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2,5-BIS-(2′-METHOXY-5′-METHYLPHENYL)-FURAN, A RARE TYPE OF COMPOUND FROM *BERBERIS UMBELLATA*

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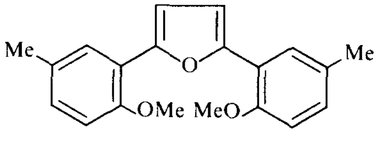
Key Word Index—*Berberis umbellata*; Berberidaceae; 2,5-bis-(2′-methoxy-5′-methylphenyl)-furan.

Abstract—The ethanolic extract of the root of *Berberis umbellata* yielded 2,5-bis-(2′-methoxy-5′-methylphenyl)-furan which has not been previously isolated from a natural source.

Berberis umbellata Wall (Berberidaceae), a native of the main Himalayan range and anterior dry ranges at 3000–4000 m from Kashmir eastwards and from Kumaon to Bhutan [1], has been reported to contain an alkaloid umbellatine [2]. Although considerable work has been carried out on the alkaloidal constituents of the genus *Berberis*, very little has been done on other components [3]. The present investigation deals with the isolation and study of a diphenylfuran.

The ethanolic extract of the root of *B. umbellata* Wall provided a non-polar compound in extremely poor yields in addition to alkaloidal constituents. The compound, $C_{20}H_{20}O_3$, mp 108–110° was characterized as 2,5-bis-(2′-methoxy-5′-methylphenyl)-furan (**1**) by comparison of the UV, IR and ^1H NMR with those reported by Majumder and Saha [3].

The compound 1,4-bis-(2′-hydroxy-5′-methylphenyl)-butan-1:4-dione, which was isolated from *B. coriaria* Royle [3] and previously reported by Thomas *et al.* [4] as a double Fries rearrangement product of di-*p*-tolyl succinate, was resynthesized and converted into compound **1** by methylation and cyclization of the methylated product with $POCl_3$ [3]. The compound **1** is probably the first naturally occurring bis-(*O*-methoxymethylphenyl)-furan.



1

EXPERIMENTAL

Isolation of 2,5-bis-(2′-methoxy-5′-methylphenyl)furan. The air-dried, finely ground roots (5 kg) of *Berberis umbellata* Wall (supplied by M/s. G. Ghose & Co., Townened, Darjeeling) was extracted exhaustively with EtOH. The solvent was removed and the residue stirred with 5% aqueous acetic acid, filtered, and the filtrate was extracted several times with $CHCl_3$, the extract washed free of acid and dried. The solvent was removed from the $CHCl_3$ extract and the concentrated brown extract was chromatographed, over a column of Si gel using a mixture of petrol–EtOAc, to provide the furan $C_{20}H_{20}O_3$ (96 mg), mp 108–110°, UV λ_{max}^{EtOH} 296, 330, IR ν_{max}^{KBr} 2938, 2862, 1605, 1500, 792, 740 cm^{-1}, NMR δ (ppm) 2.38 (6H, *s*, $ArCH_3$), 3.89 (6H, *s*, Ar–OCH_3), 6.84 (2H, *d*, Ar–H), 7.01 (2H, *s*, Ar–H), 7.03 (2H, *s*, furan protons) and 7.79 (2H, *s*, Ar–H) and MS *m/e* 308, 292, 266, 235, 159, 149, 146, 145, 116, 115, 91.

Synthesis of 2,5-bis-(2′-methoxy-5′-methylphenyl)furan (**1**). Succinic acid (1.1 g) and *p*-cresol (2 g) were heated to 115–120° on an oil bath. $POCl_3$ (1.6 g) was added dropwise to the hot mixture. After heating for 2–3 hr at 115–120°, the dark reaction mixture was allowed to cool, whereupon a reddish-brown crystalline material formed on top. This was scraped away from the black resin and mixed with 25 g of a 1:1 mixture of ice and water. The dark orange crystals were then filtered, dried and recrystallized from EtOH to give light orange crystals of di-*p*-tolyl succinate, (1.1 g), mp 118°. Found: C, 72.42, H, 6.17%. Calculated for $C_{18}H_{18}O_4$: C, 72.47, H, 6.08%.

Di-*p*-tolyl succinate (1 g), $AlCl_3$ (1.2 g) and CS_2 (50 ml) were heated to reflux for 1 hr. The CS_2 was removed and the light yellow solid remaining was heated to 130°. At 120° the solid began to melt and after heating at 130°, a light brown, spongy mass had formed. After heating for 4 hr at 130°, the material was cooled, then chipped loose and mixed with 50 g of a 1:1 mixture of ice–conc. HCl. The yellow mixture so obtained was filtered, the solid residue was mixed with 25 g of 1:1 mixture of ice and conc. HCl and the mixture stirred overnight. The next day the mixture was filtered and the residue extracted with boiling EtOH (25 ml). A light yellow residue remained which on drying at 110° turned black, chromatographed over a column of silicic acid and eluted with $CHCl_3$ to give a light brown solid (yield 250 mg), mp 184–186°, λ_{max} 257, 340 nm; IR ν_{max} 3336, 1645, 1585 cm^{-1}. Found: C, 72.58, H, 6.12%. Calculated for $C_{18}H_{18}O_4$: C, 72.47, H, 6.08%; identified as 1,4-bis-(2′-hydroxy-5′-methylphenyl)butan-1,4-dione (**2**) by mmp with the authentic sample isolated from *B. acanthifolium*.

Methylation of **2** (200 mg) with MeI and K_2CO_3 gave dimethyl ether (186 mg) mp 68°, λ_{max} 220, 250, 320, ν_{max} 2940, 2860, 1660, 1580 cm^{-1}; δ (ppm) 2.31 (6H, *s*, Ar–CH_3), 3.41 (4H, *s*, –$COCH_2$–), 3.91 (6H, *s*, Ar–OCH_3), 6.89 (2H, *d*, $J = 9$ Hz, Ar–H), 7.29 (2H, *dd*, $J = 9$ Hz and 2 Hz Ar–H), 7.60 (2H, *d*, $J = 2$ Hz, Ar–H), *m/e* 326 (M^+, 35), 177, 150, 149 (100), 134, 106, 105, 91, 78. Found: C, 73.64, H, 6.52. Calculated for $C_{20}H_{22}O_4$: C, 73.61, H, 6.49%; cyclization of the methyl ether (60 mg) was effected in $POCl_3$ under reflux for 6 hr to give the product (32 mg), mp 110 , λ_{max} 298, 330, ν_{max}^{KBr} 2932, 2860, 1605, 1500, 790, 740 identified to be compound **1** by mmp with the natural compound.

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