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# Synthesis of 2*H*-Pyran-3-(6*H*)-ones

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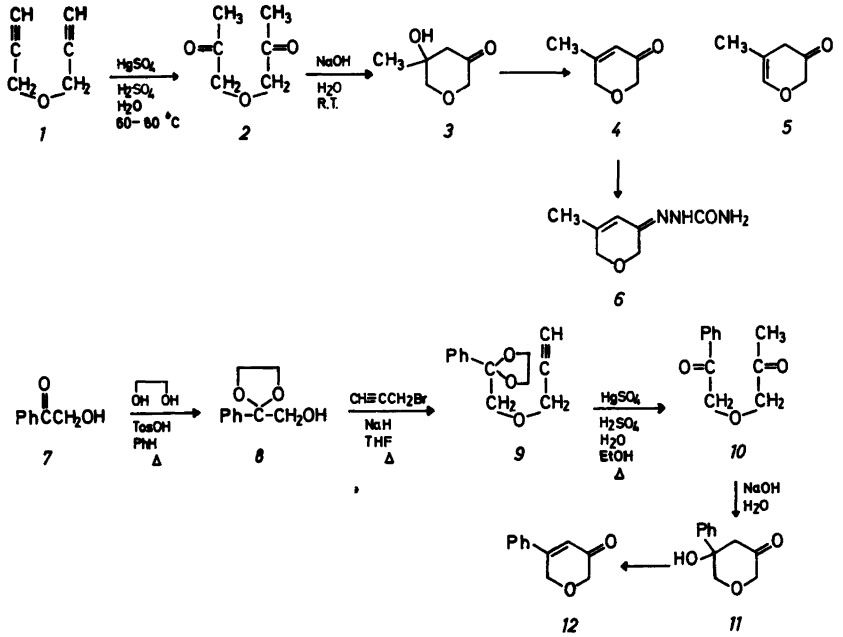
5-Substituted 2*H*-pyran-3(6*H*)-ones have been synthesised by intramolecular aldol condensation of diacetonyl and acetonyl phenacyl ethers which were accessible by hydration of corresponding 2-propynyl ethers.

The chemistry of the 2*H*-pyran-3-one systems has been little investigated. A recent patent describes reductive saturation of the olefinic bond in 2-substituted-6-alkoxy-2*H*-pyran-3(6*H*)-ones followed by elimination of the hydroalkoxy group to form 2*H*-pyran-3(4*H*)-ones.[1] Our interest in 2*H*-thiopyran-3-ones has been extended to oxygen analogues with the ultimate aim to compare properties of thiopyrylium- and pyrylium-olates.[2–4] We herein report a convenient synthesis of 2*H*-pyran-3-ones.

2*H*-Thiopyran-3(6*H*)- and 3(4*H*)-ones are available by Friedel-Crafts cyclisations of allythioacetyl chlorides.[5] A similar synthesis of the oxygen heterocycles from allyloxyacetyl chlorides seemed less attractive because ether functions are frequently affected by Lewis acids.[6] Likewise the reported[7] instability of pyran-3,5-diones discouraged their use as starting material in the synthesis of 2*H*-pyran-3(6*H*)-ones *via* enol ethers and treatment with a metal-hydride or an organometallic reagent in analogy with our versatile synthesis of thiopyran analogues.[8] Instead the synthetic routes shown in Scheme 1 were designed.




*Scheme 1.*

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Di-2-propynyl ether *1*[9] was the starting material for the synthesis of the 5-methyl derivative *4*. The hydration of *1* to the diacetonyl ether *2* was run in dilute sulfuric acid in the presence of mercuric sulfate. The intramolecular aldol condensation of *2* to *4* proceeded readily in cold dilute alkali. The intermediate aldol *3* was not isolated. Both the isomers *4* and *5* can be envisaged, but only *4* was obtained according to spectroscopy. The liquid product *4* could not be stored at room temperature, but was stable as its crystalline semicarbazone *6*.

An analogous approach was used in the synthesis of the 5-phenyl derivative *12*. Phenacyl alcohol *7*[10] was converted into the 1,3-dioxolane *8*[11] in order to avoid side-reactions in the successive condensation with 3-bromopropyne under alkaline conditions (*8*→*9*). Hydration of the triple bond in *9* with concurrent hydrolysis of the ketal function to yield the acetonyl ketone *10* was effected in dilute sulfuric acid in the presence of mercuric sulfate. Intramolecular aldol condensation of *10* in aqueous alkali gave 5-phenyl-2*H*-pyran-3(6*H*)-one *12* in 75 % yield; the 4*H*-tautomer was not seen by spectroscopy. Attempted tautomerisation in acid solution led to substantial decompositions. Presumably the 6*H*-isomer, in which the double bond and the carbonyl group are conjugated, is the thermodynamically more stable tautomer in accordance with the behaviour of 2-hydroxyfurans which exist almost exclusively as the conjugated furan-2(5*H*)-one tautomer.[12]

The IR spectra show an $\alpha,\beta$-unsaturated carbonyl group at 1690 and 1680 $cm^{-1}$ for *4* and *12*, respectively. The $^{13}C$ NMR spectra show carbonyl carbon at 194.2 and 194.6 ppm for *4* and *12*, respectively, and C5 at 160.7 and 157.8, respectively. In $^1H$ NMR the H-6 protons appear at a slightly lower field than the H-2 protons; the relative assignments are based on the assumption of allylic coupling between H-4 and H-6 protons.

## EXPERIMENTAL

*Diacetonyl ether* 2. Di-2-propynyl ether[9] (14.1 g, 0.15 mol) was added dropwise with stirring over 1 h to a mixture of mercuric sulfate (3.0 g), and concentrated sulfuric acid (4 ml) in water (100 ml) at 60 °C. After stirring for 2 h at 60 °C the temperature was increased to 80 °C and the stirring continued for 2 h. The cold reaction mixture was extracted with ether to remove unreacted di-2-propynyl ether and the product extracted into chloroform (10×). The chloroform solution was dried ($MgSO_4$), the solvent evaporated and the residue distilled; yield 11.1 g (57 %), b.p. 112–114 °C/10 mmHg. The compound slowly decomposes on storage. An analytical specimen was prepared by preparative GLC on 20 % SE 30 (column 240 cm, 3 mm) at 90–120 °C, 4 °C/min; ret.time 5 min. $^1H$ NMR ($CDCl_3$): $\delta$ 2.15 (Me), 4.18 ($CH_2$). IR (film): 3460 (br. OH), 1740 $cm^{-1}$ (CO). MS [(70 eV; *m/e* (% rel. int.)]: 130 (0.3, M), 87 (4), 57 (61), 43 (*100*).

*5-Methyl-2*H*-pyran-3(6*H*)-one* 4. 2 M NaOH (130 ml) was cooled to *ca.* 5 °C and added over 2 min to a solution of diacetonyl ether (6.5 g, 0.05 mol) in water (130 ml) at 5 °C. The cooling bath was removed after 15 min and the mixture allowed to reach room temperature and extracted with chloroform (15×). The dried ($MgSO_4$) chloroform extract was evaporated and the residue distilled; yield 3.6 g (64 %), b.p. 78–80 °C/9 mmHg. The product decomposes slowly on storage. The analytical specimen was prepared by preparative GLC on 10 % OV 17 (column 240 cm, 6 mm) at 100–140 °C, 4 °C/min; ret.time 6 min). MS: M *m/e* 112.0522. Calc. for $C_6H_8O_2$: 112.0524. $^1H$ NMR ($CDCl_3$): $\delta$ 1.96 (Me, br.s), 4.06 (2H-2,s), 4.27 (2H-6,br.s), 6.00 (H-4,br.s). $^{13}C$ NMR ($CDCl_3$): $\delta$ 19.5 (Me, *J* 128 Hz), 68.2 (*J* 144 Hz) and 71.2 (*J* 142 Hz) (C2 and C6), 123.8 (C4, *J* 169 Hz), 160.7 (C5,s), 194.2 (C3,s). IR (film): 1690 $cm^{-1}$ ($\alpha,\beta$-unsat. CO). UV [96 % EtOH (log $\varepsilon$)]: 308 (2.17), 230 (4.11) nm.

*5-Methyl-2*H*-pyran-3(6*H*)-semicarbazone* 6. A solution of 5-methyl-2*H*-pyran-3(6*H*)-one (0.5 g, 45 mmol) in ethanol (5 ml) was added to a solution of semicarbazide hydrochloride (0.5 g) and sodium acetate (0.75 g) in water (5 ml) and the mixture stirred at 70 °C for 10 min. Water (10 ml) was then added and the crystalline product collected and recrystallized from ethanol; yield 0.5 g (66 %), m.p. 196–197 °C. Anal $C_7H_{11}N_3O_2$: C, H. $^1H$ NMR (DMSO-$d_6$): $\delta$ 1.78 (Me), 4.02 (2H-6,br.s), 4.33 (2H-2,s), 5.95 (H-4,m). IR (KBr): 1700 $cm^{-1}$ (CO). MS [70 eV; *m/e* (% rel. int.)]: 169 (*100*), M.

*2-Phenyl-2-(2-propynyloxymethyl)-1,3-dioxalane* 9. A solution of 2-hydroxymethyl-2-phenyl-1,3-dioxolane[11] (9.8 g, 0.06 mol) in dry THF (100 ml) was added dropwise over 30 min at room temperature to sodium hydride (1.5 g, 0.06 mol) suspended in dry THF (50 ml). The mixture was stirred at room temperature for 2 h. 3-Bromopropyne (10.0 g, 0.08 mol) was then added at a fast rate from a dropping funnel and the mixture heated under reflux for 12 h. The mixture was filtered and most of the solvent evaporated before chloroform (150 ml) was added. The solution was washed, dried ($MgSO_4$), the solvent evaporated and the residue distilled; yield 8.1 g (62 %), b.p. 95–97 °C/0.3 mmHg). The product solidified below room temperature. The analytical specimen was prepared by preparative GLC on 20 % SE 30 (column 240 cm, 6 mm) at

190–220 °C, 4 °C/min; ret.time 5 min. $^1$H NMR ($CDCl_3$): $\delta$ 2.38 (HC≡, t, *J* 2.5 Hz), 3.71 (2-$CH_2$,s), 3.8–4.2 (–$CH_2$–$CH_2$–,m), 4.20 (–$CH_2$C≡, d, *J* 2.5 Hz), 7.2–7.6 (Ph). IR (film): 3280 (C≡C–H), 2120 cm$^{-1}$ (C≡C). MS [70 eV; *m/e* (% rel. int.)]: 218 (<1,M), 150 (11), 149 (100), 106 (5), 105 (67), 91 (5), 77 (29).

*Acetonyl phenacyl ether* 10. A solution of 2-phenyl-2-(2-propynyloxymethyl)-1,3-dioxolane (6.1 g, 0.03 mol) in 75 % aq. ethanol (50 ml) was added dropwise with stirring at room temperature over 1 h to a solution prepared from mercuric sulfate (0.6 g) and conc. sulfuric acid (3 ml) in 75 % aq. ethanol (30 ml). The mixture was refluxed for 5 h, filtered and most of the solvent distilled off. The residue was extracted with chloroform (80 ml), the chloroform solution shaken with sat. $NaHCO_3$, dried ($MgSO_4$), the chloroform evaporated and the residue distilled; yield 3.6 g (63 %), b.p. 114–116 °C/0.2 mmHg, m.p. *ca.* 25 °C. The compound is slowly decomposed on storage. The analytical specimen was prepared by preparative GLC on 20 % SE 30 (column 240 cm, 6 mm) at 150–200 °C, 4 °C/min; ret.time 9 min. $^1$H NMR ($CDCl_3$): $\delta$ 2.15 (Me), 4.23 (Ac$CH_2$,s), 4.85 (PhCO$CH_2$,s), 7.2–7.6 and 7.8–8.0 (Ph). IR (film): 1730 ($COCH_3$), 1700 cm$^{-1}$ (COPh). MS [70 eV; *m/e* (% rel. int.)]: 192 (3,M), 144 (11), 120 (35), 106 (11), 105 (*100*), 91 (31), 77 (55).

*5-Phenyl-2*H*-pyran-3(6*H*)-one* 12. Acetonyl phenacyl ether (2.9 g, 0.015 mol) was dissolved in water (130 ml) and the solution cooled to 10 °C (lower temperature gives precipitation) and 2 M NaOH (130 ml) at 10 °C added over 2 min with stirring. The mixture was stirred for another 15 min and then extracted with chloroform (5 ×). The chloroform solution was dried ($MgSO_4$), the solvent evaporated and the residue recrystallised from benzene–light petroleum (4:1); yield 2.6 g (75 %), m.p. 80–81 °C. Anal. $C_{11}H_{10}O_2$: C, H. $^1$H NMR ($CDCl_3$): $\delta$ 4.20 (2H-2,s), 4.78 (2H-6,br.s), 6.52 (H-4), t, *J* 1.5 Hz), 7.47 (Ph,s). $^{13}$C NMR ($CDCl_3$): $\delta$ 66.2 (*J* 147 Hz) and 71.6 (*J* 143 Hz) (C2 and C6), 121.7 (*J* 164 Hz) and 130.9 (*J* 158 Hz) (C4 and C4′), 126.0 (*J* 159 Hz) and 129 (*J* 163 Hz) (C2′,6′ and C3′,5′), 135.8 (C1′,s), 157.8 (C5,2), 194.6 (C3,s). IR (KBr): 1680 cm$^{-1}$ ($\alpha$,$\beta$-unsat. CO). UV [96 % EtOH (log $\varepsilon$)]: 285 (4.16), 215 (3.77) nm. MS [70 eV; *m/e* (% rel.-int.)]: 174 (18,M), 145 (12), 144 (*100*), 116 (56), 115 (91), 89 (10), 63 (12), 58 (12).

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