

3-BROMO-2,5-DIHYDROFURAN-2-ONE AND 4-BROMO-2,5-DIHYDROFURAN-2-ONE

Lothar BRECKER^{a1,*}, Wolfgang KREISER^{a2,*}, Ludger ERNST^{b1} and Henning HOPF^{b2}

^a *Naturstoffchemie, Universität Dortmund, D-44221 Dortmund, Germany; e-mail:*

¹ *brecker@orgc.tu-graz.ac.at, ² kreiser@citrin.chemie.uni-dortmund.de*

^b *Institut für Organische Chemie, Technische Universität Braunschweig, Hagenring 30, D-38106 Braunschweig, Germany; e-mail: ¹ l.ernst@tu-bs.de, ² h.hopf@tu-bs.de*

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Although 3-bromo-2,5-dihydrofuran-2-one and 4-bromo-2,5-dihydrofuran-2-one were first reported in 1894, considerable ambiguity still exists about the correct structure assignment of the two compounds. The present article gives a brief overview on the varying assignments of constitution and describes a novel method for the formation of 3-bromo-2,5-dihydrofuran-2-one. A comparison is made of the experimental ¹³C NMR chemical shifts with values predicted by increment calculations and experimental ¹J_{C-C} coupling constants are given for both compounds. Secure structural assignments are now available for both isomers.

Key words: Revision; Bromo-2,5-dihydrofuran-2-ones; Butenolides; Structure assignments; NMR spectroscopy; Lactones.

The two title compounds were first reported in 1894 by Hill and Cornelison¹. The 3-bromo-2,5-dihydrofuran-2-one (**1**), described by them formed colourless crystals characterized by a melting point of 77 °C. These authors also reported 4-bromo-2,5-dihydrofuran-2-one (**2**) as colourless crystals displaying a melting point of 58 °C. However, their assignment of the structures to the isolated compounds turned out to be wrong. We here show that the attribution of the structures to the above melting points has to be reversed. Since then, both substances have been synthesized by independent procedures and various physical characteristics have been published. But the first incorrect determination of the two structures created confusion in the literature that persists until the present time, although

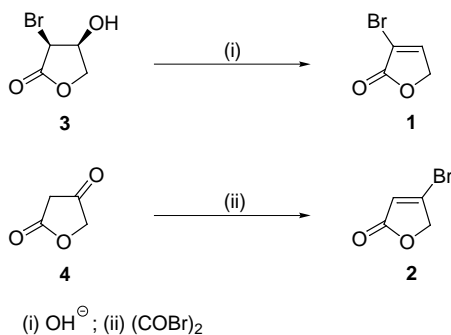
+ Present address: Institut für Organische Chemie, Technische Universität Graz, Stremayrgasse 16, A-8010 Graz, Austria.

some attempts have been made to solve the inconsistencies of the analytical data (refs^{2,3}). We have now resolved these.

RESULTS AND DISCUSSION

For the first time, 3-bromo-2,5-dihydrofuran-2-one (**1**) was correctly described by Owen and Sultanbawa⁴ and by Sukigara *et al.*^{5a} and Hata^{5b}. With reference to Hill and Cornelison¹ and Whiting², Hopf and Natsias⁶ also reported the analytical data of **1** but erroneously assigned them to structure **2**. 4-Bromo-2,5-dihydrofuran-2-one (**2**) was described and identified correctly four times (refs^{5,7-9}) but Whiting² and independently Lespieau and Viguier¹⁰ also described it and referring to Hill and Cornelison¹, wrongly assigned it to structure **1**.

With a different purpose in mind, we accidentally prepared 3-bromo-2,5-dihydrofuran-2-one (**1**) by elimination of water from (3*S*,4*S*)-3-bromo-4-hydroxytetrahydrofuran-2-one (**3**) (ref.¹¹) (Scheme 1). Since the analytical data of our product did not agree with the values given by Hopf and Natsias⁶, we undertook a directed synthesis of 4-bromo-2,5-dihydrofuran-2-one (**2**) from tetrahydrofuran-2,4-dione (**4**) using the method of Jas⁸ (Scheme 1). The analytical data of this material agreed exactly with the substance reported by Hopf and Natsias⁶.



SCHEME 1

Having both compounds in hands and comparing chemical shifts values for the vinyl H atoms in the ¹H NMR spectrum with δ 7.58 (**1**) and 6.33 (**2**) ppm, we suggest a revision of structure assignment on the basis of the deshielding effect in **1** (relative to ref.⁶). In order not to rely solely on that empirical rule, we determined and assigned the structures of the two compounds by ¹³C NMR spectroscopy. The chemical shifts were compared with the shifts calculated by the increment method. The shifts for the parent

molecule, 2,5-dihydrofuran-2-one are 121.0 ppm (C-3) and 153.2 ppm (C-4) (ref.¹²). The increment values for the bromo substituents are -8.6 ppm (α -position) and -0.9 ppm (β -position) (ref.¹³). In addition, we measured one-dimensional ^{13}C -INADEQUATE spectra of both compounds and were able to determine the exact positions of the carbon atoms in the corresponding furanone rings from the $^1J_{\text{C-C}}$ coupling constants, which confirmed the results of the increment method.

The ^{13}C NMR measurement on 3-bromo-2,5-dihydrofuran-2-one (**1**) shows chemical shifts of 110.9 ppm for C-3 and 150.5 ppm for the methyne (CH) carbon atom, and the proper signal multiplicities in the DEPT spectrum. The increment method predicts values of 112.4 and 152.3 ppm, respectively. The $^1J_{\text{C-C}}$ coupling constants of compound **1** taken from the INADEQUATE measurement are given in Fig. 1. For 4-bromo-2,5-dihydrofuran-2-one (**2**) we found chemical shift values of 121.1 ppm for the methyne carbon in the C=C double bond and 146.0 ppm for the quaternary carbon atom. The values calculated by the increment method are 120.1 and 144.6 ppm, respectively. Figure 1 also shows the $^1J_{\text{C-C}}$ coupling constants determined for compound **2**.

Evidently, there is good agreement between the calculated and experimental shifts for the carbon atoms of the C=C double bond in both compounds. In addition, the $^1J_{\text{C-C}}$ coupling constants verify that this assignment of the structures to the substances is correct. The different coupling constants between the carbonyl and the CH_2 carbon atoms and their respective neighbours are significantly different and allow unambiguous assignments.

To summarize, we have proved that the structural assignment of Hill and Cornelison¹ is *not* correct. The isomer with the melting point of 58°C is 3-bromo-2,5-dihydrofuran-2-one (**1**) and 4-bromo-2,5-dihydrofuran-2-one (**2**) is the isomer with the melting point of 77°C . Complete sets of analytical data for both substances are given in the Experimental.

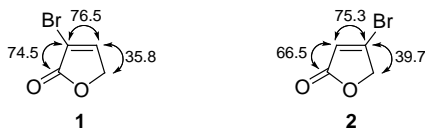


FIG. 1

$^1J_{\text{C-C}}$ Coupling constants of 3-bromo-2,5-dihydrofuran-2-one (**1**) and 4-bromo-2,5-dihydrofuran-2-one (**2**)

EXPERIMENTAL

All commercial starting materials were used without purification. TLC plates were prepared with silica gel 60 F₂₅₄ (Merck) and the spots were observed under UV light. Melting points have been measured on a Büchi 510 and are uncorrected. NMR spectra were recorded of CDCl₃ solutions on a Bruker DPX-300. Chemical shift references (δ -scale in ppm) were CHCl₃ (7.24) for ¹H and CDCl₃ (77.05) for ¹³C NMR. The IR spectra (wavenumbers in cm⁻¹) of the compounds were taken in KBr on a Nicolet Impact 400D and the MS spectra were measured on a Finnigan MAT 8200.

3-Bromo-2,5-dihydrofuran-2-one (1)

(3S,4S)-3-Bromo-4-hydroxytetrahydrofuran-2-one¹¹ (**3**; 2.7 g, 15 mmol) was dissolved in THF (20 ml) and aqueous 2 M NaOH (5 ml) was added to the solution. After stirring for 4 h, ether (75 ml) was added and the mixture was extracted with aqueous 5% Na₂CO₃. After drying the organic layer over Na₂SO₄ the solvent was removed *in vacuo* and the product purified by chromatography (silica gel, ethyl acetate-cyclohexane 1 : 1). Crystallization from ether gave colourless crystals (1.8 g, 72%), m.p. 58 °C. IR: 3 100, 2 954, 1 767, 1 606, 1 188, 1 052, 988, 717. ¹H NMR: 4.69 (2 H, d, ³J_{H-H} = 1.9, CH₂); 7.58 (1 H, t, ³J_{H-H} = 1.9, CH). ¹³C NMR: 168.6 (s, ¹J_{C-C} = 74.5, C2), 150.5 (d, ¹J_{C-C} = 76.5, 35.8, C4), 110.9 (s, ¹J_{C-C} = 76.5, 74.5, C3), 71.5 (t, ¹J_{C-C} = 35.8, C5). MS, *m/z*: 164/162 (1 : 1, 63%; M⁺), 136/134 (1 : 1, 42%; M⁺ - CO), 135/133 (1 : 1, 100%; M⁺ - CO - H), 107/105 (1 : 1, 38%; M⁺ - COOCH₂ + H), 53 (33%; M⁺ - OCH₂ - Br), 39 (36%; M⁺ - CO₂ - Br).

4-Bromo-2,5-dihydrofuran-2-one (2)

N,N-Dimethylformamide (2.25 ml, 29 mmol) was added to a suspension of tetrahydrofuran-2,4-dione (**4**; 2.25 g, 22.5 mmol) in CH₂Cl₂ (50 ml). Oxalyl dibromide (5.8 g, 27 mmol) was added at 0 °C over a period of 15 min. The reaction mixture was allowed to reach room temperature and then stirred for 3 h. After addition of water (60 ml) the organic layer was separated and the aqueous layer washed with ether (4 × 30 ml). The combined organic layers were dried over Na₂SO₄, the solvent was removed *in vacuo*, and the product purified by chromatography (silica gel, ethyl acetate-cyclohexane 1 : 1). Crystallization from ether gave colourless crystals⁸ (2.5 g, 66%), m.p. 77 °C. IR: 3 187, 3 104, 3 095, 1 742, 1 701, 1 599, 1 263, 1 151, 1 012, 865, 698. ¹H NMR: 4.84 (2 H, d, ⁴J_{H-H} = 1.9, CH₂); 6.33 (1 H, t, ⁴J_{H-H} = 1.9, CH). ¹³C NMR: 170.3 (s, ¹J_{C-C} = 66.5, C2), 146.0 (s, ¹J_{C-C} = 75.3, 39.7, C4), 121.1 (d, ¹J_{C-C} = 75.3, 66.5, C3), 74.4 (t, ¹J_{C-C} = 39.7, C5). MS, *m/z*: 164/162 (1 : 1, 52%; M⁺), 135/133 (1 : 1, 28%; M⁺ - CO - H), 83 (100%; M⁺ - Br), 53 (20%; M⁺ - OCH₂ - Br), 39 (26%; M⁺ - CO₂ - Br).

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