

Registry No. 1, 35856-82-7; 2a, 1104-21-8; 2b, 855-38-9; 2c, 1038-95-5; 2d, 13885-05-7; 2e, 603-35-0; 2f, 18437-78-0; 2g, 1159-54-2; 2h, 29949-81-3; 2i, 13406-29-6; 2j, 29949-84-6; 2k, 6224-63-1; 3a, 73116-89-9; 3b, 73116-90-2; 3c, 73116-91-3; 3d, 73116-92-4; 3e,

49595-63-3; 3f, 73116-93-5; 3g, 73116-94-6; 3h, 73116-95-7; 3i, 73116-96-8; 3j, 73116-97-9; 3k, 73116-98-0; tetramethylethylene oxide, 5076-20-0; 2,3-dimethyl-3-hydroxy-1-butene, 10473-13-9; tris(4-tolyl)phosphine oxide, 797-70-6.

New Method for Selective Monofluorination of Aromatics Using Silver Difluoride

Arnold Zweig,* Robert G. Fischer, and John E. Lancaster

Chemical Research Division, American Cyanamid Co., Stamford, Connecticut 06904

Received May 16, 1980

Fluorobenzene is obtained in 61% yield from reaction of a solution of benzene in *n*-hexane with solid argentic fluoride (AgF_2). The AgF_2 acts as both a strong oxidant and the fluoride source. Cobaltic fluoride provides only low (<8%) yields of fluorobenzene under similar conditions. The predominant reaction of benzene solutions with AgF_2 appears to proceed by a process involving initial electrophilic oxidative *cis* addition of two fluorine atoms from the solid AgF_2 lattice to the para aromatic positions, leading to *cis*-3,6-difluoro-1,4-cyclohexadiene ($\text{F}_2\text{C}_6\text{H}_4$). The reductive elimination leaves solid argentous fluoride (AgF) which is easily recoverable by filtration. Elimination of HF from the $\text{F}_2\text{C}_6\text{H}_4$ yields fluorobenzene. Reactions of haloaromatics with AgF_2 generally proceed in a similar manner. Thus, further reaction of AgF_2 with benzene or monohalo- or *p*-dihalobenzenes leads in steps to 3,3,6,6-tetrafluoro-1,4-cyclohexadiene ($\text{F}_4\text{C}_6\text{H}_4$) in up to 82% yield. The modest to high yields of mono- and specific polyfluorinated aromatics contrast sharply with reported nonselective perfluorination in vapor-phase reactions of aromatics over AgF_2 or CoF_3 . Reactions of AgF_2 or CoF_3 with solutions of nitrobenzene, acetophenone, benzoic acid, and benzonitrile give mixtures of *o*-, *m*-, and *p*-monofluoro derivatives.

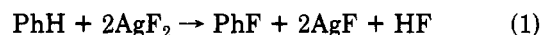
While several methods for substitutive fluorination of aromatics are known, selective monofluorination is not readily achieved. The initial reaction of fluorine with benzene provides fluorobenzene, but under preparative conditions the reaction is overwhelmed by competing processes.¹ Vapor-phase fluorination of aromatics over high-valent metal fluorides proceeds to complex mixtures of highly fluorinated products.² Electrochemical oxidation of benzene in the presence of fluoride ion is reported to provide monofluorination,³ although polyfluorination has also been noted.⁴ Chlorine trifluoride reacts directly with benzene and substituted benzenes in the presence of catalysts to give mixtures of chloro- and fluoroaromatics.⁵ Trifluoromethyl hypofluorite has been used to introduce fluorine into some electron-rich aromatics.⁶ Xenon difluoride selectively fluorinates a variety of aromatic compounds⁷ and has provided a 68% yield of fluorobenzene from benzene. While the detailed mechanism of this oxidative substitution process is not known with certainty, the evidence points to a cation radical intermediate.⁷⁻⁹

Seeking useful alternative methods for oxidative fluorination, we examined a variety of oxidants, fluoride sources, and solvents, utilizing ^{19}F NMR for detecting, characterizing, and quantitating the fluorinated products. A report¹⁰ that a high yield oxidative cleavage could be

performed by using CoF_3 in refluxing chloroform demonstrated the stability of this system and led us to investigate its effect on aromatic substrates. Exploratory reactions with a variety of aromatics gave ^{19}F NMR evidence of fluoroaromatic products in up to 12% yield based on the CoF_3 charged. An initial experiment reacting benzene with AgF_2 in chloroform provided a 19% yield of fluorobenzene, and higher yields soon followed. The scope of this reaction of aromatics diluted with relatively inert solvents with essentially insoluble high-valent metal fluorides was then explored in greater detail to evaluate its preparative potential as well as to provide information regarding the possible mechanism.

Results and Discussion

Reaction of Benzene with AgF_2 . The theoretical stoichiometry of reaction of benzene with AgF_2 is shown in eq 1. The fluorobenzene product from refluxing



benzene solutions in the presence of insoluble AgF_2 was detected and quantitated by its characteristic ^{19}F NMR spectrum (cf. Experimental Section). The HF was liberated as a gas during the course of the reaction, and the insoluble AgF was recovered by filtration as a yellow powder. Several other fluorinated compounds were also detected by ^{19}F NMR in the liquid product. These compounds, usually present in low yield, include *o*- and *p*-difluorobenzenes, identified by NMR comparison with authentic samples, and compounds where two or more fluorines have added to the benzene ring. Identification through unambiguous NMR assignments was made for 3,3,6-trifluoro-1,4-cyclohexadiene ($\text{F}_3\text{C}_6\text{H}_4$) and 3,3,6,6-tetrafluoro-1,4-cyclohexadiene ($\text{F}_4\text{C}_6\text{H}_4$) which were present in the product mixtures. A single 3,6-difluoro-cyclohexadiene ($\text{F}_2\text{C}_6\text{H}_4$) and two isomeric 3,4,5,6-tetrafluorocyclohexenes were also identified. Other ^{19}F reso-

(1) F. Cacace and A. P. Wolf, *J. Am. Chem. Soc.*, **100**, 3639 (1978); V. Grakauskas, *J. Org. Chem.*, **35**, 723 (1970), and references therein; L. C. Sams et al., *ibid.*, **43**, 2273 (1978).

(2) A. E. Pavlath and A. J. Leffler, "Aromatic Fluorine Compounds", Reinhold, New York, 1962.

(3) A. N. Rozhkov, A. V. Bukhtiarov, and I. L. Knunjanis, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **5**, 1130 (1972); *Chem. Abstr.*, **77**, 82878 (1972).

(4) Y. Inoue et al., *Bull. Chem. Soc. Jpn.*, **46**, 2204 (1973).

(5) A. E. Pavlath, Stauffer Chem. Co., U.S. Patent 2993937, July 25, 1961; J. F. Ellis and W. K. R. Musgrave, *J. Chem. Soc.*, 1063 (1953).

(6) D. H. R. Barton et al., *J. Chem. Soc., Chem. Commun.*, 806 (1968); *J. Chem. Soc., Perkin Trans. 1*, 2889 (1972).

(7) M. J. Shaw, H. H. Hyman, and R. Filler, *J. Am. Chem. Soc.*, **91**, 1563 (1969); **92**, 6498 (1970); *J. Org. Chem.*, **36**, 2917 (1971).

(8) J. Burdon, I. W. Parsons, and J. C. Tatlow, *Tetrahedron*, **28**, 43 (1972).

(9) J. Burdon and I. W. Parsons, *Tetrahedron*, **31**, 2401 (1975).

(10) G. A. Olah, J. Welch, and M. Henninger, *Synthesis*, 308 (1977).

Table I. Liquid-Phase Reactions of Benzene with AgF_2^a

solvent	solvent vol, mL	amt benzene		$T, ^\circ\text{C}$	t, h	PhF	$p\text{-F}_2^-\text{C}_6\text{H}_4$	$o\text{-F}_2^-\text{C}_6\text{H}_4$	F_2CHD	F_3CHD	F_4CHD	tetrafluoro-cyclohexenes		other	acctnt ^c
		mol	vol %									I	II		
CHCl_3	25	0.068	20	62	18	19	0.3	1.2	ND ^d	trace	0.1	ND	ND		
CHCl_3	10	0.068	38	62	18	28	2.4	2.1	ND	2.2	0.5	ND	ND		
CCl_4	25	0.068	20	76	18	36	1.4	2.4	ND	3.6	0.4	ND	ND		
CCl_4	10	0.034	23	76	18	44	3.1	2.1	ND	0.9	0.5	ND	ND		90
CH_2Cl_2	30	0.068	17	25	18	44	1.6	2.2	3.7	5.1	0.4	12.9	8.7	11	
<i>n</i> -hexane	30	0.068	17	69	18	50	2.9	3.4	ND	4.9	0.4	ND	ND	15.2	91.5
<i>n</i> -hexane	50	0.068	11	69	18	48	2.1	3.4	0.0	5.8	0.5	10.1	6.4	5	78
<i>n</i> -hexane	40	0.033	7	55	18	26	6.9	3.6	0.0	0.0	0.5	9.2	6.8	19.4	87.6
<i>n</i> -hexane	30	0.23	40	69	18	61	3.0	3.4	0.0	17.2	3.6	9.1	5.9	9.7	91.5
<i>n</i> -hexane	30	0.67	67	69	0.2	45	1.3	2.3	0.0	2.4	0.2	8.1	6.2	4.1	63.2
<i>n</i> -hexane	60	0.45	40	69	18	61	0.8	2.0	0.0	5.6	1.0	2.4	2.4	0.0	80.6
<i>n</i> -hexane	9.1	0.068	40	40	0.2	47	0.8	2.2	0.0	2.2	0.3	9.2	7.1	0.0	77

^a Employing 0.068 mol of AgF_2 ; ^b Yields determined by ^{19}F NMR and based on the amount of AgF_2 charged. ^c AgF_2 accountability as the percent of oxidizing power leading to fluorinated products. ^d ND = not determined.

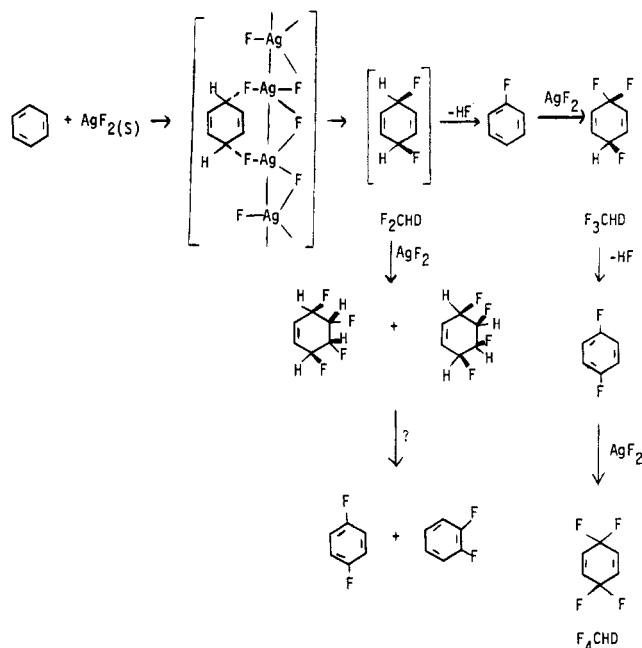


Figure 1. Proposed pathway for formation of fluorinated products from the reaction of benzene solutions with AgF_2 .

nances were sometimes present but usually in small quantity, and their positive identification was not possible. Table I describes the results obtained in experiments involving reaction of benzene solutions with AgF_2 . Initially, CHCl_3 , CH_2Cl_2 , and CCl_4 were employed as solvents, but *n*-hexane provided higher fluorobenzene yields and was thus more extensively examined. Other aliphatics such as cyclohexane behaved similarly. Since neither AgF_2 nor AgF is soluble in aliphatic hydrocarbons, the reaction must occur on the solid surface. Violent reaction occurred, and little or no fluorobenzene formed if an inert diluent was absent or if liquid HF or 1,2-dimethoxyethane was employed as the solvent. The proportion of reagents, solvent, reaction temperature, and time influenced the yield and distribution of fluorinated products as indicated in Table I. The highest yield of fluorobenzene was 61%, based on AgF_2 charged. The observed differences in yield and reaction rate in different solvents suggest a role for the latter. The benzene/ AgF_2 ratio also affects the fluorobenzene yield. If the stoichiometry of eq 1 is used, a 26% yield of fluorobenzene is obtained by using 40 vol % of benzene in *n*-hexane. A molar excess of benzene gives a 50% yield, while either a 5- or 11-fold benzene excess produces a 61% fluorobenzene yield. Significantly lower fluorobenzene yields were obtained when lower (17%) or higher (67%) volume percents of benzene in *n*-hexane were employed.

The accountability of the oxidizing power of AgF_2 in generating fluoroorganics, as determined by ^{19}F NMR, was high in most of the reactions examined. Under the conditions where fluorobenzene was obtained in 50–61% yield, the total yield of fluoroorganics was 80–93% of the theoretical¹¹ yield. When the benzene to AgF_2 reactant ratio was reduced, the ratio of other fluoroorganics to fluorobenzene increased, suggesting that further reactions of the latter or some intermediate were occurring. Independent evidence was obtained through ^{19}F NMR spectra for the following conversion sequence: fluorobenzene, F_3CHD , *p*-difluorobenzene, F_4CHD . A reaction scheme consistent with these results is shown in Figure 1. This scheme suggests that the initial step is *cis* 1,4-addition of two

(11) Although nonfluorinated oxidation products may also have been formed, no attempt was made to determine their presence.

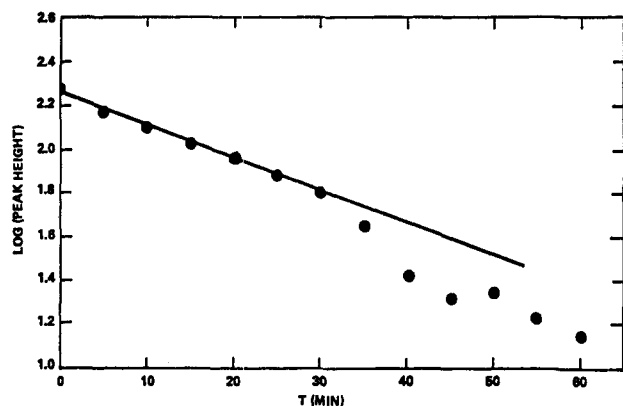
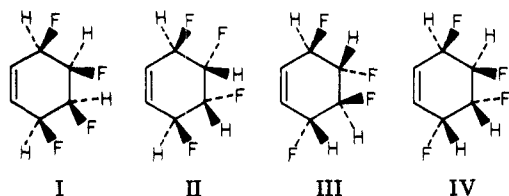


Figure 2. Disappearance of 3,6-difluoro-1,4-cyclohexadiene at 34.5 °C.

fluorines from the AgF_2 solid to the benzene ring to give *cis*-3,6-difluoro-1,4-cyclohexadiene (F_2CHD). On further examination of the ^{19}F NMR spectrum obtained from lower temperature reactions, a single metastable species was observed with $\phi_{\text{Av}} = 174.42$ (in F_3CHD , $\phi_6 = 181.82$). Consistent with its assignment as F_2CHD (either *cis* or *trans*), a complex proton coupled pattern was observed which on ^1H decoupling collapsed to a sharp singlet. This peak was observed to decrease in intensity during the course of NMR measurements. Further evidence for its assignment was the observations that it could be obtained in higher yields with shorter reaction times and lower temperature and that both it and F_3CHD completely disappeared from the ^{19}F NMR spectrum when the reaction product mixture was stirred over KOH pellets for several minutes before the NMR spectrum was obtained. The intensity of the proton-decoupled signal of the metastable product was determined as a function of time in a supernatant solution held at constant temperature. The logarithm of the relative signal intensities plotted against time (Figure 2) suggests an initial first-order decomposition with a half-life of about 20 min at 34.5 °C.

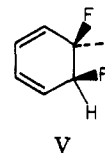
The two minor products with ^{19}F spectra consistent with isomeric 3,4,5,6-tetrafluorocyclohexenes (cf. NMR Spectral Analysis and Quantitation) were observed in a ratio of $(1.5 \pm 0.2):1$ in 14 different reactions. On proton decoupling both sets of multiplets exhibited $\text{AA}'\text{XX}'$ ^{19}F coupling patterns, eliminating two isomeric possibilities lacking the required symmetry (*cis,cis,trans* and *cis,trans,trans* fluorines). Of the remaining four (I–IV) isomeric possibilities,



I and II could arise from a combination of *cis* 1,4-addition and *cis* 1,2-addition to a remaining double bond, while I and IV could be formed from two *cis* 1,2-additions. Since 1,4- F_3CHD and 1,4- F_4CHD predominate on reaction of fluorobenzene and *p*-difluorobenzene, respectively, with AgF_2 (see the next section), 1,4-addition of fluorine seems to be the predominant mode of initial addition to the aromatic ring. Since only a single product consistent with an assignment as F_2CHD and only two tetrafluorocyclohexenes are found, I and II are the products most consistent with this mode. A mechanism involving free aromatic cation radical intermediates would result in formation of both *cis* and *trans* isomers and is thus seen as inconsistent with these results.

As seen from the data in Table I, the isomeric tetrafluorocyclohexene initially present to a greater extent is slightly reduced relative to the other isomer after treatment with KOH. Presuming relatively facile *trans* elimination of HF, these results suggest assignment of structure II (*trans, cis, trans*) to the former and structure I (*all cis*) to the latter cyclohexene.

The presence of *o*-difluorobenzene could arise from double *trans* 1,2 HF elimination from a tetrafluorocyclohexene (structure I) or HF elimination from an undetected 5,5,6-trifluoro-1,3-cyclohexadiene (V) intermediate. In



separate studies (next section) fluorobenzene was found to react with AgF_2 to give high yields of *p*-difluorobenzene but no detectable *o*-difluorobenzene (<0.1%). Thus the intermediacy of V appears precluded.

The *p*-difluorobenzene present may be formed by HF eliminations from both F_3CHD and the 3,4,5,6-tetrafluorocyclohexenes, on the basis of the results in Table I. Evidence for the former process will be discussed in the next section. No ^{19}F NMR evidence for *m*-difluorobenzene was found in any of the reaction mixtures (0.1% would have been detected).

Although the highest yield of fluorobenzene obtained was 61%, based on AgF_2 , formation of other products by the reaction path of Figure 1 requires that initial addition of two fluorines to benzene proceeds to the extent of at least 80%. Competition from further reactions, particularly a second addition of two fluorines to give the tetrafluorocyclohexenes, thus appears to limit the fluorobenzene yield. To assist HF elimination and possibly enhance the fluorobenzene yield, potassium fluoride and tri-*n*-butylamine were tested as additives. Both sharply reduced the yield of fluorobenzene as well as that of other organofluorine compounds.¹¹

Reactions of Halobenzenes with AgF_2 . Reactions of fluorobenzene, *o*- and *p*-difluorobenzene, chlorobenzene, and *p*-dichlorobenzene with AgF_2 in *n*-hexane were examined, and, except for *o*-difluorobenzene, these proved more vigorous than that of benzene as evidenced by their more rapid completion at relatively high dilution and low temperature (Table II). Quantitation by ^{19}F NMR of both substrate disappearance and product appearance in the fluorination of the fluoroaromatics provided an internal check on the analytic procedure. As seen in Table II, the accountability of the starting fluoroaromatic was nearly quantitative.

Reaction of fluorobenzene with AgF_2 in *n*-hexane yielded *p*-difluorobenzene, F_3CHD , and F_4CHD . No trace of either *o*- or *m*-difluorobenzene could be detected. As noted previously, this absence of *o*-difluorobenzene indicates that fluorobenzene is not an intermediate in its formation from benzene. Reaction of *p*-difluorobenzene with AgF_2 proceeds to F_4CHD in an 82% yield. As previously noted, F_3CHD is thermally stable at room temperature and is rapidly converted to *p*-difluorobenzene in the presence of KOH, while F_4CHD is stable under both these conditions. The facile stepwise conversion of fluorobenzene to F_3CHD to *p*-difluorobenzene to F_4CHD with all four structures unambiguously assigned by ^{19}F NMR provides conclusive evidence for the predominance of a 1,4-fluorine addition/HF elimination mode of reaction of AgF_2 with these aromatics. The finding also affords a framework for in-

Table II. Reactions of AgF_2 with Halobenzenes in Refluxing *n*-Hexane^a

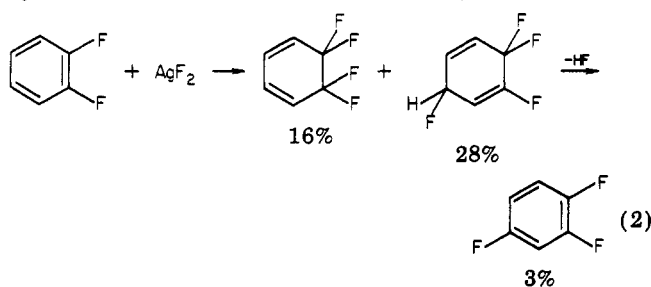
substr (amt, mol)	t, h	fluorine-containing products (% yield) ^b	accountability, %	
			SM ^c	AgF_2 ^d
fluorobenzene (0.068)	0.25	recovered SM (55), <i>p</i> -difluorobenzene (8.1), F_3CHD (36.2), F_4CHD (5.0), others (7.5)	90+	56
<i>p</i> -difluorobenzene (0.068)	0.08	recovered SM (58), F_4CHD (82), others (trace)	99	82
<i>o</i> -difluorobenzene (0.034)	2	recovered SM (55.4), 5,5,6,6-tetrafluoro-1,3-cyclohexadiene (15.7), 2,3,3,6-tetrafluoro-1,4-cyclohexadiene (28), 1,2,4-trifluorobenzene (3)	102.1	47
chlorobenzene (0.068)	18	<i>p</i> -fluorochlorobenzene (23.5), <i>o</i> -fluorochlorobenzene (11.8) (11.8), F_4CHD (10.2), <i>o</i> -difluorobenzene (2.5), <i>p</i> -difluorobenzene (2.1), 4-chloro-1,2-difluorobenzene (2.1), others (19.9)		72
<i>p</i> -dichlorobenzene (0.068)	18	F_4CHD (25.2), 2,5-dichlorofluorobenzene (11.9), 4-chloro-1,2-difluorobenzene (5.4), <i>p</i> -fluorochlorobenzene (3.7), 1,4-dichloro-3,3,6-trifluoro-1,4-cyclohexadiene (2.7), others (28.1)		77

^a 0.068 M AgF_2 and 30 mL of *n*-hexane. ^b Yields based on the amount of AgF_2 charged and eq 1. ^c Percent of fluorinated starting material (SM) accounted for. ^d Percent of oxidizing power (eq 1) leading to fluorinated products.

interpreting related reactions.

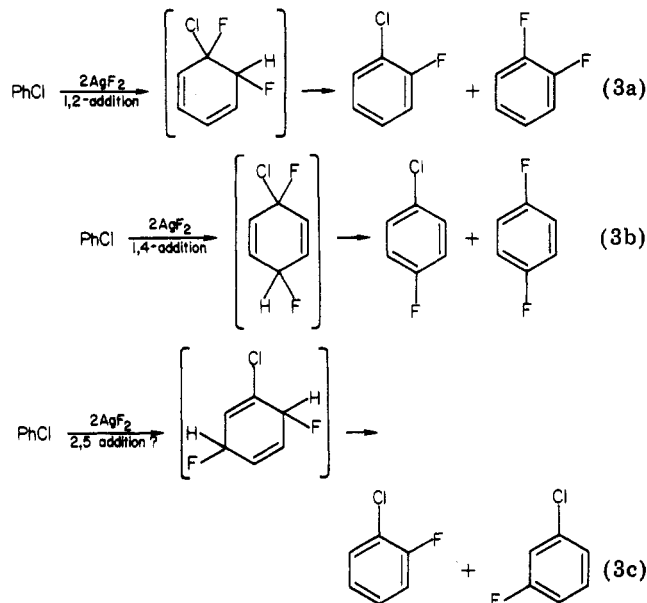
Although a stereoselective trans addition of fluorines to the aromatic ring is not ruled out, these results can be accounted for by cis 1,4-addition of two fluorines from the surface of the insoluble AgF_2 as pictured in brackets to the left in Figure 1. Simultaneous or nearly simultaneous addition of two fluorines may be facilitated by the close correspondence of the F-F distances in the complex structure of crystalline AgF_2 ¹² with the 2.8-Å distance between para positions in the benzene ring. Other factors assisting the reaction may be the thermodynamic driving force for electrophilic attack from this high-valent metal salt,¹³ the tendency of silver ion to complex with π electrons,¹⁴ and the different crystal structures¹⁵ and specific gravities of AgF (5.85) and AgF_2 (4.58), which may facilitate ablation of the surface of the latter. The minor proportion of 1,2-addition products may be formed by a similar mechanism, perhaps on an edge or corner of the AgF_2 crystal or by a more open transition state (more ion-radical character).

Reaction of *o*-difluorobenzene with AgF_2 proceeds relatively slowly as judged visually by disappearance of the dark AgF_2 solid. A 16% yield of 5,5,6,6-tetrafluoro-1,3-cyclohexadiene was obtained (eq 2) together with 28%



2,3,3,6-tetrafluoro-1,4-cyclohexadiene, indicating competitive 1,2- and 1,4-additions. The high proportion of 1,2-addition in this instance may result from the adjacent fluorines providing relatively reactive electrophilic centers. The 3% 1,2,4-trifluorobenzene was presumably formed by HF elimination from 2,3,3,6-tetrafluoro-1,4-cyclohexadiene (eq 2).

Reaction of chlorobenzene with AgF_2 in *n*-hexane provided a 72% yield of fluoroorganics (only 35% in CHCl_3). The four reaction products identified and present in the largest amounts listed in Table II suggest a combination of both 1,2- and 1,4-addition of fluorines followed by both HF and HCl elimination (eq 3a-c). The apparent favoring



of HF to HCl elimination is consistent with predominant cis addition of fluorines and trans elimination of hydrogen halide.¹⁶ The *o*- and *p*-difluorobenzenes need not arise from either cis elimination or trans addition. Instead, a mechanism indicated by the results with *p*-dichlorobenzene (see below) may be operative. In this mechanism the chlorine on the sp^3 carbon undergoes Ag-mediated meta-thesis by fluoride¹⁷ prior to elimination of the geminal fluoride. The 2,5-addition of fluorines, if it occurred, could lead to *m*-chlorofluorobenzene, which was not detected.

A relatively large proportion (19.9%) of the fluorinated products of chlorobenzene provided complex ¹⁹F NMR spectra which were not readily interpretable. The ¹⁹F chemical shifts of these materials were in the same region as those of the tetrafluorocyclohexenes. About 2% of the product was identified as 3,4-difluorochlorobenzene. After treatment of the mixture with KOH, the amount of this

(12) P. Fischer, D. Schwarzenbach, and H. M. Rietveld, *J. Phys. Chem. Solids*, **32**, 543 (1971).

(13) A. Clifford, W. Pardieck, and C. Wadley, *J. Phys. Chem.*, **70**, 3241 (1966).

(14) R. S. Mulliken and W. B. Person, "Molecular Complexes", Wiley, New York, 1969, p 272.

(15) A. F. Wells, "Structural Inorganic Chemistry", 4th ed., Clarendon Press, Oxford, 1975, p 349.

(16) D. V. Banthorpe, "Elimination Reactions", Elsevier, New York, 1963, p 12.

(17) A. M. Lovelace, D. A. Rausch, and W. Postelnek, *ACS Monogr.*, No. 138 (1958).

Table III. Liquid-Phase Reactions of Benzene and Fluorobenzene with CoF_3 ^a

moles of benzene	solvent (amt, mL)	T, °C	t, h	% yield of fluorinated products ^b		
				$\text{C}_6\text{H}_5\text{F}$	<i>p</i> - $\text{F}_2\text{C}_6\text{H}_4$	others ^c
0.05	CHCl_3 (40)	reflux	18	7.6	0.7	3.5
0.05	CHCl_3 (20)	reflux	18	6.7	trace	3.9
0.05	CCl_4 (20)	reflux	18	3.4	1.7	10
0.05 ^f	CHCl_3 (20)	25	3	0	0	0
0.22	C_6H_6 (20)	reflux	18	1.9	0.3	ND ⁱ
0.02	CHCl_3 (10)	reflux	18	4.4	0.8	4
0.05 ^g	CHCl_3 (20)	reflux	18	3.4	trace	
0.05	hexanes (30)	65	18	4.7	1.1	2.7
0.05 ^d	<i>n</i> - C_6H_{14} (30)	25	18	81 ^h	7.5	9.7 ^e

^a 0.05 mol of CoF_3 used in all runs. ^b All yields are based on the amount of CoF_3 charged. ^c Yields based on 2 mol of CoF_3 /mol of organofluorine observed. ^d Fluorobenzene. ^e F_4CHD only. ^f HF vapor added. ^g 0.1 mol of KF added. ^h Recovery. ⁱ ND = not determined.

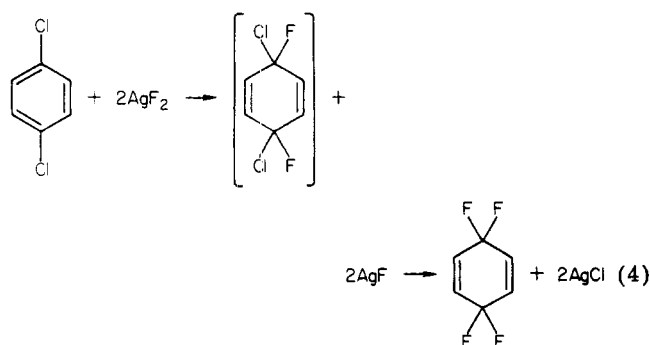
 Table IV. Liquid-Phase Reactions of Substituted Aromatics with AgF_2 and CoF_3 ^a

substr (amt, mol)	oxidant (amt, mol)	solvent (amt, mol)	t, h	% yield		ratio of o/m/p
				fluorinated products ^b	monofluoroaromatics	
$\text{C}_6\text{H}_5\text{CH}_3$ (0.15)	CoF_3 (0.05)	CHCl_3 (20)	18	4.7 ^c	c	
$\text{C}_6\text{H}_5\text{OCH}_3$ (0.05)	CoF_3 (0.05)	CHCl_3 (40)	18	trace ^d	ND ^f	
$\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2$ (0.05)	CoF_3 (0.05)	CHCl_3 (20)	72	0	0	
$\text{C}_6\text{H}_5\text{CN}$ (0.068)	AgF_2 (0.068)	CHCl_3 (25)	18	16	0.7	60:40:0
$\text{C}_6\text{H}_5\text{CN}$ (0.05)	CoF_3 (0.05)	CHCl_3 (20)	18	ND	ND	47:31:22
C_6H_5 (0.068)	AgF_2 (0.068)	CHCl_3 (10)	18	44.2	8	38:52:10
$\text{C}_5\text{H}_5\text{NO}_2$ (0.05)	CoF_3 (0.05)	CHCl_3 (20)	18	16	12.3	49:29:22
$\text{C}_6\text{H}_5\text{COCH}_3$ (0.05)	CoF_3 (0.05)	CHCl_3 (20)	18	ND	ND ^e	58:28:14
$\text{C}_6\text{H}_5\text{COOH}$ (0.05)	CoF_3 (0.05)	CHCl_3 (30)	18	5.5	4.8 ^e	51:36:12
$\text{C}_6\text{H}_5\text{CF}_3$ (0.068)	AgF_2 (0.068)	<i>n</i> - C_6H_{14} (30)	88	0	0	
$\text{C}_6\text{H}_5\text{Cl}$ (0.05)	CoF_3 (0.05)	CHCl_3 (20)	18	12.4	8.2	0:0:100
$\text{C}_6\text{H}_4\text{Cl}_2$ (0.05)	CoF_3 (0.05)	<i>n</i> - C_6H_{14} (30)	18	5.0	4.2	11:0:89

^a Reactions run at reflux. Product detected and measured by ^{19}F NMR. ^b Assuming 2 mol of MF_x /mol of organofluorine. ^c Fluorinated products not identified. ^d $\text{C}_6\text{H}_5\text{OCHF}_2$. ^e Regiospecific assignment not certain. ^f ND = not determined.

component increased substantially and two new fluoroaromatic compounds were detected. One was identified as 2,5-difluorochlorobenzene by comparison with published spectra (cf. NMR Spectral Analysis and Quantitation). The other was assigned as 2,3-difluorochlorobenzene by the ^{19}F NMR shifts and coupling pattern observed.

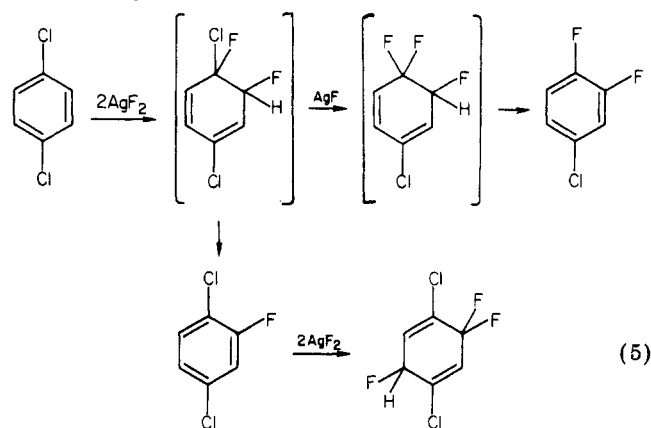
The reaction of *p*-dichlorobenzene with AgF_2 in *n*-hexane yielded mainly F_4CHD but also several unanticipated products. Although evidence for a 1,4-dichloro-1,4-difluorocyclohexadiene analogue of F_4CHD was sought through shortened contact with AgF_2 , no ^{19}F signal attributable to such a species was observed. A likely pathway to F_4CHD (eq 4) from *p*-dichlorobenzene would be through



1,4-addition of fluorines followed by metathetical substitution by AgF . Thus, through a combination of oxidative and metathetical substitution all fluorines available from AgF_2 are utilized.

The two minor products present in greatest amounts in this reaction, 2,5-dichlorofluorobenzene and 4-chloro-1,2-

difluorobenzene, could both arise from 1,2-addition as shown in eq 5. No simple irreversible process can account



for the *p*-fluorochlorobenzene present unless it arises from a chlorobenzene impurity in the *p*-dichlorobenzene. An unusual product identified in this reaction mixture was 1,4-dichloro-3,3,6-trifluoro-1,4-cyclohexadiene. The presence of only three hydrogen atoms in this molecule permitted the calculations of all the F-F and some of the H-F coupling constants to be made by using proton decoupling to obtain an unambiguous assignment of the structure. The presence of this compound is evidence for 1,4-addition of fluorines to 2,5-dichlorofluorobenzene. The latter may also have been formed through 2,5-addition of fluorines to *p*-dichlorobenzene followed by HF elimination. Because of the large proportion of unidentified products in the reaction mixture, the extent of such 2,5-addition cannot presently be ascertained.

Table V. ^{19}F NMR Data of Fluoroorganic Compounds Described in This Study

name	ϕ_{av} , ppm (vs. Freon 11)	solvent	J_{FF} , Hz	identification
Fluorinated Aromatics				
fluorobenzene	113.37	CDCl_3		authentic sample
	112.90	CCl_4		
	113.28	hexane		
<i>o</i> -difluorobenzene	112.75	C_6D_6		authentic sample
	138.78	CHCl_3		
	138.07	CCl_4		
<i>p</i> -difluorobenzene	138.45	hexane		authentic sample
	120.05	CHCl_3		
	119.67	CCl_4		
1,2,4-trifluorobenzene	ϕ_1 143.85, ϕ_2 133.69, ϕ_4 116.12	hexane	$J_{1,2} = 20.7$, $J_{1,4} = 15.2$, $J_{2,4} = 3.1$	$\phi_1 = 140.0$, $\phi_2 = 130.1$, $\phi_4 = 115.3^a$ ($J_{1,2} = -20.4$, $J_{1,4} = 15.1$, $J_{2,4} = 3.2^b$) $\phi = 115.2^a$
<i>o</i> -chlorofluorobenzene	115.78	CHCl_3		assignment ^d
	115.46	hexane		
<i>p</i> -chlorofluorobenzene	116.35	CHCl_3		$\phi = 115.7^a$
	116.55	hexane		
2,5-dichlorofluorobenzene	112.57	hexane		assignment ^d
2-chloro-1,4-difluorobenzene	$\phi_1 = 121.8$, $\phi_4 = 117.3$	CHCl_3	$J_{1,4} = 15.3$	
4-chloro-1,2-difluorobenzene	ϕ_1 135.08, ϕ_2 140.41	hexane	$J_{1,2} = 20.6$	assignment ^e
2,3-difluorochlorobenzene	ϕ_1 143.73, ϕ_2 133.58	hexane	ND	assignment ^e
<i>o</i> -fluoronitrobenzene	109.72	CHCl_3		assignment ^f
<i>m</i> -fluoronitrobenzene	118.60, 118.50, 111.49	CHCl_3		assignment ⁱ
<i>p</i> -fluoronitrobenzene	102.71, 102.79	CHCl_3		triplet of triplets, standard <i>p</i> -F pattern
<i>o</i> -fluoroacetophenone	110.30	CHCl_3		assignment ^f
<i>m</i> -fluoroacetophenone	112.66	CHCl_3		assignment ^f
<i>p</i> -fluoroacetophenone	106.29	CHCl_3		triplet of triplets, standard <i>p</i> -F pattern
<i>o</i> -fluorobenzonitrile	107.29	CHCl_3		authentic sample
<i>m</i> -fluorobenzonitrile	110.28	CHCl_3		authentic sample
<i>p</i> -fluorobenzonitrile	103.05	CHCl_3		triplet of triplets, standard <i>p</i> -F pattern, and by elimination
<i>o</i> -fluorobenzoic acid	108.4	CHCl_3		pattern very similar to nitrile above
<i>m</i> -fluorobenzoic acid	112.5	CHCl_3		by elimination
<i>p</i> -fluorobenzoic acid	104.7	CHCl_3		triplet of triplets, standard <i>p</i> -F pattern
Cyclohexenes				
<i>trans, cis, trans</i> -3,4,5,6-tetrafluorocyclohexene	ϕ_3 187.74, ϕ_4 208.76	hexane		assignment ^h
<i>cis, cis, cis</i> -3,4,5,6-tetrafluorocyclohexene	ϕ_3 194.20, ϕ_4 215.17	hexane		assignment ^h
Cyclohexadienes				
<i>cis</i> -3,6-difluoro-1,4-cyclohexadiene (F_2CHD)	174.42	hexane		assignment ^f
3,3,6-trifluoro-1,4-cyclohexadiene (F_3CHD)	ϕ_3 91.12, ϕ_3' 85.09, ϕ_6 181.82	hexane	$J_{3,3'} = 318.9$, $J_{3,6} = 15.3$, $J_{3,6'} = 11.3$, $J_{3',6'} = 14.6$, $J_{4,6'} = 43.5$, $J_{3,6'} = 8.85$, $J_{3',4} = 3.6$	definite assignment from spectrum
2,3,3,6-tetrafluoro-1,4-cyclohexadiene	ϕ_3 103.16, ϕ_3 99.33, ϕ_2 129.73, ϕ_6 179.24	hexane	$J_{3,3'} = 315.5$, $J_{3,6} = 13.8$, $J_{3,6'} = \text{ND}$, $J_{3',6} = 10.8$, $J_{3',6'} = \text{ND}$, $J_{6,6'} = 43.3$, $J_{2,3} = 21.2$, $J_{2,3'} = 20.5$, $J_{2,6} = 1.7$	definite assignment from spectrum
3,3,6,6-tetrafluoro-1,4-cyclohexadiene (F_4CHD)	96.50	hexane	$J_{1,3} = 2.3$, $J_{2,3} = 2.3$	assignment ^c
5,5,6,6-tetrafluoro-1,3-cyclohexadiene	122.74	hexane		assignment ^g

^a J. Emsley, J. Feeney, and L. Sutcliffe, *Prog. Nucl. Mag. Reson. Spectrosc.*, 7, 1 (1971). ^b V. Wray, L. Ernst and E. Lustig, *J. Magn. Reson.*, 27, 1 (1977). ^c P. L. Coe, R. G. Plevey, and J. C. Tatlow, *J. Chem. Soc. C*, 1060 (1969). ^d The ^{19}F spectrum of this compound has not previously been reported. It is not *o*-fluorochlorobenzene or 2,5-difluoro-1,4-dichlorobenzene, both of which were previously described in ref. *a*. ^e These molecules have two nonequivalent fluorines in the "ortho" region. ^f See the text for discussion of this assignment. ^g The spectrum shows the same general splitting pattern as that for F_4CHD but at higher field, possibly due to the proximity of CF_2 groups, and was derived from *o*-difluorobenzene. ^h In the products of the reaction of benzene solutions with AgF_2 , four complex multiplets are seen in the ϕ 180–200 region, corresponding to CFH groups. When proton decoupling is applied, the multiplets simplify, revealing two pairs of AA'XX'. Each pair of AA'XX' multiplets corresponds to a molecule containing four fluorines arranged with AA'XX' symmetry. A standard analysis was attempted, but because of the lack of coupling constant data for fluorinated cyclohexenes, assignment of the multiplet pairs to specific isomers by NMR analysis alone was not possible. Chemical reasoning (see text) and chemical shift considerations permit assignment of the isomer present in greater proportion (1.5 times that of the other isomer) and at lower field to *trans, cis, trans*-3,4,5,6-tetrafluorocyclohexene and the other isomer to *cis, cis, cis*-3,4,5,6-tetrafluorocyclohexene. ⁱ Assignments were made by comparison of coupling patterns to those of respective isomers of known monofluoroaromatics and by comparison of shift values to those in ref. *a*.

Reactions of Benzene and Fluorobenzene with CoF₃. Although AgF₂ and CoF₃ are both used in gas-phase perfluorination of aromatics¹⁸ AgF₂ has not previously provided any advantages.¹⁹ Since the F-F distances are shorter in CoF₃²⁰ than in AgF₂¹² (<2.7 Å vs. >2.8 Å) and since the two fluorides have quite different crystal structures, we examined their reactivity to benzene and fluorobenzene under comparable solution conditions. In most instances CoF₃ proved to be about 1 order of magnitude less efficient as a fluorinating agent for these aromatics than AgF₂. The highest yield (Table III) of fluorobenzene achieved by using CoF₃ was 8%. The accountability of the oxidizing power of CoF₃ in terms of organic fluoride products was also low. Although the other fluorinated products were not all identified, no fluorinated cyclohexenes were found in the reaction mixtures, and the absence of F₃C₆H₅ even in the products of the reaction of fluorobenzene was in striking contrast to the results with AgF₂. Since the organic reaction product was also quite dark in color, we suspect that oxidation with CoF₃ resulted in ring-opening processes.¹¹

The presence of KF or HF suppressed or eliminated the production of fluoroaromatics in these reactions. By slow addition of CoF₃, reaction with benzene could be carried out without an inert diluent, but the fluorobenzene yield was poor. The ratio of difluoro- to monofluorobenzene was much higher in the reaction of benzene with CoF₃ than in that with AgF₂. Reaction of fluorobenzene with CoF₃ gave a higher ratio of F₄C₆H₅ to *p*-difluorobenzene than did AgF₂. The results indicate that selectivity to monofluorinated products is much poorer with CoF₃ than with AgF₂ acting on benzene or fluorobenzene solutions and taken in total suggest that different mechanisms are operative.

Reactions of Other Substituted Aromatics with AgF₂ and CoF₃. Reactions with a variety of substituted benzenes were examined, and the results are detailed in Table IV. The donor substituted benzenes (toluene, anisole, and *N,N*-dimethylaniline) gave no fluoroaromatics with CoF₃ under the conditions used. Although the oxidant was consumed and color changes suggested a reaction, the identity of the nonfluorinated organic products was not established. With nitrile, nitro, acetyl, and carboxylic acid substituents on the benzene ring, all three monofluoro-substituted derivatives could be identified in the ¹⁹F NMR spectrum and their proportions established. Since the yields were low and both the products and the possible F₂C₆H₅ intermediates in their formation can also undergo reactions with the fluorinating agent, a mechanistic interpretation based on the observed regioselectivity cannot be made. Anomalous, with nitrobenzene the yield of ring-fluorinated products proved to be higher (12%) from CoF₃ than from AgF₂ (8%). The only aromatic examined, which was found to be inert to both CoF₃ and AgF₂, was α,α,α -trifluoromethylbenzene.

Experimental Section

Reagents. Reagent grade organic compounds were used as received. Fluoroaromatic reagents were assayed by ¹⁹F NMR and found to be free of extraneous absorbances. The AgF₂ and CoF₃

(reported purities 98%) were used as received from Alfa-Ventron Co. Hydrogen fluoride (reported purity 99.9%) was used as received from the Matheson Co.

Fluorination Procedure. In a 250-mL Erlenmeyer flask made of Teflon containing a magnetic stirring bar coated with Teflon and fitted with a lined condenser coated with Teflon were placed 30 mL of *n*-hexane and 20 mL (0.23 mol) of benzene. The flask was flushed with N₂ for 1 h, and 10 g (0.068 mol) of AgF₂ was added all at once. The mixture was stirred at room temperature for 15 min, brought to reflux by using a heated oil bath, and allowed to reflux for 18 h. The mixture was allowed to cool to room temperature under N₂. The resulting organic layer was pale yellow, and the color of the precipitate had changed from the dark red-brown of AgF₂ to the bright yellow of AgF. To the product mixture was added 0.2312 g of C₆F₆ diluted in approximately 5 mL of *n*-hexane. The slurry was mixed thoroughly, and the organic portion was decanted into a separatory funnel made of Teflon and washed twice with water. The organic layer was dried over sodium sulfate and analyzed by ¹⁹F NMR.

NMR Spectral Analysis and Quantitation. ¹⁹F spectra were obtained at 94.13 MHz on a Varian XL-100 operated in the FT mode, using perdeuteriobenzene to provide a deuterium lock signal. Each sample, contained in a 5-mm tube, included a measured amount of hexafluorobenzene to serve both as an internal reference and as a quantitative standard. Survey spectra of each preparation were taken of two overlapping 10-kHz ranges, covering the region from 66 to 225 ϕ [ϕ is the chemical shift in parts per million from Freon 11 (CCl₃F)]. An acquisition time of 1 s and a tipping angle of 35° were used. Narrower sweep widths and correspondingly longer acquisition times were used to examine the spin-spin multiplets in greater detail. Spectra were obtained with and without simultaneous ¹H decoupling, as appropriate for establishing component identity. The concentrations were determined from the integration of the survey spectra, including the C₆F₆ line. In reactions involving fluoroaromatic substrates, the accuracy of the analytical method was confirmed by quantitatively monitoring starting material as well as product. Analysis by ¹⁹F NMR spectroscopy thus provided the principle means of detection, identification, and quantification of fluorinated reaction products in this investigation. Table V contains the chemical shifts for all characterized compounds as well as all coupling constants determined from first-order analysis of both coupled and decoupled spectra.

Yields were calculated on the basis of the number of moles of oxidant reacted. For oxidative, additive, substitutive, or a combination of fluorination reactions, eq 6 was used to calculate the yield of fluorinated product, where RF_{*n*} = the fluorinated product, *n* = the number of fluorines in a molecule of RF_{*n*}, and *N* = the number of equivalents of oxidant required per equivalent of RF_{*n*}.

$$\text{yield of RF}_n = \frac{\text{integral RF}_n}{n(\text{integral C}_6\text{F}_6)} \frac{6(\text{moles of C}_6\text{F}_6 \text{ added})}{(\text{moles of oxidant reacted})/N} \times 100 \quad (6)$$

Registry No. I, 74298-16-1; II, 74298-17-2; 1,4-dichloro-3,3,6-trifluoro-1,4-cyclohexadiene, 74298-18-3; fluorobenzene, 462-06-6; *o*-difluorobenzene, 367-11-3; *p*-difluorobenzene, 540-36-3; 1,2,4-trifluorobenzene, 367-23-7; *o*-chlorofluorobenzene, 348-51-6; *p*-chlorofluorobenzene, 352-33-0; 2,5-dichlorofluorobenzene, 348-59-4; 2-chloro-1,4-difluorobenzene, 2367-91-1; 4-chloro-1,2-difluorobenzene, 696-02-6; 2,3-difluorochlorobenzene, 36556-47-5; *o*-fluoronitrobenzene, 1493-27-2; *m*-fluoronitrobenzene, 402-67-5; *p*-fluoronitrobenzene, 350-46-9; *o*-fluoroacetophenone, 445-27-2; *m*-fluoroacetophenone, 455-36-7; *p*-fluoroacetophenone, 403-42-9; *o*-fluorobenzonitrile, 394-47-8; *m*-fluorobenzonitrile, 403-54-3; *p*-fluorobenzonitrile, 1194-02-1; *o*-fluorobenzoic acid, 445-29-4; *m*-fluorobenzoic acid, 455-38-9; *p*-fluorobenzoic acid, 456-22-4; chlorobenzene, 108-90-7; *p*-dichlorobenzene, 106-46-7; *cis*-3,6-difluoro-1,4-cyclohexadiene, 74298-19-4; 3,3,6-trifluoro-1,4-cyclohexadiene, 74298-20-7; 2,3,3,6-tetrafluoro-1,4-cyclohexadiene, 74298-21-8; 3,3,6,6-tetrafluoro-1,4-cyclohexadiene, 22060-77-1; 5,5,6,6-tetrafluoro-1,3-cyclohexadiene, 74298-22-9; C₆H₅CH₃, 108-88-3; C₆H₅OCH₃, 100-66-3; C₆H₅N(CH₃)₂, 121-69-7; C₆H₅CN, 100-47-0; C₆H₅NO₂, 98-95-3; C₆H₅COCH₃, 98-86-2; C₆H₅COOH, 65-85-0; C₆H₅CF₃, 98-08-8; AgF₂, 7783-95-1.

(18) M. Stacey, J. C. Tatlow, and A. G. Sharpe, *Adv. Fluorine Chem.*, 1, 166 (1960); R. G. Plevy, M. P. Steward, and J. C. Tatlow, *J. Fluorine Chem.*, 3, 259 (1973).

(19) "Kirk-Othmer Encyclopedia of Chemical Technology", Vol. 9, 2nd ed., Interscience, New York, 1966, p 662.

(20) M. A. Hepworth, K. H. Jack, and R. D. Peacock, and G. J. Westland, *Acta Crystallogr.*, 10, 63 (1957).