

THE FRIEDEL-CRAFTS ACETYLATION OF 3,3'-DIMETHOXYBIPHENYL*

By P. I. MORTIMER†

Recently Campbell and Scott¹ have reported on some substitution reactions of 3,3'-dimethoxybiphenyl. They found that bromination occurred mainly in the 6,6'-positions, and that benzoyl chloride, in the presence of stannic chloride, reacted at the 6-position, the product being a fluorenol. It had earlier been found that iodination gave both 4,4'- and 6,6'-substitution,² and chloromethylation occurred at the 6,6'-position.³ Reaction with arsenic trichloride occurred at the 2- or 6-position.⁴

In contrast, Friedel-Crafts acetylations have given the 4-substituted product as the only isolated isomer. When the reaction was carried out in refluxing tetrachloroethane, monodemethylation also occurred, and the product was recognizable as an *o*-hydroxy ketone by its colour reaction with ferric chloride, by the low carbonyl frequency (1637 cm⁻¹) for which the methyl ether (carbonyl frequency 1690 cm⁻¹) provides a comparison, and by the position of the signal of the phenolic proton at very low field (δ 12.36) in the p.m.r. spectrum. Any possibility that it is the 2-isomer is excluded by its p.m.r. spectrum, which contained signals assignable to a proton adjacent to the carbonyl group. In carbon disulphide, acetylation occurred without demethylation; the resulting 4-acetyl-3,3'-dimethoxybiphenyl was also obtained by methylation of the hydroxyketone.

The Friedel-Crafts acetylation of 3,3'-dimethoxybiphenyl in the presence of aluminium chloride thus parallels the reaction with 3-methoxybiphenyl, which was shown by Bradsher, Brown, and Porter⁵ to acetylate at the 4-position. Demethylation occurred when the reaction was carried out at higher temperatures.

Experimental

Elementary analyses were by the Australian Microanalytical Service, Melbourne. Infrared spectra were run as Nujol mulls on a Perkin-Elmer Infracord, and ultraviolet spectra were determined on a Perkin-Elmer Spectracord. Proton magnetic resonance spectra were measured in deuteriochloroform with tetramethylsilane as internal standard, on a Varian A60 spectrometer. Melting points are not corrected.

Acetylation of 3,3'-Dimethoxybiphenyl in Carbon Disulphide

To a solution of 3,3'-dimethoxybiphenyl⁶ (10.7 g, 0.05 mole) in carbon disulphide (20 ml), cooled in ice, there was added ground anhydrous aluminium chloride (9.4 g, 0.07 mole) and

* Manuscript received December 15, 1966.

† C.S.R. Research Laboratories, Roseville, N.S.W.

¹ Campbell, N., and Scott, A. H., *J. chem. Soc. C*, 1966, 1050.

² Baker, W., Barton, J. W., McOmie, J. F. W., Penneck, R. J., and Watts, M. L., *J. chem. Soc.*, 1961, 3986.

³ Matarasso-Tchiroukhine, E., *Annls Chim.*, 1958, **3**, 13, 405.

⁴ Gottlieb-Billbroth, H., *J. Am. chem. Soc.*, 1927, **49**, 482.

⁵ Bradsher, C. K., Brown, F. C., and Porter, H. K., *J. Am. chem. Soc.*, 1954, **76**, 2357.

⁶ Kornblum, N., *Org. Synth.*, 1955, Coll. Vol. III, 295.

then, to the stirred mixture, over 15 min, acetic anhydride (5.1 g, 0.05 mole). A dark blue, insoluble complex formed immediately. The mixture was refluxed for 30 min, and then decomposed with ice. The organic material, in ether, was washed with water and dilute sodium hydroxide, and distilled to yield, after a fore-run of unchanged dimethoxybiphenyl (6.9 g, 64%), 4-acetyl-3,3'-dimethoxybiphenyl (1.9 g, 14%), b.p. 182° at 0.4 mm, which was purified by recrystallization from methanol and then from light petroleum, and obtained as colourless needles, m.p. 69° (Found: C, 75.4; H, 6.3. $C_{18}H_{16}O_3$ requires C, 75.0; H, 6.3%). ν_{\max} 1690 cm^{-1} ; λ_{\max} 275, 310sh $\text{m}\mu$ (ϵ 17050, 11450) in ethanol. The p.m.r. spectrum contained signals at δ 7.79 (1 proton, doublet, J 9 c/s) 6.8–7.5 (6 protons, multiplet), 3.92, 3.82, and 2.62 (each 3 protons, singlets).

The dimethoxybiphenyl ketone (0.265 g) was oxidized with sodium hypobromite as described by Johnson, Gutsche, and Offenhauer⁷ for the oxidation of 4-(4'-methoxyphenyl)-acetophenone. The crude product was purified by solution in dilute sodium bicarbonate. The recovered product (0.24 g, 89%) was recrystallized from benzene/light petroleum to yield 2-methoxy-4-(3'-methoxyphenyl)benzoic acid as colourless needles, m.p. 103–104° (Found: C, 69.7; H, 5.7. $C_{15}H_{14}O_4$ requires C, 69.8; H, 5.5%). ν_{\max} 1725 cm^{-1} ; λ_{\max} 267, 299 $\text{m}\mu$ (ϵ 17200, 10600) in ethanol; 261, 291 $\text{m}\mu$ (ϵ 16700, 10600) in 0.04N sodium ethoxide.

Acetylation of 3,3'-Dimethoxybiphenyl in Tetrachloroethane

A mixture of 3,3'-dimethoxybiphenyl (10.7 g, 0.05 mole), acetyl chloride (4.0 g, 0.05 mole), and ground aluminium chloride (7.5 g, 0.056 mole) in *sym*-tetrachloroethane (100 ml) was stirred at room temperature for 2 hr and then refluxed for 2 hr. The resulting solution and complex were stirred with water and dilute acid, and the organic phase was separated and washed with 1N hydrochloric acid, and then extracted with sodium hydroxide solution (5%, 4 portions of 100 ml). During the first two extractions, yellow sodium salts separated. Distillation of the neutral portion yielded dimethoxybiphenyl (2.3 g, 21%) and a fraction, b.p. 192°/1.4 mm (1.2 g, about 10%) containing, according to thin-layer chromatography on silica gel, the hydroxy ketone described below and traces of dimethoxybiphenyl.

The sodium salts and the alkaline extracts were combined and acidified, and the phenols were collected in light petroleum (400 ml), which left much black solid. The extraction with alkali and recovery with acid were repeated, and the phenolic fraction, from light petroleum (50 ml), yielded crude 4-acetyl-3-hydroxy-3'-methoxybiphenyl (4.0 g, 33%) as yellow crystals, m.p. 79–82°. The material (0.5 g) in the mother liquor contained, according to thin-layer chromatography, some dimethoxybiphenyl and hydroxy ketone, and possibly two minor components of lower mobility.

The hydroxy ketone was obtained from light petroleum as colourless plates, m.p. 88–89° (Found: C, 74.1; H, 5.7. $C_{15}H_{14}O_3$ requires C, 74.4; H, 5.8%). ν_{\max} 1637 cm^{-1} , λ_{\max} 284, 320sh $\text{m}\mu$ (ϵ 18800, 9900) in ethanol; 242, 284, 378 $\text{m}\mu$ (ϵ 24300, 16600, 8000) in 0.04N sodium ethoxide. The p.m.r. spectrum contained signals at δ 12.36 (1 proton, singlet), 7.70 (1 proton, doublet, J 9 c/s), 6.6–7.5 (6 protons, multiplet), 3.80 and 2.55 (each 3 protons, singlets).

An alcoholic solution of the hydroxy ketone gave a strong purple colour with ferric chloride.

The hydroxy ketone was oxidized to the hydroxy acid by the method of King, McWhirter, and Barton⁸ and gave, in 18% yield, 4-(3'-methoxyphenyl)salicylic acid, m.p. 175° (from ethanol) (Found: C, 69.1; H, 5.15. $C_{14}H_{12}O_4$ requires C, 68.85; H, 4.95%). ν_{\max} 1652 cm^{-1} ; λ_{\max} 269, 300sh $\text{m}\mu$ (ϵ 18900, 10000) in ethanol; 264, 295sh $\text{m}\mu$ (ϵ 18500, 9100) in 0.04N sodium ethoxide.

An alcoholic solution of the hydroxy acid gave with ferric chloride a strong red-purple colour.

Methylation of the Hydroxy Ketone

A solution of the hydroxy ketone (1.0 g) in acetone (50 ml) containing dimethyl sulphate (2.5 ml) and anhydrous potassium carbonate (5.0 g) was refluxed for 14 hr, and after addition

⁷ Johnson, W. S., Gutsche, C. D., and Offenhauer, R. D., *J. Am. chem. Soc.*, 1946, **68**, 1648.

⁸ King, L. C., McWhirter, M., and Barton, D. M., *J. Am. chem. Soc.*, 1954, **67**, 2089.

of ammonia and removal of solvent, the product was dissolved in ether, washed with dilute sodium hydroxide solution, and crystallized from light petroleum, to yield 4-acetyl-3,3'-dimethoxybiphenyl, m.p. 69°, not depressed by the product obtained above (yield, 9.92 g, 86%).

Acknowledgments

I am indebted to Dr A. V. Robertson, University of Sydney, for the p.m.r. spectra. The Management of the Colonial Sugar Refining Company is thanked for permission to publish.