\0,37\\0,62\\0,18\\0,40\\0,07\\0,07\\0,07\\0,07\\0,07\\0,07\\0,00\\0,01\\0\end{array}\right $

*(1) = 0.02 mole (in Expts. 1 and 6 = 0.04 mole), $Na_2S_2O_8 = 0.02$ mole, and $AgNO_3 = 0.003$ mole (in Expts. 9 and 10 = 0.001 mole).

[†] The compound was identified qualitatively.

$$R' + SH \rightarrow RH + S'$$

Butyrates (IIIb-e) are hardly hydrolyzed to (IIa) under the experimental conditions while adding the $Na_2S_2O_3$ solution. This is indicated by the very small value of the (IIIa)/(IIIb-e) ratio, which is equal to 0.08-0.1, in the reaction mixture on conclusion of adding the $Na_2S_2O_3$, and also by the absence of propane in the reaction products, the formation of which could be expected due to the generation of the propyl radical from (IIIa) if acid (IIIa) was formed before the addition of the $Na_2S_2O_3$ had been completed. Apparently, esters (Ib-e) behave in a similar manner toward hydrolysis.

According to [8], lactone (IV) can be formed by the reaction:

$$(\Pi a - e) \rightleftharpoons \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc (IV) + R'$$

$$(Va - e) \tag{3}$$

However, this path is not the sole one as regards the discussed case, since the amount of hydrocarbons RH that is formed from the R radicals by reaction (2) is substantially less than equimolar relative to lactone (IV). For example, in Experiment 3 (see Table 1) the yield of ethane was only 15% of (IV). The obtained result cannot be explained by the oxidation of the hydrocarbon radicals, since according to the data given in [7], the oxidation would lead to their predominant conversion to olefins R(-H), which were not detected in the reaction products. Consequently, still another path exists from (V) to (IV). Apparently, lactone (IV) is formed mainly via the oxidation of the cyclic (V) radicals. These radicals, due to the fact that the radical center is adjacent to two electron-donor groups, have a well-defined nucleophilic character, which facilitates their easy oxidation by the reaction:

$$(Va-e) \xrightarrow{S_2O_8^{+} - A_9^{+}}_{H_2O} \longrightarrow \underbrace{OR}_{OX} \rightarrow (IV) + ROX$$

$$X = H \text{ or } SO_8^{-}$$
(4)

The given conclusion is in agreement with the observed dependence of the mole ratios of the formed (III) and (IV) on the structure of the R substituent in acids (Ia-e) when they are decarboxylated in aqueous solutions. The (IV)/(III) ratio increases from 0.17 to 1.0 in the R series: CH_3 , C_2H_5 , $i-C_3H_7$, and H (see Table 1, Experiments 1-4). In aqueous-acetonitrile solutions, due to the low yield of lactone (IV), a similar rule could not be observed. The found dependence of (IV)/(III) on R, with the exception of $R = C_6H_5CH_2$, is not associated with a change in the rate of reaction (1) in the series of (IIa-d) radicals. This conclusion follows from the results of studying the reactivity of acids (Ia-e) as H donors in the reaction with the 3-carboxypropyl radicals (IIa), which were generated by the thermal decomposition of peroxydiglutaric acid. In estimating the H-donor capacity of acids (Ia-e) we used CCl_3COOH as the reference standard. The corresponding experimental data are given in Table 2, from which it follows that acids (Ia-d) have the same donor capacity under the experimental conditions toward radical (IIa). This result is apparently caused

(2)

TABLE 2. Relative H-donor Capacity of ROOC(CH_2)₃COOH (Ia-e) in Reaction with 3-Carboxypropyl Radicals, Generated from Peroxydiglutaric Acid (60°, 100 h, standard compound CCl₃-COOH)*

R	$\frac{(III) \dagger}{(IV) + (VII)}$	Relative donor capa- city of (I) acids
H(a)	0.11	1
CH ₃ (b)	0,11	1
C2H5 (C)	0,11	1
$t - C_3 H_7$ (d)	0,105	1
C ₆ H ₅ CH ₂ (e)	1.88	17

*(I) - 0.01 M; CCl₃COOH - 0.01 M; peroxydiglutaric acid = 0.002 M; $H_2O = 15$ ml. †(VII) = 4-chlorobutyric acid. The latter under the experimental conditions is partially converted to lactone (IV), and consequently (IV) is included

in the denominator of the ratio.

by the polar effect, and specifically by the preferential attack of the electrophilic centers of the H-donor molecules by the nucleophilic (IIa) radicals. Such centers in acids (Ia-d) are the α -CH₂ groups of the acyl fragment of the acids. As a result, a change in R hardly affects the course of the process. The substantially greater H-donor capacity of acid (Ie) when compared with acids (Ia-d) can be explained by the enhanced reactivity of the benzyl H-atoms when compared with the Hatoms of acids (Ia-d) due to the substantial difference in the stabilization energies of the radicals of the phenyl (24.5 kcal /mole [9]) and carboxyl or carbalkoxyl (~ 4 kcal/mole [10]) groups.

An increase in the (IV)/(III) ratio with increase in the nucleophilicity of the (V) radicals in the series: (Va) > (Vd) > (Vc) > (Vb) can be regarded to be an additional argument in support of the important role of oxidation reaction (4) in the process for the formation of lactone (IV).

EXPERIMENTAL METHOD

The GLC analysis of the liquid products was run on an LCM-8MD chromatograph equipped with a flame-ionization detector, while the gaseous products were analyzed on a CT-8 chromatograph equipped with a katharometer. Columns: $2 \text{ m} \times 3 \text{ mm}$ packed with 15% PEGS and 10% DS-550 (for the liquid products), $3 \text{ m} \times 4 \text{ mm}$ packed with 30% Dowtherm A, and $1 \text{ m} \times 4 \text{ mm}$ packed with Poropak Q (150-200 mesh). The solid support was Chromosorb W (0.2-0.25 mm). The carrier gas was either nitrogen or helium. The (IV) /(III) ratios were calculated taking into account the experimentally found correction factors. The yield of the reaction products was determined by the internal standard method. δ -Valerolactone, valeric acid, and methane were used as the standards. The reaction products were identified by comparison with authentic samples. The structure of lactone (IV) was also confirmed spectrophotometrically, by the characterisitc lactone absorption band (1780 cm⁻¹) [11] in the IR spectrum of the evaporated ether extract from Experiments 1 and 4 (see Table 1). The spectrum was taken on a UR-20 spectrometer in ether.

The monoesters of glutaric acid: ethyl (IIIc), isopropyl (IIId), and benzyl (IIIe) esters were obtained in 70-85% yield from the corresponding alcohols and glutaric anhydride [12, 13]. The commercial pure monomethyl glutarate was purified by vacuum-distillation. Its purity and that of the monoesters were checked by the neutralization equivalent. The pure glutaric acid, pure $Na_2S_2O_8$, analytical grade AgNO₃, and CH₃CN were used as the commercial products. All of the aqueous solutions were prepared using singly distilled water.

General Decarboxylation Method

<u>a.</u> In Aqueous-Acetonitrile Solution. To a stirred solution of 20 mmoles of acid (III) and 3 mmoles of AgNO₃ (3 ml of aqueous 1 N solution) in 20 ml of CH₃CN and 5 ml of water, after blowing the reactor with argon (15 min) and thermostatting the solution at $60 \pm 20^{\circ}$, was gradually added in 2.5-3 h a solution of 20 mmoles of Na₂S₂O₈ in 15 ml of water. Then the mixture was kept at 60° for another 2 h. A gas buret was used to check the reaction course based on the gas evolution, which nearly ceases soon after all the Na₂S₂O₈ solution had been added. The gas evolution is very slow during the first hour of reaction. The mixture on cooling to ~20° separated into an organic and an aqueous layer, which were separated, and the aqueous layer was saturated with Na₂SO₄, extracted with ether (25 ml × 5), the ether extract was evaporated to ~ 3 ml, and the residue was combined with the organic layer and analyzed by GLC. The evolved gases were analyzed chromatographically.

b. In Aqueous Solution. To a solution of 20 mmoles of acid (III) and 3 mmoles of $AgNO_3$ (3 ml of aqueous 1 N solution) in 25 ml of water (due to its poor solubility in water, the decarboxylation of acid (IIIe) was run under heterogeneous conditions) at $60 \pm 2^{\circ}$ was added in 2.5-3 h a solution of 20 mmoles of $Na_2S_2O_8$ in 15 ml of water. The mixture was kept at 60° for an additional 2 h. An induction period in the gas evolution, which is characteristic for the reaction in aqueous-acetonitrile solution, is not observed in this case. At the end of reaction the homogeneous mixture, without prior treatment, was analyzed by GLC.

CONCLUSIONS

1. The oxidative decarboxylation of glutaric acid and its monoesters (methyl, ethyl, isopropyl, and benzyl) under the influence of $Na_2S_2O_8$, in the presence of $AgNO_3$, led to the generation of the ROOC $(CH_2)_2$ CH_2 radicals, where R = H, CH_3 , C_2H_5 , $i-C_3H_7$ or $C_6H_5CH_2$.

2. The principal transformation products of these radicals are butyric acid and alkyl butyrates, and also γ -butyrolactone. The yield of the lactone relative to butyric acid and its ester increases as follows in the R series: H > i-C₃H₇ > C₂H₅ > CH₃ \approx C₆H₅CH₂.

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