Substituted γ-Lactones. 35 [1]. Reduction of 4-Aroyl-3-hydroxy-2(5*H*)-furanones

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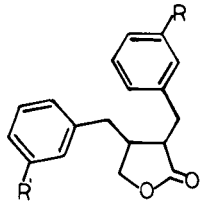
Received July 8, 1985

The reduction of 4-aroyl-3-hydroxy-2(5*H*)-furanons **1a-c** was investigated using different reducing agents. Sodium borohydride reacts with type **1** compounds by loss of water to yield 4-(arylmethylene)-2,3(4*H*,5*H*)-furandiones **2a-c**. Platinum or charcoal supported by pallodium chloride transforms **1a** to 4-benzyl-3-hydroxy-2(5*H*)-furanone (**3**). Compounds **2a** and **2b** react with *o*-phenylenediamine to give 3-(*E*-(1'-hydroxymethyl-2'-aryl)ethenyl]-2-quinoxalinones **4a** and **4b**. The lactone **3** under the same conditions splits out formaldehyde and forms 3-(2'-phenylethyl)-2-quinoxalinone (**6**). The structure assignments of the novel compounds are based on elemental analysis and nmr as well as ir spectroscopic data.

J. Heterocyclic Chem., **23**, 199 (1986).

In continuation of our investigation to use γ-lactones as readily available building blocks for the synthesis of lignans and certain dictamnine akaloids [2-4], we investigated the feasibility of 4-aroyl-3-hydroxy-2(5*H*)-furanones **1**, as starting materials for the following contemplated sequence as a convenient and fast route to lignans of the α,β-dibenzyl-γ-butyrolactone class. We are especially interested in developing a route to α,β-asymmetrically disubstituted γ-lactones (Figure 1).

Figure 1



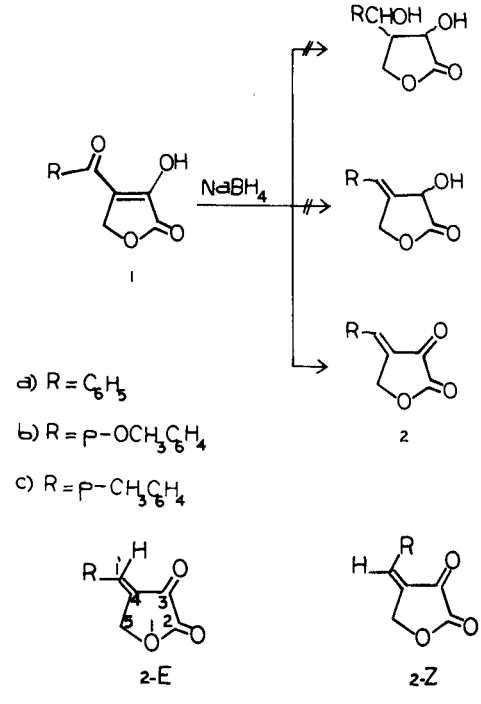
This paper reports on results of reduction of type **1** compounds.

Complex Hydrides.

The reduction of 1,3-diketones with complex hydrides has been investigated earlier. It was shown that the course of the reaction depends strongly on the structure of the 1,3-dicarbonyl compounds. Thus, Dale [5] reported the formation of 1,3-diols in excellent yields by reducing acyclic 1,3-diketones with sodium borohydride. A mixture consisting of the corresponding α,β-unsaturated aldehyde, α-hydroxymethylene species, and 3-methylcamphor was obtained when 3-methylene camphor was reduced with sodium borohydride [6]. Dreiding obtained 1,3-glycols and unsaturated alcohols as a result of a lithium aluminumhydride reduction of α-hydroxymethylene ketones nad β-ketoesters [7a]. A similar reduction of 1,3-cyclohexanedione gave 2-cyclohexenol in a high yield [7b].

Compounds **1a-c**, which were used in this study when treated with sodium borohydride gave neither a glycol nor an allyl alcohol. Instead the corresponding 4-(arylmethylene)-2,3(4*H*,5*H*)-furandiones **2a-c**, were obtained as bright yellow solids. This structure assignment is based upon elemental analysis and spectroscopic evidence (Scheme I).

Scheme I



Thus, the mass spectra show molecular ions, which are 16 units lower than those of the starting materials. The fragmentation pattern also agrees with α,β-unsaturated ke-

tones **2a-c**.

In addition, the ^{13}C-spectral evidence agrees completely with the assigned structures. Type **2** compounds were lacking the peak for the ketonic carbonyl carbon of the aryl group which was present at $\delta \sim 190$ ppm in type **1** compounds. The signals of the ^{13}C-nmr spectra of the reduction products **2a-c** at $\delta = 180$ and $\delta \sim 162$ ppm are assigned to C-3 and C-2 respectively [9].

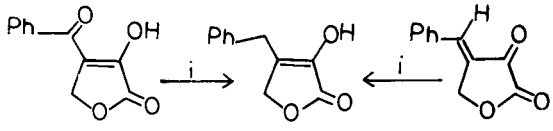
Two isomeric structures can be arrived for these products **2**-*E* and/or **2**-*Z*. By chromatographic follow-up, only one isomer was observed. The stereochemistry was conveniently elucidated on the basis of nmr data. The $J_{H\text{-}5,H\text{-}1}$, coupling constant values measured are clearly consistent with the stereochemistry of the **2**-*E* structure.

The formation of **2a-c** in this reaction can be explained to occur *via* the enolate salts. Reduction of **1a** with aluminum isopropoxide (as a hydride source) in refluxing isopropyl alcohol for 24 hours afforded in a good yield **2a** which was identical with that obtained from the previous method.

Catalytic Hydrogenation.

Using platinum on charcoal supported by palladium chloride as a catalyst to reduce **1a** afforded 4-benzyl-3-hydroxy-2(5*H*)-furanone (**3**) as a colorless product. The structure assignment is based on the following data. First, its elemental analysis and the exact mass value of m/e 190.0600 (RI = 2.57%) for the molecular ion agree with the molecular formula $C_{11}H_{10}O_3$ for this compound. Second, its ^{1}H-nmr spectrum in deuteriochloroform also is in agreement with the assigned structure. Additional evidence in support of this structure for **3** was provided by its ^{13}C-nmr which exhibited nine signals which were assigned for C-2, C-3, C-4, C-5 and C-1′ respectively, on the basis of their chemical shifts and the off-resonance decoupled spectrum. Furthermore, compound **3** also was obtained from the reduction of **2a** using the same catalyst (Scheme II).

Scheme II

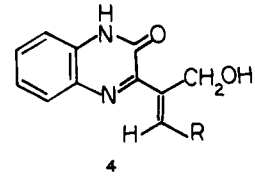


3

i = H_2 - Pt/C - $PdCl_2$

Condensation reactions of the lactones **2a**, **2b**, and **3** with *o*-phenylenediamine were investigated. Thus, when equimolar amounts of **2a** or **2b** and *o*-phenylenediamine were reacted, the expected products 3-[*E*-(1′-hydroxymethyl-2′-aryl)ethenyl]-2-quinoxalinones **4a** and **4b** were isolated. Their structure assignments also were based on their elemental analysis and spectroscopic data. However, the reaction of the lactone **3** with *o*-phenylenediamine did not afford the anticipated product 3-(3′-hydroxy-2′-phenylpropyl)-2-quinoxalinone (**5**). The elemental analysis of the isolated product agrees with its molecular formula as $C_{16}H_{14}N_2O$, indicating that the reaction followed retrograde aldol condensation [8] involving loss of formaldehyde to give 3-(2$_9$-phenylethyl)-2-quinoxalinone (**6**). Its ir spectrum showed the presence of a peak in the carbonyl frequency region in 1665 cm^{-1} indicating the presence of the OCN group. The ^{1}H-nmr and the ir-spectrum of **6** were the basis for the structure assignment. In addition, unambiguous evidence for the structure of compound **6** was provided by the reaction of benzyl pyruvic acid with *o*-phenylenediamine which gave a product identical with that obtained from the lactone **3** (Scheme III).

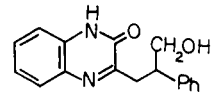
Scheme III



4

a) R = C_6H_5

b) R = p-$OCH_3C_6H_4$



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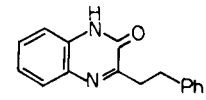

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EXPERIMENTAL

E-4-Arylidene-(4*H*,5*H*)-2,3-furandione (**2**). General Procedure.

A suspension of compound **1** (0.0024 moles) in distilled water (50 ml) was treated with sodium borohydride (0.029 mole). The mixture was stirred for 1½ hours then acidified with concentrated hydrochloric acid. The formed precipitate was filtered off and crystallized from isopropyl alcohol.

E-4-Benzylidene-(4*H*,5*H*)-2,3-furandione (**2a**).

This compound was obtained from 4-benzoyl-3-hydroxy-2(5*H*)-furanone (**1a**) 85% yield, mp 170°; ir (potassium bromide): 1790, 1780, 1730 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 5.57 (d, J = 2.5 Hz, 2H, CH_2), 7.6 (br s, 6H, H arom, and =CH); ms: m/e 188 (M$^+$) (RI = 34.8%), 144 (10.46), 131 (15.45), 116 (100), 103 (15.1), 102 (19.6), 77 (10.37), 63 (10.51), 51 (16.6).

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.20; H, 4.29. Found: C, 70.33; H, 4.43.

Alternatively, **4a** was also obtained by adding a solution of **1a** in 50 ml of isopropyl alcohol to a suspension of 0.3 moles of finely powdered aluminum isopropoxide in 450 ml of boiling isopropyl alcohol. The mixture was refluxed for 2 hours, then the solvent was removed over 24 hours using a moderate reflux ratio. The residue was acidified with concentrated hydrochloric acid.

E-4-(4-Methoxybenzylidene)-(4*H*,5*H*)-2,3-furandione (**2b**).

This compound was obtained from 4-methoxybenzoyl-3-hydroxy-2(5*H*)-furanone (**1b**), 92% yield, mp 205-208°; ir (potassium bromide):

1770, 1722 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 3.856 (s, 3H, OCH_3), 5.525 (d, J = 2.1 Hz, 2H, CH_2), 7.099, 7.607 (dd, 4H, H arom), 7.601 (t, J = 2.1 Hz, 1H, =CH); ^{13}C-nmr (DMSO-d_6): δ 180.274, 162.156, 137.184, 134.041, 125.698, 125.024, 114.986, 113.659, 68.528, 55.524; ms: m/e 218 (M^+) (RI = 99.3%), 162 (27.1), 161 (12.5), 147 (35.6), 146 (100), 133 (10.7), 131 (61.2), 117 (17.1), 115 (11.1), 103 (68.2), 102 (19.2), 89 (24.8), 77 (54.2).

Anal. Calcd. for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62. Found: C, 66.03; H, 4.67.

E-4-(4-Methylbenzylidene)-(4*H*,5*H*)-2,3-furandione (**2c**).

This compound was obtained from 4-tolyl-3-hydroxy-2(5*H*)-furanone (**1c**), 90% yield, mp 167°; ir (potassium bromide): 1770, 1730 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 2.381 (s, 3H, CH_3), 5.532 (d, J = 2.4 Hz, 2H, CH_2), 7.354, 7.519 (dd, 4H, H arom), 7.572 (t, J = 2.4 Hz, 1H, =CH); ^{13}C-nmr (DMSO-d_6): δ 180.661, 161.844, 142.097, 136.797, 131.696, 130.383, 129.962, 126.617, 68.548, 21.120; ms: m/e 202 (M^+) (RI = 93.2%), 187 (13.8), 159 (10.4), 145 (20.1), 131 (44.5), 130 (95.6), 129 (74.7), 128 (30.3), 115 (100), 91 (34.7), 89 (20.4), 77 (20.7).

Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.28; H, 4.99. Found: C, 71.25; H, 5.00.

4-Benzyl-3-hydroxy-2(5*H*)-furanone (**3**). A).

In a Parr bottle, 5 g of **2a**, 0.5 g 5% Pt/C, 1 ml aqueous palladous chloride solution and 150 ml methanol were combined. The mixture was hydrogenated under 50 psi for 30 minutes. The catalyst was filtered off and the solvent was removed *in vacuo*. A small amount of benzene was added followed by enough hexane to cause cloudiness and the mixture was left in the refrigerator for 24 hours. The colorless precipitate was filtered off under dry nitrogen and recrystallized from benzene-hexane, 75% yield, mp 86°; ir (potassium bromide): 3320, 1720 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.33 (s, 2H, CH_2), 3.50 (s, 2H, OCH_2), 7.23 (s, 5H, H arom), 7.53 (s, 1H, OH is deuterium oxide exchangeable); ^{13}C-nmr (deuteriochloroform): δ 171.770 (C_2), 137.226 (C_3), 136.868, 132.241 (C_4), 128.776, 126.804, 69.591 (C_5), 30.769 (C_1); ms: m/e 190.06 (M^+) (RI = 2.57), 91.0552 (100).

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.17; H, 5.43.

B) The work-up procedure is the same as above using **1a** instead of **2a**. The hydrogenation was achieved after 24 hours.

3-[*E*-(1'-Hydroxymethyl-2'-aryl)ethenyl]-2-(1*H*)-quinoxalinone (**4**). General Procedure.

To a solution of 0.005 mole of compound **3** in 30 ml methanol was added a solution of 0.005 mole of *o*-phenylenediamine. The mixture was refluxed for 1 hour. The formed precipitate was filtered and recrystallized from isopropyl alcohol.

3-[*E*-(1'-Hydroxymethyl-2'-phenyl)ethenyl]-2(1*H*)-quinoxalinone (**4a**).

This compound was obtained from **2a**, 75% yield, mp 218°; ir (potassium bromide): 3540, 3200-2700, 16509 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 4.7 (s, 2H, CH_2), 4.8 (br s, 1H, OH is deuterium oxide exchangeable), 7.5, 7.8, 7.9 (m, s, s, 10H, H arom and =CH), 12.4 (br s, 1H, NH is deuterium oxide exchangeable).

Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.05; N, 10.07. Found: C, 73.09; H, 5.00; N, 10.23.

3-[*E*-(1'-Hydroxymethyl-2'-anisyl)ethenyl]-2(1*H*)-quinoxalinone (**4b**).

This compound was obtained from **2b**, 70% yield, mp 180-183°; ir (potassium bromide): 3520-2700, 1650 cm^{-1}.

Anal. Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.11; H, 5.23; N, 9.09. Found: C, 70.33; H, 5.24; N, 9.05.

3-(2'-Phenylethyl)-2(1*H*)-quinoxalinone (**6**).

A solution of 1.9 g of compound **3** and 1.1 g of *o*-phenylenediamine in 20 ml of ethanol and two drops of acetic acid was heated on a steam-bath for 4 hours. The reaction mixture was concentrated and the product that separated out was filtered off and recrystallized from ethanol, 52% yield, mp 207-209°; ir (potassium bromide): 1665 cm^{-1} (C=O); ^{1}H-nmr (DMSO-d_6): δ 3.10 (s, 4H, CH_2CH_2), 7.33, 7.74 (m, 9H, H arom), 12.37 (s, 1H, NH, is deuterium oxide exchangeable).

Anal. Calcd. for $C_{16}H_{14}N_2O$: C, 76.8; H, 5.6; N, 11.2. Found: C, 77.13; H, 5.73; N, 11.09.

Acknowledgement.

Financial support by the National Science Foundation toward the Kratos MS 80 instrument through Grant PCM 8219912 is greatly appreciated.

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