Difunctional Tetrafluorobenzene Compounds from Fluoroaromatic Organolithium Intermediates[1]

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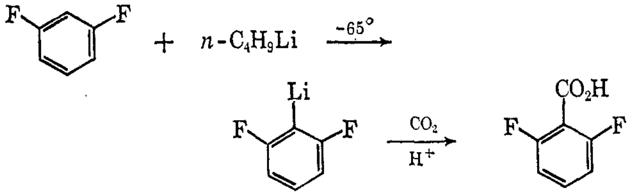
Received August 19, 1965

Metal–hydrogen interconversion reactions have been carried out on a series of monosubstituted tetrafluorobenzenes which have been subsequently carbonated to yield the corresponding tetrafluoromonosubstituted benzoic acids. In addition, the preparation of the monohydrotetrafluorobenzenes is presented.

Metalation (hydrogen–metal interconversion) of a hydrogen atom *ortho* to a fluorine atom has been demonstrated in the original work of Wittig, *et al.*,[2a] on benzyne formation from fluorobenzene. At the temperatures used by these investigators (approximately 0°), the intermediate *o*-fluorophenyllithium is unstable and readily forms benzyne. It was later demonstrated by Gilman and Gorsich[2b] that a lithium–bromine interconversion between *n*-butyllithium and *o*-fluorobromobenzene at −60° yielded a stable intermediate *o*-fluorophenyllithium at these low temperatures. Carbonation of this lithium intermediate afforded *o*-fluorobenzoic acid in 83% yield.

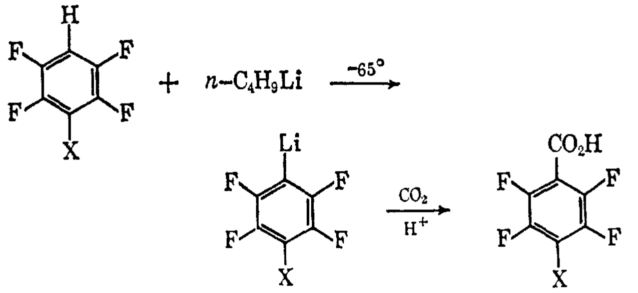
We have shown[3] that 1,3-difluorobenzene will metalate[4] in the 2-position when subjected to a lithium–hydrogen interconversion at −65° with *n*-butyllithium.



Carbonation of this intermediate, stable at −65°, afforded 2,6-difluorobenzoic acid in 87.5% yield.

From the above examples it was apparent that low temperatures (*ca.* −65°) are required to stabilize the *o*-fluoroaryllithium intermediates. At some higher temperature the *o*-fluoroaryllithium intermediates will decompose with elimination of LiF and formation of the reactive benzyne species.

We have recently demonstrated[5] that lithium–hydrogen interconversion can be extended to polyfluorinated aryl compounds. The presence of a functional group, *e.g.*, COOH in 2,3,5,6-tetrafluorobenzoic acid, does not interfere with the formation of a monolithioaryl organometallic. We now wish to report on a further extension of the lithium–hydrogen interconversion reactions in various substituted monohydrotetrafluorobenzene compounds, *p*-HC_6F_4X (I). The substituent X in I has now been extended to include OH, NH_2, SH, CF_3, CH_3, CN, and *p*-HC_6F_4. If the group contains an acidic hydrogen atom (*e.g.*, OH, NH_2, SH, COOH), an equivalent amount of *n*-butyllithium must be added to form the lithium salt in addition to the *n*-butyllithium necessary to form the aryllithium intermediate. By this general synthesis procedure a wide variety of polyfluorinated arylorganolithium intermediates containing various substituents can be prepared. In this study only carbonation reactions have been performed with the various organolithium compounds.



X = F, H, CO_2H

Other studies, however, on reactions of polyfluorinated aryllithium compounds have shown their reactivity towards metallic and metalloidal halides,[6] ethyl formate,[7] N-methylformanilide,[7] benzaldehyde,[7] halogens,[5b,7] sulfur,[5b] and water.[5b,7] It thus seems likely that the polyfluorinated phenyllithium compounds reported here may offer convenient synthesis procedures for a host of mono- or disubstituted polyfluoroaryl compounds.

Table I summarizes the various acids prepared from the substituted polyfluoroaryllithium intermediates. As can be seen from Table I, all the substituted monohydrotetrafluorobenzene compounds yielded the desired organolithium intermediate with the exception of the nitrile.[8]

Certain monohydrotetrafluorophenyl compounds (I) required for the metalation studies were synthesized *via* the oxidation of the hydrazino intermediates (see Table II). It has been previously shown by Birchall, *et al.*,[9] that pentafluorophenylhydrazine is

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[1] Presented at the 3rd International Symposium on Fluorine Chemistry, Munich, Germany, Sept. 1965.

[2] (a) G. Wittig, G. Pieper, and G. Fuhrman, *Ber.*, **73**, 1193 (1940); (b) H. Gilman and R. D. Gorsich, *J. Am. Chem. Soc.*, **78**, 2217 (1956).

[3] C. Tamborski and E. J. Soloski, unpublished studies.

[4] G. Wittig and W. Merkle [*Ber.*, **75**, 1491 (1942)] have originally demonstrated the ability to metalate the 2-position in 1,3-difluorobenzene with phenyllithium. However, the reaction temperatures used were sufficiently high enough to decompose the 2,6-difluorophenyllithium *via* a sequence of benzyne formation and reaction with phenyllithium to yield *m*-terphenyl. Because of the higher reaction temperatures, they were not able to derivatize the 2,6-difluorophenyllithium intermediate.

[5] (a) R. J. Harper, E. J. Soloski, and C. Tamborski, *J. Org. Chem.*, **29**, 2385 (1964); (b) C. Tamborski and E. J. Soloski, *ibid.*, **31**, 743 (1966).

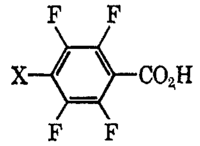
[6] C. Tamborski, E. J. Soloski, and S. M. Dec, *J. Organometal. Chem.*, **4**, 446 (1965), and references cited therein.

[7] P. L. Coe, R. Stephens, and J. C. Tatlow, *J. Chem. Soc.*, 3227 (1962).

[8] A similar observation was noted by H. Gilman and D. S. Malstrom [*J. Am. Chem. Soc.*, **70**, 4177 (1948)] in their attempted synthesis of *p*-cyanophenyllithium. In our studies a reaction was observed between *n*-butyllithium and 2,3,5,6-tetrafluorocyanobenzene; however, none of the desired 4-cyano-2,3,5,6-tetrafluorobenzoic acid was isolated on carbonation. It is not known definitely whether the *n*-butyllithium reacted with the hydrogen or the nitrile group. The bulk of the crude reaction product, however, indicated absence of a nitrile band. It can be assumed that the *n*-butyllithium either reacted with the nitrile to form an imine or ketone or with the hydrogen to form the *p*-cyanoaryllithium which further reacted intermolecularly to form a polymeric imine or ketone.

[9] J. M. Birchall, R. N. Haszeldine, and A. R. Parkinson, *J. Chem. Soc.*, 4966 (1962).

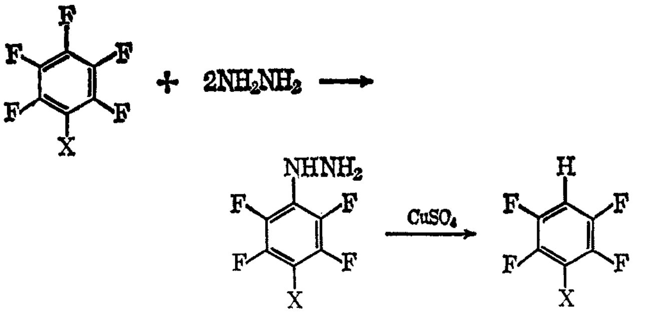
TABLE I



X	M.p., °C.	% yield
OH	154–156[a]	82
NH_2	182–184	37
SH	156–158	77
CH_3	169.5–171	88
CF_3	110–111.5	77
p-HC_6F_4	318–320 dec.	92
CN	. . .	0
H[b,c]	152–154	85
F[b,c]	103–104	68–85
Br[b,d]	144.5–145.5	71
CO_2H[b,c]	276–278	94

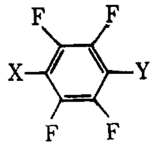
[a] The product crystallizes as the monohydrate, HOC_6F_4-$COOH \cdot H_2O$. [b] These compounds have been previously reported by us and are listed here only for comparison reasons (see ref. 5b). [c] Prepared through metal–hydrogen interconversions. [d] Prepared through metal–halogen interconversions.

oxidized easily with aqueous copper sulfate to yield pentafluorobenzene (77%) and a small amount of 2,3,5,6-tetrafluorobenzene (4%). The same procedure has now been extended to other hydrazino derivatives of monosubstituted pentafluorobenzenes. F^{19} n.m.r. analysis indicated that the substituents were *para* oriented in all cases. There was no evidence for any other isomer formation.[10] All the oxidations of the monohydrazino compounds with copper sulfate were carried out on material shown by n.m.r. to contain only the *para* isomer. It was interesting to note that the oxidation of 4-bromo-2,3,5,6-tetrafluorophenylhydrazine produced, besides the expected 4-bromo-2,3,5,6-tetrafluorobenzene (46.6% yield), an 8.0% yield of 1,2,4,5-tetrafluorobenzene. The mechanism by which *p*-bromine is eliminated is not known. Birchall, *et al.*,[9] previously observed *p*-fluorine elimination in their studies on the copper sulfate oxidation studies of pentafluorophenylhydrazine. These two examples of oxidation of perfluorophenylhydrazines by copper sulfate do indicate that this procedure may lead to more than one product and as such cannot be used with assurance in identifying only the position of a hydrazino group in perfluoroarylhydrazines.



X = Br, CH_3, CF_3, CN

TABLE II



X	Y = $NHNH_2$ M.p., °C.	% yield	Y = H B.p., °C.	% yield
Br	78–79.5	55	143[a]	47
CH_3	90.5–91.5	32	125–125.5	77
CF_3	82–83	97	111–112	70
CN	145–146	94	40–41	53

[a] This compound has not been used in this study. It is listed only for its preparative value. As shown previously,[5b] the Br reacts preferentially to the H in reactions with *n*-butyllithium.

Experimental Section[11]

Metalation of 1,3-Difluorobenzene.—1,3-Difluorobenzene (17.1 g., 0.15 mole) in 20 ml. of tetrahydrofuran was added dropwise to a precooled (−70°) solution of *n*-butyllithium[12] (100 ml. of hexane solution, 0.148 mole) in 200 ml. of anhydrous tetrahydrofuran. Addition of the 1,3-difluorobenzene required 8 min. Fifteen minutes after the addition was complete, Color Test IIA[13] was negative. The reaction mixture was stirred an additional 35 min. and then carbonated by bubbling carbon dioxide into the reaction. After 40 min. the cooling bath was removed, and the reaction warmed to room temperature with continued carbonation. The reaction was then hydrolyzed with 300 ml. of 6 *N* HCl and phase separated, and the organic layer was extracted with 500 ml. of 5% NaOH. The basic aqueous layer was then acidified and again extracted with diethyl ether, phase separated, and dried over sodium sulfate. The diethyl ether was removed by distillation, yielding 20.5 g. (87.5%) of crude product, m.p. 160–162°. Recrystallization from carbon tetrachloride yielded 2,6-difluorobenzoic acid, m.p. 161–162°. An F^{19} n.m.r. analysis[14] in methanol indicated a triplet at 35.3 p.p.m. and was consistent with the proposed structure.

Anal. Calcd. for $C_7H_4F_2O_2$: C, 53.17; H, 2.55; F, 24.03. Found: C, 53.46; H, 2.64; F, 23.88.

4-Bromo-2,3,5,6-tetrafluorophenylhydrazine.—Bromopentafluorobenzene (25.0 g., 0.101 mole) and 95+% anhydrous hydrazine (6.94 g., 0.202 mole) were heated in 175 ml. of *p*-dioxane. After 6 hr. at reflux temperature, water (500 ml.) was added to the reaction solution. The precipitate was removed by filtration and thoroughly washed with water. After drying, the crude product, 14.5 g. (55%), had a melting point of 75.5–78.5°. Recrystallization from petroleum ether (b.p. 90–120°) afforded the analytical sample, m.p. 78–79.5°.

Anal. Calcd. for $C_6H_3BrF_4N_2$: C, 27.81; H, 1.16; Br, 30.86; F, 29.35; N, 10.81. Found: C, 27.75; H, 1.12; Br, 30.59; F, 29.41; N, 11.10.

The F^{19} n.m.r. spectrum in deuterated benzene is consistent with the proposed structure. Two multiplets of 57.0 and 77.6 p.p.m. were observed for the two different types of fluorine.

2,3,5,6-Tetrafluorobromobenzene.—A copper sulfate (111.4 g., 0.446 mole) solution (300 ml. of water) was added to 4-bromo-2,3,5,6-tetrafluorophenylhydrazine (57.7 g., 0.223 mole) with stirring. An immediate green color was noted. The reaction solution was refluxed for several hours. The organic layer, collected in a Dean–Stark trap, was diluted with diethyl ether (25 ml.) and dried over magnesium sulfate. The organic liquid was filtered and fractionated on a spinning-band column. Three fractions were collected. The first fraction was diethyl ether, the second was 1,2,4,5-tetrafluorobenzene, 2.73 g. (8.0%), b.p. 88.0° (identified by v.p.c. analysis), and the third, the desired product, was 2,3,5,6-tetrafluorobromobenzene, 23.8 g. (46.6%), b.p. 143°, n^{20}_D 1.4690.

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(10) It is possible that if any *o*- or *m*-hydrazino isomer was formed in small quantities, it may have been lost during recrystallization of the *p*-hydrazino product and thus not appear in the characterization n.m.r. studies on the purified samples.

(11) All organolithium reactions were carried out in an atmosphere of dry, oxygen-free nitrogen. All melting points are uncorrected.

(12) Commercially prepared in hexane solution, Foote Mineral Co., Exton, Pa.

(13) H. Gilman and J. Swiss, *J. Am. Chem. Soc.*, **62**, 1847 (1940). This is a qualitative color test indicating the presence of an alkyllithium reagent.

(14) The F^{19} spectra were run on a Varian V-4300-2 D.P. spectrometer at a 40.0 Mc./sec. Chemical shifts are reported in parts per million from trifluoroacetic acid.

Anal. Calcd. for C_6HBrF_4: C, 31.47; H, 0.44; Br, 34.90; F, 33.19. Found: C, 31.59; H, 0.65; Br, 34.71; F, 33.01.

4-Methyl-2,3,5,6-tetrafluorophenylhydrazine.—2,3,4,5,6-Pentafluorotoluene (50.34 g., 0.277 mole) and 95+% anhydrous hydrazine (18.59 g., 0.581 mole) were heated in 300 ml. of *p*-dioxane. After 22 hr. of refluxing, the reaction solution was poured into 1500 ml. of cold water. The mixture was phase separated and the water layer was washed four times with 100-ml. aliquots of diethyl ether. The organic layer and the ether washings were then combined and dried over magnesium sulfate. The dried ether layer was aspirated and yielded 17.1 g. (31.7%) of 4-hydrazino-2,3,5,6-tetrafluorotoluene, m.p. 89–90°. Recrystallization from petroleum ether gave the analytical sample, m.p. 90.5–91.5°.

Anal. Calcd. for $C_7H_6F_4N_2$: C, 43.29; H, 3.09; F, 39.17; N, 14.43. Found: C, 43.40; H, 3.27; F, 39.43; N, 14.40.

The F^{19} n.m.r. spectrum in deuterated benzene is consistent with the proposed structure. Two multiplets of 67.3 and 80.6 p.p.m. were observed for the two different types of fluorine.

2,3,5,6-Tetrafluorotoluene.—A 250-ml. solution of copper sulfate (31.0 g., 0.126 mole) was added to a slurry of 4-hydrazino-2,3,5,6-tetrafluorotoluene (12.2 g., 0.063 mole) in 50 ml. of water and refluxed for several hours. The organic layer, collected in a Dean–Stark trap, was added to 100 ml. of diethyl ether and dried over magnesium sulfate. After drying, the material was distilled on a spinning-band column. The distillation afforded 7.96 g. (77%) of pure 2,3,5,6-tetrafluorotoluene, b.p. 125.0–125.5°.

Anal. Calcd. for $C_7H_4F_4$: C, 51.22; H, 2.44; F, 46.34. Found: C, 51.82; H, 2.49; F, 45.91.

4-Trifluoromethyl-2,3,5,6-tetrafluorophenylhydrazine.—Octafluorotoluene (118 g., 0.5 mole), 95+% anhydrous hydrazine (33.6 g., 1.0 mole), and 400 ml. of absolute ethanol were stirred and heated at reflux temperature for 2 hr. The reaction mixture was poured into 1.2 l. of water. After vigorous stirring, the white crystalline product, 120.2 g. (97%), m.p. 77–79.5° (lit.[15] m.p. 84°), was filtered. Recrystallization from petroleum ether elevated the melting point to 82–83°.

4H-Perfluorotoluene.—To a stirred suspension of 4-trifluoromethyl-2,3,5,6-tetrafluorophenylhydrazine (66.9 g., 0.27 mole) in 300 ml. of water at 80°, was slowly added 400 ml. of a copper sulfate (135 g., 0.54 mole) solution. The addition was conducted in such a manner that the reaction temperature was maintained at 80°. After 1.5 hr., a Dean-Stark trap connected to the condenser contained 31 ml. of pale yellow liquid. This distillate was collected, dissolved in ether, and dried over magnesium sulfate. The ether solution was distilled and afforded 41.2 g. (70.0%) of colorless product, b.p. 111–112°, $n^{23}\text{D}$ 1.3781 (lit.[15] b.p. 111–112°).

4-Cyano-2,3,5,6-tetrafluorophenylhydrazine.—To a stirred solution of pentafluorobenzonitrile (48.3 g., 0.25 mole) dissolved in 200 ml. of ethyl alcohol (95%) was slowly added 37 ml. of a hydrazine solution (16.8 g., 0.50 mole, in ethyl alcohol). The addition required 45 min. while maintaining the temperature below 23°. The reaction mixture was then stirred an additional 1.25 hr. followed by hydrolysis with 1000 ml. of ice–water. The resultant white crystals were filtered, yielding 48.4 g. (94.4%) of 4-cyano-2,3,5,6-tetrafluorophenylhydrazine. An analytical sample was obtained by recrystallization from benzene, m.p. 145–146°.

Anal. Calcd. for $C_7H_3F_4N_3$: C, 40.99; H, 1.47; F, 37.05; N, 20.49. Found: C, 40.90; H, 1.64; F, 37.22; N, 19.40.

2,3,5,6-Tetrafluorobenzonitrile.—To a stirred suspension of 4-hydrazino-2,3,5,6-tetrafluorobenzonitrile (41.0 g., 0.20 mole) in 200 ml. of water at 80° was slowly added 300 ml. of a copper sulfate (99.9 g., 0.40 mole) solution. During the addition the reaction temperature was maintained between 75 and 90°. During an additional 1.5 hr. of heating, a colorless organic layer was collected in a Dean–Stark trap connected to the reflux column. Diethyl ether was added to the organic layer. The ether solution was dried over magnesium sulfate and distilled at reduced pressure. The fraction collected at 88–90° at 45 mm. solidified on cooling. In this manner 18.5 g. (52.8%) of pure 2,3,5,6-tetrafluorobenzonitrile, m.p. 40–41°, was obtained.

Anal. Calcd. for C_7HF_4N: C, 48.02; H, 0.58; F, 43.41. Found: C, 48.12; H, 0.85; F, 42.86.

The F^{19} n.m.r. spectrum in carbon tetrachloride is consistent with the proposed structure. Two multiplets of 52.9 and 55.4 p.p.m. were observed for the two different types of fluorine. Infrared analysis indicated the C≡N band at 2250 cm.$^{-1}$.

4-Hydroxy-2,3,5,6-tetrafluorobenzoic Acid.—2,3,5,6-Tetrafluorophenol (16.6 g., 0.1 mole) dissolved in 50 ml. of freshly distilled tetrahydrofuran was added dropwise to a precooled (−70°) solution of *n*-butyllithium (140 ml. of a hexane solution, 0.2 mole) in 400 ml. of tetrahydrofuran. Time of the addition was 15 min. Fifteen minutes after the addition was complete, Color Test IIA was negative. After an additional 35 min., carbon dioxide was bubbled into the reaction mixture. Forty-five minutes later the cooling bath was removed, and the reaction mixture warmed to room temperature with continued carbonation. The mixture was then hydrolyzed with 300 ml. of 6 *N* HCl and phase separated, and the organic layer was dried over sodium sulfate. The solvent was distilled under reduced pressure to yield 17.3 g. (82.5%) of crude product. Recrystallization of a sample from xylene yielded 4-hydroxy-2,3,5,6-tetrafluorobenzoic acid monohydrate, m.p. 154–156° (lit.[15a] m.p. 157°).

Anal. Calcd. for $C_7H_4F_4O_4$: C, 36.85; H, 1.76; F, 33.31. Found: C, 37.05; H, 1.80; F, 33.13.

4-Amino-2,3,5,6-tetrafluorobenzoic Acid.—2,3,5,6-Tetrafluoroaniline (16.5 g., 0.1 mole) dissolved in 35 ml. of anhydrous tetrahydrofuran was added dropwise to a precooled (−70°) solution of *n*-butyllithium (195 ml. of a hexane solution, 0.3 mole) in 450 ml. of tetrahydrofuran. Time of addition was 15 min. Three hours after the addition was complete, Color Test IIA was negative. Carbon dioxide was then bubbled into the reaction mixture. After 30 min. the cooling bath was removed, and the reaction mixture warmed to room temperature with continued carbonation. The mixture was then hydrolyzed with 250 ml. of 3 *N* HCl and phase separated, and the organic layer was dried over magnesium sulfate. Distillation of the solvent yielded 9.43 g. (45.1%) of crude product. Recrystallization from benzene yielded 7.72 g. (36.9%) of pure 4-amino-2,3,5,6-tetrafluorobenzoic acid, m.p. 182–184° (lit.[16] m.p. 182°).

Anal. Calcd. for $C_7H_3F_4NO_2$: C, 40.21; H, 1.44; F, 36.34; N, 6.69. Found: C, 40.16; H, 1.54; F, 36.42; N, 6.87.

4-Thiol-2,3,5,6-tetrafluorobenzoic Acid.—2,3,5,6-Tetrafluorothiophenol (27.32 g., 0.15 mole) dissolved in 60 ml. of anhydrous diethyl ether was added dropwise to a precooled (−70°) solution of *n*-butyllithium (195 ml. of a hexane solution, 0.3 mole) in 400 ml. of diethyl ether. Time of the addition was 34 min. Thirty minutes after the addition was complete, Color Test IIA was negative. After an additional 30 min., carbon dioxide was bubbled into the reaction mixture. After 30 min. the cooling bath was removed, and the reaction mixture warmed to room temperature with continued carbonation. The mixture was then hydrolyzed with 300 ml. of 6 *N* HCl and phase separated, and the organic layer was dried over magnesium sulfate. Distillation of the solvent under reduced pressure afforded 27.8 g. (82.0%) of crude product. Recrystallization from petroleum ether yielded 26.0 g. (76.5%) of yellow, crystalline 4-thiol-2,3,5,6-tetrafluorobenzoic acid, m.p. 156–158°.

Anal. Calcd. for $C_7H_2F_4O_2S$: C, 37.18; H, 0.89; F, 33.60; S, 14.18. Found: C, 37.33; H, 0.86; F, 32.76; S, 14.74.

4-Methyl-2,3,5,6-tetrafluorobenzoic Acid.—*n*-Butyllithium (162.5 ml. of a hexane solution, 0.25 mole) was added dropwise to a precooled (−70°) solution of 2,3,5,6-tetrafluorotoluene (41.0 g., 0.25 mole) in 500 ml. of anhydrous diethyl ether. The *n*-butyllithium was added over a period of 45 min. Thirty-five minutes after the addition was complete, Color Test IIA was negative. After an additional 30 min., carbon dioxide was bubbled into the reaction mixture. Thirty minutes later the cooling bath was removed, and the reaction mixture warmed to room temperature with continued carbonation. The mixture was then hydrolyzed with 250 ml. of 6 *N* HCl and phase separated, and the organic layer was dried over magnesium sulfate. The ether was distilled under vacuum and yielded 52.0 g. of crude product. Recrystallization from benzene yielded 45.7 g. (87.8%) of pure 4-methyl-2,3,5,6-tetrafluorobenzoic acid, m.p. 169.5–171° (lit.[15a] m.p. 174°).

4-Trifluoromethyl-2,3,5,6-tetrafluorobenzoic Acid.—*n*-Butyllithium (71 ml. of a hexane solution, 0.11 mole) was added

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(15) (a) D. J. Alsop, J. Burdon, and J. C. Tatlow, *J. Chem. Soc.*, 1801 (1962); (b) D. G. Holland, G. J. Moore, and C. Tamborski, Air Force Materials Laboratory Technical Report 64-367, Wright-Patterson AFB, Ohio.

(16) G. G. Yakobson, V. N. Odinokov, T. D. Petrova, and N. N. Vorozhtsov, Jr., *Zh. Obshch. Khim.*, **39**, 2953 (1964); *Chem. Abstr.*, **62**, 470 (1965).

dropwise to a precooled (−70°) solution of 2,3,5,6-heptafluorotoluene (21.8 g., 0.10 mole) in 200 ml. of anhydrous tetrahydrofuran. The temperature was maintained below −60°. The solution was carbonated by bubbling gaseous carbon dioxide through the reaction mixture for 1 hr. The reaction was allowed to warm to room temperature with continued carbonation. The mixture was then hydrolyzed with 300 ml. of 6 N hydrochloric acid. The two-phase solution was distilled until only the aqueous phase remained. This solution was cooled, yielding a white precipitate which on recrystallization from benzene afforded 20.3 g. (77%) of white crystalline product, m.p. 107.5–110.5°. The analytical sample, m.p. 110–111.5° was obtained by an additional recrystallization from benzene.[15b]

Anal. Calcd. for $C_8HF_7O_2$: C, 36.66; H, 0.38; F, 50.7. Found: C, 36.72; H, 0.41; F, 50.6.

2,2′,3,3′,5,5′,6,6′-Octafluorobiphenyl-4,4′-dicarboxylic Acid.—A solution of 2,2′,3,3′5,5′,6,6′-octafluorobiphenyl (28.9 g., 0.1 mole) in 55 ml. of anhydrous tetrahydrofuran was added dropwise over a period of 18 min. to a precooled (−70°) solution of *n*-butyllithium (137 ml. of a hexane solution, 0.2 mole) in 250 ml. of anhydrous tetrahydrofuran. Thirty minutes after the addition was complete, Color Test IIA was negative. After an additional 30 min., carbon dioxide was bubbled through the reaction mixture for 0.5 hr. The mixture was then allowed to warm to room temperature with continued carbonation and then hydrolyzed with 250 ml. 6 N HCl, and the resulting mixture was phase separated. The aqueous layer was then washed three times with diethyl ether, combined with the organic layer, and dried over magnesium sulfate. After drying, solvents were removed by aspiration, yielding 38.4 g. (96.7%) of the desired 2,2′,3,3′,5,5′,6,6′-octafluorobiphenyl-4,4′-dicarboxylic acid, m.p. 313–319°. The analytical sample, m.p. 318–320° dec., was obtained by slurrying the above product in boiling petroleum ether, yielding 35.5 g. (91.9%).

Anal. Calcd. for $C_{14}H_2F_8O_4$: C, 43.54; H, 0.52; F, 39.36. Found: C, 43.24; H, 0.62; F, 39.40.

Attempted Preparation of 4-Cyano-2,3,5,6-tetrafluorobenzoic Acid.—To a cooled (−70°) stirred solution of 2,3,5,6-tetrafluorobenzonitrile (10.0 g., 0.057 mole) dissolved in 220 ml. of diethyl ether was added 0.057 mole of *n*-butyllithium (37 ml. of a hexane solution) over a period of 1 hr. During the addition the color of the reaction mixture changed from pale yellow to amber and finally to brown. Forty-five minutes after the addition was complete, Color Test I was positive and Color Test IIA was negative. The reaction was stirred another 45 min. and then carbon dioxide was bubbled in. During carbonation the appearance of the mixture became much lighter. The mixture was then warmed to room temperature, hydrolyzed with ice, acidified, extracted with diethyl ether, and dried over magnesium sulfate. Distillation of the dried organic layer yielded a pale yellow semisolid. Attempted crystallization from a variety of solvents as well as silica gel chromatographic separation produced no tractable material. Infrared analysis of the crude materials indicated the presence of a nitrile band at 2250 cm.$^{-1}$.

Acknowledgment.—The authors wish to thank J. V. Pustinger, Jr., of the Monsanto Research Corporation for the determination and interpretation of the n.m.r. spectra reported in this work. We also wish to thank Mr. John P. Ward for the synthesis of some of the intermediate compounds.

The Acylation of 1,3,5-Triphenylbenzene. The Solvent Effect

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Received October 15, 1965

The aluminum chloride catalyzed acetylation of 1,3,5-triphenylbenzene gives only the peripheral-ring *para*-substitution product in nitrobenzene, dichloroethane, and carbon disulfide. Benzoylation of 1,3,5-triphenylbenzene gives only central-ring substitution in carbon disulfide and dichloroethane. The central-ring:peripheral-ring product ratio for benzoylation decreases by at least 10^3 as the solvent is changed from dichloroethane through various dichloroethane–nitrobenzene mixtures. The ratio is unity at a solvent composition containing between 15 and 20% nitrobenzene (nitrobenzene:benzoyl chloride molar ratio of approximately 5). The mechanism of the solvent effect is discussed.

It had been shown previously[1] that the normal position of electrophilic attack on 1,3,5-triphenylbenzene (**1**) is the central ring, but that Friedel–Crafts acetylation in nitrobenzene gives only an abnormal orientation product, 1-(*p*-acetylphenyl)-3,5-diphenylbenzene (**6**), resulting from attack at a *para* position of one of the peripheral rings. In contrast to this result, the literature records, for reactions of 1,3,5-triphenylbenzene, acetylation, phthaloylation, and aminoformylation giving only central-ring products (no yields or solvents recorded);[2] benzoylation giving a 90% yield of central-ring product (no solvent recorded);[3] benzoylation in carbon disulfide giving a 75% yield of central-ring product;[4] and benzoylation in carbon disulfide giving a 98% yield of central-ring product.[5]

In this laboratory acetylation with acetic anhydride has been found to give only 1-(*p*-acetylphenyl)-3,5-diphenylbenzene in each of the solvents, nitrobenzene, 1,2-dichloroethane, and carbon disulfide. These results are summarized in Table I. The examination by nmr of the crude reaction mixtures in each solvent confirmed the specificity of the reaction. Only a single methyl signal, that of the peripheral-ring *p*-acetyl derivative at τ 7.45,[1] was observed under conditions that would have produced a detectable signal (at τ 8.11[1]) for a 2% yield of the central-ring isomer.

TABLE I

ACETYLATION OF 1,3,5-TRIPHENYLBENZENE[a]

Solvent	Recovered **1**, %	Yield of **6**, %
CS_2	63	36
$C_2H_4Cl_2$	31	60
$C_6H_5NO_2$	30	72

[a] At 20° for 2 hr; triphenylbenzene and acetic anhydride 0.015 M; $AlCl_3$ 0.053 M. Percentages are ±2%.

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