2,3,9,10-Tetrachlorobenzo[1,2-*b*: 4,5-*b'*]bis[1,4]benzodioxin, a Homologue of TCDD

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Received January 24, 1978

Catechol and 4,5-dichlorocatechol have been condensed with 1,5-dichloro-2,4-dinitrobenzene to provide benzo[1,2-*b*: 4,5-*b'*]bis[1,4]benzodioxin and its 2,3,9,10-tetrachloro derivative, respectively. The latter compound is a novel homologue of the extremely toxic 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD).

J. Heterocyclic Chem., 15, 689 (1978)

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD, **1**) is one of the most toxic compounds known, and other halogenated dibenzo-*p*-dioxins display toxicological properties dependent on the degree and position of halogenation (1). Poland, *et al.*, (2) have attempted to correlate chloracnegenic activities of chlorinated dibenzo-*p*-dioxins, dibenzofurans, and azobenzenes with their abilities to induce aryl hydrocarbon hydroxylase, and have indicated that the chemically dissimilar compounds are able to compete for binding sites because of their abilities to assume similar molecular configurations. The shape of the molecule cannot be the only factor, however, because 2,3,7,8-tetrachloro-1,4-dioxino[2,3-*b*: 5,6-*b'*]dipyridine, which should also be nearly isosteric with **1**, has an LD_{50} in rats of 300 mg./kg. (compared to 0.022-0.045 mg./kg. for **1**) (3). The dithia analog of **1** has recently been reported (4), but we know of no toxicological data on this material.

The syntheses of dibenzo-*p*-dioxins by condensation of catechols with *o*-halonitrobenzenes have been described by Pohland and Yang (5) and by Gray, *et al.*, (6). It occurred to us that an appropriately substituted dihalodinitrobenzene might undergo condensation with two equivalents of a catechol and thus provide homologues of the dibenzo-*p*-dioxins. Indeed, under conditions similar to those reported, 1,5-dichloro-2,4-dinitrobenzene was found to react with catechol and with 4,5-dichlorocatechol to provide benzo[1,2-*b*: 4,5-*b'*]bis[1,4]benzodioxin (**2**) and its 2,3,9,10-tetrachloro derivative (**3**), respectively.

Both **2** and **3** are high-melting (m.p. > 350°), poorly-soluble solids, and **3** was almost impossible to purify, since the only recrystallization solvent we were able to find was *m*-cresol at its boiling point (203°).

Mass spectra of **2** and **3** were consistent with the assigned structures. The molecular ion in each was by far the

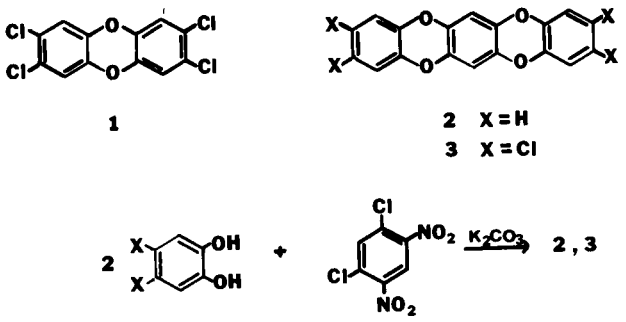

Figure 1

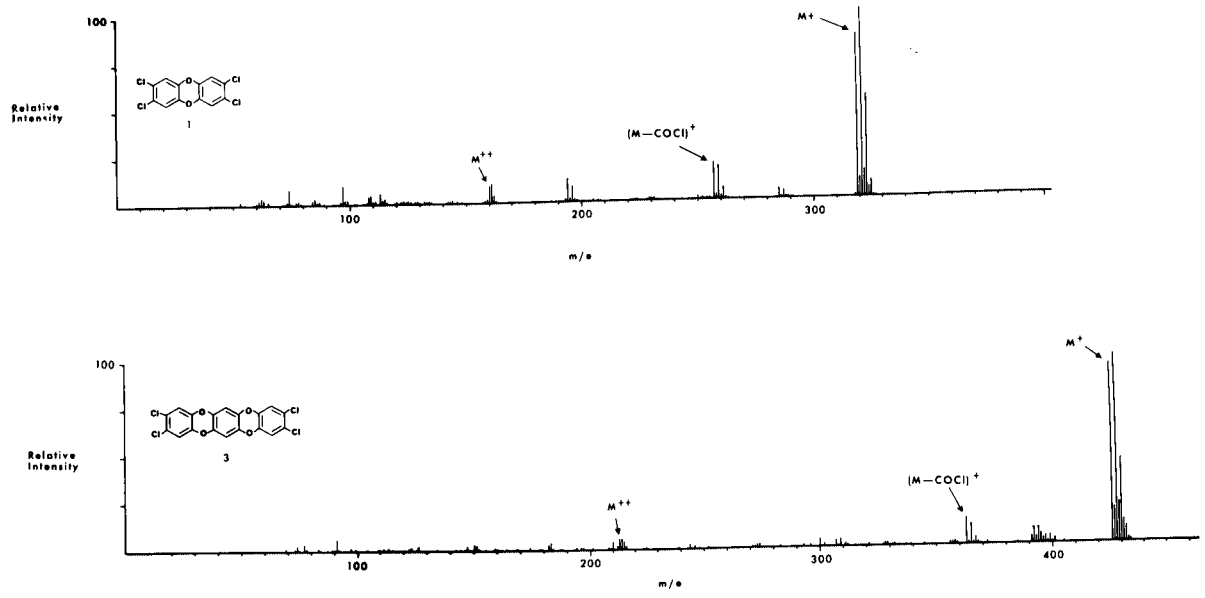

Figure 2

most prominent with little fragmentation occurring, and in each spectrum, an ion with m/e corresponding to half fo the molecular weight was assigned to the doubly charged molecular ion. The remarkable similarity of the mass spectra of **3** and **1** are illustrated in Figure 2.

Although **1** is a relatively unreactive compound, we anticipated that the central ring of **3**, being substituted by four oxygen atoms, should be activated toward electrophilic reagents. This proved to be difficult to verify, since the extreme insolubility of the compound made reactions difficult to effect as well as to follow. A sample of **3** was recovered unchanged after refluxing overnight in tetrachloroethane with excess sulfuryl chloride. Suspensions of both **3** and **1** in acetic acid containing a little sulfuric acid were resistant to nitration by concentrated nitric acid. Both **3** and **1** reacted rapidly with fuming nitric acid in concentrated sulfuric acid to provide yellow, water-soluble products which we have not characterized. The extreme insolubility of **3** has also made an assessment of its biological activity very difficult, but we hope to report on this aspect of the problem in the future.

EXPERIMENTAL

Melting point determinations were performed on a Kofler Micro Hot Stage apparatus. Mass spectra were obtained with a DuPont 491B mass spectrometer. The samples were analyzed *via* direct probe with a source temperature of 220°.

Benzo[1,2-*b*: 4,5-*b'*]bis[1,4]benzodioxin (**2**).

A mixture of pulverized potassium carbonate (2.8 g., 20 mmoles) and catechol (1.0 g., 10 mmoles) in dimethylformamide (25 ml.) was warmed (70°) under nitrogen 0.5 hour, then a solution of 1,5-dichloro-2,4-dinitrobenzene (1.2 g., 5 mmoles) in dimethylformamide (5 ml.) was added and the resulting mixture was refluxed overnight. After cooling, water was added and a tan solid (1.1 g., m.p. > 350°) was collected by filtration. Recrystallization from chlorobenzene (with decolorizing carbon) provided pure **2** as a silver mat, m.p. > 350°; ms (70 eV) m/e (relative intensity): 290 (100%, M+), 261 (12.1%, M-HCO), 145 (10.5%, M++).

Anal. Calcd. for $C_{18}H_{10}O_4$: C, 74.48; H, 3.47. Found: C, 74.78; H, 3.36.

2,3,9,10-Tetrachlorobenzo[1,2-*b*: 4,5-*b'*]bis[1,4]benzodioxin (**3**).

4,5-Dichlorocatechol (7) (0.90 g., 5 mmoles) was condensed with 1,5-dichloro-2,4-dinitrobenzene (2.5 mmoles) as described for the preparation of **2**, except the mixture was heated 4 hours in this instance. The grey product (0.60 g., m.p. > 350°) was purified by refluxing with charcoal in *m*-cresol then quickly filtering through a hot Buchner funnel containing a pad of Celite. The product quickly separated from the filtrate and was collected and washed with alcohol to give **3** as a light buff mat, m.p. > 350°; ms (70 eV) m/e (relative intensity): 426, 428, 430, 432 (67.0, 100, 48.4, 15.7%, respectively, M+), 363, 365, (4.8 and 3.6%, M-COCl), 213, 214, 215, (6.3, 12.3, and 3.2%, respectively, M++).

Anal. Calcd. for $C_{18}H_6Cl_4O_4$: C, 50.50; H, 1.41; Cl, 33.13. Found: C, 50.92; H, 1.45; Cl, 33.66.

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