course of the reaction the temperature was raised gradually until there was a gentle refluxing of the solvent. After concentrating the clear chlorobenzene solution under reduced pressure the product was distilled and 26.3 g. (62%) of colorless 2,5-dichlorophenyl isocyanate was obtained; b. p. 83–84° at 3–4 mm. The isocyanate was identified by means of the crystalline di-(2,5-dichlorophenyl)-urea; m. p. 289° (cor.).

Anal. Calcd. for $(C_6H_3Cl_2)_2(NH)_2CO$: N, 8.0; Cl, 40.1. Found: N, 7.9; Cl, 40.0.

2,4,6-Trichlorophenyl Isocyanate.—Phosgene was passed through a suspension of 50 g. of 2,4,6-trichloraniline hydrochloride in 500 ml. of chlorobenzene. The temperature was raised gradually to the reflux point. The bulk of the suspended material dissolved. The small amount of crystalline compound that was separated by filtration proved to be the disubstituted urea derivative. The clear filtrate was concentrated under reduced pressure until free of chlorobenzene. The hot residue was transferred to a crystallizing dish and stored in a vacuum desiccator in which upon cooling the product crystallized. The yield of crude 2,4,6-trichlorophenyl isocyanate was 29.2 g. (61%). Pure material was obtained on recrystallization from petroleum ether; m. p. 64–65°.

Anal. Calcd. for $C_6H_2Cl_3NCO$: N, 6.3; Cl, 47.9. Found: N, 5.9; Cl, 47.3.

The crystalline di-(2,4,6-trichlorophenyl)-urea was prepared; m. p. 295° (cor.).

2,4,6-Tribromophenyl Isocyanate.—Dry hydrogen chloride was passed into a solution of 107 g. of 2,4,6-tribromoaniline in 500 ml. of chlorobenzene until a voluminous precipitate of the hydrochloride was formed. Phosgene was then passed into the reaction mixture in a steady stream with continuous stirring until solution of the 2,4,6-tribromoaniline hydrochloride was effected. The reaction mixture was heated gradually during the course of the reaction to the reflux temperature of the solvent. An appreciable amount of the crystalline disubstituted urea was formed and this product was separated by filtration. The clear filtrate was concentrated under reduced pressure until free of solvent and the hot liquid residue transferred to a crystallizing dish. After cooling in a vacuum desiccator a crystalline mass was obtained. The yield of crude 2,4,6-tribromophenyl isocyanate was 44.6 g. (39%). Pure material was obtained on recrystallization from petroleum ether; m. p. 92–94°.

Anal. Calcd. for $C_6H_2Br_3NCO$: N, 3.9; Br, 67.5. Found: N, 3.9; Br, 66.8.

The addition of water to a pyridine solution of the isocyanate yielded the di-(2,4,6-tribromophenyl)-urea; m. p. 323° (cor.).

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The Chloromethylation of Veratrole[1]

BY OSCAR GAWRON

In connection with a synthesis of a compound of pharmaceutical interest, a large supply of 4-chloromethyl-veratrole was needed. Recourse to the literature showed several unsuccessful attempts[2,3] at chloromethylation of veratrole by the usual procedures and a successful attempt[4] by a two phase chloromethylation. The unsuccessful attempts yielded 2,3,6,7-tetramethoxy-9,10-dihydroanthracene as a condensation product.[3,4]

The successful Bide and Wilkinson[4] procedure was tried and found to give somewhat erratic results, probably due to the critical conditions involved, −2 to +2°, rate of stirring, and rate of passage of the hydrogen chloride. In addition, temperature control of large scale laboratory preparations was difficult, although this was partially solved by the direct addition of dry ice to the reaction mixture from time to time.

Since the above procedure did not prove entirely satisfactory, several chloromethylation experiments were run with chloromethyl ether in glacial acetic acid. These were found to be satisfactory. The conditions used were essentially those employed by Vavon, Bolle and Calin[5] in their study of the influence of substituents on rates of chloromethylation of aromatic compounds.

The procedure finally adopted was as follows: In a one-liter, three-necked, round-bottom flask, equipped with a thermometer, a mercury seal stirrer, and a calcium chloride tube, were placed 282 g. of glacial acetic acid, 247 g. of veratrole (1.8 moles) and 288 g. of chloromethyl ether (3.6 moles). The stirrer was started and the initial temperature was noted. If below 20°, the reaction mixture was gently warmed to 20 to 21°. The reaction was then allowed to proceed for seven hours. In four to six hours the temperature rose to 30° and subsequently the reaction mixture was kept below 30° by means of a cold water-bath. The reaction, which had proceeded to almost 50% completion (analytical method of Vavon, Bolle and Calin[5]) at the end of seven hours was then stopped by pouring with stirring, onto 800 g. of cracked ice and 400 ml. of chloroform. Stirring was continued until most of the ice had melted. The chloroform layer was then separated and the water layer extracted twice with 100-ml. portions of chloroform. The combined chloroform extracts were washed once with 50 ml. of water and then dried over anhydrous sodium sulfate. The chloroform was removed *in vacuo* and the residue distilled at less than 1 mm. The fore run was unchanged veratrole and then the 4-chloromethylveratrole distilled at 100–103°. It crystallized on cooling the receiver; m. p. 48–50°; yield, 62 g. (54%), based on recovered veratrole.

Further preparatory studies and kinetic studies on the mechanism of the general chloromethylation reaction are in progress.

(1) Work done at the New York Quinine and Chemical Works, Inc., Brooklyn, N. Y.

(2) Carré and Liberman, *Compt. rend.*, **199**, 791 (1934).

(3) Fitscher and Bogert, *J. Org. Chem.*, **4**, 71 (1939).

(4) Bide and Wilkinson, *J. Chem. Soc.*, 84 (1945).

(5) Vavon, Bolle and Calin, *Bull. soc. chim.*, [5] **6**, 1025 (1939).

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Substituted Quinolyl Dodecyl Sulfides

BY HENRY GILMAN AND SAMUEL P. MASSIE

The therapeutic activities of some quinoline ethers and the germicidal activities of some aryl sulfides[1] suggested the preparation of some quinoline sulfides for pharmacological testing. It was also considered desirable to incorporate a fat-soluble group into the molecule, so as to increase the possibility of absorption of the drug by the animal body. These considerations initiated the preparation of some high-molecular weight alkyl quinolyl sulfides for therapeutic investigation.

(1) Foss, Dunning and Jenkins, THIS JOURNAL, **56**, 1978 (1934).