Tetrahedron Letters No.47, pp. 4095-4096, 1969. Pergamon Press. Printed in Great Britain.

TRIFLUOROMETHYLATION OF AROMATIC COMPOUNDS

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(Received in Japan 4 August 1969; received in UK for publication 4 September 1969)

We wish to report on a new method to introduce CF_3 group into the desired position of the aromatic ring.

Recently, McLoughlin et al. (1) showed the way to introduce a perfluoroalkyl group possessing more than three carbon atoms into the aromatic ring by heating the perfluoroalkyl halide, the aromatic halide, and metallic copper in an aprotic solvent. However, trifluoromethyl compounds are quite different from higher perfluoroalkyl homologues in both chemical and physical characters. Namely, CF_3I is a gas at room temperature and McLoughlin's procedure of carrying out the reaction in an open vessel or a sealed glass tube is not technically applicable. Moreover, there is a considerable difference in the reactivity of C_3F_7I and CF_3I to form R_fLi- (2) and R_fMgX- (3) type compounds and, therefore, it was of great interest to investigate whether the reaction would proceed with CF_3I.

$$\mathrm{ArX} \quad + \quad \mathrm{CF_3I} \xrightarrow{\mathrm{Cu}} \mathrm{Ar{-}CF_3} \quad + \quad \mathrm{CuXI}$$

$$X = \mathrm{I,\ Br,\ Cl}$$

First, iodobenzene was heated at 130-140° with CF_3I (15 mole equiv.) in a stainless steel tube with mechanical shaking. Investigation of the reaction showed that dimethylformamide among other aprotic solvents affords benzotrifluoride in the highest yield (based on the starting material) and that, as regards metal copper, that precipitated from the aqueous solution of copper sulfate by adding zinc powder (4) gives the desired product in a better yield

(73.6%) than the commercial copper powder (treatment (5) with I_2 and acetone did not improve the yield).

Next, under the same reaction conditions, the reactions with the series of aromatic and heteroaromatic halides were carried out, the results of which are shown in Table I.

TABLE I

Starting Material	Product	Yield (%)
o-iodotoluene	o-CF_3-toluene	28
m-iodotoluene	m-CF_3-toluene	68
o-iodobenzene trifluoride	o-hexafluoroxylene	80
o-diiodobenzene	"	32
p-nitroiodobenzene	p-nitrobenzene trifluoride	51
2-chloroquinoline	2-CF_3-quinoline	10
2-iodoquinoline	"	60
3-iodoquinoline	3-CF_3-quinoline	11
4-chloroquinoline	4-CF_3-quinoline	11
6-bromoquinoline	6-CF_3-quinoline	28
1-chloroisoquinoline	1-CF_3-isoquinoline	30

This method is superior to the known methods, which substituted Cl in CCl_3 group by F or converted carboxyl group to CF_3 group by SF_4 and, consequently, involved only the modification on the carbon atom originally existing in the compound, whose application being limited. Furthermore, o-CF_3-toluene could not be obtained by the above two methods.

REFERENCES

1. V.C.R. McLoughlin and J. Thrower. U.S. Pat. 3,408,411.
2. O.R. Pierce, E.T. McBee, and G.F. Judd, J. Am. Chem. Soc., 74, 474 (1954).
3. R.N. Haszeldine, J. Chem. Soc., 1954, 1273.
4. R.Q. Brewster and T. Groening, Org. Syn. Coll. Vol, 2, 446 (1943).
5. R.C. Fuson and E.A. Cleveland, Org. Syn. Coll. Vol, 3, 339 (1955).