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GAS-SOLID REACTIONS OF METHYLAMINE WITH POLYFLUORINATED AROMATIC COMPOUNDS[1]

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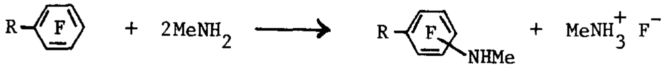
Gas-solid reactions have received increasing attention for the stereochemical control they can exert over a reaction. Some examples are an asymmetric synthesis in a single crystal which is optically active[2], and the dehydrohalogenation of solid meso-dihaloadipates to form only trans, trans dienes.[3] In these reactions the stereochemistry of the products is dependent upon the conformation of the reactants in the solid.

Polyfluorinated aromatic compounds are usually very susceptible to substitution of aromatic fluorine by different nucleophiles.[4] It was of interest to determine if crystalline fluoroaromatic compounds would retain their high solution reactivity in a solid-gas reaction with gaseous nucleophiles and whether the substitution patterns would change in a solid-state reaction. Thus, the solid-gas reactions of some pentafluorobenzene derivatives with methylamine were examined with these points in mind. The results of these reactions are given in the Table and discussed below.

F-Biphenyl, **1**, reacts very rapidly with $MeNH_2$ in benzene solution. The predominant product is 4,4'-bis(N-methylamino)-F-biphenyl and the intermediate product is 4-N-methylamino-F-biphenyl. The reaction of powdered single crystals leads to rapid formation of the disubstituted product. The reaction is accompanied by extensive liquid phase (melt) formation between the reactants and products and an extensive amount of the reaction occurs in this liquid phase. Attempts to eliminate this melt formation by reducing the amount of $MeNH_2$ present in the reaction vessel were unsuccessful.

Diphenyl-F-phenylphosphine, **2**, shows solution and solid-gas reactivities similar to **1**, also melt formation occurs during the solid-gas reaction. This was eliminated, however, by raising the reaction temperature to 55°C and by using less than a stoichiometric amount of $MeNH_2$. But, the rate becomes very slow with ca. 1/2% yield after five days. (Melt formation is indicative of reaction and is a eutectic mixture of reactant, products, and $MeNH_2$. Exposure of the powdered organic products from **1**, **2**, or **3** to excess $MeNH_2$ did not

Table



R	Cmpd No.	mp, °C	Reaction Conditions[a]		Product Yield[b]	
			Solution	Solid-Gas[c]	Solution	Solid-gas
C_6F_5-	**1**	69-70	C_6H_6,r.t. 24 hr	r.t.,20 hr	30% para 70% di-sub.	95% di-sub.
Ph_2P-	**2**	68-70[d]	EtOH,reflux, 3 d.	r.t.,3 d.	> 95% para	> 95% para
$Ph_2P(O)$-	**3**	122-4[e]	C_6H_6,50°, 24 hr	55°,2 d.	93% ortho[f] 7% para	≤ 2% ortho ≥ 98% para
			-	55°,7 d.[g]	-	ca. 5% para[h]
Ph-	**4**	110-2[i]	EtOH,reflux, 10 d.	r.t.,10 d.	> 95% para	No Reaction
C_6F_5-/Ph-Ph[j]	**5**	115-7	-	r.t.,3 d.	-	< 5% total

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a. all reactions used excess amine unless indicated; b. the structures of new products were confirmed by ^{19}F NMR and mass spectral analysis; c. reactions were between powdered single crystals and dry $MeNH_2$, the reaction vessel was flushed with dry N_2 prior to the introduction of the $MeNH_2$; d. Ref. 5; e. Ref. 6; f. these values compare favorably with the ratio of 88/12 reported in Ref. 6; g. reaction stoichiometry: 2:1 - fluoroaromatic: $MeNH_2$; h. the ortho isomer was not detected; i. Ref. 7; j. a 1:1 crystalline, molecular complex between F-biphenyl and biphenyl

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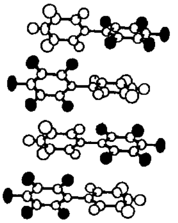
lead to the formation of a liquid phase. The by-product of the reaction, $MeNH_3^+ F^-$, apparently dissociates and escapes from either the melt or solid phase as gaseous $MeNH_2$ and HF. This was suggested by elemental analysis of reaction mixtures after excess $MeNH_2$ had been removed.)

The reactions of diphenyl-F-phenylphosphine oxide, **3**, are especially intriguing. As shown in the Table, a substantial amount of _ortho_ substitution occurs when the reaction is performed in benzene. Switching to a hydrogen-bonding solvent (EtOH) causes the _para_ isomer to be favored (≥95% para).[6] Two reasonable explanations have been proposed to account for the unusually large amount of _ortho_ substitution: hydrogen-bond formation between the amine and the oxygen of **3**[9]; and internal-solvation which energetically favors attack at the _ortho_ position.[10] (There are a number of normally _para_-directing substituents which lead to predominant _ortho_ substitution under certain conditions: nitro[9]; nitroso[11]; carboxyl[12]; and formyl[13].) The reaction of **3** with excess $MeNH_2$ results in the formation of a melt but the predominant product is now the _para_ isomer. This can be explained by the reaction medium being excess $MeNH_2$, which excludes hydrogen bonding. This is confirmed by solution reactions in benzene where excess $MeNH_2$ causes a decrease in the ortho/para ratio.

The exposure of powdered crystals of 3 to less than a stoichiometric amount of $MeNH_2$ at 55° prevents the formation of any liquid phase during the reaction. The reaction rate is quite slow as after one week only a 5% yield of the para product is found, the ortho isomer could not be detected by glpc analysis. X-ray powder pattern analysis reveals only diffraction from 3. Under microscopic examination powdered 3 becomes slightly opaque during the reaction and a color change from white to very light yellow occurs. Single crystals, however, remain unchanged and do not appear to react with the gas. Thus, the reaction is probably dependent upon the presence of defects in the solid which allows the gas to penetrate the crystal lattice. The predominance of the para product cannot be completely explained at present. The preliminary results of an x-ray structure determination indicate that the conformation of 3 is similar to triphenylphosphine oxide[14] and that the phosphine oxide group is shielded by neighboring molecules. Thus it may not be possible for $MeNH_2$ to approach the P=O group and yield ortho substitution.

The solution reactivity of pentafluorobiphenyl, 4, is slightly less than compounds 1 - 3. However, it is totally unreactive in the gas-solid reaction with $MeNH_2$. This total lack of solid-state reactivity appears to be related to the crystal structure of 4.[15] The molecular packing in crystalline 4 is similar to the packing found in the 1:1 crystalline complexes between F-benzene and aromatic hydrocarbons. The molecular packing is shown below, for a crystallographic R of 0.032. As can be seen in the figure, the C_6H_5 and C_6F_5 rings form columns of alternating rings. These mixed stacks are similar to those found by Dahl[16] in the crystalline complexes of F-benzene with p-xylene, mesitylene, durene, and hexamethylbenzene. The interplanar separation within the stacks in 4 is 3.43 Å, which is approximately the same as reported by Dahl (ca. 3.5 Å). The melting point of 4 is 40° higher than the melting point of 1 or biphenyl (70-71°). This increase in melting point indicates that the intermolecular interactions in 4 are similar to those in the crystalline 1:1 molecular complexes of F-benzene.



The high quality of the crystals of 4 prompted the preparation of the previously unreported biphenyl/F-biphenyl 1:1 molecular complex. Evaporation of an ether solution containing equal amounts of biphenyl and F-biphenyl led to the formation of single crystals of the 1:1 complex, 5. The crystals are colorless prisms; mp = 115-7°, Dm = 1.55 g/cc, Cc or C2/c, a = 21.99, b = 7.57, c = 12.83 Å, β = 112.3°. The crystal structure is currently being determined. [The 1:1 complex between naphthalene (mp = 81°) and F-naphthalene (mp = 88°) has been reported, mp = 131-3°.[8]] It is anticipated that the crystal structure of this complex will be similar to the structures of the F-benzene complexes.

The gas-solid reaction between $MeNH_2$ and powdered crystals of 5 is a very slow reaction. After 3 days, less than a 5% yield of substituted products can be detected by glpc. The gas-solid reactions of **4** and **5** occur without melt formation even when excess $MeNH_2$ is used. This is due to the strong intermolecular attractions between the hydrocarbon and perfluorocarbon rings which prevent the melt formation. In general, each of these gas-solid reactions (when unaccompanied by liquid phase formation) exhibit a substantial decrease in the reactivity of the pentafluorophenyl derivative compared to the solution reactions.

We are currently examining the solid-state chemistry of other pentafluorobenzene derivatives and will report these in due course.

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