Chemistry of Heterocyclic Compounds, Vol. 34, No. 7, 1998

CATALYTIC OXIDATION OF FURAN AND HYDROFURAN COMPOUNDS.

3.* SYNTHESIS OF 2,5-DIETHOXY-2,5-DIHYDROFURAN IN THE FURAN–HYDROGEN PEROXIDE–AQUEOUS ETHANOL–VANADYL SULFATE SYSTEM

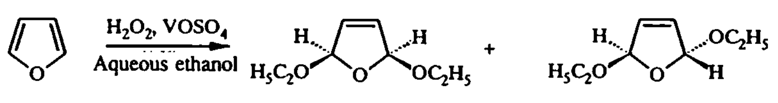
V. V. Poskonin, L. A. Badovskaya, and L. V. Povarova

2,5-Diethoxy-2,5-dihydrofuran was synthesized for the first time by the oxidation of furan with hydrogen peroxide in an aqueous ethanol medium in the presence of vanadyl sulfate. The reaction product was characterized by PMR, ^{13}C NMR, and IR spectroscopy and chromato-mass spectrometry. It was found that diethoxydihydrofuran is formed as a mixture of cis and trans isomers in a ratio of 2.5:1. The corresponding dihydrazone of malealdehyde was obtained from the isolated product and 2,4-dinitrophenylhydrazine.

1,4-Dicarbonyl compounds are highly active synthons, but as a result of their instability they are mainly used in the form of their stable derivatives — 2,5-dialkoxy-2,5-dihydrofurans [2-6] — mainly obtained by sensitized photochemical oxygenation [6, 7] and electrochemical alkoxylation [8, 9] of furan compounds. However, these methods have a series of disadvantages, which prevent their widespread use (the significant energy content, the length of the process, the need to use special equipment and highly toxic reagents, etc.). In this connection the search for convenient methods for the specific synthesis of dialkoxydihydrofurans continues to remain an urgent problem. The oxidation of furans by peracids and hydrogen peroxide was previously considered [10-13] for the potential precursors — 1,4-dicarbonyl compounds and 2,5-dihydroxy-2,5-dihydrofurans. However, the proposed conditions proved unsuitable for the preparative synthesis of these unstable products. Earlier we reported on the possibility of using the oxidation of furan with hydrogen peroxide, catalyzed by vanadium compounds, for preparative purposes [14]. It was assumed that the introduction of ethanol into the reaction medium would promote not only its homogenization but also the accumulation of intermediate products in the form of more stable ethoxy derivatives, including 2,5-diethoxy-2,5-dihydrofuran (I).

In the present work we realized for the first time the synthesis of compound (I) by the oxidation of furan in a system containing hydrogen peroxide, aqueous ethanol, and $VOSO_4$ (Scheme 1).

Scheme 1



cis-I   trans-I

The reaction was conducted at 20°C (furan–hydrogen peroxide–vanadyl sulfate molar ratios 1:2:0.02) with vigorous agitation. A 30% aqueous solution of hydrogen peroxide in ethanol with a hydrogen peroxide–ethanol molar ratio of 1:3 was used for oxidation. At the beginning of the process the pH of the reaction mixture was 4.5-5.0, and at the end it was about 1. The reaction was continued until the hydrogen peroxide had been completely transformed; the yield of compound (I) was 12% on the reacted furan.

---

*For Communication 2, see [1].

Kubansk State Technological University, Krasnodar 350072, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 893-897, July, 1998. Original article submitted September 9, 1997; revision submitted January 27, 1998.

0009-3122/98/3407-0771$20.00

The structure of the diethyl acetal (I) was established by spectroscopic methods (mass spectrometry, IR, PMR, ^{13}C NMR spectroscopy) and was confirmed by data on the structure of the product from its reaction with 2,4-dinitrophenylhydrazine — malealdehyde dihydrazone (II).

In the IR spectrum of compound (I) there is a group of strong bands in the region of 1115-1130 cm^{-1}, corresponding to the absorption of the C–O–C groups. The absorption of the C=C bond is observed at 1635 cm^{-1}. In the PMR spectrum there are characteristic signals for the protons of the two OC_2H_5 groups, i.e., a triplet for the methyl protons in the region of 1.24 and a multiplet for the four methylene protons in the region of 3.68 ppm. The protons at the $C_{(2)}$ and $C_{(5)}$ atoms of the ring appear in the spectrum in the form of two multiplets at 5.68 and 5.86; the protons at the C=C bond also appear in the form of two multiplets at 6.07 and 6.09 ppm; the integral intensity ratio for each pair of signals is 2.5:1. Analogous splitting of the signals of the carbon atoms is observed in the ^{13}C NMR spectrum; there are distinguishable doublets in the regions of 14.09-15.00 (CH_3), 62.2-62.7 (OCH_2), 105.9-107.4 ($C_{(2)}$ and $C_{(5)}$), and 131.0-131.4 ppm ($C_{(3)}$ and $C_{(4)}$). The weaker downfield signals of H and C atoms can be assigned to the *trans* isomer (I), since the anisotropy that arises during the formation of a hydrogen bond or under the influence of the characteristic magnetic field of the alkyl group can only appear for this isomer [15]:

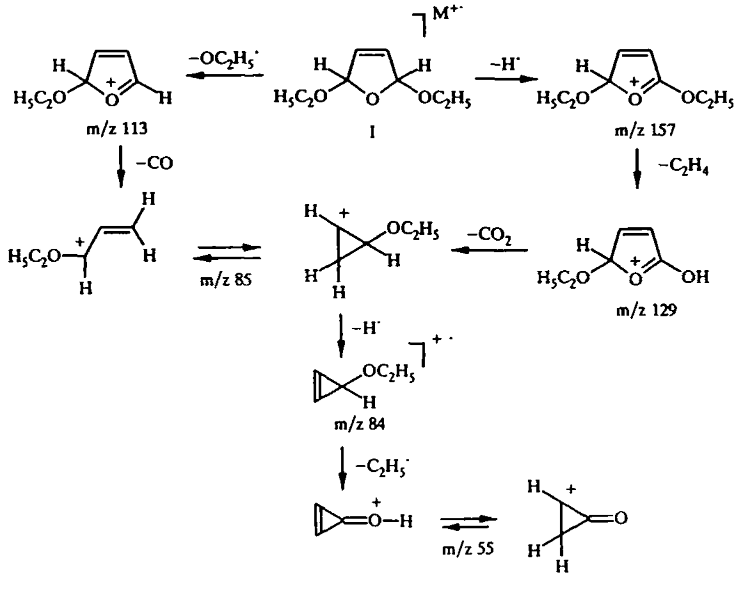
trans-I

The ^{13}C NMR data make it possible to consider that the product (I) in the investigated reaction is formed as a mixture of *cis* and *trans* isomers (Scheme 1) with a substantial preponderance of the *cis* form. This conclusion is confirmed by the results of chromato-mass spectrometry. Thus, on the chromatogram of the product (I) there are two peaks with an area ratio of 2.5:1. The corresponding mass spectra coincide in the composition of the main fragment ions, and the signals of the identical fragments have, with a small exception, approximately equal intensity. The most likely scheme of the main fragmentation paths of the molecular ions for the isomers of 2,5-diethoxy-2,5-dihydrofuran (I) is shown in Scheme 2.

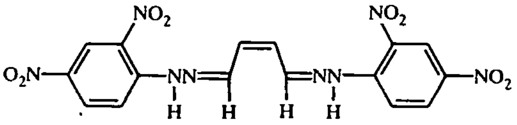
The molecular ion is not observed in the spectra of either isomer, but there is a fragment with *m/z* 157, clearly formed as a result of the loss of a hydrogen atom by the $M^{+\cdot}$ ion. The elimination of C_2H_5 and OC_2H_5 radicals characteristic of ethoxy-containing compounds leads to fragments with *m/z* 129 and 113 respectively. The elimination of a CO_2 molecule from the first of them and a CO molecule from the second results in the formation of the strongest ion at *m/z* 85, the dissociation of which with ejection of the H and C_2H_5 particles leads to the stable ion at *m/z* 55. The formation of the fragment with *m/z* 99 can be explained by the alternative dissociation of the ion with *m/z* 129 with the ejection of a C_2H_6 molecule.

Treatment of compound (I) with 2,4-dinitrophenylhydrazine gave a 96% yield of malealdehyde bis(dinitrophenylhydrazone) (II).

Scheme 2

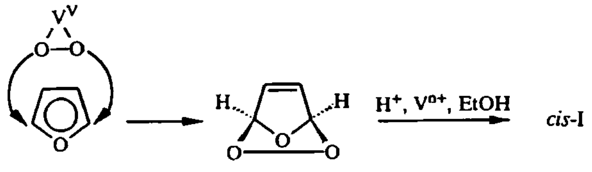


In the IR spectrum of the dihydrazone (II) there are a series of bands in the region of 1495-1615 cm^{-1}, due to the absorption of the C=C and C=N bonds, and there is also a band for the N−H group at 3300 cm^{-1}. In the ^{13}C NMR spectrum of this compound there are signals in the region of 115 and 116 ppm, belonging to the carbon atoms of the aliphatic C=C bond and the $C_{(arom)}-N$ bond. The signals of the carbon atoms of the benzene ring attached to hydrogen are found at 123 ppm, and those attached to the nitro group are found at 130 ppm. The azomethine C atoms are observed in the region of 146 ppm. The PMR spectrum of compound (II) could not be obtained on account of its low solubility in the available deuterated solvents.



II

The stereoselectivity of the formation of the diacetal (I) with a preference for the *cis* form can be explained by the reaction of a complex cation of V^V, containing a peroxo group O_2^{-2}, with the π system of the furan. The possibility of such a reaction is demonstrated by the formation of peroxo compounds of vanadium in the $V^{IV,V}-H_2O_2$ system [16, 17] and by the ability of the ions of this metal to form π complexes with compounds of the aromatic [18] and furan [19] series. In view of the familiar ability of electron-excessive π systems to add the O−O group during reaction with the peroxo complexes of vanadium [20] it can be supposed that complexation of the reaction components promotes preferential attack on the heterocycle by the active form of the oxidizing agent from the side closest to the catalyst. The rapid dissociation of the unstable *cis*-endoperoxide (III) [21] presumably formed here leads to the corresponding isomer of the diacetal (I):



III

The stereoselective formation of 2,5-dialkoxy-2,5-dihydrofurans was observed during the photochemical oxygenation of 2-alkyl- and 2,5-dialkylfurans in the presence of V_2O_5 [8] (ratio of *cis* and *trans* isomers of the products 3:2). Such an analogy confirms the important role of the catalyst in the stereochemical orientation of attack by the oxidizing agent on the furan ring. The data presented above, our other data, and published data make it possible to suppose that the elementary event in the oxidation of the furan ring takes place in the inner coordination sphere of the complex catalytic ion without the appreciable participation of free radicals.

The new path that we have discovered for the production of 2,5-diethoxy-2,5-dihydrofuran based on the reaction of furan with hydrogen peroxide in the presence of aqueous ethanol and the vanadium catalyst can be regarded as a promising alternative to the photochemical and electrochemical methods.

EXPERIMENTAL

The chromato-mass spectra of 2,5-diethoxy-2,5-dihydrofuran (I) were obtained on a Hitachi M-80B instrument fitted with a quartz capillary column with CE-30 stationary phase (phenylmethylsilicone), $l = 25$ m, $d_{int} = 0.1$ mm. The carrier gas was nitrogen. The chromatographic conditions were as follows. For 5 min after introduction of the sample the column was thermostated at 40°C. The temperature was then raised to 280°C at 8 deg/min. The injector temperature was 250°C. Fragmentation of the separated components was realized by direct injection into the ion source. The temperature of the ionization chamber was 200°C, and the energy of the ionizing electrons was 70 eV. The PMR and ^{13}C NMR spectra of the products (I) and (II) were recorded on a Bruker AC-200P instrument in deuterochloroform and DMSO-d_6 with TMS as internal standard. The IR spectra were obtained in Vaseline oil on a UR-20 spectrometer.

The gas-liquid chromatograms of the product (I) were recorded on a Crom-4 chromatograph with a flame-ionization detector and a glass column (300 × 0.3 cm). The carrier gas was nitrogen at 30 ml/min. The samples were chromatographed on polymethylphenylsiloxane oil (PMFS-4) deposited at the rate of 15% on Chromaton N-AW DMCS at a column temperature of 150°C, evaporator temperature 220°C, detector temperature 220°C. The emergence time of compound (I) was 170 sec.

Thin-layer chromatography of the reaction mixture and of the products (I) and (II) was conducted on Silufol UV-254 plates in chloroform and in the 3:1 chloroform–acetone system. The chromatograms were developed with dilute solutions of potassium permanganate and 2,4-dinitrophenylhydrazine and also with an alcohol solution of bromophenol blue and with iodine vapor.

2,5-Diethoxy-2,5-dihydrofuran (I). A mixture of 23.8 g (0.35 mole) of furan, 75 ml (0.70 mole) of 30% hydrogen peroxide, and 2.1 g (0.007 mole) of vanadyl sulfate in 100 ml of ethanol was stirred at room temperature for 6 h. The reaction mixture was extracted with ether, and the extract was dried over sodium sulfate. The mixture was filtered, and the solvent was distilled. Vacuum distillation of the residue gave 6.6 g of the product (I). The yield was 12% on the reacted furan; mp 70-75°C (10 mm Hg), n_D^{20} 1.4340, d_4^{20} 1.0031. Published data: bp 71-73°C (12 mm Hg), n_D^{20} 1.4309, d_4^{20} 1.0019 [9]. IR spectrum, cm^{-1}: 1115 and 1130 (C–O–C), 1350 and 1370 (C_2H_5), 1635 (C=C), 2895, 2940, and 2990 (C–H). ^{13}C NMR spectrum (deuterochloroform), ppm: *cis* isomer, 14.92 (CH_3), 62.27 (O–CH_2), 105.88 ($C_{(2)}$ and $C_{(5)}$), 130.98 ($C_{(3)}$ and $C_{(4)}$); *trans* isomer, 15.03 (CH_3), 62.67 (O–CH_2), 107.36 ($C_{(2)}$ and $C_{(5)}$), 131.41 ($C_{(3)}$ and $C_{(4)}$). PMR spectrum (deuterochloroform), ppm: *cis* isomer, 1.24 (6H, t, CH_3); 3.68 (4H, m, OCH_2); 5.68 (2H, m, 2- and 5-H); 6.07 (2H, m, 3- and 4-H); *trans* isomer, 1.24 (6H, t, CH_3); 3.68 (4H, m, OCH_2); 5.68 (2H, m, 2- and 5-H); 6.07 (2H, m, 3- and 4-H); *trans* isomer, 1.24 (6H, t, CH_3); 3.68 (4H, m, OCH_2); 5.86 (2H, m, 2- and 5-H); 6.09 (2H, m, 3- and 4-H). Found %: C 60.54; H 8.86. $C_8H_{14}O_3$. Calculated %: C 60.74; H 8.92.

Malealdehyde Dihydrazone (II). To an alcohol solution of 0.79 g (0.005 mole) of the diacetal (I) we added 2.48 g (0.0125 mole) of 2,4-dinitrophenylhydrazine in the form of a 10% aqueous alcohol solution acidified with sulfuric acid. The precipitate was filtered off, washed with water and alcohol, and dried. We obtained 2.48 g of red-orange crystals of the product (II). The yield was 96%; mp 310°C (decomp.). IR spectrum, cm^{-1}: 1365 ($C_{(arom)}$–NH); 1495, 1520, 1585, 1610, and 3300 (C=C, C=N, $C_{(arom)}$–H, and N–H). ^{13}C NMR spectrum (DMSO-d_6), ppm: 115.38 ($C_{(aliph)}$–H); 116.53 ($C_{(arom)}$–NH); 122.68 ($C_{(arom)}$–H); 129.57 (C–NO_2); 146.23 (C=N). Found %: C 43.41; H 2.78; N 25.18. $C_{16}H_{12}N_8O_8$. Calculated %: C 43.27; H 2.70; N 25.23.

REFERENCES

1. V. V. Poskonin and L. A. Badovskaya, Khim. Geterotsikl. Soedin., No. 6, 742 (1998).
2. A. A. Ponomarev and I. A. Markushina, Uch. Zap. Saratov. Gos. Un-ta. Vyp. Khim., **71**, 135 (1959).
3. Samizu Kiyohiro and Ogasawara Kanio, Heterocycles, **38**, 1745 (1994).
4. A. Stoll, B. Becker, and E. Jucker, Helv. Chim. Acta, **35**, 1265 (1952).
5. I. Saito, Y. H. Kuo, and T. Matsuura, Tetrahedron Lett., **27**, 2757 (1986).
6. Z. Ogumi, S. Ohhashi, and Z. Takehara, J. Chem. Soc. Jpn., No. 11, 1788 (1984).
7. G. O. Schenk, Lieb. Ann. Chem., **584**, 156 (1953).
8. B. L. Feringa and R. J. Butselaar, Tetrahedron Lett., **23**, 1941 (1982).
9. N. Clauson-Kaas, F. Limborg, and J. Fakstrop, Acta Chem. Scand., **2**, 109 (1948).
10. F. Catala and J. Defaye, Comp Rend. Acad. Sci., **258**, 4094 (1964).
11. S. Foot and S. Wexler, J. Am. Chem. Soc., **86**, 3879 (1964).
12. V. P. Gvozdetskaya, Thesis for Candidate of Chemical Sciences [in Russian], Krasnodar (1974).
13. N. Clauson-Kaas and J. Fakstrop, Acta Chem. Scand., **1**, 415 (1947).
14. V. V. Poskonin, L. V. Povarova, and L. A. Badovskaya, Khim. Geterotsikl. Soedin., No. 5, 633 (1996).
15. I. B. Ionin, B. A. Ershov, and A. I. Kol'tsov, NMR Spectroscopy in Organic Chemistry [in Russian], Khimiya, Leningrad (1983), pp. 30, 37, 38.
16. R. A. Sheldon and J. Kochi, Metal-Catalyzed Oxidations of Organic Compounds, Interscience, New York (1981).
17. I. I. Vol'nov, Peroxo Complexes of Vanadium, Niobium, and Tantalum [in Russian], Nauka, Moscow (1987).
18. Y. Luo, K. Kustin, and I. R. Epstein, Inorg. Chem., **27**, 2489 (1988).
19. P. O. I. Virtanen and Puutio, Finn. Chem. Lett., No. 1, 49 (1981).
20. A. E. Gekhman, N. I. Moiseeva, and I. I. Moiseev, Izv. Akad. Nauk. Ser. Khim., No. 4, 605 (1995).
21. K. Gollnick and A. Griesbeck, Tetrahedron, **41**, 2057 (1985).