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THE EFFECT OF CHARCOAL ON THE TRIFLUOROMETHYLATION OF ARYL CHLORIDES USING BURTON'S REAGENT

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The reactivity of the trifluoromethylating system copper-dibromodifluoromethane-N, N-dimethylacetamide towards aryl chlorides can be enhanced by the addition of charcoal.

The introduction of the CF_3 group into aromatic compounds can greatly affect their physiological activity and this has resulted in considerable academic and industrial interest in the development of inexpensive and convenient rates to trifluoromethylated aromatics. We have recently reported that the $Cu-CF_2Br_2$-amide solvent reaction system originally described by Burton[1] can be extended to reaction of electronically activated chloroaromatics possessing ortho groups capable of interacting with the metal although rates of reaction and product yields are sometimes rather low[2]. The mechanism of reaction of this trifluoromethylating system probably involves the species $CuCF_3$ and we have already shown that the reactivity of some Cu(I) species such as CuCN[3] and CuI[4] can be significantly enhanced by the presence of charcoal. We now wish to report our preliminary results from a study of the effect of charcoal on the reaction of Burton's reagent with some chloroaromatics. The development of efficient trifluoromethylating systems based on readily available substrates such as chloroaromatics and halofluorocarbons would clearly be very desirable.

In order to investigate the effect of charcoal, chloro-2,4-dinitrobenzene (5 mmole), copper metal (30 mmole) and dibromodifluoromethane (10 mmole) were reacted together in the presence of charcoal (1g, dried at 280°C) in N, N-dimethylacetamide (7.5 cm^3) at 100°C under nitrogen to give 87% conversion to 2,4-dinitrobenzotrifluoride after 2h. An identical experiment carried out in the absence of the charcoal gave only 21% conversion after the same period of time. Table 1 shows the effect of charcoal on the trifluoromethylation of some other activated chloroaromatics. Increasing the amount of charcoal results in a steady increase in the rates of reaction as illustrated for the model reaction of chloro-2, 4-dinitrobenzene in Figure 1 although very large amounts of charcoal can make the reactions difficult to stir efficiently.

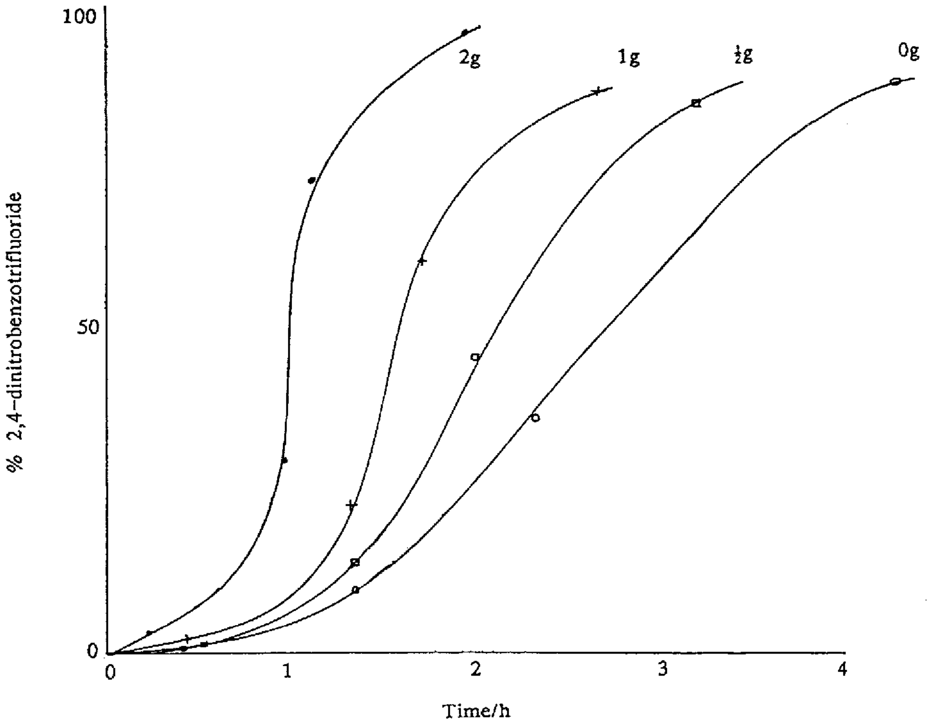
TABLE 1. Trifluoromethylation of Aryl Chlorides[a]

Substrate	Time/h	% Trifluoromethylation[b]	
		With added Charcoal (1g)	Without charcoal
Chloro-2,4-dinitrobenzene	2	87	21
2-Chloronitrobenzene	4	89	24
2,3-Dichloronitrobenzene	2	100	33
4-Chloro-3-nitrobenzotrifluoride	4	98	41
2-Chloro-5-nitropyridine	8	45[c]	35[d]

[a] Reactions were carried out as described in the text.
[b] G.c. yields; products were identified by mass-spectrometry and ^{19}F n.m.r. spectroscopy.
[c] Along with 45% perfluoroalkylpyridines, $Ar(CF_2)_nCF_3$, n = 1-3.
[d] Along with 7% perfluoroalkylpyridines.

The reaction of 2-chloro-5-nitropyridine does not show a significant increase in the rate of formation of the desired product 2-trifluoromethyl-5-nitropyridine on addition of charcoal although the rate of reaction of the substrate is significantly enhanced. The increased amount of higher perfluoroalkylated products resulting from this substrate can be attributed to the added stabilisation of $CuCF_3$ (the trifluoromethylating reagent formed in these systems) by the pyridine allowing it to react with $:CF_2$ (formed from decomposition of the CF_2Br_2[1]) to give $Cu(CF_2)_nCF_3$ species. One possible solution to this problem might be to increase the rate of the primary trifluoromethylation by offering $CuCF_3$ a more reactive substrate. In order to test this we replaced the charcoal with the supported reagent CuI-charcoal (an effective reagent for the conversion of chloro- and bromoaromatics to iodoaromatics[4]) which might convert the substrate to the more reactive 2-iodo-5-nitropyridine while hopefully maintaining the positive charcoal effect. Copper (I) iodide can also autocatalyse copper (I) nucleophilic reactions by removal of halide ion in the rate limiting step forming $CuIX^-$ as a better leaving group[5,6]. The effect of this supported reagent was to increase the yield of the desired 5-nitro-2-trifluoromethylpyridine product to 68% after 8h with very little higher perfluoroalkylation being observed. Interestingly, a blank reaction carried out with no CF_2Br_2 present gave no detectable iodinated product suggesting that the CuI was showing an autocatalytic effect.

Figure 1. Rate of Trifluoromethylation of Chloro-2, 4-dinitrobenzene in the presence of Charcoal[a]



[a]Reactions were carried out as described in the text using the indicated quantities of added dry charcoal.

We believe that the positive effect of charcoal in these reactions can be rationalised in two ways. Firstly the active but highly unstable $CuCF_3$ species can be stabilised on the support surface by a bonding interaction between a vacant 4p orbital on the copper and the electron rich aromatic π-system of the charcoal. Secondly the charcoal can effectively restrict the dimensionality of the system and thus increase the reactive species concentration. It seems clear from our results that these effects can be usefully exploited in designing trifluoromethylating systems based on $CuCF_3$.

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