CHEMISTRY LETTERS, pp. 1719-1720, 1981.

A CONVENIENT TRIFLUOROMETHYLATION OF AROMATIC HALIDES WITH SODIUM TRIFLUOROACETATE

Kiyohide MATSUI, Etsuko TOBITA, Midori ANDO, and Kiyosi KONDO
Sagami Chemical Research Center
Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229

Regiospecific trifluoromethylation by substitution of the halogen in aromatic halides was achieved by the use of sodium trifluoroacetate and copper(I) iodide. The reaction proceeded smoothly in dipolar aprotic solvents in good to high yields.

A number of trifluoromethyl-substituted aromatic compounds have been known to be physiologically active. It is essential to exist trifluoromethyl group at specific position on aromatic ring for the aimed activity. The known methods to introduce a trifluoromethyl group into the desired position, however, possess some serious disadvantages, e.g., use of highly toxic or expensive reagents and/or vigorous reaction conditions.[1] Recently, Yagupolskii et al. reported a novel method using bis(trifluoromethyl)mercury instead of gaseous trifluoroiodomethane.[2] The use of toxic mercury, however, strongly diminished the synthetic utility of the method.

This paper presents a convenient trifluoromethylation of aromatic halides with easily available sodium trifluoroacetate in the presence of copper(I) iodide. The reaction was exemplified by the following: A mixture of iodobenzene (Ia) (5 mmol), sodium trifluoroacetate (20 mmol), and copper(I) iodide (10 mmol) in N-methylpyrrolidone (NMP) (40 ml) was heated under argon atmosphere. Evolution of CO_2 began at around 140°C. After 4 h stirring at 160°C, work-up of the resulting mixture afforded (trifluoromethyl)benzene (IIa) in 72% yield (GLC).[3] The reaction can be carried out in glass apparatus under normal pressure. Table I shows some other examples which reveal the regiospecificity of the reaction and the wide applicability of the present method.

The reaction also proceeded smoothly in other dipolar aprotic solvents such as N,N-dimethylacetamide or hexamethylphosphoric triamide. The extent of the conversion of I to II depends on the substrate concentration and the use of ca. 5% (w/v) solution was recommended. The intrusion of moisture should be avoided because the moisture favored the reduction of the starting aromatic halides (I) resulting in the formation of corresponding aromatic hydrocarbons (ArH).[4]

Thus, our new method is superior to the known methods in the easiness of operations and the availability of the source of trifluoromethyl group.

$$\underset{\text{I}}{\text{ArI}} \xrightarrow{\text{CF}_3\text{CO}_2\text{Na/CuI}} \underset{\text{II}}{\text{ArCF}_3}$$

Table I. Trifluoromethylation of aromatic halides[a]

Aromatic compound	Product[b]	Yield (%)[3]
m-Iodotoluene (Ib)	m-(Trifluoromethyl)toluene	88
p-Iodonitrobenzene (Ic)	p-Nitro(trifluoromethyl)benzene	47 (39)[c]
p-Chloroiodobenzene (Id)	p-Chloro(trifluoromethyl)benzene	68
p-Iodomethoxybenzene (Ie)	p-Methoxy(trifluoromethyl)benzene	59 (42)[c]
1-Iodonaphthalene (If)	1-(Trifluoromethyl)naphthalene	82 (78)[c]
m-Bromotoluene (Ig)	m-(Trifluoromethyl)toluene	58
2-Bromopyridine (Ih)	2-(Trifluoromethyl)pyridine	41

[a] Reaction was carried out in NMP as described above.

[b] No existence of position isomers were confirmed by GLC, GLC-MS, and ^{1}H NMR after isolation by means of GLC or column chromatography (silica-gel).

[c] Yields isolated by column chromatography (silica-gel).

References

1) (a) Use of SbF_3 or HF: J. H. Simons and C. J. Lewis, J. Am. Chem. Soc., 60, 492 (1938), (b) Use of SF_4: Org. Reactions, Vol. 21, 1 (1974), (c) Use of CF_3I: Y. Kobayashi and I. Kumadaki, Tetrahedron Lett., 1969, 4095; V. C. R. McLoughlin and J. Thrower, Tetrahedron, 25, 5921 (1969); Y. Kobayashi, I. Kumadaki, S. Sato, N. Hara, and E. Chikai, Chem. Pharm. Bull., 18, 2334 (1970); Y. Kobayashi, K. Yamamoto, and I. Kumadaki, Tetrahedron Lett., 1979, 2071.

2) N. V. Kondratenko, E. P. Vechirko, and L. M. Yagupolskii, Synthesis, 1980, 932.

3) Yields were determiend by GLC (2% EGA, 2m), after dilution of the reaction mixture with ether-hexane (1:1), filtration through celite layer, washing with water (3 times), and dried ($MgSO_4$).

4) Similar reduction of aromatic iodide was reported in the trifluoromethylation with CF_3I: K. Hosokawa and K. Inukai, Nippon Kagaku Kaishi, 1977, 1163.

(Received September 16, 1981)