First synthesis of 5-hydroxycyclohexane-1,3-dione

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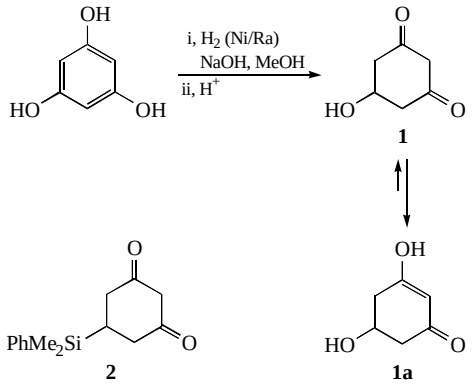
A simple synthetic scheme for 5-hydroxycyclohexane-1,3-dione **1**, existing in solution mainly in the enolic form **1a**, is proposed for the first time.

Recently, we described the synthesis and utilization of 4-hydroxycyclohexane-1,3-dione.[1] Here, we propose a simple preparative synthesis of a regioisomer, 5-hydroxycyclohexane-1,3-dione **1**, by the Ni/Ra-catalysed hydrogenation of phloroglucinol in an alkaline methanolic solution. Hydroxy diketone **1** is stable in the form of its sodium salt, but dehydrates in strongly acidic solution affording resorcinol. The ^{1}H NMR spectrum of diketone **1** in [$^2H_5$]pyridine solution shows only the enolic form of dione **1**. In contrast, the ^{1}H NMR spectrum in [$^2H_6$]acetone shows that dione **1** exists predominantly as the enolic tautomer **1a**, with only 15–20% of the diketo tautomer.



5-Hydroxycyclohexane-1,3-dione **1** was found earlier[2] in the products of metabolism of phloroglucinol by *Pseudomonas* sp. Nevertheless, a chemical synthesis of the compound **1** was thought to be problematic due to the known instability of -hydroxy ketones, and the authors[3] had proposed a complex and multistage scheme for a synthetic equivalent of **1**, 5-phenyldimethylsilylcyclohexane-1,3-dione **2**.

Dione **1**, synthesised by us,[†] yields esters or ethers from its enolic or hydroxy group, easily and with good chemoselectivity, depending on the reaction conditions. The use of dione **1** in the synthesis of natural polyketides will be reported separately.

References

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† 5-*Hydroxycyclohexane*-1,3-*dione* **1**. A mixture of 1.05 g (6.5 mmol) of phloroglucinol dihydrate, 0.29 g (7.2 mmol) of NaOH in 10 ml methanol and 0.5 g of freshly prepared Ni catalyst was stirred for 2 h at 100 bar H_2 and room temperature. Catalyst was then filtered off and the filtrate was passed through a column containing 5 g sulfoacidic cationite in H^+ form. The column was additionally washed with 50 ml MeOH. The combined effluents were evaporated *in vacuo* giving 0.95 g (~100%) of the monohydrate of 5-hydroxycyclohexane-1,3-dione **1**, a viscous oil, which crystallised when cooling. Mp 44–45 °C. ^{1}H NMR ([$^2H_5$]pyridine) δ: 2.93, 2.99 (2dd, 4H, 4,6-H, *J* 4.5, 17 Hz and 7, 17 Hz), 4.65 (septet, 1H, 5-H, *J* 4.5, 7 Hz), 5.87 (s, 1H, 2-H), 7.45 (br. s, >1H, enolic H). ^{1}H NMR ([$^2H_6$]acetone) δ: 2.39 (ddd, 1.7H, 4-H for **1a**, *J* 4, 7 and 17 Hz), 2.62 (dt+d, 2.1H, 6-H for **1a** and 4-H for **1**, *J* 4.5, 17 + 16 Hz), 2.95 (d, 0.4H, 4-H for **1**, *J* 16 Hz), 3.16 and 3.65 (2m, 0.4H, 2-H for **1**), 4.29 (m, 0.85H, 5-H for **1a**), 4.52 (m, 0.15H, 5-H for **1**), 5.39 (m, 0.7H, 2-H for **1a**). IR (KBr, ν/cm^{-1}): 3440 (br), 2680 (br), 1710 (weak), 1620, 1230, 1165, 1060. Found (%): C, 49.23; H, 6.96. Calc. for $C_6H_{10}O_4$ (%): C, 49.31; H, 6.85.