A SYNTHESIS OF 2,2,4-TRIMETHYL-4-HYDROXYTETRAHYDROFURAN, A PRODUCT OF THE PHOTOLYSIS OF 4-METHYL-4-METHOXY-2-PENTANONE

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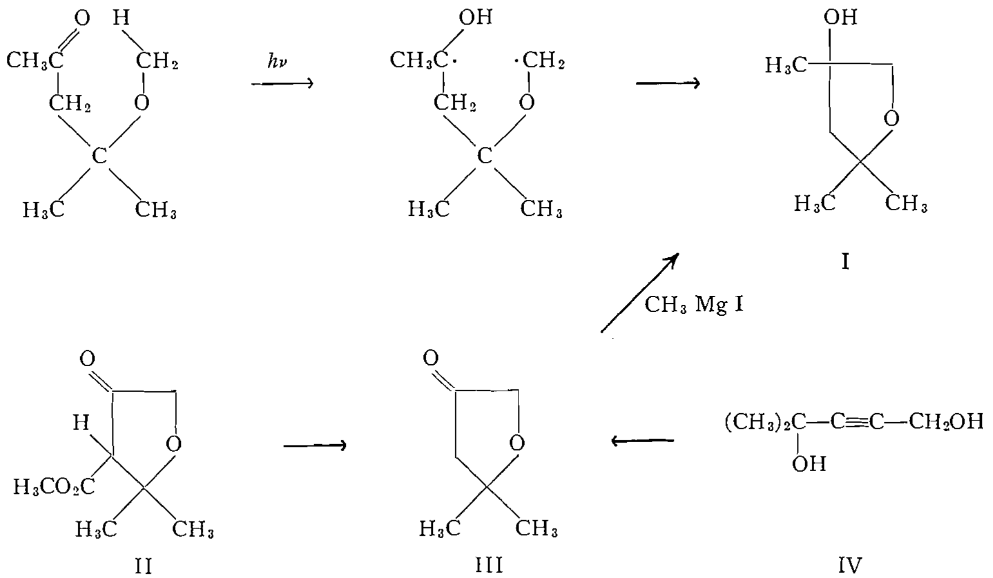
It has recently been reported (1) that the photolysis of 4-methyl-4-methoxy-2-pentanone yields methanol, acetone, mesityl oxide, and a "hydroxyfuran." The elemental analysis and the spectral properties suggested that this latter substance should have structure I, which could be derived from the methoxyketone via a seven-membered ring intermediate (1). However, this important product of the photolytic reaction was not compared with a synthetic sample.

We wish to report that compound I can be conveniently obtained by reacting methyl β-methylcrotonate with the oxanion of methyl glycolate in dimethyl sulfoxide, decarboxylating the resultant β-ketoester (2,2-dimethyl-3-carbomethoxytetrahydrofuran-4-one, II) and treating the 2,2-dimethyltetrahydrofuran-4-one so obtained (III) with methylmagnesium iodide. The syntheses of the intermediates II and III were patterned after those of other tetrahydrofuranone derivatives which have been recently prepared in this laboratory (2).

When the synthesis of the intermediate III was attempted by treatment of 4-methylpent-2-yn-1,4-diol (IV) with mercuric oxide and sulfuric acid, a mixture resulted, whose main constituent was identical with a sample of III prepared from II. Two other substances, isolated from the reaction mixture by vapor phase chromatography (v.p.c.) and not submitted to elemental analysis, had infrared spectra which are compatible with the structures of two anticipated by-products of the reaction, i.e., 4-methylpent-4-en-2-yn-1-ol and 4-methylpent-4-en-3-on-1-ol. It was found, however, that the use of the less acidic catalyst described by Colonge *et al.* (3) (mercuric sulfate with no excess of sulfuric acid) suppresses the formation of these by-products and permits another convenient synthesis of III.



I

II III IV

The identity of synthetic I with the "hydroxyfuran" obtained by photolysis of 4-methyl-4-methoxy-2-pentanone was proved by a comparison of the spectral properties of the two substances (infrared, nuclear magnetic resonance (n.m.r.), and mass spectra), effected through the courtesy of Dr. Petersen of the Aerospace Corporation, El Segundo, California (1).

The potentialities of the now easily available (2) tetrahydrofuran-3-ones as intermediates in the synthesis of 2,3-dihydrofurans (via tosylhydrazones), furans, and γ-lactones are currently being investigated.

EXPERIMENTAL

The infrared spectra were determined on CCl_4 solutions. The n.m.r. spectra were measured in CCl_4 at 60 Mc, with tetramethylsilane as internal standard; chemical shifts are in p.p.m. The mass spectra were determined on a CEC 21-103C instrument. The v.p.c. retention times (R_T) are expressed in minutes and refer to the following conditions: 2m × 0.25 in. silicone rubber column, 15% on acid-washed Chromosorb W (60–80 mesh), 75°, 70 ml He/min.

2,2-Dimethyl-3-carbomethoxytetradrofuran-4-one (II)

This compound was prepared in 40% yield from methyl glycolate and methyl β-methylcrotonate by a procedure completely analogous to that previously employed for the synthesis of other tetrahydrofuranone derivatives (2). Boiling point 41–42° at 0.1 mm; n_D^{23} 1.4497; infrared bands at 5.58, 5.69, 5.92, and 6.07 μ indicate the coexistence of keto and enol forms.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.87; H, 7.25.

Methyl 3-methoxyisovalerate, the only important by-product of the reaction, was isolated by v.p.c. of the forerun of distillation, and was identified by comparison of its infrared spectrum and retention time with those of an authentic sample (4).

2,2-Dimethyltetrahydrofuran-4-one (III)

The decarboxylative hydrolysis of II was effected by 1 h refluxing in 10% H_2SO_4. The usual work-up (ether extraction, drying over Na_2SO_4, removal of the solvent, and distillation) gave III in 73% yield. Boiling point 64° at 50 mm; R_T 5.6; n_D^{25} 1.4259; $\lambda_{CO}^{CCl_4}$ 5.63 μ; $\lambda_{C-O-C}^{CCl_4}$ 9.36 μ; n.m.r.: singlets at $\delta = 3.88$, 2.23, and 1.35, in ratios of 1:1:3.

Anal. Calcd. for $C_6H_{10}O_2$: C, 63.13, H, 8.83. Found: C, 62.98; H, 8.93.

Semicarbazone, m.p. 187–188°.

Anal. Calcd. for $C_7H_{13}N_3O_2$: N, 24.55. Found: N, 24.36.

Treatment of 4-methylpent-2-yn-1,4-diol (IV) as described for the synthesis of 2,2,5,5-tetramethyltetrahydrofuran-3-one from 2,5-dimethylhex-3-yn-2,5-diol (5) resulted in a mixture, which was separated into its components by v.p.c. The main constituent (R_T 5.6) was identical (R_T, infrared) with a sample of III prepared from II. The principal infrared bands of two by-products (see text) occur at the following wavelengths: Compound A (R_T 7.6): 2.75 and 2.90 μ, free and bonded O—H stretching; 3.22 μ, asymmetric stretching olefinic CH_2; 5.54 μ, overtone of δ_{C-H} out-of-plane; 6.15 μ, C═C stretching; 9.80 and 9.90 μ, C—O stretching; 11.10 μ, δ_{C-H} out-of-plane. Compound B (R_T 13.1): 2.85 μ, O—H stretching (intramolecular bond); 5.85, 6.08, and 9.65 μ, C═O, C═C, and C—O stretching; 10.95 μ, δ_{C-H} out of plane; λ_{max}^{EtOH} 231 mμ. However, when a less acidic reaction medium was employed (see text and ref. 3), the formation of compounds A and B was suppressed, and III was obtained in 30% yield.

2,2,4-Trimethyl-4-hydroxytetrahydrofuran (I)

Refluxing for 2 h an ether solution of compound III and methylmagnesium iodide (10% excess) gave, after the usual work-up and distillation, an 87% yield of I. Boiling point 63–64° at 12 mm; n_D^{25} 1.4259; n.m.r.: doublet, 2 protons, centered at $\delta = 3.60$; singlet, 1 proton, $\delta = 3.27$; doublet, 2 protons, centered at $\delta = 1.80$; singlet, 6 protons, $\delta = 1.30$; singlet, 3 protons, $\delta = 1.20$. The mass spectrum showed an extremely weak molecular ion peak ($m/e = 130$); the principal peaks were at the following m/e values: 43 (100%), 85 (69%), 57 (31%), 115 (30%), and 41 (27%).

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.68; H, 10.83.

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