Paper Partition Chromatography.[8]—The technique of one-dimensional paper partition chromatography was helpful in the identity of the isolated pigment. Ethyl acetate, 40% butanol–50% water–10% acetic acid and *m*-cresol were each used as the flowing solvent. The isolated pigment was chromatographed alone and in a mixture with a known pure sample of isoquercitrin. The R_f values for the isolated pigment are as follows: ethyl acetate: 0.65; butanol–acetic acid–water: 0.72; and *m*-cresol: 0.30. The corresponding values with pure isoquercitrin were: 0.63–0.65, 0.72, and 0.29. This method was also used in the identification of the aglycone obtained after hydrolysis. The R_f values are as follows: ethyl acetate 0.93; butanol–acetic acid–water 0.81; and *m*-cresol, 0.45. The corresponding values for quercetin were 0.93, 0.83 and 0.44.

Chromogenic Reagents.—The fluorescence in ultraviolet light of a dried spot of a solution of the unknown pigment on filter paper, after being sprayed with various chromogenic reagents,[8] was also of assistance in the identification of the isolated flavonoid pigment: alcoholic aluminum chloride, yellow; aqueous lead acetate, orange yellow; aqueous basic lead acetate, orange; aqueous sodium carbonate, yellowish-brown; boric acid–citric acid,[9] yellow. The same colors were obtained with pure isoquercitrin.

Acknowledgment.—The pure isoquercitrin was kindly furnished by the Pharmacology Laboratory, Bureau of Agricultural and Industrial Chemistry, Albany, California. This investigation was supported by a grant from the Division of Research Grants and Fellowships of the National Institute of Health, U. S. Public Health Service.

Summary

A flavonoid pigment has been isolated from the seed pods of *Cercis canadensis* and identified as isoquercitrin. The identity was also confirmed by paper partition chromatography.

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(8) Wender and Gage, *Science*, **109**, 287 (1949).

(9) Wilson, THIS JOURNAL, **61**, 2303 (1939).

NORMAN, OKLAHOMA RECEIVED MARCH 4, 1949

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

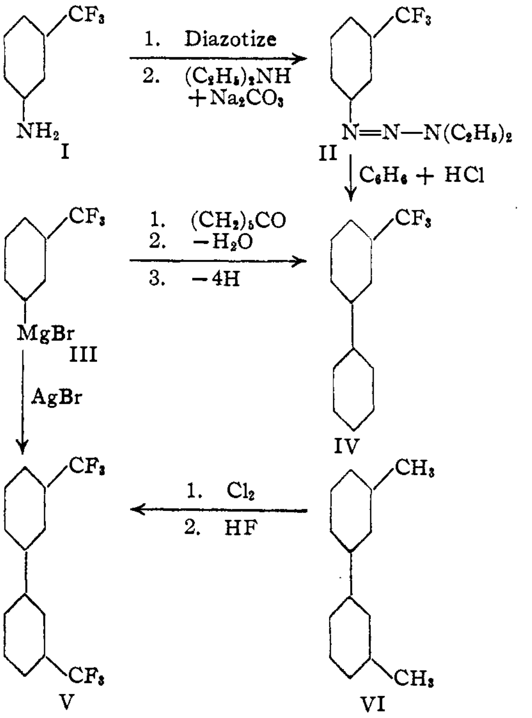
Trifluoromethyl Biphenyls[1]

BY CHARLES K. BRADSHER AND JEAN B. BOND[2]

The literature affords no example of a biphenyl compound containing one or more trifluoromethyl groups. It has been found that such compounds may be prepared from trifluoromethyl benzene derivatives by application of the classical biaryl syntheses, or, in at least one case, from methylbiphenyls by an indirect fluorination process.

The first method studied was the recently developed triazene modification of the diazo reaction.[3,4] It was found that the triazene (II) produced by addition of diethylamine to diazotized *m*-(trifluoromethyl)-aniline,[5] could be decomposed in benzene solution to give a 24% yield of 3-trifluoromethylbiphenyl (IV). When benzotrifluoride or bis-trifluoromethylbenzene was used instead of benzene, no coupling was observed.[6]

The action of *m*-trifluoromethylphenylmagnesium bromide[7] (III) on cyclohexanone followed by dehydration and dehydrogenation[8] with chloranil[9] gave *m*-trifluoromethylbiphenyl (IV). When the same Grignard reagent (III) was treated with anhydrous silver bromide, 3,3′-bis-(trifluoromethyl)-biphenyl (V) was obtained in 60% yield. The same product was prepared from *m,m′*-bitolyl (VI) by complete chlorination of the methyl groups followed by halogen interchange with liquid hydrogen fluoride under pressure.



Ullmann reactions, carried out using 3-nitro-4-chlorobenzotrifluoride and 4-chloro-5-nitro-1,3-bis-(trifluoromethyl)-benzene, yielded 2,2′-dinitro-4,4′-bis-(trifluoromethyl)-biphenyl (VII)

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(1) The work reported here was carried out under contract N6ori-107 with the Office of Naval Research.

(2) Office of Naval Research Fellow.

(3) U. S. Patent 2,280,504; *C. A.*, **36**, 5658 (1942).

(4) Elks and Hey, *J. Chem. Soc.*, 441 (1943).

(5) Swarts, *Bull. Acad. roy. Belg.*, [3] **35**, 388 (1898).

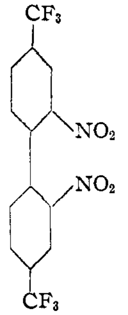
(6) The triazenes from *meta*- and *para*-nitroaniline were likewise without effect on the trifluoromethylbenzenes.

(7) We were unable to prepare the related 2-chloro-5-trifluoromethyl-phenylmagnesium bromide from what is believed to be 3-bromo-4-chlorobenzotrifluoride.

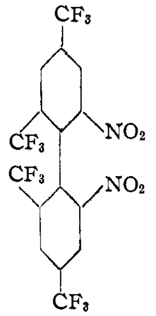
(8) *Cf.* Weiss and Woidick, *Monatsh.*, **46**, 453 (1925).

(9) Arnold and Collins, THIS JOURNAL, **61**, 1407 (1939).

and 2,2'-dinitro-4,4',6,6'-tetrakis-(trifluoromethyl)-biphenyl (VIII).



VII



VIII

Experimental

1-(3-Trifluoromethylphenyl)-3,3-diethyltriazene (II).—A mixture consisting of 161 g. of 3-aminobenzotrifluoride, 250 ml. of 12*M* hydrochloric acid and 500 g. of crushed ice was stirred while a solution of 69 g. of sodium nitrite in water was added slowly. To the diazotized solution was added slowly 69.3 g. of diethylamine followed by 106 g. of sodium carbonate in 400 ml. of water. Care was taken to prevent the rise of the temperature of the solution above 10° during the addition. After one-half hour at room temperature, the brown oil which had separated was taken up in ether, the ethereal solution dried (sodium sulfate) and concentrated, and the residue distilled. The fraction boiling at 118–120° (6 mm.) was yellow in color; yield 116 g. (49%)

Anal.[10] Calcd. for $C_{11}H_{14}N_3F_3$: F, 23.3. Found: F, 23.3.

3-Trifluoromethylbiphenyl. (a) By the Triazene Method.—The distilled 1-(3-trifluoromethylphenyl)-3,3-diethyltriazene obtained from 80 g. of 3-aminobenzotrifluoride was dissolved in 500 ml. of benzene and the solution refluxed for four hours while dry hydrogen chloride was passed through. At the end of this period, the solution was washed, dried, and concentrated, and the residue distilled under reduced pressure yielding 29 g. (24% based on amine) of a colorless oil, b. p. 118–119 (13 mm.), $n^{25}\mathrm{D}$ 1.5302.

(b) **By the Grignard Reaction.**—The Grignard reagent prepared from 32 g. of 3-bromobenzotrifluoride was allowed to react with 17 ml. of cyclohexanone dissolved in ether. The reaction mixture was decomposed in the usual way and the crude cyclohexanol was dehydrated by heating at 125° for one-half hour followed by vacuum distillation. The crude cyclohexene thus obtained was dehydrogenated by refluxing it for eighteen hours in 200 ml. of xylene containing 60 g. of chloranil. The filtered solution was concentrated and the residue distilled, yielding 8 g. (25%) of 3-trifluoromethylbiphenyl, b. p. 117–118° (13 mm.), $n^{25}\mathrm{D}$ 1.5299.

Anal. Calcd. for $C_{13}H_9F_3$: F, 25.7. Found: F, (a) 25.4, (b) 25.5.

3(?)-Bromo-4-chlorobenzotrifluoride.—One-half mole of *p*-chlorobenzotrifluoride[11] was brominated at 60° using an iron catalyst. The product, washed, dried and distilled, was a colorless liquid, b. p. 188–190°, $n^{25}\mathrm{D}$ 1.4973; yield, 51.5%. It was found that this material failed to give a Grignard reagent under ordinary conditions.

Anal. Calcd. for $C_7H_3F_3ClBr$: F, 22.0. Found: F, 21.9.

3,3'-bis-(Trifluoromethyl)-biphenyl (V). (a) By the Grignard Reaction.—The Grignard reagent prepared from 90 g. of 3-bromobenzotrifluoride was cautiously treated with 90 g. of anhydrous silver bromide and then stirred for twelve hours at room temperature. Evaporation of the filtered ethereal solution, and distillation of the residue under reduced pressure, gave 33 g. (60%) of a nearly colorless liquid, b. p. 93–94° (3 mm.), $n^{25}\mathrm{D}$ 1.4887.

(b) **By Indirect Fluorination of *m,m'*-Bitolyl.**—The bitolyl[12] was heated to 100° and irradiated with a mercury arc lamp while chlorine was passed through slowly for four hours. The chlorination rate was then increased and the temperature allowed to rise to 130° and maintained for seventeen hours longer. At the end of this period, the weight of product was 297 g. or approximately the theoretical value for complete chlorination of the methyl groups. The viscous yellow liquid was used directly in the fluorination. A solution of 140 g. of the crude material was dissolved in 110 ml. of benzotrifluoride and placed in an autoclave provided with a stirrer and a reflux condenser. Five grams of phosphorus pentachloride and 5 g. of antimony pentachloride were added to the autoclave, after which 280 g. of liquid hydrogen fluoride was forced in under nitrogen pressure. The mixture was maintained at 50° for two and one-half hours, hydrogen chloride being valved off to prevent the pressure rising above 250 lb./sq. in.[11,13] After evaporation of excess hydrogen fluoride, the crude product was washed, dried and distilled under reduced pressure, yielding 20 g. of an oil, b. p. 93–100° (3 mm.). Redistillation gave 14 g. (13%) of liquid, b. p. 93–94° (3 mm.); $n^{24}\mathrm{D}$ 1.4897. This was probably less pure than the material obtained by procedure a.

Anal. Calcd. for $C_{14}H_8F_6$: F, 39.2. Found: (a) 39.1, (b) 39.5.

2,2'-Dinitro-4,4'-bis-(trifluoromethyl)-biphenyl (VII).—When 20 g. of 3-nitro-4-chlorobenzotrifluoride[13a] was refluxed for five hours with half the calculated quantity of copper powder and the product crystallized from ethanol, 4 g. of yellow plates was obtained, m. p. 121–122°.

Anal. Calcd. for $C_{14}H_6N_2O_4F_6$: F, 29.9. Found: F, 30.4.

4-Chloro-5-nitro-1,3-bis-(trifluoromethyl)-benzene.—To 77.5 g. of 4-chloro-1,3-bis-(trifluoromethyl)-benzene[14,15] heated on a steam-bath, a mixture of 200 ml. of concentrated sulfuric acid and 200 ml. of fuming nitric acid (d. 1.5) was added over the course of one-half hour. After heating for four hours longer, the reaction mixture was poured on ice, separated, and the organic layer washed, dried and fractionated. The product was a light yellow oil, b. p. 208–210°; yield 68 g. (74%).

Anal. Calcd. for $C_8H_2O_2NClF_6$: F, 38.8. Found: F, 39.8.

2,2'-Dinitro-4,4',6,6'-tetrakis-(trifluoromethyl)-biphenyl (VIII).—When 4-chloro-5-nitro-1,3,bis-(trifluoromethyl)-benzene was heated with copper powder as described for VII above, a small quantity of nearly colorless needles, m. p. 135–135.5°, was obtained.

Anal. Calcd. for $C_{16}H_4N_2O_4F_{12}$: F, 44.2. Found: F, 44.3.

Summary

By use of conventional methods of synthesis, some new biphenyl derivatives containing one or more trifluoromethyl groups have been prepared.

DURHAM, N. C. RECEIVED MARCH 9, 1949

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[10] All analyses were done by Mrs. Mary Taylor Gilbert under the direction of Dr. J. H. Saylor. The method used for the titration of fluoride ion was that of Saylor and Larkin (*Anal. Chem.*, **20**, 194 (1948)). A paper by Saylor and Gilbert describing the application of this method to the analysis of organic fluorides will appear in *Analytical Chemistry*.

[11] German Patent 575,593, *Chem. Zentr.*, **104**, II, 609 (1933).

[12] Kornblum, *Org. Syntheses*, **21**, 30 (1941).

[13] (a) French Patent 745,293, *Chem. Zentr.*, **104**, II, 2061 (1933). (b) British Patent 395,227, *Chem. Zentr.*, **104**, II, 4374 (1933).

[14] U. S. Patent 2,394,442, *C. A.*, **40**, 3209 (1946).

[15] McBee, Bolt, Graham and Tebbe, THIS JOURNAL, **69**, 947 (1947).