Preliminary note

Preparation and reactions of the 2,3,5,6-tetrafluoropyridylcopper reagent

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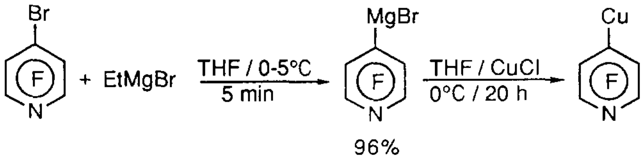
Abstract

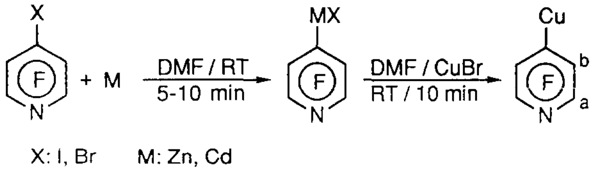
4-Iodotetrafluoropyridine and 4-bromotetrafluoropyridine react readily with acid-washed cadmium or zinc powder in DMF at room temperature to give the 2,3,5,6-tetrafluoropyridylcadmium or 2,3,5,6-tetrafluoropyridylzinc reagent in quantitative yield. Metathesis of the cadmium or zinc reagent with CuBr at room temperature gives the stable 2,3,5,6-tetrafluoropyridylcopper reagent. The 2,3,5,6-tetrafluoropyridylcopper reagent couples with allylic halides, vinyl iodides, aryl iodides and acyl halides to give the corresponding adducts in high yield.

The synthesis of perfluoroarylcopper reagents via metathesis of the corresponding perfluoroaryllithium or perfluoroarylmagnesium compounds with cuprous halides (Cl, Br, I) at low temperature has been reported [1]. This method is limited by the thermal stability of perfluoroaryl-lithium or -magnesium reagents. Recently, we reported the preparation of *F*-alkenyl- and *F*-aryl-cadmium, -zinc and -copper reagents such as *F*-vinyl [2], *F*-allyl [3], *F*-acetylenic [4], *F*-phenyl [5]. These reagents have found utility in the synthesis of organofluorine compounds [6].

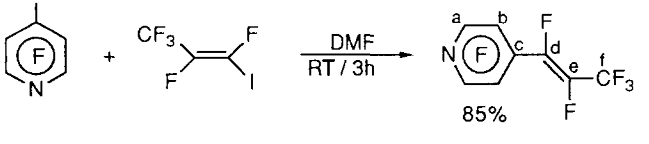
The only method reported for the preparation of the 4-tetrafluoropyridylcopper reagent is via metathesis of 4-tetrafluoropyridylmagnesium bromide with CuBr at 0 °C in THF [7].



In contrast to the lithium and Grignard reagents, the 4-tetrafluoropyridyl-cadmium and -zinc reagents are very stable [8]. In our laboratory, the 2,3,5,6-tetrafluoropyridylcopper reagent was prepared by treatment of the 4-iodo- or 4-bromo-2,3,5,6-tetrafluoropyridine with acid-washed cadmium or zinc powder in DMF at room temperature under an argon atmosphere to form the 4-tetrafluoropyridyl-cadmium and -zinc reagents in quantitative yield. This reaction is rapid, exothermic, and complete in 5–10 min. The cadmium and zinc reagents undergo metathesis with CuBr at room temperature (10 min) to give the corresponding copper reagent. In a degassed sealed tube, the 2,3,5,6-tetrafluoropyridylcopper reagent exhibits excellent thermal stability at room temperature. When a solution of the 2,3,5,6-tetrafluoropyridylcopper reagent was heated at 90 °C for 3 h, the color of the solution changed slightly from brown to dark brown, but the ^{19}F NMR spectrum of the copper reagent exhibited no significant changes [^{19}F NMR ($CFCl_3$, DMF) δ: -99.3 (m, $2F_a$); -117.4 (m, $2F_b$) ppm]. The copper reagent readily undergoes coupling with aryl iodides, terminal vinyl iodides, allyl halides and acid chlorides at room temperature to give high yields of the expected coupling products. The results of this study are summarized in Table 1. The coupling reaction proceeded with retention of stereochemistry in all cases and no metal–halogen exchange was detected by ^{19}F NMR analysis of the reaction mixture. The stereochemistry of the *E* and *Z* isomers was verified by the NMR coupling constants of the vinylic fluorines or vinylic hydrogens of the products.



A typical experimental procedure is described for the preparation of (*E*)-1-(2,3,5,6-tetrafluoropyridyl)-pentafluoropropene.



A dry, two-necked, 50 ml round-bottomed flask, equipped with an argon inlet, septum port and a Teflon coated stir-bar, was charged with 5 ml of dry DMF and 1.3 g (5.0 mmol) of (*Z*)-1-iodopentafluoropropene

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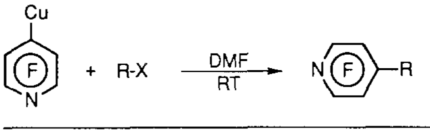
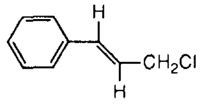
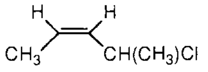
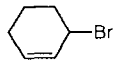
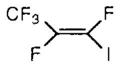
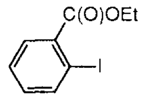
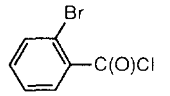
TABLE 1. Reaction of 2,3,5,6-tetrafluoropyridylcopper reagent with allylic halides, vinyl iodide, aryl iodide and acid chlorides



Entry No.	R−X	Reaction time (h)	Yield (%)[a,b]
1		1.5	86
2		2	74
3		1	82
4		3	85
5		2	80
6	$CH_3OC(O)CH_2CH_2C(O)Cl$	1.5	83
7		2	85

[a] Isolated yields based on the 4-tetrafluoropyridylcopper reagent.
[b] All compounds gave satisfactory ^{19}F, ^{1}H, ^{13}C NMR, FT-IR and GC/MS data.

[9]. The solution was stirred under an argon atmosphere at room temperature, then a solution of the 2,3,5,6-tetrafluoropyridylcopper reagent (5.0 mmol) was added dropwise via a syringe. After stirring at room temperature for 3 h, the copper reagent had been completely consumed as determined by ^{19}F NMR analysis. The mixture was poured into 200 ml of water and extracted with 3×100 ml of CH_2Cl_2. The organic layer was separated, washed with 3×100 ml of water, dried over anhydrous $MgSO_4$, gravity filtered, then concentrated using a rotary evaporator. The crude product was introduced onto a silica gel column, 3.5 cm o.d.×20 cm long (Baker, 40 μm), and eluted with hexane. The eluate containing the product was collected and the solvent removed by rotary evaporation followed by evaporation under vacuum to give 1.2 g (85% yield) of (*E*)-1-(2,3,5,6-tetrafluoropyridyl)pentafluoropropene as a clear liquid. The GLPC purity was 99.5%. ^{19}F NMR ($CFCl_3$, $CDCl_3$) δ: −68.7 (dd, $^3J_{F-F}=20.4$, $^4J_{F-F}=10.2$ Hz, 3F$_f$); −87.9 (m, 2F$_a$); −137.5 (m, 2F$_b$); −141.7 (dm, $^3J_{F-F}=140.0$ Hz, 1F$_d$); −157.0 (dm, $^3J_{F-F}=140.0$ Hz, 1F$_e$) ppm. ^{13}C NMR ($CDCl_3$, TMS) δ: 144.5 (dm, $J_{C-F}=245.1$ Hz, C$_a$); 142.6 (ddq, $J_{C-F}=259.7$, $^2J_{C-F}=42.3$, $^2J_{C-F}=42.3$ Hz, C$_e$); 140.9 (ddm, $J_{C-F}=260.9$, $^2J_{C-F}=46.3$ Hz, C$_d$); 140.1 (dm, $J_{C-F}=270.6$ Hz, C$_b$); 119.9 (m, C$_c$); 118.6 (qdd, $J_{C-F}=273.4$, $^2J_{C-F}=35.3$, $^3J_{C-F}=4.6$ Hz, C$_f$) ppm. FT-IR (CCl_4) (cm^{-1}): 2905.9 (w); 1643.6 (w); 1481.1 (s); 1380.8 (m); 1223.5 (s); 1170.7 (s); 967.9 (m). GC/MS (*m/z*): 281 (M$^+$, 4.8); 135 (5.0); 117 (100.0); 105 (20.6); HR-MS: Calc. for C_8F_9N, 280.9887. Obs., 280.9879.

Acknowledgement

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References

1 (a) C. Tamborski, E.J. Soloski and R.J. DePasquale, *J. Organomet. Chem., 15* (1968) 494; (b) A. Cairncross and W.A Sheppard, *J. Am. Chem. Soc., 90* (1968) 2186; (c) S.S. Dua, A.E. Jukes and H. Gilman, *J. Organomet. Chem., 12* (1968) 24; (d) R.J. DePasquale and C. Tamborski, *J. Org. Chem., 34* (1969) 1736.

2 (a) D.J. Burton and S.W. Hansen, *J. Fluorine Chem., 31* (1986) 461; (b) S.W. Hansen, T.D. Spawn and D.J. Burton, *J. Fluorine Chem., 35* (1987) 415; (c) T.D. Spawn and D.J. Burton, *Bull. Soc. Chim. Fr.*, (1986) 876.

3 D.J. Burton, Y. Tarumi and P.L. Heinze, *J. Fluorine Chem., 50* (1990) 257.

4 D.J. Burton and T.D. Spawn, *J. Fluorine Chem., 38* (1988) 119.

5 D.J. Burton, Z.Y. Yang and K.J. MacNeil, *J. Fluorine Chem., 52* (1991) 251.

6 (a) P.L. Heinze and D.J. Burton, *J. Org. Chem., 53* (1988) 2714; (b) P.L. Heinze and D.J. Burton, *J. Fluorine Chem., 31* (1986) 115; (c) D.J. Burton, G.D. Hartgraves and J. Hsu, *Tetrahedron Lett., 26* (1990) 3699; (d) D.J. Burton and G.D. Hartgraves, *J. Fluorine Chem., 49* (1990) 155; (e) W.R. Dolbier, Jr., H. Koroniak, D.J. Burton, P.L. Heinze, A.R. Bailey, G.S. Shaw and S.W. Hansen, *J. Am. Chem. Soc., 109* (1987) 219; (f) J.P. Gillet, R. Sauvetre and J.F. Normant, *Synthesis*, (1986) 538; (g) F. Tellier, R. Sauvetre and J.F. Normant, *J. Organomet. Chem., 331* (1987) 281; (h) S.K. Choi and Y.T. Jeong, *J. Chem. Soc., Chem. Commun.* (1988) 1478.

7 E.J. Soloski, W.E. Ward and C. Tamborski, *J. Fluorine Chem., 2* (1972/73) 361.

8 P. Satori and H. Adelt, *J. Fluorine Chem., 3* (1973/74) 275.

9 P.L. Heinze, T.D. Spawn, D.J. Burton and S. Shin-Ya, *J. Fluorine Chem., 38* (1988) 131.