Aerobic Oxidative Trifluoromethylation of Arenes Catalyzed by Phosphovanadomolybdcic Acids

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The trifluoromethyl (CF$_3$) group is becoming of increasing importance in pharmaceuticals, agrochemicals, polymers, and liquid crystals because the physical and chemical properties of molecules, such as metabolic stability, membrane permeability, and bioactivity, can be remarkably modified by installation of CF$_3$ group(s). Therefore, the development of efficient trifluoromethylation methods has attracted considerable attention. Recently, significant progress has been achieved in radical-based C–H trifluoromethylation using various kinds of CF$_3$ sources.[1] Sodium trifluoromethanesulfinate (NaSO$_2$CF$_3$) is one of the most preferable trifluoromethylation reagents because it is relatively stable, easy-to-handle, and inexpensive. Although efforts have been devoted to develop the catalytic direct C–H trifluoromethylation of (hetero)arenes using NaSO$_2$CF$_3$ as the source of CF$_3$ radicals, the previously reported systems typically require superstoichiometric amounts of organic and inorganic oxidants. The NaSO$_2$CF$_3$-based trifluoromethylation of (hetero)arenes using O$_2$ as the terminal oxidant has been remained unexplored until now.

In this study, we report for the first time that phosphovanadomolybdic acids can act as efficient catalysts for oxidative direct C–H trifluoromethylation of (hetero)arenes using NaSO$_2$CF$_3$ as the source of CF$_3$ radicals, and the previously reported systems typically require superstoichiometric amounts of organic and inorganic oxidants. The NaSO$_2$CF$_3$-based trifluoromethylation of (hetero)arenes using O$_2$ as the terminal oxidant has been remained unexplored until now.

In the presence of catalytic amounts of phosphovanadomolybdic acids, such as H$_6$PV$_3$Mo$_9$O$_{40}$, various kinds of structurally diverse (hetero)arenes, such as substituted benzenes, naphthalene, pyrazine, pyridine, quinolone, and thiophene, could be efficiently converted into the corresponding trifluoromethylated products (Fig. 1). The reaction proceeded without dechlorination for 1,4-dichlorobenzene and 1,2-dichlorobenzene, and no hydration or hydrolytic decomposition proceeded for benzonitrile. Based on the several experimental results, we propose a radical-based reaction mechanism for the present trifluoromethylation.

Scheme 1 Direct C–H trifluoromethylation of (hetero)arenes using NaSO$_2$CF$_3$ as the CF$_3$ source and O$_2$ as the terminal oxidant.

**REFERENCES**