

Trimerization of 2-Chloro-, 2-Hydroxy-, and 2-Mercaptobenzimidazoles

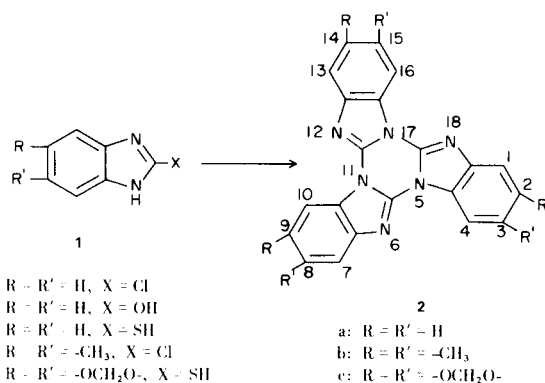
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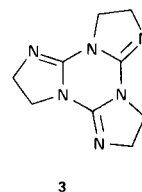
Harrison *et al.* (1) observed that heating 2-chlorobenzimidazoles above the melting point caused release of hydrogen chloride and formation of high-melting solids. A similar product was also produced by treating 2-hydroxybenzimidazole with phosphorus oxychloride. Because of the insoluble nature of these solids, they were not fully investigated; and it was speculated that they were condensation polymers.

We have found that the product obtained by heating 2-chlorobenzimidazole (**1a**), neat or in solution, can be purified to give a crystalline compound to which we have assigned the trimer structure **2a**.



Compound **2a** was also obtained by treating 2-hydroxybenzimidazole (**1b**) and 2-mercaptobenzimidazole (**1c**) with phosphorus oxychloride. The highly crystalline nature of **2a** was confirmed by the appearance of clearly defined lines in the X-ray powder diffraction pattern. Structural assignment is based on the following: the elemental analysis corresponds to empirical formula, C₂₁H₁₂N₆; the molecular weight, determined by mass spectrometry, is 348, the calculated value; the nmr spectrum reveals only aromatic protons; and the ir spectrum has a strong band at 1626 cm⁻¹ assigned to -C=N absorption. Trimers **2b** and **2c** were prepared from benzimidazoles **1d** and **1e**, respectively. Their physical properties are in agreement with the *s*-triazine structure. Compound **2** appeared to be a new ring system, however, while the manuscript was being revised, the publication of Gofen, Kadyrov and Kosyakovskaya (2) came to our

attention wherein these authors had prepared **2a** by heating 2-chlorobenzimidazole and urethane in toluene for 18 hours at 180-200°. The *s*-triazine **3** which lacks the three aromatic rings has been described (3-5).



EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. The nmr spectra were determined on a Varian HA-60 instrument. Chemical shifts are reported in ppm relative to TMS. The ir spectra were determined on a Perkin-Elmer Model 221 Spectrophotometer. Mass spectra were measured on a CEC 21-110 mass spectrometer. X-ray diffraction patterns were obtained for *s*-triazines **2a**, **2b**, and **2c**. They are on file in the X-ray diffraction laboratory of Eli Lilly and Company. In all the experiments described no attempt was made to optimize yields.

Trisbenzimidazo[1,2-*a*:1',2'-*c*:1'',2''-*e*]-*s*-triazine (**2a**).

Method A.

Five g. (0.0327 mole) of **1a** contained in a flask was immersed in an oil bath preheated to 195°. As **1a** melted and resolidified, hydrogen chloride gas was evolved. When gas evolution ceased, the reaction mixture was cooled to room temperature and the solid was recrystallized from nitrobenzene. The fluffy white needles were collected, washed with ethanol, then ether, and dried to yield 2.1 g. of **2a**, m.p. 391-393°; ir (Nujol) cm⁻¹ 1626 (-C=N); 1600, 1580, 1470 (phenyl); nmr (trifluoroacetic acid) δ 7.85 (6H, M, ar.H, *m* to the ring junction), 8.10 (3H, M, Ar.H), 8.64 (3H, M, Ar.H); molecular weight 348 (mass spec.).

Anal. Calcd. for C₂₁H₁₂N₆: C, 72.40; H, 3.47; N, 24.13. Found: C, 72.25; H, 3.48; N, 23.91.

Method B.

Five g. (0.0327 mole) of **1a** was refluxed in 250 ml. of nitrobenzene for 24 hours. After cooling to room temperature, the solid that separated was collected, washed with ethanol, then ether, and dried to give 1.4 g. of fluffy white needles, identical with **2a** obtained by Method A.

Method C.

Twenty g. (0.15 mole) of 2-hydroxybenzimidazole (**1b**) was

suspended in 260 ml. of phosphorus oxychloride and heated to reflux with stirring. A clear solution was obtained after refluxing for 20 minutes. After 16 hours a crystalline mass had appeared. The reaction mixture was cooled to room temperature and the crystals were collected and washed successively with ethanol, water and acetone to yield after drying, 2.5 g. of material identical to that obtained by Method A.

Method D.

Twenty g. (0.13 mole) of 2-mercaptobenzimidazole (**1c**) and 260 ml. of phosphorus oxychloride was heated under reflux with stirring for 16 hours. The reaction mixture was cooled to room temperature and the solid present was collected, washed successively with ethanol, water, acetone and then dried to yield 4.1 g. of **2a**. 2,3,8,9,14,15-Hexamethyltribenzimidazo[1,2-*a*:1'*2'*-*c*:1''*2''*-*e*]-*s*-triazine (**2b**).

2-Chloro-5,6-dimethylbenzimidazole (**1d**) (2.1 g.) (6) and 100 ml. of nitrobenzene was refluxed with stirring for 24 hours. The dark-colored reaction mixture was cooled to room temperature and the solid was collected and washed with ethanol, then ether. Recrystallization from nitrobenzene afforded 300 mg. of **2b** as a tan solid, m.p. >400°; ir (Nujol) cm^{-1} 1637 (-C=N); 1608, 1572 (phenyl); nmr (trifluoroacetic acid) δ 2.44 (3Me, S, Ar.CH₃), 2.47 (3Me, S, Ar.CH₃), 7.66 (3H, S, Ar.H), 8.11 (3H, S, Ar.H); mol. wt. 432 (mass spec.).

Anal. Calcd. for C₂₇H₂₄N₆: C, 74.98; H, 5.59; N, 19.43. Found: C, 75.19; H, 5.57; N, 19.30.

2-Mercapto-5,6-methylenedioxybenzimidazole (**1e**).

To a mixture of 48.0 g. (0.3 mole) of 4,5-methylenedioxy-*o*-phenylenediamine (7), 110 ml. of water, 540 ml. of ethanol and 19.7 g. (0.3 mole) of 85% potassium hydroxide pellets was added 55 ml. of carbon disulfide over a 5-10 minute period at 20°. The reaction mixture was then heated slowly to reflux and refluxed with stirring for one hour. After cooling and addition of 20 ml. of carbon disulfide, the reaction mixture was again refluxed for one hour, cooled to 10° and acidified with 35 ml. of concentrated hydrochloric acid. The solid product was collected, washed with ethanol, then water, dried and recrystallized from DMF-water, using carbon to give 45 g. of **1e** as yellow crystals, m.p. 350°;

nmr (DMSO) δ 6.02 (2H, S, -O-CH₂-O-), 6.75 (2H, S, aromatic), 12.33 (2H, S, -NH-C(=O)-NH-).

Anal. Calcd. for C₈H₆N₂O₂S: C, 49.47; H, 3.12; N, 14.43. Found: C, 49.42; H, 3.26; N, 14.49.

2,3:8,9:14,15-Trismethylenedioxytribenzimidazo[1,2-*a*:1'*2'*-*c*:1''*2''*-*e*]-*s*-triazine (**2c**).

2-Mercapto-5,6-methylenedioxybenzimidazole (**1e**) (19.4 g., 0.1 mole) was stirred in 200 ml. of phosphorus oxychloride and brought to reflux. After 15 minutes the reaction mixture became very thick and stopped the stirrer. An additional 300 ml. of phosphorus oxychloride was added, and refluxing was continued for 16 hours. After cooling to room temperature, the solid product was collected and washed with 20 ml. of phosphorus oxychloride. Since the material was insoluble in all the common organic solvents, it was purified by washing successively with 500 ml. portions of ethanol, 2 *N* sodium hydroxide, and water to afford 1.8 g. of cream colored fluffy **2c**, m.p. > 400°; ir (Nujol) cm^{-1} 1634 (-C=N); 1600 (phenyl); mol. wt. 480 (mass spec.).

Anal. Calcd. for C₂₄H₁₂N₆O₆: C, 60.01; H, 2.52; N, 17.49. Found: C, 60.01; H, 2.63; N, 17.28.

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