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Preparation of 1,7-Bis(*p*-hydroxyphenyl)heptane

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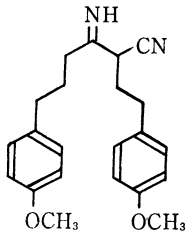
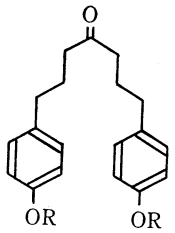
We prepared 1,7-bis(*p*-hydroxyphenyl)heptane in order to study the intramolecular oxidative coupling of phenolic compounds.

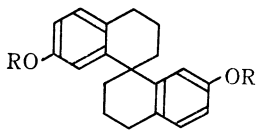
Treatment of 4-(*p*-methoxyphenyl)butyronitrile[1] with lithium methylanilide afforded an iminonitrile I. Hydrolysis of I with boiling sulfuric acid gave 1,7-bis(*p*-methoxyphenyl)-heptanone-4 (IIa). In addition to IIa a compound having no carbonyl group was isolated as a by-product by silica gel chromatography. The structure of this compound was assigned as 7,7'-dimethoxy-1,1'-spirobitetralin (IIIa) by NMR and MS spectra. The same compound was obtained easily by boiling IIa with hydrobromic acid to produce a phenolic compound IIIb followed by methylation with dimethyl sulfate. Huang Minlon reduction of IIa gave 1,7-bis(*p*-methoxyphenyl)heptane (IVa), and a phenolic compound IVb was also obtained by demethylation of IVa.



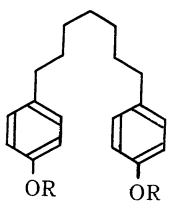
I



II a, R=CH_3
b, R=H



III a, R=CH_3
b, R=H



IV a, R=CH_3
b, R=H

Experimental

*3-Cyano-1,7-bis(*p*-methoxyphenyl)-4-iminoheptane (I).* Phenyllithium was prepared by adding bromobenzene (4.7 g) to lithium (0.4 g) in ether (40 m*l*) under nitrogen atmosphere. To this solution was added methylaniline (6.4 g) dissolved in ether (20 m*l*). After refluxing for 1 hr, 4-(*p*-methoxyphenyl)-butyronitrile (5.2 g) in ether (30 m*l*) was added dropwise to the above solution at room temperature. The solution was refluxed for 1 hr, then quenched with water. The organic layer was washed with water, dried and evaporated. The product (3.7 g, 74%) was obtained by distillation, bp 240—245°C/0.02 mmHg. IR: ν^{neat} 3480, 3380, 3250, 2300 cm^{-1}.

Hydrolysis of the Iminonitrile (I). I (9.3 g) was dissolved in 1:1 sulfuric acid (300 m*l*). The solution was heated at 60°C for 30 min and then under reflux for 30 min. The solution was diluted with water and extracted with ether. The ethereal extract was washed with water, dried and evaporated. Chromatography of the crude product on silica gel (elution with benzene) resulted in the separation of two compounds. Evaporation of the first fraction gave IIIa (0.7 g, 8.3%), mp 88 —89°C. IR: ν^{Nujol} 1615, 1575, 1275, 1235, 1040, 880, 845, 810 cm^{-1}. NMR: δ (CCl_4) 1.6—2.2 (8H, m), 2.6—3.0 (4H, m), 3.6 (6H, s), 6.25 (2H, d, J=3 Hz), 6.6 (2H, d-d, J=8—3 Hz), 6.95 ppm (2H, d, J=8 Hz). MS: *m/e* 308 (100), 280 (15.7), 279 (61.3), 249 (18.8), 248 (18.7), 221 (10.4), 174 (46.5), 159 (14.2), 147 (23.6), 134 (25.2), 121 (24.7%).

Found: C, 82.05; H, 7.85%. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84%.

The second fraction gave IIa (4.3 g, 50%), mp 31—33°C. IR: ν^{Nujol} 1705, 1615, 1585, 1305, 1240, 1030, 835, 815 cm^{-1}. NMR: δ(CCl_4) 1.9 (4H, q, J=6 Hz), 2.4 (4H, t, J=6 Hz), 3.8 (6H, s), 6.8 (4H, d, J=9 Hz), 7.1 ppm (4H, d, J=9 Hz).

Found: C, 77.39; H, 7.94%. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03%.

IIa (300 mg) was dissolved in 48% hydrobromic acid (50 m*l*) and heated for 1 hr under reflux. The reaction mixture was evaporated to dryness and extracted with ether. The ethereal extract was washed with sodium carbonate solution and water, dried and evaporated. The residue was recrystallized from chloroform to give IIIb (120 mg, 40%), mp 157—159°C. IR: ν^{Nujol} 3340, 3180, 1620, 1585, 1290, 1230, 1035, 860, 845 cm^{-1}. NMR: δ ($CDCl_3$), 1.6—2.3 (8H, m), 2.6—3.0 (4H, m), 4.2 (2H, broad s), 6.2 (2H, d, J=3 Hz), 6.6 (2H, d-d, J=3—8 Hz), 7.0 ppm (2H, d, J=8 Hz). MS: *m/e* 280 (91.4), 252(25.3), 251(100), 224 (17.3), 223(28.9), 160(38.3), 145(17.9), 133(19.8), 120(16.7), 107(25.3%).

Found: C, 81.09; H, 7.18%. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19%.

This compound was converted by treatment with dimethyl

1) Ki-U Kim, *J. Pharm. Soc. Japan*, **63**, 376 (1943).

sulfate into a dimethyl ether, which was identical with IIIa in IR spectra.

*1,7-Bis(*p*-hydroxyphenyl)heptanone-4 (IIb).* Ethylmagnesium bromide was prepared by adding ethyl bromide (21.8 g) to magnesium (4.8 g) in ether. To this solution was added diethylamine (14.6 g) and heated for 30 min under reflux. IIa (3.3 g) in ether was added to the solution. The reaction was carried out for 2 hr under reflux. The solvent was removed and the residue was heated to 179—190°C for 45 min. The reaction mixture was cooled, diluted with water and extracted with ether. The ethereal extract was washed with sodium carbonate solution and water. The ethereal layer was extracted with dilute potassium hydroxide solution and the aqueous layer was acidified with 6N hydrochloric acid and extracted with ether and dried. On evaporation of the solvent, the product solidified, (2.6 g, 80%). Recrystallization from ether-petroleum ether gave IIb, mp 115—117°C. IR: ν^{Nujol} 3320, 1685, 1610, 1590, 1510, 1220, 830 cm^{-1}. NMR: δ (CD_3OD), 1.8 (4H, q), 2.4 (4H, t), 2.5 (4H, t), 6.7(4H, d, J=8 Hz), 7.0 ppm (4H, d, J=8 Hz).

Found: C, 76.24; H, 7.41%. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43%.

*1,7-Bis(*p*-methoxyphenyl)heptane (IVa).* A mixture of IIa (3.3 g) potassium hydroxide (10 g), 80% hydrazine hydrate (40 m*l*) and triethylene glycol (10 m*l*) was heated for 2 hr at 140—160°C and then for 3 hr at 190—210°C. Water (300 m*l*) and 6N hydrochloric acid (30 m*l*) were added to the cooled solution. The product was extracted with chloroform and the chloroform extract was washed with water, dried and evaporated. Distillation of the residual oil gave IVa (2.2 g, 70%), bp 180—190°C/0.01 mmHg. IR ν^{neat} 1610, 1585, 1455, 1295, 1240, 1170, 1035, 820 cm^{-1}. NMR: δ(CCl_4), 1.2—1.6 (10H, m), 2.5 (4H, t, J=7 Hz), 4.75 (6H, s), 6.7 (4H, d, J=8 Hz), 7.0 ppm (4H, d, J=8 Hz).

Found: C, 80.89; H, 9.01%. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03%.

*1,7-Bis(*p*-hydroxyphenyl)heptane (IVb).* IVa (3.0 g) was dissolved in acetic acid (100 m*l*) and 48% hydrobromic acid (100 m*l*) and then heated under reflux for 30 min. The solution was evaporated *in vacuo*, and ether was added to the residue. The ethereal solution was washed with sodium carbonate solution and water, and then extracted with potassium hydroxide solution. The aqueous extract was acidified with 6N hydrochloric acid and reextracted with ether. On evaporation of the solvent, the product solidified (2.6 g, 85%). Recrystallization from benzene gave IVb, mp 98—99°C. NMR: δ ($CDCl_3$), 1.3—2.0 (10H, m), 2.7 (4H, t, J=7 Hz), 4.2 (2H, m), 6.95 (4H, d, J=8 Hz), 7.25 ppm (4H, d, J=8 Hz). MS: *m/e* 284(20), 107(100%).

Found: C, 80.06; H, 8.45%. Calcd for $C_{19}H_{24}O_2$; C, 80.24; H, 8.51%.