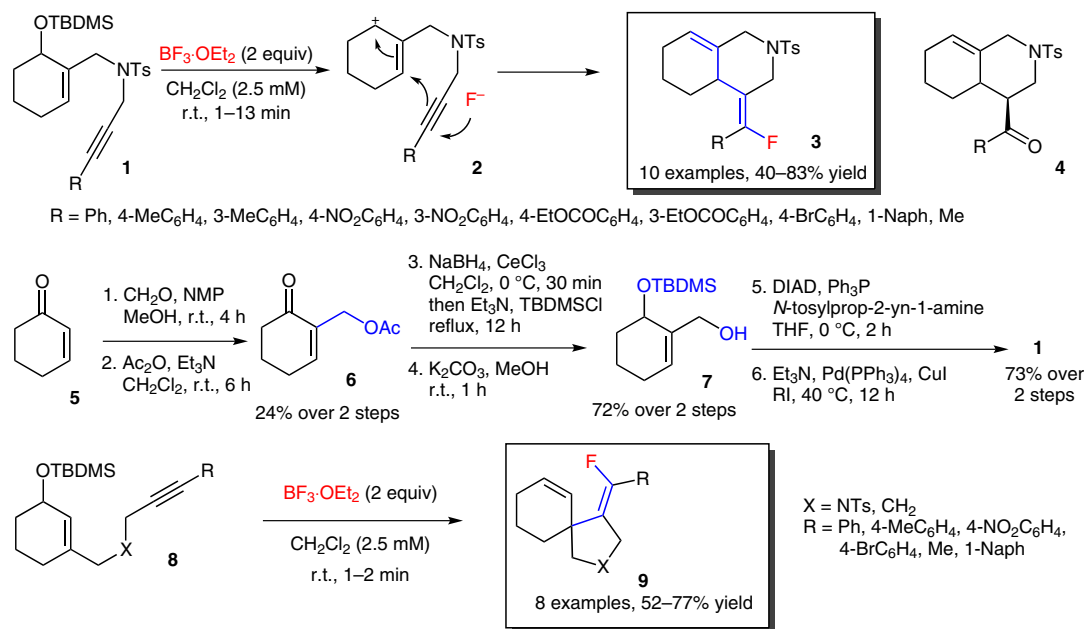


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 Transition-Metal-Free Carbofluorination of TBS-Protected Nitrogen-Containing Cyclic Enynols: Synthesis of Fluorinated Azabicycles
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Synthesis of Fluorinated Azabicycles



Significance: Described is the regio- and stereo-selective synthesis of fluorinated azabicycles **3** from arylpropargyl tosylaminomethyl-tethered cyclohex-2-en-1-ols **1**. Inexpensive $\text{BF}_3 \cdot \text{OEt}_2$ is used for this transformation, which serves both as a Lewis acid and a fluorinating agent. Moreover, the reaction is carried out at room temperature and is complete within minutes. The starting material is prepared in six steps starting from cyclohex-2-en-1-one and formaldehyde under Baylis–Hillman conditions followed by reaction with an N-protected propargylamine using Mitsunobu chemistry. Subsequent Sonogashira coupling of the resulting terminal alkyne with aryl iodides gives **1**. The reaction may be envisaged to occur via intermediate **2** as shown above. This method was extended to the synthesis of the fluorinated spiro compounds **9** from the analogous TBDMS-protected enynols.

Comment: A fluoro substituent has the promise of incorporating biological activity in an organic molecule (K. Müller, C. Faeh, F. Diederich *Science* **2007**, *317*, 1881). There are many methods for the synthesis of alkenyl fluorides: fluorination of vinylstannanes, silver-catalyzed aminofluorination of alkynes, palladium-catalyzed tandem fluorination of enynes and (NHC)gold-catalyzed hydrofluorination of alkynes, amongst others (J. A. Akana, K. X. Bhattacharyya, P. Müller, J. P. Sadighi *J. Am. Chem. Soc.* **2007**, *129*, 7736). However, Lewis acid promoted direct fluorination of unactivated alkynes has not been reported up to date. Optimization by tuning the combination of the solvent, reaction time, and substrate concentration was carried out, and the azabicycles **3** were obtained in 40–83% yield. In the presence of water or acid, ketones **4** are formed instead. The scope of the substituent R^1 is limited and the cyclization proceeds well with neutral and electron-poor aryls as well as with methyl, but fails with electron-rich aryls.

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