HETEROATOM-FACILITATED ORTHO CARBON-CARBON BOND FORMATION IN NUCLEOPHILIC F-PHENYL SUBSTITUTION

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Regioselective ortho-substitutions in F-phenyl carboxylic acid and its derivatives were accomplished by conversion into F-phenyloxazoline (1a) or F-phenyldihydrooxazine (1b), followed by nucleophilic displacements of one or two ortho-fluorines with organometallic reagents in nonpolar solvents. Requisite 1a and 1b were readily prepared by treating F-benzoyl chloride with 2-amino-2-methyl-1-propanol, and F-benzonitrile with 2-methyl-2,4-pentanediol, respectively. Treating 1a or 1b with either Grignard reagents (CH_3MgI, C_2H_5MgBr, n-C_3H_7MgBr) or organolithium reagents (CH_3Li, n-C_4H_9Li) gave appreciable yields of the 2-substituted F-phenyloxazoline (2a) or F-phenyldihydrooxazine (2b), while no 4-substituted ones were identified. The use of an excess of the organometallic reagents afforded 2,6-disubstitution in preference to 2,4-disubstitution. The ortho-directing effects here observed are conceivably caused through a mechanism like that suggested by Meyers(Tetrahedron Lett., 223(1978)).