Short Communications

Complex Dibenzofurans

XIII.* Further Studies on the Dehydration of 2,2'-Dihydroxy-biphenyls

BRIAN G. PRING **

Institute of Organic Chemistry, University of Stockholm, Stockholm, 50, Sweden
and
NILS E. STJERNSTRÖM

Research Laboratories, AB Astra, Södertälje, Sweden

During previous investigations on the acid-catalysed dehydration of 2,2'-di-hydroxybiphenyls, it was found that derivatives of hydroquinone and resorcinol were especially susceptible to ring closure.[1] However, monophenolic and catechol groupings do not facilitate this reaction.[2,3] We now wish to report some further experiments concerning the aptitude to ring closure of 2,2'-dihydroxybiphenyl, 2,3,2'-trihydroxybiphenyl, 2,3,2',3'-tetra-hydroxybiphenyl, and 2,6,2',6'-tetrahydroxybiphenyl.

Dehydration of 2,2'-dihydroxybiphenyl has previously been effected by fusion with zinc chloride.[4] We have not been able to bring about dehydration by prolonged refluxing with hydrobromic acid. However, single phenolic hydroxyl groups can be displaced by hydroxyl-^{18}O, alkoxyl, and alkylthio groups under more forcing conditions in the presence of hydrochloric acid.[5-7] These results led us to believe that acid-catalysed dehydration of 2,2'-dihydroxy-

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** Present address: Research Laboratories, AB Astra, Södertälje, Sweden.

biphenyl might be brought about under similar conditions and such was the case. When the compound was heated with a mixture of 48 % hydrobromic acid and glacial acetic acid in an ampoule at 180° for 48 h, dibenzofuran was formed together with a considerable amount of ether-insoluble material. Paper chromatography indicated the absence of 2,2'-dihydroxybiphenyl.

The ring closure reaction effected by refluxing hydrobromic acid is believed to proceed *via* protonated intermediates.[8] Exchange of the nuclear hydrogens of phenol for deuterium takes place slowly in heavy water in the presence of hydrochloric acid, even at 100°.[9] By analogy, nuclear protonation of 2,2'-dihydroxybiphenyl may be expected to be slow in refluxing acid solution, but at 180° the conditions are favourable for ring closure.

Although the end product of the reaction of 2,3,2'-trimethoxybiphenyl with refluxing hydrobromic acid is 2,3,2'-trihydroxybi-phenyl,[2] we obtained a small amount of 4-hydroxydibenzofuran on heating the tri-hydroxy-compound with hydrobromic acid at 180°. 2,3,2',3'-Tetrahydroxybiphenyl was the end product of the reaction between its tetramethyl ether and refluxing hydrobromic acid. Even at 180°, no ring closure product was obtained. Both cate-chol derivatives gave considerable amounts of ether-insoluble material in the reactions at 180°. Zinc chloride fusion of 2,3,2'-tri-hydroxybiphenyl gave a better yield of ring closure product. Similar treatment of 2,3,2',3'-tetrahydroxybiphenyl invariably resulted in the formation of intractable tars.

The inertness of catechol derivatives in this type of reaction is not easily explained. However, intramolecular hydrogen bonding between the catechol hydroxyl groups (*cf.* Ref. 10) may be an important factor in decreasing the reactivity of the 2-carbon atom in the protonated intermediate to-wards nucleophilic attack by the 2'-hy-droxyl group. In this connection, it must

be pointed out that it is not certain which of the *ortho*-hydroxyl groups is eliminated during dehydration of 2,3,2′-trihydroxybiphenyl.

It has been found previously that the ring closure of 2,6,2′-trihydroxybiphenyl with refluxing hydrobromic acid is somewhat retarded in comparison to that of 2,4,2′-trihydroxybiphenyl.[2] In the present investigation, it has been found that this retardation is even more predominant in the case of 2,6,2′,6′-tetrahydroxybiphenyl. Refluxing with hydrobromic acid for seven days is required for completion of the reaction. These velocity differences may depend to some extent on intramolecular hydrogen bonding between the hydroxyl group of one ring and the π-electron cloud of the other (*cf.* Refs. 11, 12). An additional factor may be steric hindrance in the ring-closure transition state by the hydroxyl groups at the *ortho*-positions.

Experimental. Demethylation experiments. General procedure. The course of the demethylation experiments described below were followed by paper chromatography (*cf.* Ref. 2). Samples of the reaction mixtures were withdrawn at certain intervals, extracted with ether and the extracts dried over sodium sulphate. The ether extracts were chromatographed on Whatman No. 1 paper using the solvent system formamide-ether. The chromatograms were investigated under ultraviolet light before spraying with bis-diazotised benzidine followed by 10 % sodium carbonate solution.

When the reactions were complete, the reaction mixtures were poured into water and extracted with ether. The ether solutions were washed with water and dried over magnesium sulphate. After removal of the solvent, the crude product was purified by recrystallisation from a suitable solvent and sublimation *in vacuo*.

Demethylation of 2,2′-dimethoxybiphenyl. The biphenyl[13] (0.5 g) was refluxed with 48 % hydrobromic acid (4 ml) and glacial acetic acid (4 ml) in an argon atmosphere. Two phenols were detected. 2-Hydroxy-2′-methoxybiphenyl (R_F 0.85, yellow-orange) was detected after 2 min and the end product, 2,2′-dihydroxybiphenyl (R_F 0.73, orange), after 7 min. Demethylation was complete within 1 h. Thin layer chromatography of the ether extracts on silica using isopropyl ether as the moving phase showed that no dibenzofuran (R_F *ca.* 0.7) was formed, not even after 24 h. After working up the residual reaction mixture, 2,2′-dihydroxybiphenyl (0.16 g, 37 %) was obtained, m.p. 108−110° (after recrystallisation

from toluene and sublimation *in vacuo*) (lit.[4] m.p. 109°).

Demethylation of 2,3,2′,3′-tetramethoxybiphenyl. The compound [14] (3.0 g) was refluxed with 48 % hydrobromic acid (25 ml) and glacial acetic acid (25 ml) in an inert atmosphere. Eight phenols were detected, the end product, 2,3,2′,3′-tetrahydroxybiphenyl (R_F 0.10, brown), being detected after 20 min. Demethylation was complete within 5 h. No further spot was detected, not even after 30 h. Yield of 2,3,2′,3′-tetrahydroxybiphenyl 1.46 g; 61 %, m.p. 223−224° (after recrystallisation from dioxane and sublimation *in vacuo*) (lit.[15] m.p. 220−222°).

Demethylation of 2,6,2′,6′-tetramethoxybiphenyl. The biphenyl [16] (1.0 g) was refluxed with 48 % hydrobromic acid (8 ml) and glacial acetic acid (8 ml) in an inert atmosphere. The chromatographic pattern was complex, eight phenols being detected altogether. Six phenols were detected after 5 min. 2,6,2′,6′-Tetrahydroxybiphenyl [17] (R_F 0.0, red) was traced after 10 min and the end product, 1,9-dihydroxydibenzofuran (R_F 0.87, brown) after 1.5 h. Only these two phenols could be detected after 1.5 h, but the reaction required *ca.* 7 days for completion. Yield of 1,9-dihydroxydibenzofuran 0.32 g, 44 %, m.p. 204−205° (after recrystallisation from water and sublimation *in vacuo*) (lit. m.p. 215°[17] and m.p. 205−206°[18]).

Dehydration experiments with hydrobromic acid at 180°. General procedure. The polyhydroxybiphenyl (0.5 g) was heated in a vacuum-sealed ampoule with 48 % hydrobromic acid (4 ml) and glacial acetic acid (4 ml) for 24 h at 180°. After this time, the ampoules were opened, the contents diluted with water and extracted with ether. The ether solutions were dried over magnesium sulphate and investigated by means of paper chromatography in the manner described previously. After removal of the solvent, the residues were worked up for the end product as indicated below.

Dehydration of 2,2′-dihydroxybiphenyl. After 24 h, paper chromatography indicated that the dihydroxybiphenyl was still present in the reaction mixture. According to thin layer chromatography on silica using isopropyl ether as the moving phase, two ether-soluble substances were detectable, namely 2,2′-dihydroxybiphenyl (R_F *ca.* 0.4) together with dibenzofuran (R_F *ca.* 0.7). The reaction was then carried out for 48 h. After this time, the only ether-soluble reaction product detectable by thin layer chromatography was dibenzofuran, though a considerable amount of ether-insoluble material was formed. Dibenzofuran was isolated from this reaction mixture by steam distillation. The product was recrystal-

lised from ethanol and sublimed *in vacuo*. Yield of dibenzofuran 65 mg, 14 %, m.p. 76 — 78° (lit.[19] m.p. 82.8 —, 83°). A mixed melting point with an authentic sample of dibenzofuran (m.p. 81 — 83°) showed no depression (m.p. 78 — 82°).

Dehydration of 2,3,2'-trihydroxybiphenyl. Paper chromatography indicated that a little 2,3,2'-trihydroxybiphenyl[2] (R_F 0.43, brown) was present after 24 h, but the main spot was ascribable to 4-hydroxydibenzofuran (R_F 0.90, brown). Much ether-insoluble material was formed during the reaction. The ether-soluble residue was recrystallised from water and sublimed *in vacuo*. Yield of 4-hydroxydibenzofuran 31 mg, 7 %, m.p. 99 — 101° (lit.[20] 102°).

Attempted dehydration of 2,3,2',3'-tetrahydroxybiphenyl. Only a small amount of ether-soluble material (12 mg) was present in the reaction mixture after 24 h. Paper chromatography of this material gave one spot (R_F 0.0, brown). The material could not be sublimed *in vacuo*.

Dehydration experiments with zinc chloride. General procedure. The polyhydroxybiphenyl (30 mg) and anhydrous zinc chloride (300 mg) were thoroughly mixed and heated at 300° for 5 min in an argon atmosphere. After cooling, the mixture was treated with dilute hydrochloric acid and extracted with ether. The ether solution was dried over magnesium sulphate and investigated by means of paper chromatography.

Zinc chloride fusion of 2,3,2'-trihydroxybiphenyl. The only phenol detected after the reaction was 4-hydroxydibenzofuran (R_F 0.90, brown). After removal of the ether, the residue was recrystallised from water and sublimed *in vacuo*. Yield of 4-hydroxydibenzofuran 10 mg, 37 %, m.p. 99 — 100° (lit.[20] 102°).

Zinc chloride fusion of 2,3,2',3'-tetrahydroxybiphenyl. Only ether-insoluble material was formed in the reaction.

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A Stable Carbamic Acid Anhydride

J. LARS G. NILSSON, HANS SIEVERTSSON and RICHARD DAHLBOM

Department of Chemistry, Kungl. Farmaceutiska Institutet, Stockholm, Sweden

When *N*-(2-chloro-6-methylphenyl)-*N*-methylcarbamoyl chloride (I) was reacted with the sodium salt of *N*-ethyl-3-hydroxypiperidine in refluxing toluene, a crystalline compound was obtained as a byproduct. Spectral and chemical data characterize the compound as *N*-(2-chloro-6-methylphenyl)-*N*-methylcarbamic acid anhydride (II) which appears to the first reported stable anhydride of a carbamic acid.