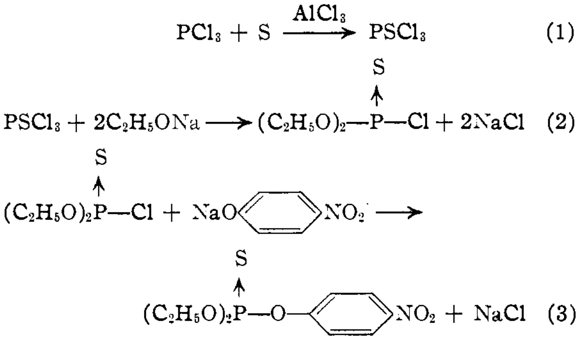
combination of sulfur and phosphorus trichloride in the presence of anhydrous aluminum chloride produces thiophosphoric trichloride[3] in 97% yield. The steps in the synthesis of parathion are



$$PCl_3 + S \xrightarrow{AlCl_3} PSCl_3 \quad (1)$$

$$PSCl_3 + 2C_2H_5ONa \longrightarrow (C_2H_5O)_2-\overset{S\uparrow}{P}-Cl + 2NaCl \quad (2)$$

While the insecticide may be tagged with C^{14}, P^{32} or S^{35}, from the radiation detection standpoint, cost and waste disposal, it seemed advisable in this preliminary experimentation to label with P^{32}. Although not previously reported in the literature, if labeled phosphorus trichloride could be produced by neutron bombardment of phosphorus trichloride, the starting material could be obtained in this manner. Complicating factors in this procedure are the production of S^{35} by a (*n,p*) reaction on Cl^{35} isotopes in the phosphorus trichloride molecule and the subsequent recoil energies given to the molecule both by this reaction and the (n,γ) reaction producing P^{32}. As the recoil energies are sufficient to break the phosphorus-chlorine bonds, the production of labeled phosphorus trichloride depends on the recombination of fragments. Experimentally, one gram of phosphorus trichloride irradiated in the Oak Ridge reactor for three weeks did contain labeled phosphorus trichloride. Further, either the chemical form of S^{35} was such as to be incorporated in the thiophosphoric trichloride in step I or trace amounts of labeled thiophosphoric trichloride were synthesized by the recombination of fragments during bombardment. In any event, the insecticide was labeled with both P^{32} and S^{35}.

Since the preparation of labeled parathion was to be carried out on a semi-micro basis (1 g. PCl_3 starting weight), several syntheses were performed with inactive materials on this scale. When consistent, although low yields, for the individual steps and over-all process (25% based on starting weight of PCl_3) had been attained and the purity of the product established by the standard colorimetric method,[4] radioactive parathion was synthesized from the irradiated PCl_3. An over-all yield of 26% was obtained with a specific activity of 2 microcuries/mg. of parathion.

The chemical purity of the active parathion was established by the method of Averell and Norris[4] and found to be 94% parathion. The radiochemical purity of the insecticide was established by absorption of the emitted radiations in aluminum. Analysis of this information indicated that only P^{32} and S^{35} were present in the final product.

As a result of the covalent bonding of the phosphorus atom in parathion, it is unlikely that exchange would take place between that atom and other phosphorus atoms. However, this possibility was tested by shaking mixtures of inactive parathion and P^{32}-labeled phosphate ion in the presence of various radiation sources for periods of several hours. No exchange took place. In similar tests with the radioactive parathion, no exchange of the labeled phosphorus or sulfur atoms with the substrate occurred.

Experimental

Thiophosphoric Trichloride.—Anhydrous aluminum chloride (0.1–0.2 g.) was added to 1 g. of phosphorus trichloride and 0.24 g. of powdered sulfur. On heating in a water-bath to the b.p. of phosphorus trichloride (74°) the reaction proceeded rapidly (30 sec.) particularly with 0.2 g. of aluminum chloride. After the solution was cooled, the aluminum chloride was extracted in 0.3 ml. of water and the thiophosphoric trichloride layer dried with calcium chloride. The thiophosphoric trichloride was then distilled (at 124–126°) into the second reaction vessel. The average yield for three runs with inactive materials for this step was 78%. The yield with active phosphorus trichloride was 61%.

O,O-Diethyl Chlorothiophosphate.—The method of synthesis for the trial runs and active compound was very similar to that described by Fletcher and colleagues.[1] Because of the semi-micro scale the organic layer was transferred by capillaries rather than filtering. The average yield on this step for two inactive runs was 42.5%. Because of better stirring techniques the yield with active thiophosphoric trichloride was 69%.

Parathion.—The general procedure for *p*-nitrophenyl thiophosphates as reported by Fletcher, *et al.*,[2] was followed in this step with the exception again that the transferring of the active compound was done by capillaries. The average yield for two inactive runs was 51% and for the active material a 69% yield was obtained.

Acknowledgment.—The authors are grateful to E. W. Robb, P. A. Dahm and F. C. Fountaine for their interest and aid in this problem. This work was supported in part by funds from the American Cyanamid Company.

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RECEIVED NOVEMBER 8, 1951

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[3] F. Knotz, *Osterr. Chem. Z.*, **50**, 128 (1949).

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Cholesteryl Laurate[1]

BY DAVID KRITCHEVSKY AND MARGARET E. ANDERSON

Several isomorphic modifications of cholesteryl laurate have been reported. Page and Rudy[2] prepared the ester, m.p. 91°, $[\alpha]_D$ −27.6°, by heating cholesterol and lauric acid in a current of carbon dioxide; Jaeger[3] used the same method to obtain an ester m.p. 100°; Cataline and co-workers[4] heated the sterol and acid in benzene in the presence of benzene sulfonic acid to obtain this compound m.p. 92° and Abderhalden and Kautzsch[5] heated a chloroform solution of cholesterol and lauroyl chloride to obtain a product sintering at 78°, m.p. 110°; $[\alpha]_D$ −31.3°. In our hands, heating a pyridine solution of the sterol and acid chloride[6] yielded an

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[1] This work was sponsored by the U. S. Atomic Energy Commission.

[2] I. H. Page and H. Rudy, *Biochem. Z.*, **220**, 304 (1930).

[3] F. M. Jaeger, *Rec. trav. chim.*, **25**, 334 (1906), quoted by Page and Rudy.

[4] E. L. Cataline, L. Worrell, S. F. Jeffries and S. A. Aronson, *J. Am. Pharm. Assoc.*, **33**, 107 (1944).

[5] E. Abderhalden and K. Kautzsch, *Z. physiol. Chem.*, **65**, 69 (1910).

[6] D. Kritchevsky, THIS JOURNAL, **65**, 480 (1943).

ester, m.p. 78–78.5°; $[\alpha]^{21}\text{D}$ −30.3°. Two other preparations of this ester following the methods of Page[2] and of Cataline[4] gave material melting at 75–76° and 74–75°, respectively. Crystallizations from acetone, ethanol or chloroform–methanol did not alter the melting point in any case. A sample of our material maintained at 75° for 100 hours melted over the range 75–85°. Another sample, maintained at 80° for 100 hours melted, after solidification, over the range 60–78°.

Our preparation would appear to be a hitherto unreported isomorphic modification of cholesteryl laurate.

Experimental[7]

Starting Materials.—Cholesterol (Amerchol), m.p. 141–143°; Lauric Acid (Eastman Kodak), m.p. 37°. The acid chloride gave quantitative yields of the amide, m.p. 99° (lit.[8] 98°) and anilide, m.p. 75° (lit.[8] 76°) when treated with ammonium hydroxide and aniline, respectively.

Cholesteryl Laurate.—A solution of 28 g. of cholesterol and 17.5 g. of lauroyl chloride in 25 cc. of pyridine was heated to boiling, and, after one minute, allowed to cool. The brown solid obtained on cooling was dissolved in ether, washed free of excess pyridine and acid and the ether dried over anhydrous sodium sulfate. Distillation of the ether left a tan solid, m.p. 73–76°. Three crystallizations from chloroform-methanol yielded 33 g. (80%) of white needles, m.p. 78–78.5°, $[\alpha]^{21}\text{D}$ −30.3° ($CHCl_3$).

Anal.[9] Calcd. for $C_{39}H_{68}O_2$: C, 82.33; H, 12.05. Found: C, 82.21; H, 11.99.

Cholesteryl Laurate.[2]—Lauric acid (4 g.) and cholesterol (2 g.) were heated in a stream of carbon dioxide at 200° for 3 hours. After removal of excess acid the ester was obtained as white needles from chloroform–methanol, m.p. 75–76°; $[\alpha]^{19}\text{D}$ −30.2° ($CHCl_3$). Mixed melting point with first preparation, 75–76°.

Cholesteryl Laurate.[4]—A solution of 5.8 g. of cholesterol, 3 g. of lauric acid and 0.13 g. of *p*-toluenesulfonic acid in 75 cc. of benzene was allowed to reflux, under constant water take-off, for 3 hours. After removal of all acidic material, the ester was crystallized from chloroform–methanol, m.p. 74–75°, $[\alpha]^{21}\text{D}$ −28.8° ($CHCl_3$). Mixed melting point with the initial preparation, 74–75°; mixed melting point with the second preparation, 75–76°.

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[7] All melting points corrected.

[8] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 223.

[9] Analysis by Mr. V. Tashinian of the microanalytical laboratory, University of California, Berkeley.

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Trifluoromethyl Substituted Biphenyls and Diphenyl Ethers

BY MOUSHY MARKARIAN

The recent interest in trifluoromethyl substituted biphenyls and diphenyl ethers[1,2] prompts us to report the syntheses of 3,3′-bis-(trifluoromethyl)-biphenyl, 4,4′-bis-(trifluoromethyl)-biphenyl, 3-trifluoromethyl diphenyl ether, 3-trifluoromethyl-4′-chlorodiphenyl ether, 3-trifluoromethyl 3′-ethyldiphenyl ether and 3-trifluoromethyl phenyl-α-naphthyl ether; the two bis-(trifluoromethyl)-biphenyls were prepared by coupling the appropriate Grignard reagent with either silver bromide[1] or cupric chloride.[3] For the preparation of 4,4′-bis-(trifluoromethyl)-biphenyl, the necessary starting material is *p*-bromobenzotrifluoride,[4] and we have developed a simple two-step preparation of this material. The *m*-bromobenzotrifluoride was obtained by the method of Simons and Ramler.[5]

The trifluoromethyl diphenyl ethers were all prepared by the method of Ullman and Sponagel.[6]

Experimental[7]

3,3′-Bis-(trifluoromethyl)-biphenyl.—*m*-Bromobenzotrifluoride (225 g.) was reacted with magnesium turnings (24.5 g.) and anhydrous cupric chloride (140 g.) in dry ether (750 cc.). After refluxing for two hours, the reaction mixture was poured onto ice and treated with excess concentrated hydrochloric acid to dissolve the copper chloride. The ether layer was washed with water and dilute sodium hydroxide and dried over anhydrous magnesium sulfate. The ether was removed and the residue was fractionated at 1 mm. pressure to yield 62 g. (42.7%) of colorless liquid; b.p. 79–80°; $n^{20}\text{D}$ 1.4899.

Anal. Calcd. for $C_{14}H_8F_6$: C, 57.92; H, 2.78. Found: C, 58.00, 57.88; H, 2.90, 2.78.

***p*-Bromobenzotribromide.**—Bromine (48 g.) was added dropwise to *p*-bromotoluene (17.1 g.) heated to 120–130° and illuminated with a 150-watt bulb. The temperature was gradually increased during the course of the addition and attained 210° when the bromine addition was completed. This final temperature was maintained another 10 minutes. The reaction mixture was then cooled and poured into an evaporating dish where it solidified to a crystalline mass; m.p. 72–76°; yield 38 g. (93%). Recrystallization from hexane raised the m.p. to 81–82°.

Anal. Calcd. for $C_7H_3Br_4$: C, 20.62; H, 0.99. Found: C, 20.71, 20.50; H, 1.00, 0.82.

***p*-Bromobenzotrifluoride.**—*p*-Bromobenzotribromide (175 g., 0.43 mole) and antimony trifluoride (89.4 g., 0.50 mole) were ground together in a mortar and placed in a 250-cc. flask equipped with a condenser for distillation. The mixture was heated with a free flame until reaction took place with distillation, and heating was maintained until distillation became negligible. The distillate and benzene extracts of the flask residue were steam distilled and then distilled at atmospheric pressure to yield 59 g. (60.9%) of *p*-bromobenzotrifluoride; b.p. 153–155°; $n^{25}\text{D}$ 1.4705.

4,4′-Bis-(trifluoromethyl)-biphenyl.—The Grignard reagent prepared from 6.2 g. of *p*-bromobenzotrifluoride was treated with 6.2 g. of anhydrous silver bromide and stirred overnight at room temperature. The ether solution was filtered, washed with water, and dilute sodium hydroxide and dried over anhydrous magnesium sulfate. The ether was removed to give 3 g. of solid, m.p. 75–85° which on recrystallization from methanol gave 1 g. (25%), m.p. 91–92°.

Anal. Calcd. for $C_{14}H_8F_6$: C, 57.92; H, 2.78; F, 39.30; mol. wt., 290. Found: C, 57.78, 57.90; H, 2.95, 2.72; F, 39.32, 39.53; mol. wt. (Rast), 310.

3-Trifluoromethyl Diphenyl Ether.—Phenol, 118 g. (1.25 moles) and 85% potassium hydroxide, 56 g. (0.85 mole) were placed in a one-liter three-neck flask equipped with stirrer, reflux condenser with Dean and Stark trap, and thermometer. Stirring was started and the mixture was heated to 140–150° until all of the potassium hydroxide had dissolved. The mixture was then cooled to 110° and 1 g. of copper powder was added, followed by 225 g. (1 mole) of *m*-bromobenzotrifluoride. The temperature of the reaction mixture was gradually raised until refluxing began with separation of water in the Dean and Stark trap. The water was periodically removed and the *m*-bromobenzotrifluoride returned to the reaction. As the reaction progressed, the temperature gradually rose to 190° with separation of potassium bromide and the amount of water separating became negligible. The reaction mixture was maintained at 190°

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[1] C. K. Bradsher and J. B. Bond, THIS JOURNAL, **71**, 2659 (1949).

[2] J. K. Wolfe, U. S. Patent 2,547,679.

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[4] For another preparation of *p*-bromobenzotrifluoride see R. G. Jones, THIS JOURNAL, **69**, 2346 (1947).

[5] J. H. Simons and E. O. Ramler, *ibid.*, **65**, 389 (1943).

[6] F. Ullman and P. Sponagel, *Ber.*, **38**, 2211 (1905).

[7] The microanalyses are by Dr. Carl Tiedcke.