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Note

A convenient synthesis of 1-phenyl-heptane-1,5-dione

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An efficient synthesis of the title compound **9** has been developed *via* Friedel-Craft acylation of benzene and subsequent manipulation of the functionalities of the condensation product **3** for generation of the required 1,5-dione moiety.

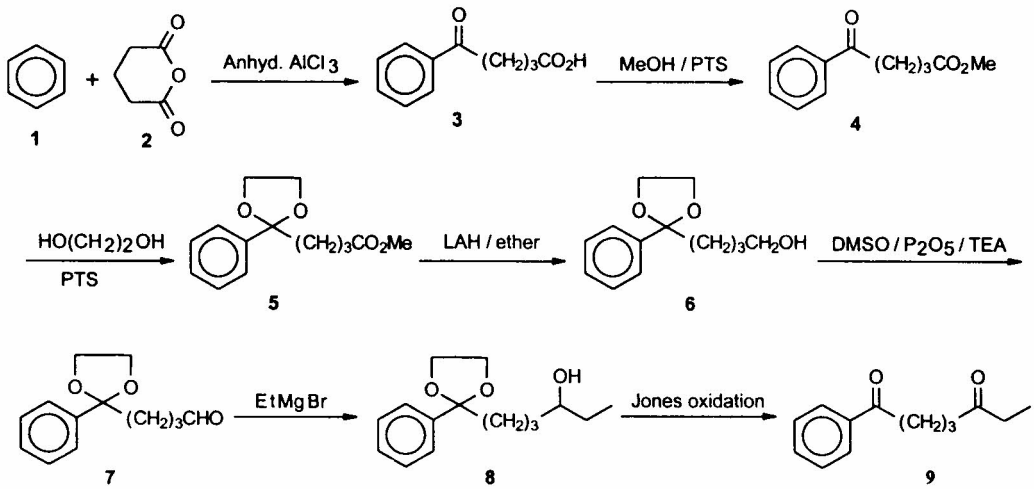
Different phenylheptanes have been isolated[1] from the decayed heartwood of aspens infected with the fungus *Phellinus tremulae*. Subsequently, the isolation of 1-phenylheptane-1,5-dione **9** from the fungus has been reported[2] in 1993. Recently, there has been a report for the synthesis of this diketone which involves Michael addition of a nitroketone[3]. This prompted us to develop a practical approach for the synthesis of the title compound utilising Friedel-Craft condensation of cheaply available benzene to generate the precursor of the required 1,5-dione functionality.

Condensation of **1** with glutaric anhydride **2** followed by esterification gave the ketoester **4**. This on ketalisation followed by $LiAlH_4$ reduction of the resulting ester **5** furnished the alcohol **6**. Oxidation of **6** to the aldehyde **7** has been effected very nicely with DMSO/phosphorus pentoxide/ triethylamine[4] where the acetal functionality remained unaltered. Grignard addition to **7** resulted in the formation of **8.** The latter on Jones' oxidation and simultaneous deketalisation in the strong acidic reaction medium directly gave the dione **9**. The spectral data of the final product were in good agreement with that of the reported compound[3].

Experimental Section

All b.ps and m.ps are uncorrected. ^1H NMR spectra were recorded in $CDCl_3$ on a Varian EM-360 instrument (60 MHz). Chemical shifts were recorded relative to internal TMS. IR spectra were recorded on a Perkin Elmer 783 spectrophotometer as thin film and only the pertinent bands are expressed in cm^{-1}. Mass spectra were recorded on a Shimadzu QP-1000A GC-MS instrument. For all the anhydrous reactions, freshly dried solvents and reagents were used. Unless otherwise mentioned, organic extracts were dried over anhydrous Na_2SO_4.

Methyl 4-benzoylbutanoate 4. To a stirred solution of benzene **1** (200 mL, 2.25 moles) and glutaric anhydride **2** (38.76 g, 0.34 mole), anhydrous aluminium chloride (92.4 g, 0.7 mole) was added in small portions over a period of 4 hr. After addition of dry benzene (100 mL) the reaction mixture, was refluxed for 1 hr, poured into a chilled 20% HCl solution and extracted with ether. The combined organic extract was washed



with water and brine and then dried. After solvent removal, the residue was esterified using methanol (100 mL) and PTS (100 mg). Removal of methanol and usual extraction of the residue with ether gave **4** as a colourless oil: (50.0 g, 71%), b.p 120° / 0.1 mm Hg; IR (neat): 3056, 1737 (C=O), 1686 (Ar-C=O); NMR: δ 1.1-1.4 (m, 2H, H-3), 2.1 (t, J = 6 Hz, 2H, H-2), 3.06 (t, J=8 Hz, 2H, H-4), 4.2 (s, 3H,-OCH_3), 7.4-8.0 (m, 5H, aromatic). Anal. Found: C 69.69, H 6.92. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84 %.

5-Ethylenedioxy-5-phenylpentan-1-ol 6. A mixture of **4** (15.45 g, 0.075 mole), ethylene glycol (4.7g, 0.075 mole) and PTS (500 mg) in benzene (150 mL) is refluxed in a Dean-Stark apparatus for 4 hr with continuos removal of water. The benzene solution was washed successively with 10 % aqueous $NaHCO_3$, water and brine and dried. Solvent removal afforded the acetal **5** in quantitative yield. A solution of the latter in dry ether (100 mL) was added dropwise to a cold suspension of LAH (2.8 g, 0.075 mole) in ether (100 mL) over a period of 1 hr followed by refluxing. The reaction was terminated by dropwise addition of saturated solution of Na_2SO_4 to the ice-cooled mixture till a white crystalline precipitate appeared which was filtered. The filterate was concentrated and the residue distilled to furnish **6** as a colourless oil, 13.8 g (83.4%); b.p 110° C at 0.5 mm Hg; IR (Neat): 3600, 3045, 1640; δ ^{1}H NMR: 1.1-1.4 (m, 6H, H-2, H-3, H-4), 3.3-3.6 [m, 6H, H-1, O-$(CH_2)_2$ -O-], 2.9 (bs, -OH, exchangeable with D_2O), 7.4-8.0 (m, 5H, aromatic). Anal. Found: C, 70.48, H 8.34, Calcd. for $C_{13}H_{18}O_3$: C, 70.24, H 8.16 %.

5-Ethylenedioxy-5-phenylpentanal 7. To a cooled (0°C) solution of **6** (4.44 g, 20 mmoles) in CH_2Cl_2 (50 mL) were added DMSO (3.12 g, 40 mmoles) and P_2O_5 (5.68 g, 40 mmoles) successively. The mixture was brought to room temperature and stirred for 2 hr. Triethylamine (7.1 mL, 70 mmoles) was added. The mixture was stirred for 4 hr at room temperature and treated with water. The aqueous layer was extracted with CH_2Cl_2. The combined organic extract was washed with 10 % HCl, water, brine and dried. Solvent removal under reduced pressure afforded the aldehyde **7**. The aldehyde being unstable was immediately subjected to the next step without purification. Yield 3.3 g (75%); IR (Neat): 3060, 3027, 2733, 1724; ^{1}H NMR: δ 1.1-1.4 (m, 4H, H-3, H-4), 2.3 (t, J = 6 Hz, 2H, H-2), 3.4-3.6 [m, 4H, O-$(CH_2)_2$-O-], 7.4-8.0 (m, 5H, aromatic), 9.7 (t, J = 1.5 Hz, -CHO).

3-Hydroxy-7-ethylenedioxy-7-phenylheptane 8. To a cooled (10°C) suspension of Grignard reagent, prepared from Mg (114 mg, 4.75 mmoles) and C_2H_5Br (0.52 g, 4.7 mmoles) in THF (30 mL), was added a solution of **7** (0.7g, 3.18 mmol) in THF (20 mL) and stirring further continued for 4 hr. The reaction was terminated by the addition of a saturated solution of NH_4Cl and extracted with ether. Usual work-up and removal of solvent followed by distillation afforded the alcohol **8** as a viscous oil; 600 mg (75%), b.p 127°/ 0.5 mm Hg; IR (Neat): 3466, 3050, 1685 cm^{-1}; ^{1}H NMR: δ 0.9 (t, J = 5 Hz, 3H, CH3), 1.2-1.8 (m, 8H), 3.4-3.6 (m, 5H), 2.9 (bs, -OH, exchangeable with D_2O), 7.4-8.0 (m, 5H, aromatic). Anal. Found : C, 71.69, H 8.62 Calcd for $C_{15}H_{22}O_3$: C, 71.96, H 8.86 %.

1-Phenylheptane-1,5-dione 9. Following a standard procedure for Jones' oxidation, compound **8** (500 mg, 2.0 mmoles) in acetone (15 mL) was added dropwise over a period of 1 hr to a stirred and cooled (0-5 °C) solution of Jones' reagent (50 mL, 2.0 M solution). The mixture was stirred further for 2 hr at this temperature and the reaction quenched by the addition of *iso*-propanol (3 mL). The reaction mixture was brought to room temperature and extracted with ether. An usual work up followed by solvent removal gave the residue which was crystallized from EtOAc-cyclohexane to furnish **9** as a white solid, 248 mg (61%), m.p. 62° (lit.[3] m.p. 64°); IR (KBr): 1712 (C=O),1680 (ArC=O); ^{1}H NMR δ 1.03 (t, J = 7.3 Hz, 3H, H-7), 2.02 (m, 2H, H-3), 2.46 (q, J = 7.3 Hz, 2H, H-6), 2.53 (t, J = 7 Hz, 2H, H-4), 3.07 (t, J = 7 Hz, 2H, H-2), 7.4-8.0 (m, 5H, aromatic); MS (EI, 70 eV): (m/z) 204 (M+, 11 %), 175 (12), 147(29), 133 (15), 120 (28), 105 (100), 77 (45), 57 (14).

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