

Diels–Alder Reaction–Fragmentation of Pyridinium Salts and Alkynes

Category

Synthesis of Heterocycles

Key words

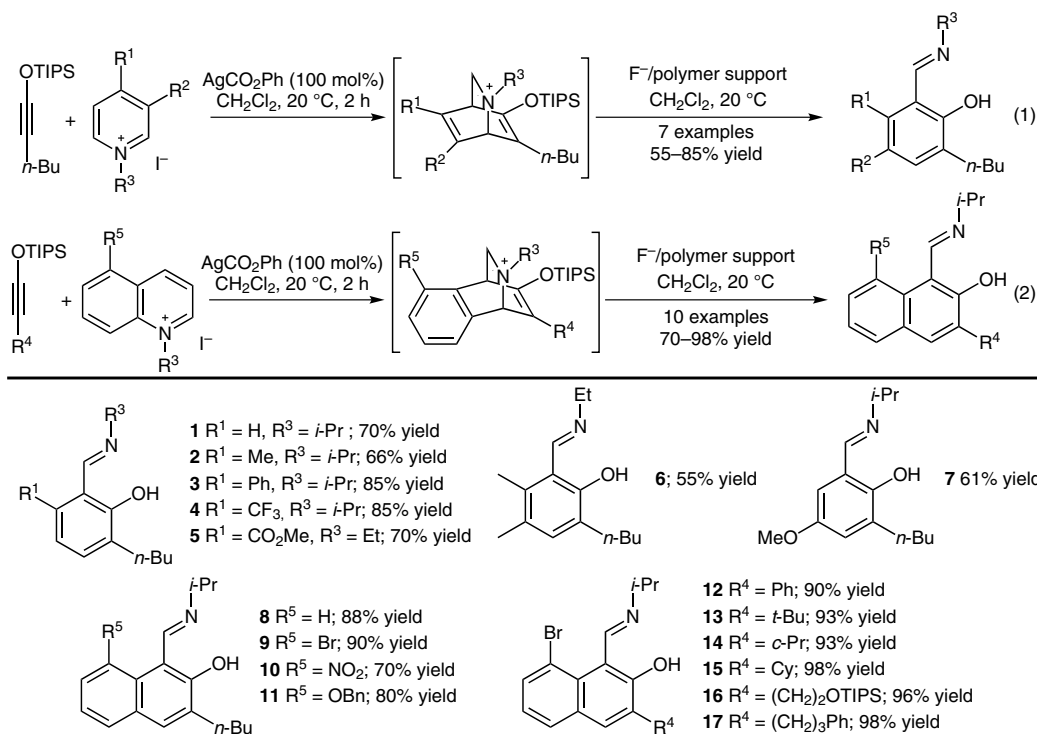
benzannulation

siloxoalkynes

Diels–Alder reaction

aromatics

SYNFACT
of the month



Significance: Reported is a de novo synthesis of substituted phenols and naphthols generated via silver(I)-promoted sequential Diels–Alder reaction–fragmentation from siloxyalkynes with readily available pyridinium or isoquinolinium salts. The generation of substituted aromatics via benzannulation of isoquinolinium salts has been explored extensively (S. Saito, Y. Yamamoto *Chem. Rev.* **2000**, 100, 2901) and the present report by Kozmin employs a benzannulation strategy to provide substituted aromatics using pyrones and isoquinoline *N*-oxides as dienes (*Nature Chem.* **2013**, 5, 423). The chemistry presented is a useful extension of the method, as pyridinium salts are employed as Diels–Alder cycloaddition synthons, where pyridine *N*-oxides previously failed.

Comment: Optimization of the silver(I) source revealed AgCO_2Ph as the ideal promoter for the transformation at 20 °C, albeit stoichiometric amounts are required for efficient conversion. Pyridinium counterions were examined, revealing iodide as the optimal counterion. A variety of substituted pyridinium salts undergo the transformation (eq. 1, **1–7**); however, the 4-OMe-substituted pyridinium salt did not afford product. This result is likely due to the electronic incompatibility of the inverse-demand Diels–Alder cycloaddition, since 3-OMe pyridinium salt (**7**) does not impede the reaction. Substituted isoquinolinium salts also undergo the reaction (**8–11**), and substitution of the siloxyalkyne is well tolerated (**12–17**). Noteworthy is the formation of 1,2,3-trisubstituted naphthalenes, which are synthesized with difficulty.