Synthesis of 1-Phenylheptane-1,5-dione, a New Natural Product Found in Phellinus tremulae

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SYNTHESIS OF 1-PHENYLHEPTANE-1,5-DIONE, A NEW NATURAL PRODUCT FOUND IN *PHELLINUS TREMULAE*

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ABSTRACT.—1-Phenylheptane-1,5-dione, **4**, has been synthesized to corroborate the structure proposed following its recent isolation.

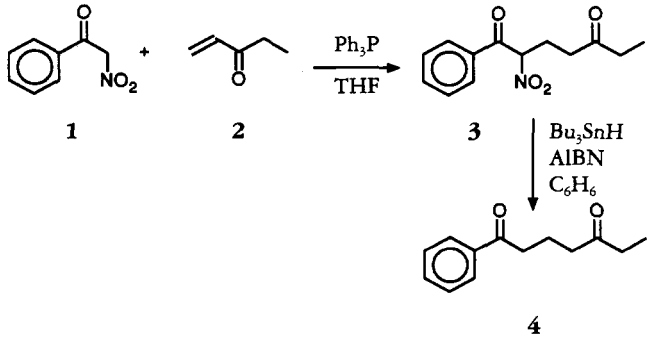
Different phenylheptanes have been isolated (1) from the decayed heartwood of aspens infected with the fungus *Phellinus tremulae* (Bond.) Bond & Borisov (Hymenochaetaceae). The isolation of 1-phenylheptane-1,5-dione [**4**] directly from the fungus, was reported in 1993 (2). This was the first documentation of compound **4** as natural product. In this report we describe the synthesis of **4** which is identical in all respects with the natural product described by Lewis *et al.* (2).

Our synthesis is straightforward and utilizes the well-known versatility of α-nitro ketones for the preparation of natural products (3–5). Michael addition of the commercially available nitro ketone **1** to ethyl vinyl ketone [**2**] (Scheme 1) in THF and in the presence of a catalytic amount of triphenylphosphine, gave **3** in 71% yield. Denitration of **3** was carried out (6) by heating a stirred mixture of **3**, tributyltin hydride, and azobis(isobutyronitrile) (AIBN), in C_6H_6. The 1-phenylheptane-1,5-dione **4** was obtained in 70% yield (49.7% overall yield). Physical properties of the synthetic sample agree well with those reported by the original authors (2).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The ^1H- and ^{13}C-nmr spectra were recorded in $CDCl_3$ at 200 and 50 MHz, respectively, on a Varian Gemini 200 spectrometer. Chemical shifts were recorded relative to internal TMS. Ir spectra were recorded with a Perkin-Elmer spectrophotometer. Mass spectra were determined on a Hewlett-Packard gc/ms 5988A. All the products were monitored by gc performed on a Carlo Erba Fractovap 4160 using a capillary column of Duran glass (0.32 mm×25 m), stationary phase OV-1 (film thickness 0.4–0.45 μm). Microanalyses were performed by using a C, H, N Analyzer Model 185 from Hewlett-Packard Co. The α-nitro ketone **1** was purchased from Aldrich.

1-Phenyl-2-nitroheptane-1,5-dione [**3**].—A THF (40 ml) solution of benzoylnitromethane [**1**] (2.0 g, 12 mmol), ethyl vinyl ketone [**2**] (1.0 g, 12 mmol) and a catalytic amount of Ph_3P, was stirred at room temperature for 24 h. The solution was then washed with 2 N HCl (2×15 ml), dried, evaporated, and flash chromatographed over Si gel. Elution with cyclohexane-EtOAc (8:2) afforded pure **3**: oil (2.13 g, 71%); ir (dry film) ν max 1710 (C=O), 1695 (ArC=O), 1550 (NO_2) cm^{-1}; ^1H nmr δ 1.08 (3H, t, J=7.2 Hz, H-7), 2.4–2.5 (4H, t+q, H-4 and H-6), 2.65–2.7 (2H, m, H-3),



1 2 3 4

SCHEME 1. Synthesis of 1-Phenylheptane-1,5-dione.

6.3–6.4 (1H, m, H-2), 6.5–6.7 (3H, m, H-3′, H-4′, and H-5′), 8.1–8.15 (2H, m, H-2′ and H-6′). *Anal.* calcd for $C_{13}H_{15}NO_4$, C 62.64, H 6.07, N 5.62; found C 62.8, H 6.18, N 5.49.

1-Phenylheptane-1,5-dione [**4**].—To a dry C_6H_6 solution (70 ml) of **3** (2 g, 8 mmol) and azobis(isobutyronitrile) (AIBN, 0.626 g, 3.84 mmol), under N_2, tributyltin hydride (3.5 g, 12 mmol) was added and the resulting solution was refluxed for 3 h. After cooling, the solvent was evaporated and the crude product purified by chromatography. Elution with cyclohexane-EtOAc (8:2) afforded pure **4** as a white solid: mp 63–64° (1.15 g, 70%); ir (KBr) ν max 1710 (C=O), 1680 (ArC=O) cm^{-1}; ^1H nmr δ 1.03 (3H, t, J=7.3 Hz, H-7), 2.02 (2H, m, J=7 Hz, H-3), 2.42 (2H, q, J=7.3 Hz, H-6), 2.55 (2H, t, J=7 Hz, H-4), 3.02 (2H, t, J=7 Hz, H-2), 7.4–7.6 (3H, m, H-3′, H-4′, and H-5′), 7.92–8.0 (2H, m, H-2′ and H-6′); ^{13}C nmr δ 8.29 (q, C-7), 18.78 (t, C-3), 36.38, 37.99, 41.68 (t, C-2, C-4, and C-6), 128.51, 129.54 (d, C-2′, C-3′, C-5′, and C-6′), 133.54 (d, C-4′), 137.27 (s, C-1′), 200.3 (s, C-1), 211.68 (s, C-5); eims (70 eV) *m/z* $[M]^+$ 204 (11), 175 (10), 147 (29), 133 (13), 120 (28), 105 (100), 77 (43), 57 (12). *Anal.* calcd for $C_{13}H_{16}O_2$, C 76.44, H 7.9; found C 76.58, H 8.02.

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