HETEROCYCLES, Vol. 24, No. 9, 1986

OXIDATION OF CYCLOBUTANONES TO γ-BUTYROLACTONES WITH HYDROGEN PEROXIDE IN 2,2,2-TRIFLUOROETHANOL

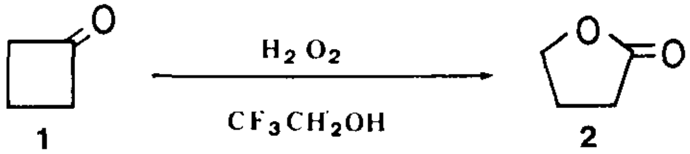
Masakatsu Matsumoto* and Hisako Kobayashi
Sagami Chemical Research Center,
Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229, Japan

Abstract—Cyclobutanones were selectively oxidized to yield γ-butyrolactones with hydrogen peroxide in 2,2,2-trifluoroethanol.

The Baeyer-Villiger oxidation of cyclobutanones is an important entry to γ-butyrolactones and has been attained by means of various oxidation systems.[1,2] We wish to report here a facile method where cyclobutanones are simply treated to yield γ-butyrolactones with aqueous hydrogen peroxide in 2,2,2-trifluoroethanol.

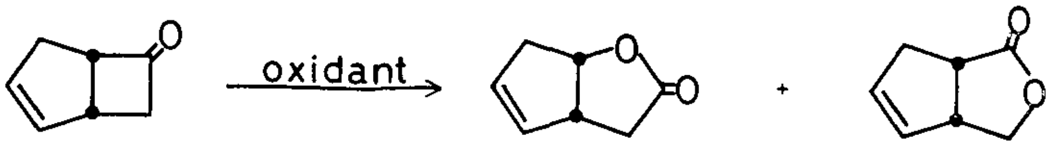
Recently, we have found that benzaldehydes are smoothly oxidized into phenols and/or methyl benzoates with hydrogen peroxide in acidic methanol.[3] As an extension of the work, we investigated the oxidation of carbonyl compounds with hydrogen peroxide in 2,2,2-trifluoroethanol, which is itself a weak acid and has unique characters as a solvent,[4,5,6] and found that the hydrogen peroxide/trifluoroethanol system is remarkably effective for the conversion of cyclobutanones to γ-butyrolactones.

Cyclobutanone (1) was stirred with 1.1 equivalents of hydrogen peroxide (30% aqueous solution) in trifluoroethanol at room temperature. After 24 h, the ketone 1 was completely consumed and γ-butyrolactone (2) was produced in a 98% yield.



The present system was applied to the conversion of bicyclo[3.2.0]hept-2-en-6-one (3) into 6-oxabicyclo[3.3.0]oct-2-en-7-one (Corey's lactone, 4), which is an important intermediate of prostaglandin synthesis.[2a,7] The oxidation proceeded at room temperature to afford the desired lactone 4 in a 91% yield. The NMR analysis showed, however, the lactone 4 was contaminated with a slight amount of a new compound 5. There have been no literatures described about the formation of the by-product in the oxidation of the butanone 3. Thus, we examined the oxidation of 3 by means of older system to know whether the byproduct 5 formed. When the ketone 3 was treated with $K_2S_2O_8$, which is a typical oxidant for the Baeyer-Villiger reaction,[1] in acidic methanol, the lactone 4 was produced together with a considerable amount of the compound 5. By careful chromatographic separation (Al_2O_3/CH_2Cl_2), the compound 5 was obtained as a colorless oil, whose spectral properties were as follows: NMR($CDCl_3$) δ 2.6-2.9 (m, 2H), 3.14 (ddd, J = 8.0, 6.0, and -2 Hz, 1H), 3.82 (dd with fine coupling, J = 8.0, 7.0, and -2Hz, 1H), 4.24 (q_{AB} with d, J_{AB} = 9.0 Hz, J = 1.8 Hz, 1H), 4.46 (q_{AB} with d, J_{AB} = 9.0 Hz, J = 7.0 Hz, 1H), and 5.78 (center)(q_{AB} with fine coupling, J_{AB} = 5.8 Hz, J = ~2Hz, 1H)ppm; IR (liquid film) 2910, 1760, 1367, and 1135 cm^{-1}; MS (m/z, %) 124 (M^+, 8), 79 (32), and 66 (100). Based on these spectral deta, the compound 5 was determined as an isomeric lactone, 7-oxabicyclo[3.3.0]oct-2-en-6-one.

Next, we examined the oxidation of the ketone 3 with hydrogen peroxide in various acidic solvents and summarized the results in the table. The isomeric lactone 5 was produced even in the hydrogen peroxide/acetic acid system,[8] which is the first used for the preparation of the lactone 4 from the butanone 3.[2a] The isomeric mixture of the lactone 4 and 5 was also obtained in the other systems, $H_2O_2/KHSO_4/MeOH$ or EtOH and $H_2O_2/KHSO_4/CH_3CN$. Conclusively, the results in the table showed that the isomeric lactone 5 formed as a by-product in all the oxidation of the ketone 3 examined here, and the hydrogen peroxide/trifluoroethanol system was superior to the others for the selective transformation of the ketone 3 to the lactone 4.[9]

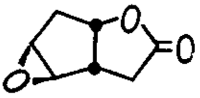


3 4 5

Table. Oxidation of Bicyclo[3.2.0]hept-2-en-6-one.[a)]

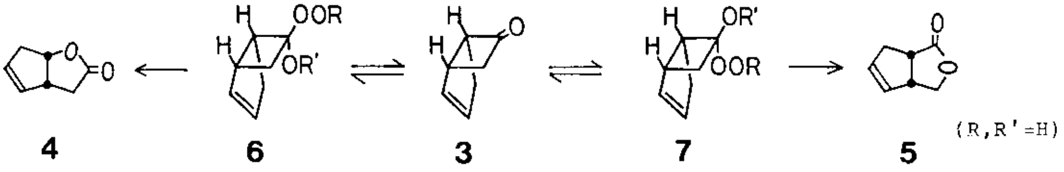
Entry	System	Reaction Time (h)	Yield (4 + 5) (%)	Ratio of 4/5
1	$H_2O_2/KHSO_4/MeOH^{b,c)}$	9	91	6
2	$H_2O_2/KHSO_4/EtOH^{b,c)}$	6	77	8
3	$H_2O_2/KHSO_4/CH_3CN^{b,c)}$	24	75	6
4	$H_2O_2/CF_3CH_2OH^{b)}$	17	91	~100
5	$H_2O_2/AcOH^{d)}$	24	$85^{e)}$	12
6	$K_2S_2O_8/H_2SO_4/MeOH^{f)}$	24	88	5

a) All the reactions were carried out at room temperature. The ratio of 4/5 was determined by NMR spectral analysis. b) The ketone 3 (5mmol) and H_2O_2 (30% aq. solution, 6mmol) were stirred in the solvent (10ml). c) 0.17mmol of $KHSO_4$ was used. d) The ketone 3 (3mmol), H_2O_2 (30%, 7mmol), and AcOH (8ml) were used. e) An epoxylactone, 4-epoxy, was produced in a 5% yield. f) The ketone 3 (5mmol), $K_2S_2O_8$ (5.2mmol), and H_2SO_4 (5.4mmol) were reacted in methanol (10ml).



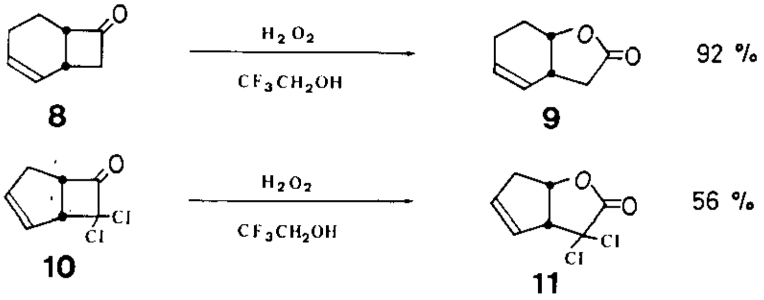
4-epoxy

The oxidation of 3 probably proceeds through intermediary α-hydroxy hydroperoxide which successively rearranges to the lactone 4 and 5 with loss of water by the catalysis of acid. The bicyclic ketone 3 is capable of leading to exo-hydroperoxide 6 and its endo-isomer 7, of which the former 6 may be sterically more stable and more easily formed than the latter 7. According to the mechanism proposed for the regiospecificity in the Baeyer-Villiger oxidation of norcamphor and epicamphor with peracid,[10] the exo-isomer 6 might rearrange to the lactone 4 whereas the endo-isomer 7 might give the lactone 5. The total reaction paths were illustrated in the scheme, where trifluoroethanol may just



(R,R'=H)

fit as a weakly acidic medium[4] for biasing the reaction path to the left. The trifluoroethanol system effected the oxidation of bicyclo[4.2.0]oct-2-en-7-one (8) and 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (10) into the corresponding lactones 9 and 11. Benzaldehydes were also subjected to the Baeyer-Villiger oxidation with H_2O_2 in trifluoroethanol, though the efficiency was far less than the hydrogen peroxide/methanol system and the products were somewhat different from the case. 2,3,4-Trimethoxybenzaldehyde gave 2,3,4-trimethoxyphenol and its formate in 55 and 26% yield, respectively. p-Nitrobenzaldehyde afforded only a slight amount of p-nitrobenzoic acid. On the other hand, by the use of the hydrogen peroxide/methanol system, the trimethoxy- and the nitrobenzaldehyde produce respectively the trimethoxyphenol and methyl nitrobenzoate in high yields.[3] These facts just mean that the intermediates are likely α-hydroxy hydroperoxides but not peroxyhemiacetals[11] such as α-trifluoroethoxy hydroperoxide, in the oxidation of carbonyls with hydrogen peroxide in trifluoroethanol.



REFERENCES AND NOTES

1. For reviews on the Baeyer-Villiger oxidation, see: C. H. Hassal, Org. React., 1957, 9, 73. W. S. Trahanovsky,"Oxidation in Organic Chemistry", Academic Press, New York, Part C, p254, 1978.

2. For oxidation of cyclobutanones, see: (a) With hydrogen peroxide/acetic acid; E. J. Corey, Z. Arnold, and J. Hutton, Tetrahedron Lett.,1970, 307. E. J. Corey and R. Noyori, ibid., 1970, 311. P. A. Grieco, J. Org. Chem., 1972, 37, 2363. (b) With hydrogen peroxide/ arsonated polystyrene; S. E. Jacobson, F. Mares, and P. M. Zambri, J. Am. Chem. Soc., 1979, 101, 6938. (c) With hydrogen peroxide/ acetonitrile; D. H. Gibson and J. T. Joseph, Tetrahedron

Lett., 1972, 3483. (d) With NaOOH; Y. Tsuda, T. Tanno, A. Ukai, and K. Isobe, ibid., 1971, 2009. M. J. Bogdanowicz, T. Ambelang, and B. M. Trost, ibid., 1973, 923. B. M. Trost and J. Bogdanowicz, J. Am. Chem. Soc., 1973, 95, 5321. B. M. Trost, P. Buhlmayer, and M. Mao, Tetrahedron Lett., 1982, 23, 1443. (e) With HOCl; J. A. Horton, M. A. Laura, S. M. Kalbag, and R. C. Petterson, J. Org. Chem., 1969, 34, 3366. (f) With bis(trimethylsilyl)peroxide; M. Suzuki, H. Takada, and R. Noyori, ibid., 1982, 47, 902.

3. M. Matsumoto, H. Kobayashi, and Y. Hotta, J. Org. Chem., 1984, 49, 4740.
4. Physical properties of trifluoroethanol are as follows: pKa = 12.5 (ethanol: pKa = 15.9), μ(D) at 25 °C = 2.03, ε(25 °C) = 26.14, and b.p. = 73.6 °C. The self-association of trifluoroethanol is less than that of ethanol although it forms stronger complexes than ethanol with other bases such as ethers, ketones and so on.[5] Thus, we thought that trifluoroethanol could act both as an unique acid catalyst and as a polar solvent which was easily removed after the reaction.
5. For a review on trifluoroethanol, see: "Catalog of Trifluoroethanol" from Halocarbon Product Co. (USA).
6. Trifluoroethanol was generously gifted from Japan Halon Co.
7. As a recent report, see: E. W. Collington, C. J. Wallis, and I. Waterhouse, Tetrahedron Lett., 1983, 24, 3125.
8. In the present work, the reaction conditions (see Entry 5 in the Table) were partly different from those in the previous work, where the ketone 3 has been oxidized with H_2O_2 in 90% aqueous acetic acid at°0 C for 24 h.
9. Another merit in the present system is the easy workup of the reaction mixture; the crude products are simply obtained by azeotropic removal of the solvent, trifluoroethanol containing water.
10. J. Meinwald and E. Frauenglass, J. Am. Chem. Soc., 1960, 82, 5235. R. R. Sauer and G. P. Ahearn, ibid., 1961, 83, 2759. See also ref. 1.
11. In the Baeyer-Villiger oxidation of benzaldehydes with H_2O_2 in acidic methanol, the reaction proceeds through peroxyhemiacetals, ArCH(OMe)OOH.[3] Accordingly, in the reaction of the ketone 3 with $H_2O_2/KHSO_4/MeOH$ or EtOH, the intermediary peroxyhemiacetals can not be completely ruled out.

Received, 20th June, 1986