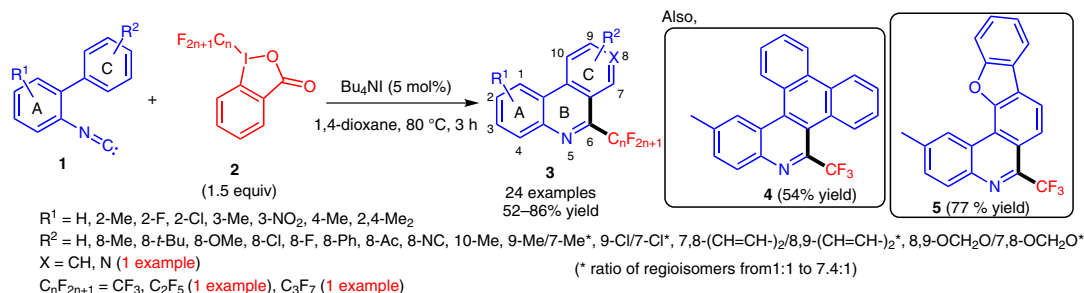


B. ZHANG, C. MÜCK-LICHTENFELD, C. G. DANILIUC, A. STUDER* (WESTFÄLISCHE WILHELMS-UNIVERSITÄT MÜNSTER, GERMANY)

6-Trifluoromethyl-Phenanthridines through Radical Trifluoromethylation of Isonitriles
Angew. Chem. Int. Ed. **2013**, 52, 10792–10795.

Synthesis of 6-Trifluoromethyl-Phenanthridines from Diaryl Isonitriles



Significance: Reported is the synthesis of 6-trifluoromethyl phenanthridines (**3–5**) from the reaction of readily available isonitriles **1** with the Togni reagent (**2**, $n = 1$) involving a radical trifluoromethylation reaction. Initially, transition metals (salts of copper, iron, nickel, and cobalt) were used to carry out this transformation, but later it was realized that Bu_4NI can be successfully used as a radical initiator. A range of 6-trifluoromethyl-phenanthridines were obtained in moderate to good yields. For *meta*-substituted ring-C derivatives of **1**, cyclization preferably occurred at the position distal to the *meta* substituent, but regiocontrol was low (1:1 to 7.4:1). The method was also applied to the synthesis of 6-perfluoroalkylated phenanthridines ($\text{C}_n\text{F}_{2n+1}$, $n = 2, 3$). The reaction did not proceed in the presence of TEMPO, suggesting a radical mechanism involving the addition of CF_3 radical to the isonitrile group, followed by a cyclization event.

Reviews: X.-F. Wu, H. Neumann, M. Beller *Chem. Asian J.* **2012**, 7, 1744–1754; H. Liu, Z. Gu, X. Jiang *Adv. Synth. Catal.* **2013**, 355, 617–626; T. Besset, C. Schneider, D. Cahard *Angew. Chem. Int. Ed.* **2012**, 51, 5048–5050.

Comment: Trifluoromethylated (hetero)arenes are important structural motifs for drug discovery programs. Classic methods for the synthesis of CF_3 -substituted (hetero)arenes rely mostly on the commercial availability of CF_3 -bearing starting materials usually obtained by industrially unviable Swarts-type reactions (G. K. S. Prakash, J. Hu, J. Simon, D. R. Bellew, G. A. Olah *J. Fluorine Chem.* **2004**, 125, 595). In more recent developments, the CF_3 group has been introduced by transition-metal-mediated cross-coupling reactions or direct C–H trifluoromethylation (see Reviews below). Despite some modest improvement in this field, new routes for the high-yielding and site-selective introduction of CF_3 groups on (hetero)arenes are required. The present method utilizes readily prepared isonitriles and provides 6-perfluoroalkylated phenanthridines without transition-metal-based catalysis. However, the Togni reagent is potentially explosive and should be handled with care (N. Fiederling, J. Haller, H. Schramm *Org. Process Res. Dev.* **2013**, 17, 318). Conceptually, this method is similar to Zhou's approach (Q. Wang, X. Dong, T. Xiao, L. Zhou *Org. Lett.* **2013**, 15, 4846) in which, instead of the Togni reagent, a combination of $\text{PhI}(\text{OAc})_2$ and the Ruppert–Prakash reagent (TMSCF_3) was used at room temperature to obtain similar derivatives.

SYNFACTS Contributors: Victor Snieckus, Suneel P. Singh (Snieckus Innovations)

Synfacts 2014, 10(1), 0016 Published online: 13.12.2013

DOI: 10.1055/s-0033-1340419; Reg-No.: V15013SF

2014 © THIEME STUTTGART • NEW YORK