

B<sub>1a</sub>(C<sub>1a</sub>) constellations, one has to reconsider the A<sub>2a</sub> types. The larger the energy gap between the lowest energy S-S and the T-T absorption bands in this type of chromophore the lower the T-T absorption over the fluorescence region of the substituted compound (the A<sub>2c</sub> type of laser dye) will be. All the A<sub>2c</sub> type of commercially available laser dyes we discussed had either naphthalene or anthracene (or their heterocyclic derivatives such as coumarin and xanthene) as chromophores. In both compounds, the energy gap between the lowest energy S-S and T-T absorption bands is not very large. As a result of this situation, after substitution, the spec-

tral region of laser action still falls on a region of considerable T-T absorption. However, improvements in laser dye performance can be expected if one starts with chromophores which have a larger energy gap. We have not emphasized the reduction of intersystem crossing rates, but certainly T-T absorption can be minimized by this approach.

Obviously, the final conclusion of this paper has already been made. At the moment, the chain-type compounds present a very large pool of promising molecules. Among them, there should be many candidates possessing promising A<sub>2a</sub> constellations.

## Gas Phase Fluorination of Benzene, Fluorobenzene, *m*-Difluorobenzene, and Trifluoromethylbenzene by Reactions of Thermal Fluorine-18 Atoms<sup>1</sup>

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**Abstract:** Thermal fluorine-18 atoms have been reacted in the gas phase with benzene, fluorobenzene, *m*-difluorobenzene, and trifluoromethylbenzene. The <sup>18</sup>F atoms were formed at high kinetic energies by the <sup>19</sup>F(n,2n)<sup>18</sup>F nuclear reaction and then thermalized by multiple collisions with SF<sub>6</sub>. The yields of <sup>18</sup>F/H are small and pressure independent in the absence of oxygen. With O<sub>2</sub> present, the yields increase substantially, reaching >60% for C<sub>6</sub>H<sub>5</sub><sup>18</sup>F from C<sub>6</sub>H<sub>6</sub>. The yield from substitution of thermal <sup>18</sup>F for H ortho to another F substituent is decreased by O<sub>2</sub>, while that in meta and para positions is substantially increased. No such diminution of yield in the ortho position is found for CF<sub>3</sub> as a substituent. The substitution of thermal <sup>18</sup>F for aromatically bonded F atoms is observed in low yields only.

Relatively few experimental investigations have been carried out which unambiguously involve the reactions of atomic fluorine with aromatic systems despite the considerable interest in such reactions.<sup>2</sup> However, radioactive <sup>18</sup>F atoms (*t*<sub>1/2</sub> = 110 min) can be produced by various nuclear reactions, including the <sup>19</sup>F(n,2n)<sup>18</sup>F reaction with fast neutrons, and these atoms can be brought to thermal energies without bond formation by multiple collisions with suitable inert moderators.<sup>3-13</sup>

In the last several years, research in this laboratory has utilized such thermal <sup>18</sup>F atoms for reaction studies with olefins,<sup>6,7,9,10</sup> acetylene,<sup>8</sup> various RH compounds,<sup>11</sup> and a variety of inorganic species.<sup>12,13</sup>

Several earlier studies have been made of <sup>18</sup>F atomic reactions in aromatic systems, but these have generally involved either a neat fluoroaromatic substrate or else a relatively high concentration of aromatic substrate, such that the observed reaction products are formed by a mixture of kinetically hot and thermal processes.<sup>14-23</sup> In those experiments, none of the high moderation systems were studied in which the observed products are essentially those of thermal origin. Condensed phase experiments have involved <sup>18</sup>F atoms from either the (n,2n) or (γ,n) reactions on fluorinated sub-

(1) This research was supported by A.E.C. Contract No. (04-3)-34, Agreement No. 126.

(2) Many experiments result in fluorination of aromatic compounds but under conditions in which both atomic and molecular fluorination mechanisms can be readily postulated. See, for example, V. Grakauskas, *J. Org. Chem.*, **35**, 723 (1970); V. Grakauskas, *Intra-Sci. Chem. Rep.*, **5**, 85 (1971).

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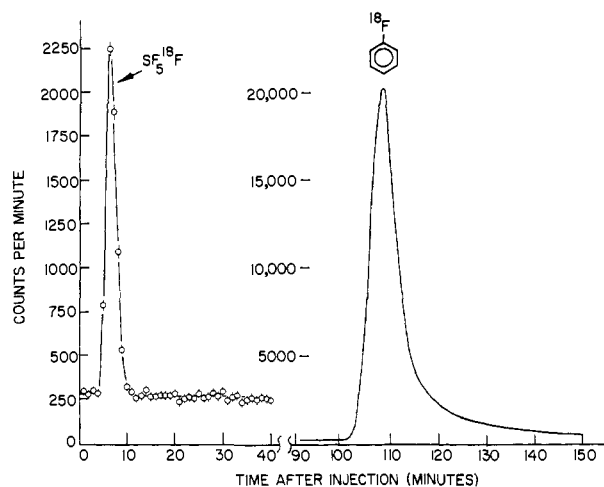
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**Figure 1.** Radio gas chromatogram of  $C_6H_5^{18}F$  and  $SF_5^{18}F$  formed in gaseous  $SF_6-C_6H_6-O_2$  mixture at 3000 Torr.

strates,<sup>14-22</sup> or from solutions containing both oxygen and lithium through the thermal neutron-induced double nuclear reaction,  ${}^6Li(n,\alpha){}^3H$  plus  ${}^{16}O({}^3H,n){}^{18}F$ .<sup>23</sup> An esr investigation of  ${}^{18}F$  atom reactions with benzene was conducted at 4°K by Cochran, *et al.*<sup>24</sup>

A gas phase investigation was made of the isomer distribution of difluorobenzenes from  ${}^{18}F$  reactions with neat fluorobenzene by Brinkman and Lindner.<sup>25</sup> Since energetic  ${}^{18}F$  atom reactions are quite feasible under these conditions, the resulting products again represent a mixture of hot and thermally initiated reactions. Recently, Sams and Vasek have investigated the gas phase reactions with bromobenzene of  ${}^{18}F$  atoms formed in plasma discharges.<sup>26</sup>

We have now applied our radiochemical techniques to the reactions of thermal  ${}^{18}F$  atoms with benzene, fluorobenzene, *m*-difluorobenzene, and trifluoromethylbenzene. The initially energetic  ${}^{18}F$  atoms have been formed by the  ${}^{19}F(n,2n){}^{18}F$  reaction in  $SF_6$  and have been moderated to thermal energies by many non-reactive collisions with  $SF_6$  prior to reaction with the aromatic compounds included as minor components in each system. Most of our experiments have been carried out in the gas phase, usually at about 3000 Torr total pressure, and always near 10°. The radioactive products have been assayed by radio gas chromatography.

## Experimental Section

**General.** Discussions of the experimental aspects of  ${}^{18}F$  recoil atom chemistry as carried out in this laboratory have been presented earlier<sup>3-13</sup> and are now available in full detail as a project report.<sup>27</sup> Our present experiments are rather similar, and extensive description is given only for those aspects in which appreciable differences have necessitated alternative treatment.

As before, the  ${}^{18}F$  atoms are created by bombardment of gaseous  $SF_6$  in 11-ml glass ampoules with 14 MeV neutrons from a Kaman A711 fast neutron generator. Approximately  $10^8$  atoms of  ${}^{18}F$  are formed in a typical 10-20 min irradiation. The samples are maintained at about 10° by proximity to the cooling water flowing around the zirconium tritide target in the neutron generator.

(24) E. L. Cochran, F. J. Adrian, and V. A. Bowers, *J. Phys. Chem.*, **74**, 2083 (1970).

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(27) R. S. Iyer and F. S. Rowland, A.E.C. Report UCI-1973-1, available on request from the authors.

When  $SF_6$  is present at mole fraction  $\geq 0.95$ , about 1% of the  ${}^{18}F$  atoms react while hot to form  $SF_5^{18}F$  and the remaining  ${}^{18}F$  atoms are well thermalized by multiple collisions with  $SF_6$  before reaction with the aromatic substrate can occur. The essentially complete thermalization of these  ${}^{18}F$  atoms has been established through the lack of effect of further dilution with  $SF_6$  on the excitation energy of the  $C_2H_4^{18}F^*$  radicals formed by  ${}^{18}F$  addition to substrate  $C_2H_4$ .<sup>10</sup>

**Calibration of Proportional Counter vs. Scintillation Counter (for Monitor).** The more volatile  ${}^{18}F$ -labeled products (except  $H^{18}F$ ) were separated and assayed by radio gas chromatography. Absolute yields were determined from the activity induced in an external Teflon monitor surrounding the glass ampoule.<sup>5,6,27</sup> In our system, the comparison of sample contents with the Teflon monitor involves counting the former with an external flow proportional counter and the latter with a NaI scintillation detector and requires cross-calibration of each to correct for the differences in efficiency of the two counting systems. This calibration factor (in our laboratory, designated the P/S ratio) is determined by assaying a particular aliquot of a volatile  ${}^{18}F$ -labeled compound in a glass ampoule in the scintillation detector (S) followed by injection of the material into the radio gas chromatograph for measurement with the proportional counter (P). The normal routine determination of the P/S ratio has utilized a mixture of three radioactive gases ( $CF_2^{18}FCHF_2$ ,  $CHF_2^{18}F$ , and  $C_2F_3^{18}F$ ) formed from  ${}^{18}F$  reaction with  $C_2F_4$ . The P/S ratio should be independent of the identity of the  ${}^{18}F$ -gaseous component, as long as the physical behavior of the gases is the same in the two assay situations. With higher boiling  ${}^{18}F$ -labeled compounds, the passage of such gases through tubing and the external counter without delay from surface adsorption becomes a less certain assumption, and the P/S ratio has been determined for several of the reaction products actually found in this study. As shown in Table I, all of these aromatic molecules have substantially higher P/S ratios than for the usual more volatile calibration gases.

**Table I.** Measured Calibration Ratios of Proportional and Scintillation Counters for Various  ${}^{18}F$ -Labeled Compounds

${}^{18}F$ -labeled compd	P/S calibration ratio	Boiling point, °C
$CF_2^{18}FCHF_2$	3.24	-48.5 <sup>a</sup>
$CHF_2^{18}F$	3.27	-82.2 <sup>b</sup>
$C_2F_3^{18}F$	3.28	-76.3 <sup>b</sup>
<i>m</i> - $C_6H_4F^{18}F$	6.57	+82.5 <sup>b</sup>
$C_6H_5^{18}F$	6.70	+84.8 <sup>b</sup>
	6.72	
<i>p</i> - $C_6H_4F^{18}F$	5.62	+88.5 <sup>b</sup>
<i>m</i> - $CF_3C_6H_4^{18}F$	7.58	+100 <sup>c</sup>

<sup>a</sup> D. S. Young, N. Fukuhara, and L. A. Bigelow, *J. Amer. Chem. Soc.*, **62**, 1171 (1940). <sup>b</sup> M. Hudlicky, "Chemistry of Organic Fluorine Compounds," Macmillan, New York, N. Y., 1962. <sup>c</sup> K. E. Seiler, M. A. Durrance, and L. C. Sams, *J. Chromatogr.*, **63**, 375 (1971).

The  ${}^{18}F$ -labeled fluorobenzene peak from the external proportional counter is shown in Figure 1 for a typical  $O_2$ -scavenged sample. Although the peak exhibits some tailing, it is reasonably normal in shape. Nevertheless, on the average, each  $C_6H_5^{18}F$  molecule remained in the proportional counter-sensitive region for approximately 2.05 times as long as the residence time for the He carrier molecules (about 1 min) and hence gave 2.05 times as many decays as would have been observed if both He and  $C_6H_5^{18}F$  passed through the counting volume at the same rate.

In a separate experiment, the transit times for air and fluorobenzene were determined between two thermal conductivity cells in series with the proportional counter between them. While the transit times between thermal conductivity detectors for the two molecules were essentially the same without the counter between, the interposition of the counter increased the incremental peak-to-peak transit time for fluorobenzene to  $1.9 \pm 0.1$  times that found for air.

In the present study, all absolute yields have been estimated with P/S calibration factors appropriate to the particular molecule being measured, using the values of Table I. These ratios can be seen to increase with increasing boiling point and dipole moment. The increase in residence time in the counter for these experiments is quite consistent from run to run and is unaffected by the presence or

absence of small carrier quantities of unlabeled material with the radioactive products. We have made no further effort to determine the precise physical origin of the longer residence times for these particular molecules in this particular counter type.

An alternate method now used in our laboratory for higher boiling products is the heating of the counting volume to about 100°, with consequent reduction of the residence time for otherwise mildly adsorbed species.<sup>28</sup>

In an earlier publication, the yield of C<sub>6</sub>H<sub>5</sub><sup>18</sup>F from <sup>18</sup>F reactions with benzene-O<sub>2</sub> mixtures was identified as approaching 95% with increasing O<sub>2</sub>.<sup>29</sup> The lower yields (shown later in Figure 3) reflect the change required by the measurement of the actual P/S calibration factor for fluorobenzene.

**Identification of Products.** The trace radioactive components were identified by coincidence of gas chromatographic retention times with those of known materials, except in the case of 1,2,3-trifluorobenzene. On these analytical columns, the order of elution for the various fluorobenzenes roughly corresponds to the increasing boiling points of the molecules. The peak for 1,2,3-trifluorobenzene was assigned from its boiling point and location relative to the known peaks for *m*-difluoro-, 1,2,4-trifluoro-, and 1,3,5-trifluorobenzene.

The order of elution (shown later in Figure 4) for the difluorobenzenes differs from that given by Grakauskas in ref 2 for a column of similar material.<sup>30</sup> We have checked with nmr measurements that our commercial difluorobenzenes were indeed the compounds indicated.

The samples of the isomeric CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>F molecules were kindly furnished by R. A. Gorse, Jr., K. E. Al-Ani, and W. A. Noyes, Jr., of the University of Texas at Austin. These molecules emerged from the gas chromatograph in increasing order of their dipole moments.

**Gas Chromatographic Columns.** The columns used for analysis were: (A) 0.25-in. × 25-ft 30% Dow-Corning 705 silicone oil on 40-60 mesh Chromosorb P; (B) 0.25-in. × 50-ft 27% XF-1150 on 30-50 mesh Chromosorb P (HMDS); and (C) 0.25-in. × 12-ft 15% Bentone 34-5% UCON on 60-80 mesh Chromosorb W (acid washed).

The relative retention times obtained with column B at 84° were: *m*-C<sub>6</sub>H<sub>4</sub>F<sub>2</sub>, (1.00); C<sub>6</sub>H<sub>5</sub>F, 1.19; *p*-C<sub>6</sub>H<sub>4</sub>F<sub>2</sub>, 1.27; and *o*-C<sub>6</sub>H<sub>4</sub>F<sub>2</sub>, 1.46. At 78° with column B, these relative retention times were observed: 1,3,5-C<sub>6</sub>H<sub>3</sub>F<sub>3</sub>, 0.59; *m*-C<sub>6</sub>H<sub>4</sub>F<sub>2</sub>, (1.00); 1,2,4-C<sub>6</sub>H<sub>3</sub>F<sub>3</sub>, 1.16; and 1,2,3-C<sub>6</sub>H<sub>3</sub>F<sub>3</sub>, 1.38. At 30 ml/min the retention time of *m*-C<sub>6</sub>H<sub>4</sub>F<sub>2</sub> was 146 min at 78° and 125 min at 84°.

The radioactive products from <sup>18</sup>F reactions with CF<sub>3</sub>C<sub>6</sub>H<sub>5</sub> showed these retention times on column C at 60°: *p*-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>F, 43 min; *m*-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>F, 73 min. Between 107 and 116 min, the column temperature was manually programmed to 106°, while maintaining flow rate constant at 30 ml/min. The parent compound emerged with negligible <sup>18</sup>F radioactivity at 127 min, and *o*-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>F came out at 162 min.

Column A was used for the analysis of the SF<sub>6</sub><sup>18</sup>F and C<sub>6</sub>H<sub>5</sub><sup>18</sup>F formed in SF<sub>6</sub>-benzene mixtures.

## Results and Discussion

**<sup>18</sup>F Reaction with Benzene.** The only radioactive molecules observed by radio gas chromatography of the contents of an irradiated SF<sub>6</sub>-benzene (70:1) mixture at 3000 Torr total pressure are SF<sub>5</sub><sup>18</sup>F (1%) and C<sub>6</sub>H<sub>5</sub><sup>18</sup>F (9%). An increase in the SF<sub>6</sub>-benzene moderator ratio to 200:1 gave no change in the observed product distribution. No other organic products were observed in the boiling point range accessible to the chromatography; dimeric or polymeric materials would not have eluted during the available time. No search was made for H<sup>18</sup>F in these experiments, although small yields are anticipated from H atom abstraction from benzene; this H<sup>18</sup>F presumably reacted on the glass ampoule walls.

The observation of C<sub>2</sub>H<sub>3</sub><sup>18</sup>F from thermal <sup>18</sup>F reaction

(28) F. S.-C. Lee and F. S. Rowland, unpublished experiments.

(29) F. S. Rowland, J. A. Cramer, R. S. Iyer, R. Milstein, and R. L. Williams, "Radiopharmaceuticals and Labeled Compounds," Vol. 1, International Atomic Energy Agency, Vienna, 1973, p 383.

(30) The column used in ref 2 was coated with 10% XF-1150 on Anakrom AS (90-100 mesh).

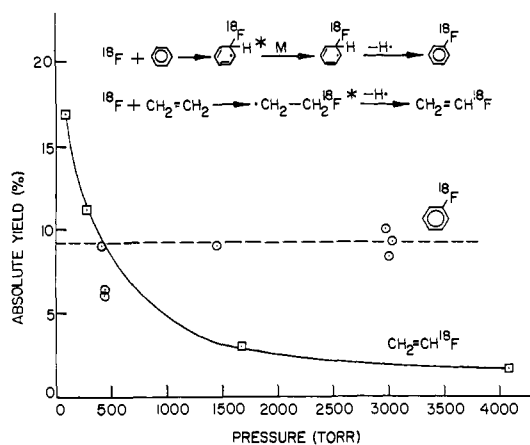
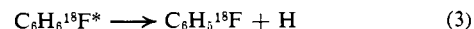
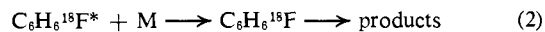
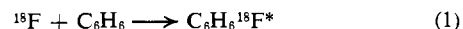


Figure 2. Yield of C<sub>6</sub>H<sub>5</sub><sup>18</sup>F vs. pressure from SF<sub>6</sub>-C<sub>6</sub>H<sub>6</sub> mixtures, as compared to SF<sub>6</sub>-C<sub>2</sub>H<sub>4</sub> mixtures (ref 10): O, C<sub>6</sub>H<sub>5</sub><sup>18</sup>F; □, C<sub>2</sub>H<sub>3</sub><sup>18</sup>F.

with C<sub>2</sub>H<sub>4</sub> has been definitely shown to arise from a two-step sequence of addition to the olefin to form C<sub>2</sub>H<sub>4</sub><sup>18</sup>F\*, followed by H atom loss leaving C<sub>2</sub>H<sub>3</sub><sup>18</sup>F as the residual molecule.<sup>10, 31-33</sup> Variation of the total pressure in C<sub>2</sub>H<sub>4</sub> mixtures with SF<sub>6</sub> (also CF<sub>4</sub><sup>32-33</sup> or NF<sub>3</sub><sup>33</sup>) shows an increasing yield of C<sub>2</sub>H<sub>3</sub><sup>18</sup>F at lower pressures, consistent with a lifetime of about 10<sup>-9</sup> sec for C<sub>2</sub>H<sub>4</sub><sup>18</sup>F\* radicals from thermal <sup>18</sup>F addition. On the other hand, no evidence has been found for decomposition by H atom loss from the CH<sup>18</sup>F=CH\* radicals obtained from thermal <sup>18</sup>F addition to CH≡CH.<sup>8</sup>

The possible pressure dependence of the formation of C<sub>6</sub>H<sub>5</sub><sup>18</sup>F by the sequence of reactions 1 to 3 was tested, as shown in Figure 2, with negative results.



Evidence has been obtained from esr studies, for the existence of the C<sub>6</sub>H<sub>6</sub>F fluorocyclohexadienyl radical after photodissociation of F<sub>2</sub> with benzene in a solid argon matrix at 4°K.<sup>24</sup> Although large variations are found for C<sub>2</sub>H<sub>3</sub><sup>18</sup>F yields in this pressure range, as illustrated, the data of Figure 2<sup>34</sup> indicate no formation of C<sub>6</sub>H<sub>5</sub><sup>18</sup>F by decomposition of C<sub>6</sub>H<sub>6</sub><sup>18</sup>F\*. The absence of a pressure-dependent yield for C<sub>6</sub>H<sub>5</sub><sup>18</sup>F of course does not mean that no C<sub>6</sub>H<sub>6</sub><sup>18</sup>F\* was formed; rather, if formed, such radicals must always be stabilized by collision before decomposition can occur, just as observed for CH<sup>18</sup>F=CH\* radicals.

The precursor of C<sub>6</sub>H<sub>5</sub><sup>18</sup>F in these unscavenged SF<sub>6</sub>-benzene mixtures is probably thermalized C<sub>6</sub>H<sub>6</sub><sup>18</sup>F, reacting either by H atom transfer to another molecule of benzene or by disproportionation with some other radical in the system.

### <sup>18</sup>F Reactions with Benzene Plus Molecular Oxygen.

The inclusion of O<sub>2</sub> in the reaction system at 3000 Torr

(31) N. Colebourne, J. F. J. Todd, and R. Wolfgang, "Chemical Effects of Nuclear Transformations," Vol. 1, International Atomic Energy Agency, Vienna, 1965, p 149.

(32) J. F. J. Todd, N. Colebourne, and R. Wolfgang, *J. Phys. Chem.*, 71, 2875 (1967).

(33) J. P. Frank and F. S. Rowland, *J. Phys. Chem.*, 78, 850 (1974).

(34) Numerical values for the points illustrated in Figures 2, 3, 5, and 8 are given in Tables III-VI in the microfilm. See paragraph at end of paper regarding supplementary material.

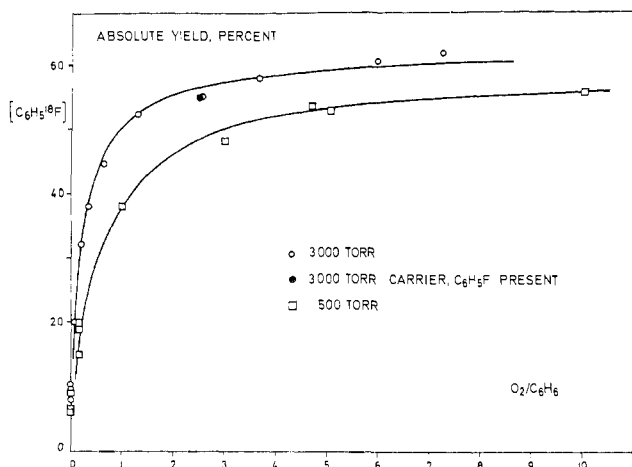


Figure 3. Enhancement of yields of  $C_6H_5^{18}F$  by the presence of molecular  $O_2$  in 60:1  $SF_6-C_6H_6$  mixtures. Total pressure:  $\circ$ , 3000 Torr;  $\bullet$ , 3000 Torr (carrier  $C_6H_5F$  present);  $\square$ , 500 Torr.

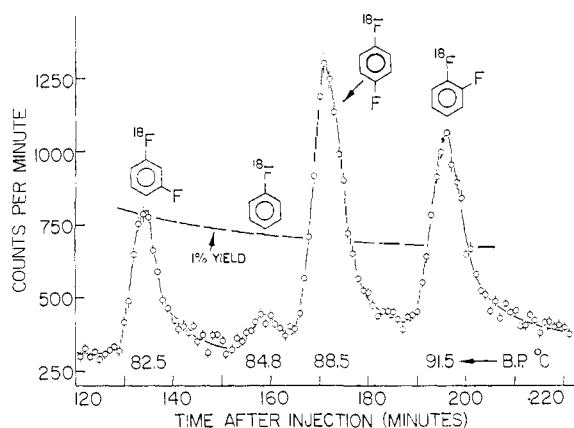
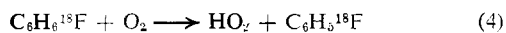


Figure 4. Radio gas chromatogram of  $^{18}F$ -labeled aromatic compounds from 80:1  $SF_6-C_6H_5F$  mixtures at 3000 Torr: ---, approximate peak height expected for 1% absolute yield.

of total pressure results in a dramatic increase in the  $C_6H_5^{18}F$  yield, as shown in Figures 1 and 3.<sup>34</sup> The continuous curve of Figure 3 represents the yield of  $C_6H_5^{18}F$  expected for direct competition for  $C_6H_6^{18}F$  radicals between  $O_2$  and benzene (or some species with concentration proportional to benzene), with relative rates of  $k_{O_2}/k_{PhH} = 3.7$  at 3000 Torr and 1.3 at 500 Torr. The nature of the reactions of  $C_6H_6^{18}F$  with  $C_6H_6$  is not experimentally known.

A possible mechanism for the formation of excess  $C_6H_5^{18}F$  in  $O_2$ -scavenged  $SF_6$ -benzene mixtures is the direct reaction of thermalized  $C_6H_6^{18}F$  with  $O_2$ , as shown in (4). However, this mechanism does not account for the differing values of the ratio  $k_{O_2}/k_{PhH}$  at 500 and 3000 Torr. Alternatively, the reaction between  $C_6H_6^{18}F$  and  $O_2$  might lead to an intermediate peroxy radical  $C_6H_6^{18}FO_2$ , whose subsequent unimolecular decomposi-



tion by  $HO_2$  loss would leave the observed  $C_6H_5^{18}F$  product in amounts varying with pressure. The presence of carrier  $C_6H_5F$  in one experiment had no effect on the yield of  $C_6H_5^{18}F$ , suggesting the absence of any unexpected trace level reactions affecting the  $C_6H_5^{18}F$  yield.

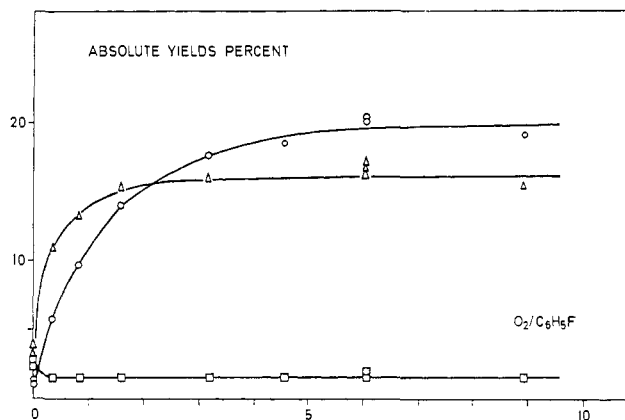


Figure 5. Effect of  $O_2$  on yields of  $^{18}F$ -labeled compounds from 80:1  $SF_6-C_6H_5F$  mixtures at 3000 Torr.  $C_6H_4F^{18}$  yields:  $\Delta$ , para;  $\circ$ , meta;  $\square$ , ortho.

These data do not conclusively eliminate the possible involvement of  $^{18}FO_2$  radicals formed by direct reaction of  $^{18}F$  with  $O_2$ . However, comparable experiments with  $SF_6-C_2H_4-O_2$  mixtures<sup>13</sup> demonstrate (a) no enhancement of  $C_2H_3^{18}F$  yields by  $O_2$  and (b) no removal of  $^{18}F$  from the system by reaction with  $O_2$ . Since  $FO_2$  radicals are known to exist (in low-temperature matrices),<sup>35</sup> the lack of observed  $^{18}F + O_2$  reaction in these gas phase experiments presumably reflects the rapid reverse decomposition without stabilization of any  $^{18}FO_2$  radicals temporarily formed. We therefore conclude that atomic  $^{18}F$ , and not  $^{18}FO_2$ , is the species reacting with benzene in these  $O_2$ -scavenged systems.

**$^{18}F$  Reactions with Fluorobenzene.** Four  $^{18}F$ -containing organic products were observed from the reactions of thermal  $^{18}F$  atoms with fluorobenzene in the absence of scavenger. The assay of these radioactive products is illustrated in Figure 4 for an 87:1  $SF_6-C_6H_5F$  mixture at 3000 Torr of total pressure. When corrected for the decay of  $^{18}F$  during chromatography, the difluorobenzene yields (*para*, 3.4%; *meta*, 1.1%; *ortho*, 2.6%) do not correspond to a 1:2:2 statistical pattern. Replacement of F by  $^{18}F$  is always much less probable than any of the  $^{18}F$  for H replacements, with yields of  $\leq 0.3\%$  with, and without,  $O_2$  present. Yields in the 0.1% range can be found for hot substitution reactions with mixtures in the 50:1 to 100:1 range.

The effect of molecular oxygen on the observed yields is different for each of the difluorobenzenes as illustrated in Figure 5.<sup>34</sup> While both *p*- and *m*- $C_6H_4F^{18}$  yields are substantially enhanced by  $O_2$  (although not parallel in dependence on it), the yield of the *ortho* molecule is depressed by the inclusion of  $O_2$ . This "negative *ortho*" effect has also been observed with *m*- $C_6H_4F_2$  as substrate as described below. Since the precursor difluorocyclohexadienyl radicals do not always lead to the difluorobenzenes, as shown by the wide variations in *ortho*-*meta*-*para* yields and in the ratios of these yields, we cannot draw any firm conclusions from our data about the relative probability of initial  $^{18}F$  attack on the various positions in fluorobenzene.

(35) V. I. Vedenev, Yu. M. Gershenson, A. P. Dement'ev, A. B. Nalbandyan, and O. M. Sarkisov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1438 (1970).

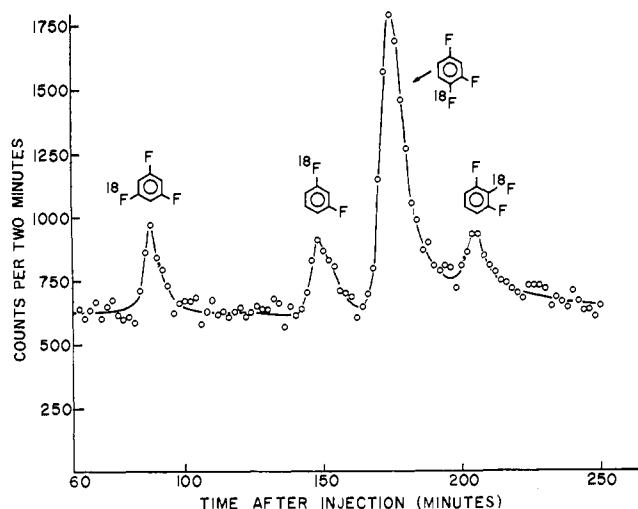


Figure 6. Radio gas chromatogram of  $^{18}\text{F}$ -labeled products from 60:1  $\text{SF}_6$ - $m$ - $\text{C}_6\text{H}_4\text{F}_2$  mixtures at 3000 Torr.

$^{18}\text{F}$  Reaction with  $m$ -Difluorobenzene. Four  $^{18}\text{F}$ -containing organic products were again observed from the reactions of thermal  $^{18}\text{F}$  atoms with  $m$ -difluorobenzene in the absence of scavenger, as illustrated in Figure 6. The products have been identified as the  $^{18}\text{F}$  for F and the three possible  $^{18}\text{F}$  for H products. The effect of including  $\text{O}_2$  during irradiation is shown in Table II. Attack on 1,3-difluorobenzene at the 2 posi-

Table II. Absolute Yields from Thermal  $^{18}\text{F}$  Reactions with  $m$ -Difluorobenzene in  $\text{SF}_6$ - $\text{C}_6\text{H}_4\text{F}_2$ - $\text{O}_2$  Gaseous Mixtures

Composition, Torr	$\text{SF}_6$	$m$ - $\text{C}_6\text{H}_4\text{F}_2$	$\text{O}_2$	Absolute yields, % <sup>a</sup>			
				1,3,5-	1,2,4-	1,2,3-	$m$ - $\text{C}_6\text{H}_4\text{F}^{18}\text{F}$
2968	59	0	0	0.38	2.7	0.48	0.52
2636	53	322	322	8.9	1.9	0.14	0.17
			Ratio $\text{O}_2$ /unscavenged	24	0.7	0.3	0.3

<sup>a</sup> P/S ratios used for calculation (see text) = 6.57 for 1,2,4- $\text{C}_6\text{H}_3\text{F}_2^{18}\text{F}$ , 1,2,3- $\text{C}_6\text{H}_3\text{F}_2^{18}\text{F}$ , and  $m$ - $\text{C}_6\text{H}_4\text{F}^{18}\text{F}$  and 5.62 for 1,3,5- $\text{C}_6\text{H}_3\text{F}_2^{18}\text{F}$ .

tion is ortho to both fluorine substituents, and the reduction in yield with  $\text{O}_2$  is the greatest for this molecule. Attack at either the 4 or 6 positions to form 1,2,4-trifluorobenzene is ortho to one F atom and again is suppressed by the presence of  $\text{O}_2$ . Attack at the 5 position is not ortho to either substituent F position, and  $\text{O}_2$  causes a striking increase in the yield of  $^{18}\text{F}$ -labeled 1,3,5-trifluorobenzene over the yield in the unscavenged system.

$^{18}\text{F}$  Reactions with Trifluoromethylbenzene. Thermal  $^{18}\text{F}$  atoms react with trifluoromethylbenzene to form three major products, the isomeric trifluoromethylfluorobenzenes, as shown in Figure 7. The yield from the  $^{18}\text{F}$ -F reaction in the  $\text{CF}_3$  group is very small and probably originates from hot  $^{18}\text{F}$  atom reactions. In this case, the addition of  $\text{O}_2$  enhances the yields of all three of the isomeric  $\text{CF}_3\text{C}_6\text{H}_4^{18}\text{F}$  molecules, as shown in Figure 8.<sup>34</sup>

The total yield of the three isomeric  $\text{CF}_3\text{C}_6\text{H}_4^{18}\text{F}$  molecules in high  $\text{O}_2$  is about 38%, and no "negative ortho" effect is found for  $\text{CF}_3$  as a substituent.

**Competitive Reactions of  $^{18}\text{F}$  with  $\text{C}_2\text{H}_2$  and Benzene.** The relative reactivities of  $\text{C}_2\text{H}_2$  and  $\text{C}_2\text{H}_4$  toward

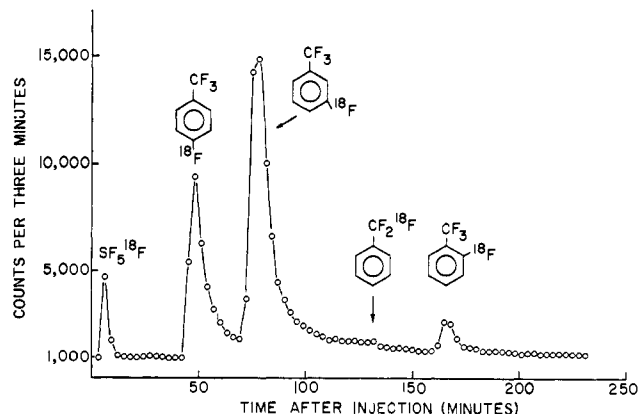


Figure 7. Radio gas chromatogram of  $^{18}\text{F}$ -labeled products from 300:1:0.5  $\text{SF}_6$ - $\text{CF}_3\text{C}_6\text{H}_5$ - $\text{O}_2$  mixtures at 3000 Torr total pressure.

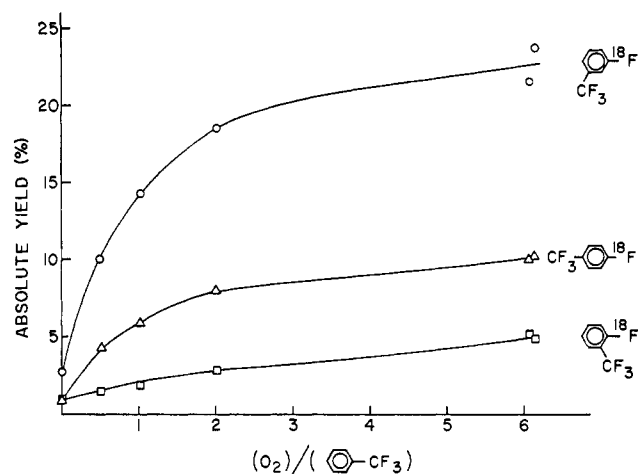


Figure 8. Enhancement of yields of  $\text{CF}_3\text{C}_6\text{H}_4^{18}\text{F}$  molecules by presence of  $\text{O}_2$  in 300:1  $\text{SF}_6$ - $\text{CF}_3\text{C}_6\text{H}_5$  mixtures at 3000 Torr.  $\text{CF}_3\text{C}_6\text{H}_4^{18}\text{F}$  yields:  $\Delta$ , para;  $\circ$ , meta;  $\square$ , ortho.

thermal  $^{18}\text{F}$  atoms have been measured in direct competition to be in the ratio 1.0:0.83.<sup>13</sup> We have also measured the relative reactivities of  $\text{C}_2\text{H}_2$  and  $\text{C}_6\text{H}_6$  by including both as substrates in excess  $\text{SF}_6$ . Activity as  $\text{C}_2\text{H}_3^{18}\text{F}$  in an HI-scavenged 1:1 mixture is reduced to about 28% from the 80% typical of  $\text{C}_2\text{H}_2 + \text{HI}$  alone, which suggests that benzene is  $1.5 \pm 0.5$  as reactive as acetylene in removing thermal  $^{18}\text{F}$  atoms. The  $\text{C}_2\text{H}_2$  reaction is in turn calibrated *vs.* abstraction by  $^{18}\text{F}$  of H from  $\text{CH}_4$  ( $\text{C}_2\text{H}_2/\text{CH}_4 = 1.0:0.41$ ),<sup>11</sup> a reaction shown by direct kinetic measurements in a flow stream to have a reaction efficiency such that only 2-5 collisions with  $\text{CH}_4$  are required for reaction.<sup>36</sup> All three of these  $\pi$ -bond additions are thus very reactive, with collision efficiencies greater than 1 in 10.

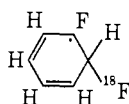
**Directional Effects with Substituted Benzenes.** Intramolecular experiments with olefinic molecules have shown that the directional effects are relatively small for thermal  $^{18}\text{F}$  atoms: the terminal/central attack ratio is about 1.35 for  $\text{CH}_3\text{CH}=\text{CH}_2$ ,<sup>9</sup> 1.0 for  $\text{CH}_2=\text{C}=\text{CH}_2$ ,<sup>37</sup> and attack on the  $\text{CH}_2$  end is favored by about a factor of 5 over the  $\text{CF}_2$  end in  $\text{CH}_2=\text{CF}_2$ .<sup>7</sup> As in-

(36) H. G. Wagner, J. Warnatz, and C. Zetzch, *An. Assoc. Quim. Argent.*, **59**, 169 (1971).

(37) R. S. Iyer, R. L. Williams, and F. S. Rowland, Abstracts of 7th International Symposium on Fluorine Chemistry, Santa Cruz, California, July, 1973.

licated above,  $^{18}\text{F}$  atoms react about equally well with  $\text{C}_2\text{H}_2$ ,  $\text{C}_2\text{H}_4$ , and  $\text{C}_6\text{H}_6$  and hence do not exhibit very strong intermolecular selectivity either.

We do not believe that our present data permit us to draw any strong conclusions about the intramolecular selectivity of attack by  $^{18}\text{F}$  on substituted aromatic compounds. Our interpretation of our experiments is that most of the thermal  $^{18}\text{F}$  atoms react by addition to the aromatic ring in each of these systems to form a substituted cyclohexadienyl radical. In the absence of  $\text{O}_2$ , most of these radicals probably react with another aromatic substrate molecule or a radical present in the system, and we do not observe the resulting dimeric (or polymeric) product. In the presence of  $\text{O}_2$ , some of these radicals are able to react with it to release  $\text{HO}_2$ , leaving an enhanced yield of the corresponding fluoroaromatic product. However, we have no means for confirming that *all* of the particular fluorocyclohexadienyl radicals lose  $\text{HO}_2$  in reaction with  $\text{O}_2$ ; in particular, it seems quite probable that, for example, the radical



after initially being formed by ortho addition of  $^{18}\text{F}$  to  $\text{C}_6\text{H}_5\text{F}$  does not undergo a reaction with  $\text{O}_2$  which leads to the release of  $\text{HO}_2$ . (The "ortho" effect may involve conjugative interaction of the nonbonding electrons of F atom substituents with the aromatic ring, with resulting deactivation of an unpaired ring electron at the F substituent position. There can be no conjugative interaction of this type for  $\text{CF}_3$  as a substituent, and an  $\text{O}_2$ -induced yield reduction for the ortho substitution product is not observed in the  $\text{CF}_3\text{C}_6\text{H}_5$  system.)

Determination of the relative rates of  $^{18}\text{F}$  attack on various aromatic positions will require total determina-

tion of all organic products, including dimers and polymers, for several systems. Since isomeric dimers may be present, the problem is quite complex, especially when the available analysis time is severely limited by the 110 minute half-life of  $^{18}\text{F}$ .

**Absolute Yields from  $^{18}\text{F}$  Reactions in Aromatic Systems.** The 60% yield found for  $\text{C}_6\text{H}_5^{18}\text{F}$  accounts for the major fraction of the  $^{18}\text{F}$  formed in this system. The yield for abstraction of H from  $\text{C}_6\text{H}_6$  may account for much of the remaining  $^{18}\text{F}$  activity, as is postulated to be the case for  $\text{C}_2\text{H}_4$  from which a 60% yield of addition products is found.

In the other systems, a lesser total yield of  $^{18}\text{F}$ -labeled aromatics has been observed, and the activity not accounted for is in the majority. Since it is doubtful that the abstractability of H from different aromatic positions varies too widely, much of the additional "missing" activity in reactions of  $^{18}\text{F}$  with the substituted aromatics probably could be found as dimeric or polymeric products, and not as  $\text{H}^{18}\text{F}$ .

When high yields of carrier-free  $^{18}\text{F}$ -labeled products can be directly obtained *in situ* with the addition of  $\text{O}_2$ , the procedure becomes of potential interest for rapid synthesis of particular compounds, either for immediate use or as precursors for further synthetic reactions.<sup>29</sup> The 60% yield of  $\text{C}_6\text{H}_5^{18}\text{F}$  indicates that direct synthesis of some useful labeled aromatic molecules by thermal  $^{18}\text{F}$  atom addition may be feasible and suggests additional experiments with other types of ring compounds.

**Supplementary Material Available.** Tables III-VI (numerical values for the points illustrated in Figures 2, 3, 5, and 8) will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JACS-74-6579.