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# TRIFLUOROACETOXYLATION OF BENZENE DERIVATIVES WITH LEAD TETRAKISTRIFLUOROACETATE (LTTFA) IN TRIFLUOROACETIC ACID (TFA)

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The literature contains only limited data[1-3] concerning reactions of LTTFA with organic substrates and under the reported conditions its reactions with benzene derivatives follow a complex course[1,3]. However, by analogy with our ideas concerning the Wessely acetoxylation[4], we believed that in polar media the reactions of LTTFA with aromatic substrates could proceed by an electrophilic substitution mechanism and thus afford a convenient method for direct introduction of the oxygen function into aromatic nuclei. Further, due to the electron withdrawing effect of the trifluoroacetoxy group[5], it appeared possible that trifluoroacetoxylation with LTTFA should not proceed beyond monosubstitution, thus increasing its potential synthetic utility.

LTTFA, prepared by the method described by Partch[1], was used as an approximately 0.3 molar solution in TFA in an equimolar ratio to the aromatic substrate. Either the reagent was added to the neat substrate at 0° or a solution of the substrate in TFA was added to the reagent at 0°. Generally, the reaction mixture was allowed to stand at 0°C for 20 minutes and work up was accomplished by adding pentane and washing the organic layer with ice cold water. Product analysis was carried out by a combination of GLC and NMR methods. The results summarized in table 1 refer to runs performed by both methods of addition and the ranges quoted thus span some systematic differences as well as experimental uncertainties.

The following observations support our hypothesis that the reactions of benzene derivatives with LTTFA in TFA proceed primarily, if not exclusively, by an electrophilic substitution mechanism:

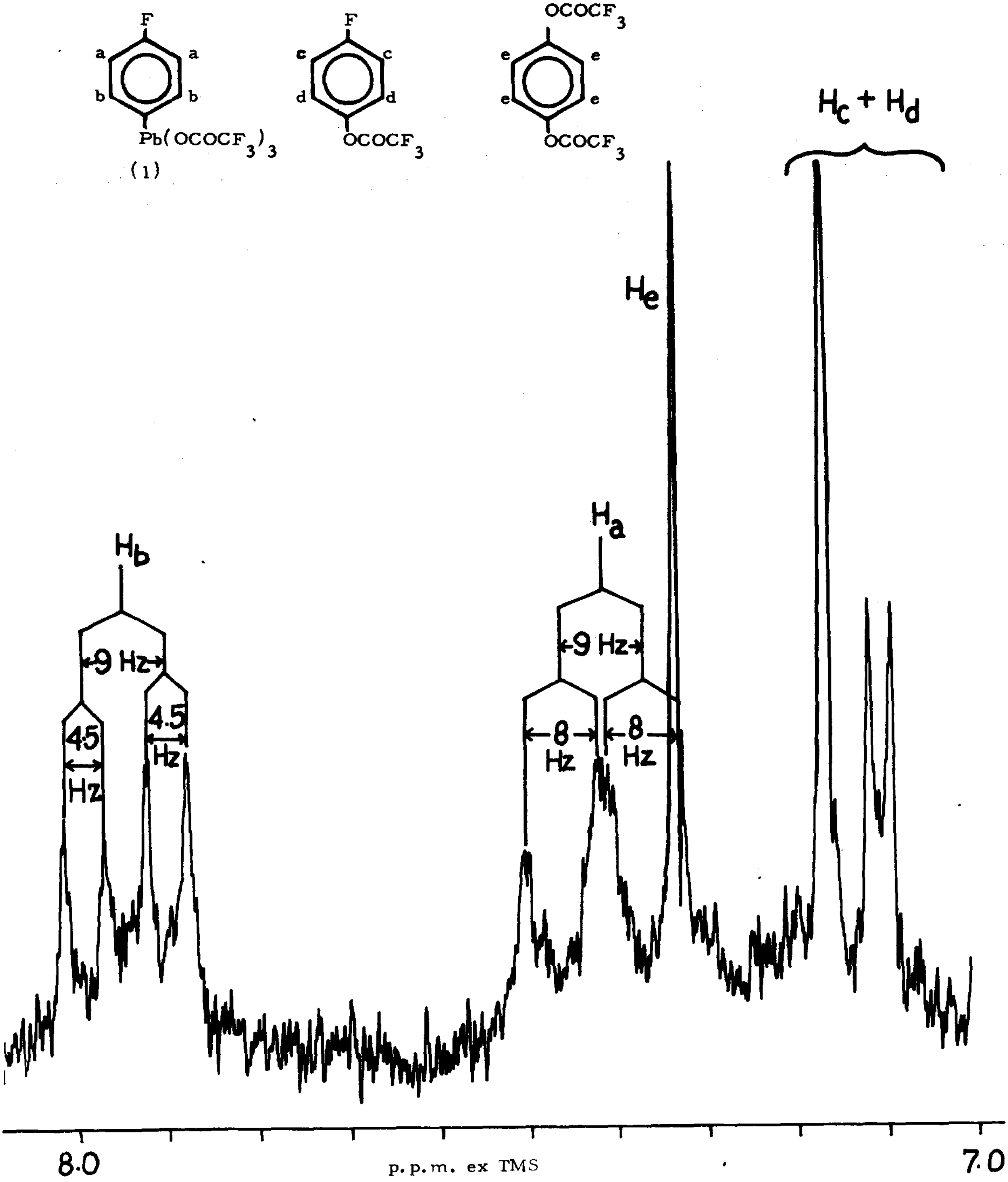
(i) The substitution pattern is characteristic of SE reactions (Table 1). (ii) The appearance of dealkylated products, together with the corresponding alkyl trifluoroacetates when cumene or tert. butylbenzene were used as substrates (Table 1) is best explained in terms of cationic intermediates. (iii) The pattern of reactivity of substrates towards LTTFA is that expected for SE reactions. Thus, of the reactions listed in table 1, those of alkylbenzenes were faster than those of halobenzenes, while nitrobenzene failed to react after two weeks at room temperature and anisole reacted too violently to allow us to obtain reliable data. We have also carried out a quantitative comparison of the reaction rates of toluene and benzene with LTTFA in TFA and found that both the partial rate factors and the selectivity factors are characteristic of aromatic electrophilic substitution, the latter being between the values for nitration and bromination[6].

TABLE 1: Product distribution (mole %) from the reaction of LTTFA with monosubstituted benzenes (PhX)

| X | $C_6H_4X(OH)$ + $C_6H_4X(OCOCF_3)$ | | | PhX | Other | Total accounted for |
|---|---|---|---|---|---|---|
| | ortho | meta | para | | | |
| H | 76.4 - 78.6 | | | 6.3-7.3 | - | 83.7-84.9 |
| Me | 11.2-18.5 | 1.8-4.2 | 40.0-51.0 | 13.6-18.5 | $PhCH_2OCOCF_3$ 0.2-3.3 | 73.0-83.0 |
| Et | 11.8-20.2 | 1.8-5.0 | 42.7-54.5 | 9.0-22.2 | - | 78.5-84.4 |
| $CHMe_2$ | 5.0-8.9 | 1.7-2.2 | 42.4-63.0 | 3.8-17.9 | $PhOCOCF_3$ 4.0-8.0<br>$CHMe_2OCOCF_3$ 8.4 | 75.2-92.0 |
| $CMe_3$ | 2.0-5.4 | 3.1-3.7 | 60.9-66.9 | 7.6-9.3 | $PhOCOCF_3$ 7.5-10.2<br>$CMe_3OCOCF_3$ 8.1 | 85.9-89.6 |
| F | 6.7 | | 62.3 | 23.1 | p-$C_6H_4(OCOCF_3)_2$ ca 6 | ≥90 |
| Cl | 1.4-5.3 | ≤1 | 68-70 | 4.0-4.4 | - | 76.4-77.5 |
| Br | 4.6-10.5 | 0.6-1.0 | 40.6-48.5 | 14.4-16.5 | - | 62.3-76.5 |

The site of electrophilic reactivity in LTTFA is most likely to be either oxygen or lead and for the possibly analogous reactions with activated aromatic substrates, Norman[3,7] has produced evidence of lead tetracarboxylates acting as ambident electrophiles. We have obtained direct evidence that, at least for the formation of para-trifluoroacetoxy derivatives of fluoro, chloro and bromobenzene, the initial attack gives a transient intermediate which

Fig. 1


F
a
b
Pb(OCOCF$_3$)$_3$
(1)
F
c
d
OCOCF$_3$
OCOCF$_3$
e
OCOCF$_3$
$H_c + H_d$
$H_e$
$H_a$
9 Hz
8 Hz
8 Hz
$H_b$
9 Hz
4.5 Hz
4.5 Hz
8.0
p.p.m. ex TMS
7.0

rearranges to the final product. Figure 1 shows the 100 MHz NMR spectrum of a 0.3 molar solution of fluorobenzene and LTTFA (0.3 molar) in TFA after a few minutes at room temperature. Direct comparison with authentic samples permitted us to identify the signals due to the major final product (p-fluorotrifluoroacetoxybenzene) and a by-product, (p-bis-trifluoroacetoxybenzene) while remaining signals can be rationalized in terms of a *para* substituted fluorobenzene. On standing the latter signals were observed to decrease in intensity with a corresponding increase in the signals due to p-fluorotrifluoroacetoxybenzene and the process can be completed by mild heating for five minutes. We believe that the transient intermediate is the lead-containing compound (1) shown in Fig. 1. Exactly analogous results were also obtained for reactions with chlorobenzene and bromobenzene.

## ACKNOWLEDGMENTS

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