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GAS PHASE ISOPROPYLATION OF AROMATIC HYDROCARBONS. FLUORINE AND METHYL SUBSTITUENT EFFECTS ON REACTIVITY AND ORIENTATION.

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Abstract: The isopropylation of substituted benzenes by $\underline{s}$-$C_3H_7^+$ cations is studied to evaluate the directive effects of fluorine, methyl group and their combinations as ring substituents in the gas-phase aromatic substitution.

In recent years, application of radiolytic techniques[1] to the investigation of gas-phase ionic reactions allowed **the study of** alkylation of aromatic substrates by free and structurally well defined carbenium ions, in the absence of any counterions and solvation phenomena. Furthermore, in this approach, the isomeric composition of products, and hence the directive effects of substituents, can be measured by using traditional solution chemistry methods, including the isolation and analysis of the neutral end products.

The present preliminary results illustrate the reactivity and selectivity of the attack by gaseous $\underline{s}$-$C_3H_7^+$ cations on the isomeric fluorinated benzenes and toluenes, as apparent from the relative yields of isopropylated products, in competitive reactions with benzene.

The gaseous systems, enclosed in sealed pyrex bulbs, contained propane as the bulk constituent (720 torr), together with traces of the aromatic substrate(s) (ca 1 torr) and a few torr of O_2, employed as a thermal radical scavenger. They were irradiated in a ^{60}Co 220- Gammacell from Nuclear Canada Ltd., at 30°C and to a total dose of 2.0 Mrad, delivered at 0.5 Mrad hour^{-1}. The reaction mixtures were then extracted with methanol and analyzed by glc using: i)a 20 ft x 1/8 in o.d. glass column, filled with 10% SP-1000 on Supelcoport and operated from 65 to 130°C; ii)a 12m Carbowax 20 M fused silica capillary column, operated at 40°c; iii)a 150ft x 0.01in Ucon LB-550-X stainless steel capillary column, operated at 120°C. The products were identified by comparison of their retention volumes, on at least two different columns, with those of authentic samples and their identity was further checked by GC-MS, using a VG -Micromass mod. ZAB-2f mass spectrometer.

The results obtained from the isopropylation of fluorobenzene, toluene, isomeric fluorotoluenes and difluorobenzenes, in competitive reactions with benzene, are summarized in Table I. Control runs were carried out to verify the independence of the **relative** products yields over a tenfold variation of the radiation dose.

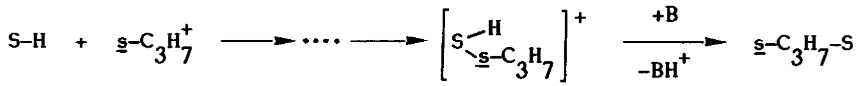
TABLE I. Gas-phase electrophilic aromatic isopropylation of fluoroarenes.

System composition (torr)[a]		$k_{SH}/k_{C_6H_6}$	**Isomeric composition of isopropylated products (%)**[b]
Substrate (SH)	C_6H_6		
Fluorobenzene, 1.1			(2),86.1;(3), 4.5;(4), 9.4
Fluorobenzene, 1.2	1.1	1.4	(2),86.1;(3), 4.5;(4), 9.4
Toluene, 1.1	1.2	0.8	(2),54.2;(3),28.5;(4),17.3
2-Fluorotoluene, 1.5	1.5	1.0	(3),68.7;(5),18.5;(6),12.2;(4),0.6
3-Fluorotoluene, 1.0	1.1	1.2	(4),47.3;(2),40.6;(6),11.3;(5),0.7
4-Fluorotoluene, 1.3	1.6	1.1	(3),86.3;(2),13.7
1,2-Difluorobenzene, 1.0	0.8	1.0	(3),82.0;(4),18.0
1,3-Difluorobenzene, 1.0	0.9	0.4	(2),45.0;(4),55.0
1,4-Difluorobenzene, 0.9	0.6	0.4	(2),100

[a] All systems contained 720 torr C_3H_8 and 10 torr O_2. [b] Ring positions bearing the isopropyl group in parentheses. Standard deviation of data ca 10%.

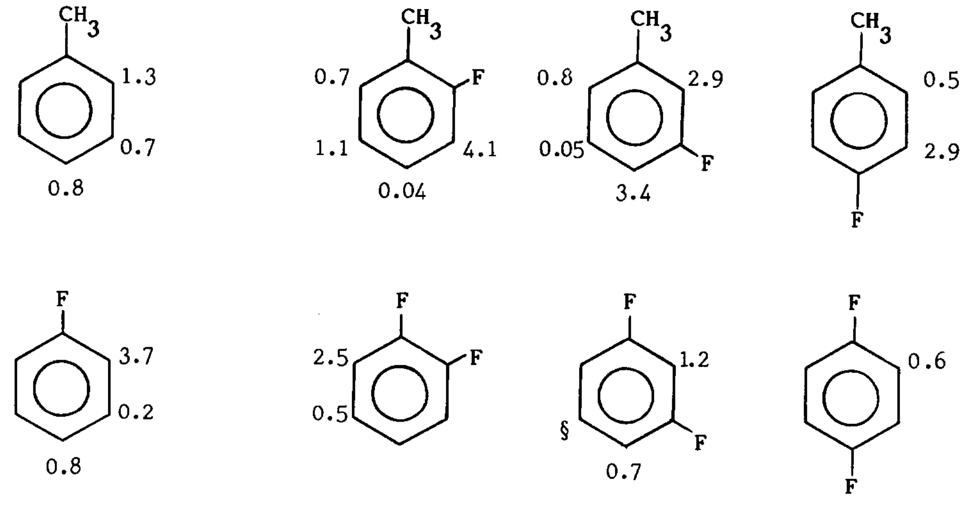
The presence of oxygen in the irradiated systems, as a radical scavenger, allows to rule out any contribution of radical reactions to the formation of the observed products. This can be traced, on the contrary, to purely ionic pathways, as definitely shown by the sharp decrease of the alkylated products yields that were observed in systems containing a good carbenium ion interceptor like ammonia, in addition to the other gaseous components.[2]

The isopropyl cations are by far the major ionic species from the radiolysis of propane, formed either directly or following hydride-ion abstraction by the primary carbenium ions from the parent hydrocarbon.[3] The large excess of C_3H_8 furthermore ensures complete collisional thermalization of the ionic reagent before interaction with the substrate molecules. The isopropylated aromatic products are therefore originated from the attack of s-$C_3H_7^+$ cations on the substrates , which leads to formation of substituted arenium ions. These eventually lose a proton either to a base added to the system (NH_3) or to another substrate molecule.



Anyhow, since both the isomeric composition of products and the relative alkylation rates, measured in competitive runs, were not appreciably affected by the concentration of the base, the deprotonation step is not rate limiting in the case of the present substrates. The results show exceedingly high substitution ortho to fluorine, confirming the earlier suggestion that the free gaseous electrophile selectively interacts with the n-donor substituent, prior to rearranging to the arenium ion.[4,5] In addition, the data allow to evaluate, in the gas-phase isopropylation, the combined directive effects of two fluorine atoms, and of fluorine and the methyl group, as illustrated in Table II.

TABLE II. Partial rate factors in gas-phase isopropylation.



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§ Below detection limit.

A word of caution seems appropriate before discussing the present results. In fact, the proton affinity values of the substrates are all slightly above that of propene,[6,7] the conjugated base of isopropyl cations. This makes thermochemically permissible a proton transfer process, which would be competitive with alkylation and not directly detectable under the experimental conditions employed, i.e.:

$$s\text{-}C_3H_7^+ \quad + \quad SH \longrightarrow C_3H_6 \quad + \quad SH_2^+$$

However, were this reaction to appreciably affect the reactivity order of the substrates in the alkylation, it would favor the difluorobenzenes over fluorobenzene, in view of the higher proton affinity of the latter,[8] and p-$C_6H_4F_2$ over o-$C_6H_4F_2$, which is in contrast with the experimental evidence. Furthermore, the bulk gas, employed in the present experiments at relatively high pressure (720 Torr) and acting as an effective thermal bath, is expected to favor the collapse of the adduct between the electrophile and the substrate to an addition intermediate, rather than its unimolecular decomposition into propene and the protonated haloarene.

The partial rate factors reported are therefore likely to represent the correct reactivity order of the ring positions in the substrates investigated, and, being measured in the dilute gas state, to reflect the true electronic effects of the substituents, independently of solvent interactions. Comparison of the data from toluene and fluorobenzene with those of disubstituted benzenes shows that the substituents effects do not fit the "additivity principle".[9] The ring position meta to a fluorine substituent appears strongly deactivated. An interesting exception is provided by the position 3 of o-$C_6H_4F_2$, whose high reactivity cannot be justified by π-donation and coordination of the electrophile by the second F atom alone, which can both take place in the para isomer as well. A possible explanation may be sought i) in a peculiar interaction of the electrophile with the two ortho fluorine atoms, that, preceding the rearrangement to the Wheland intermediate, perturbs the electronic effects of the substituents on the ring, and ii) in a more efficient capture of the reagent by the substrate, owing to its high dipole moment. Further investigation is required to substantiate these points.

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