

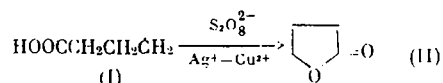
OXIDATIVE CYCLIZATION OF ω -CARBOXYALKYL RADICALS

Yu. N. Ogibin, É. I. Troyanskii,
and G. I. Nikishin

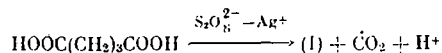
UDC 542.943:66.095.252:541.515

Oxidative cyclization, with the formation of five- and six-membered rings, is one of the characteristic reactions of aryl-substituted alkyl and benzoyloxy radicals [1-8]. The ions Cu(II) [2, 6], Pb(IV) [3, 6, 7], and Mn(III) [8], and the system $S_2O_8^{2-}$ -Ag(I) [4, 5] are usually used as the oxidizing agents in this reaction. The 3-carboxy- and 3-carbalkoxypropyl radicals, which are generated by the catalytic decomposition of peroxydiglutamic acid [9] or by the oxidative decarboxylation of glutamic acid and its monoalkyl esters under the influence of $Na_2S_2O_8$ and $AgNO_3$ [10], also undergo oxidative cyclization. However, together with oxidative cyclization, the product of which is γ -butyrolactone, these radicals undergo a number of other transformations, and specifically they undergo dimerization, cleave a hydrogen atom from a hydrogen donor, and are oxidized to vinylacetic acid. As a result, the contribution of oxidative cyclization to the sum of the transformations of the 3-carboxy- and 3-carbalkoxypropyl radicals does not exceed 50%.

In the present paper we report the selective oxidative cyclization of the 3-carboxypropyl radicals. A complete selectivity of the reaction was achieved by using the system $Na_2S_2O_8$ - $AgNO_3$ - $CuSO_4$ as the oxidizing agent.



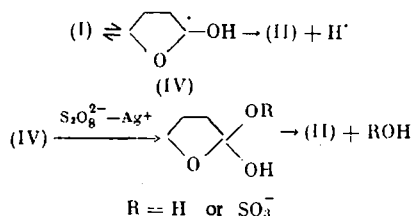
The (I) radicals were generated from glutamic acid at 60°C in aqueous solution under the influence of $Na_2S_2O_8$ in the presence of a catalytic amount of $AgNO_3$ [10]. The selectivity of the reaction is upset if



$CuSO_4$ is excluded from the oxidation system and, besides lactone (II), butyric acid (III) is obtained in an approximately equal amount. The latter is formed from the (I) radicals via the cleavage of H atoms from an H donor (SH), which can be either the starting glutamic acid or the reaction products.



According to the data given in [10, 11], in the absence of copper ions the formation of lactone (II) can proceed by two schemes:



A complete suppression of reaction (1) when copper ions are added to the system is due to their active participation in the processes for the oxidation of radicals (I) and (IV), which can be depicted by the following reactions. The ability of hydrated copper ions to cause the oxidation of alkyl radicals to the corresponding

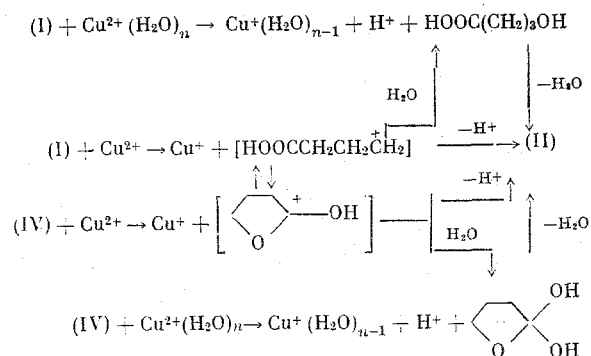
N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya*, No. 11, pp. 2522-2526, November, 1974. Original article submitted March 21, 1974.

© 1975 Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.

TABLE 1. Oxidative Decarboxylation of Glutaric Acid
(60°C, 3 h, solvent = 40 ml of water, and 20 mmoles each
of glutaric acid and Na₂S₂O₈)

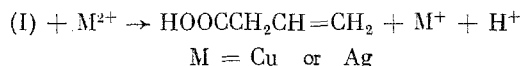
Reagents, mmoles			Reaction products, mole/mole of Na ₂ S ₂ O ₈ (mole/mole of CO ₂)			
AgNO ₃	CuSO ₄	NaOH	CO ₂	(II)	(III)	Σ
—	—	20 *	0,28	0,11 (0,38)	0,11 (0,38)	0,22 (0,76)
3	—	—	0,60	0,24 (0,40)	0,24 (0,40)	0,48 (0,80)
—	4	20 *	0,25	0,21 (0,84)	—	0,21 (0,84)
3	4	—	0,55	0,50 (0,91)	—	0,50 (0,91)
3	4	20	0,55	0,50 (0,91)	—	0,50 (0,91)

*Run at 100°.

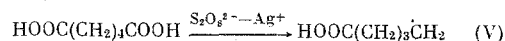


hydroxy compounds is known [12]. The involvement of the carbocation states in the processes for the oxidation of alkyl radicals by copper ions, especially when they are coordinated with hard ligands, is confirmed by the data given in [13]. The Ag²⁺ ions that are formed in the reaction of Ag⁺ with S₂O₈²⁻ [14] apparently oxidize radicals (I) and (IV) in a similar manner, but less efficiently.

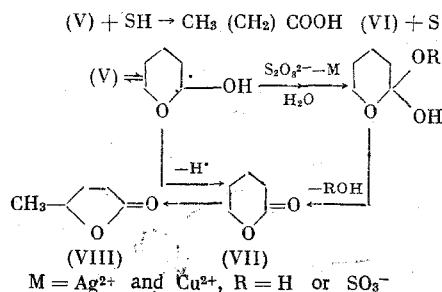
The oxidation of the (I) radicals by the oxidative elimination mechanism, which is characteristic for copper and silver ions [14, 15], was not observed under the experimental conditions (Table 1).



The adjacent homolog of radical (I), namely the 4-carboxybutyl radical (V), which was generated from adipic acid, undergoes similar transformations in the absence of copper ions, but with each transformation making a somewhat different contribution. The majority of the (V) radicals (~2/3) is converted to



valeric acid (VI), while the remainder is converted to δ-valerolactone (VII) (Table 2). Under the experimental conditions lactone (VII) is partially isomerized to γ-valerolactone (VIII), and is also oxidized to



butyrolactone (II). Thus, (VII) under the influence of an equimolar amount of Na₂S₂O₈, in the presence of AgNO₃ and CuSO₄, is converted in 3 h (60°C) to the extent of 53% to (II), while under the influence of a

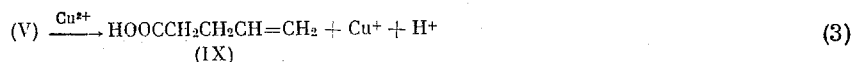
TABLE 2. Oxidative Decarboxylation of Adipic Acid (60°C, 3 h, solvent = 40 ml of water, and 20 mmoles each of acid and Na₂S₂O₈)

Expt. No.	Reagents, mmoles		Reaction products, mole/mole of Na ₂ S ₂ O ₈ (mole/mole of CO ₂)						
	AgNO ₃	CuSO ₄	CO ₂	(VI)	(VII)	(VIII)	(IX)	(II)	Σ
1	3	—	0,41	0,22 (0,54)	0,10 (0,24)	0,03 (0,07)	—	+	0,35 (0,85)
2*	3	4	0,35	—	0,16 (0,46)	0,06 (0,16)	0,03 (0,07)	0,06 (0,17)	0,31 (0,86)

*The (VII)/(VIII) ratio = 2.75 (immediately after adding the Na₂S₂O₈), 2.70 (after 2 h), and 2.66 (after 5 h).

threefold molar amount of NaHSO₄ it is converted to the extent of 10% to lactone (VIII). In addition, the isomerization of (VII) to (VIII) testifies to a decrease in the (VII)/(VIII) ratio with increase in the time of heating the reaction mixture after adding the Na₂S₂O₈ (see Expt. 2, Table 2).

In the presence of copper ions the behavior of radical (V) differs from that of radical (I). The main difference is the less selective character of the oxidative cyclization: besides conversion to lactone (VII), the (V) radicals are partially converted to allylactic acid (IX) via their oxidation by copper ions by the oxidative elimination mechanism. Lactone (VII) (taking into account its isomerization to (VIII) and oxidation to (II)) and acid (IX) are formed in an ~10:1 ratio.



The formation of the unsaturated acid (IX), together with lactone (VII), in the oxidation of radical (V) by the system S₂O₈²⁻—Ag⁺—Cu²⁺, and the absence of its lower homolog in the oxidation product of radical (I), are apparently due to the different ability of radicals (I) and (V) to be oxidized to lactones (II) and (VII). We postulate that this difference is determined by the substantial difference in the rates of the homolytic cyclization reactions, which respectively lead to five- and six-membered systems. Thus, in most cases, where cyclization of the radical with the competing formation of five- and six-membered rings is possible, the reaction that leads to the five-membered system is either the predominant or exclusive reaction [16]. The selective oxidation of radical (I) to lactone (II) is the direct consequence of this trait of homolytic cyclization. Under the investigated conditions the cyclization of radical (I), and the subsequent oxidation of the formed cyclic radical (IV), apparently proceed at a substantially faster overall rate than the competing reactions, for example, (1) and (2). Due to the smaller ability of radical (V) to undergo cyclization the overall rate of its conversion to lactone (VII) under the influence of the system Na₂S₂O₈—Ag⁺—Cu²⁺, relative to the rate of reaction (3), decreases and does not assure a selectivity of the process.

In conclusion it should be mentioned that in the decarboxylation of adipic acid the copper ions exert an effect not only on the conversion of the (V) radicals, but also on the isomerization of lactone (VII) to lactone (VIII) and the oxidation of (VII) to lactone (II). The yield of (VIII) and (II) increases sharply when the reaction is run in the presence of CuSO₄ (see Table 2).

EXPERIMENTAL

The GLC analysis was run on an LCM-8MD chromatograph equipped with a flame-ionization detector; nitrogen served as the carrier gas. The columns were: 1 m × 3 mm with 15% FFAP, and 2 m × 3 mm with 15% PEGS deposited on Chromosorb W (0.2–0.25 mm). The yield of the reaction products was determined via the internal standard method, taking into account the experimentally found calibration coefficients. As the standards we used δ-valerolactone, butyric acid, and valeric acid. The reaction products were identified by comparison with authentic specimens, while lactones (II) and (VIII) were also identified via IR spectroscopy by the characteristic absorption band at 1780 cm⁻¹ [16]. The spectra were taken on a UR-20 spectrometer in ether solution.

The glutaric and adipic acids (labeled pure), and the Na₂S₂O₈, AgNO₃, and CuSO₄ (labeled analytical grade) were commercial products and were used without further purification. All of the aqueous solutions were prepared using distilled water.

General Procedure. To a stirred solution of 20 mmoles of the dicarboxylic acid and 3 mmoles of AgNO₃, and also 4 mmoles of CuSO₄ (in a number of experiments), in 25 ml of water, after purging the

reactor with argon for 15 min and thermostating at 60°C for 2 h, was added a solution of 20 mmoles of $\text{Na}_2\text{S}_2\text{O}_8$ in 15 ml of water. On completion of adding the $\text{Na}_2\text{S}_2\text{O}_8$ solution the mixture was kept at 60°C for 1 h in order to completely decompose the $\text{S}_2\text{O}_8^{2-}$ ions. The course of the reaction was checked by the gas evolution using a gas buret, which was connected to the reactor. On completion of reaction the reaction mixture was cooled and analyzed by GLC: without prior workup in the experiments with glutaric acid, and after filtering the partially precipitated unreacted acid in the experiments with adipic acid. For a spectroscopic study of the reaction products the mixture was extracted with ether (50 ml \times 5), and the extract was dried, evaporated, and analyzed.

Oxidation of δ -Valerolactone (VII) with $\text{Na}_2\text{S}_2\text{O}_8$ in the Presence of Silver and Copper Ions. To a solution of 20 mmoles of (VII), 3 mmoles of AgNO_3 , and 4 mmoles of CuSO_4 in 25 ml of water, heated to 60°C, was added 20 mmoles of Na_2S in 15 ml of water in 2 h. The reaction product contained 6.9 mmoles of unreacted (VII) (65.5% conversion) and 10.6 mmoles of γ -butyrolactone. Lactone (VII) was obtained from 5-chlorovaleric acid as described in [17].

Isomerization of δ -Valerolactone (VII) to γ -Valerolactone (VIII). A solution of 5 mmoles of (VII) and 16.6 mmoles of NaHSO_4 in 40 ml of water was heated at 60°C for 3 h. The reaction products contained 4.5 mmoles of (VII) (10% conversion) and 0.45 mmoles of (VIII). The conversion of vinylacetic acid to γ -butyrolactone, and of allylacetic acid to (VII) and (VIII), was not observed under analogous conditions.

CONCLUSIONS

1. The 3-carboxypropyl and 4-carboxybutyl radicals were generated by the respective decarboxylation of glutaric and adipic acids at 60°C in aqueous solution under the influence of $\text{Na}_2\text{S}_2\text{O}_8$ in the presence of a catalytic amount of AgNO_3 , and their transformations under the decarboxylation conditions were studied, and also the effect of added copper ions on these transformations.

2. The system $\text{Na}_2\text{S}_2\text{O}_8$ — AgNO_3 — CuSO_4 causes an efficient oxidative cyclization of the studied ω -carboxyalkyl radicals, in which connection the 3-carboxypropyl radicals are selectively converted to γ -butyrolactone, while the 4-carboxybutyl radicals are converted to δ -valerolactone to the extent of 90%.

3. Oxidative cyclization also occurs in the absence of copper ions, but its contribution to the sum of the transformations of the 3-carboxypropyl radicals does not exceed 50%, and not over 30% in the case of the 4-carboxybutyl radicals.

LITERATURE CITED

1. M. Julia, J. M. Salard, and J. C. Chottard, *Bull. Soc. Chim. France*, 2478 (1973).
2. J. K. Kochi and R. C. Gilliom, *J. Am. Chem. Soc.*, **86**, 5251 (1964).
3. D. I. Davies and C. Waring, *J. Chem. Soc.*, C 1639 (1967); 1865, 2332, 2337 (1968).
4. P. M. Brown, J. Russell, R. H. Thompson, and A. G. Walie, *J. Chem. Soc.*, C 842 (1968).
5. J. Russell and R. H. Thompson, *J. Chem. Soc.*, 3379 (1962); R. H. Thompson and A. G. Walie, *J. Chem. Soc.*, C 321 (1966).
6. J. C. Chottard, M. Julia, and J. M. Salard, *Tetrahedron*, **25**, 4967 (1969); J. C. Chottard and M. Julia, *Tetrahedron*, **28**, 5616 (1972).
7. M. Julia, *Accounts Chem. Res.*, **4**, 386 (1971).
8. E. I. Heiba and R. M. Dessau, *J. Am. Chem. Soc.*, **94**, 2888 (1972).
9. E. K. Starostin, S. I. Moryashova, and G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2048 (1974).
10. Yu. N. Ogibin, É. I. Troyanskii, and G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2239 (1974).
11. G. I. Nikishin, E. K. Starostin, and B. A. Golovin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 825 (1973).
12. C. Walling and S. Kato, *J. Am. Chem. Soc.*, **93**, 4275 (1971).
13. J. K. Kochi and A. Bemis, *J. Am. Chem. Soc.*, **90**, 4038 (1968); J. C. Jenkins and J. K. Kochi, *Ibid.*, **94**, 843 (1972); J. K. Kochi, A. Bemis, and J. C. Jenkins, *Ibid.*, **90**, 4616 (1968).
14. J. M. Anderson and J. K. Kochi, *J. Am. Chem. Soc.*, **92**, 1651 (1970).
15. J. D. Bacha and J. K. Kochi, *Tetrahedron*, **24**, 2215 (1968).
16. K. Nakanishi, *Infrared Absorption Spectroscopy* [Russian translation], Mir (1965).
17. R. M. Joyce, W. E. Hanford, and J. Harmon, *J. Am. Chem. Soc.*, **70**, 2529 (1948).