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Synthesis of the Parent and Substituted Tetracyclic ABCD Ring Cores of Camptothecins via 1-(3-Aryl-2-propynyl)-1,6-dihydro-6-oxo-2-pyridinecarbonitriles
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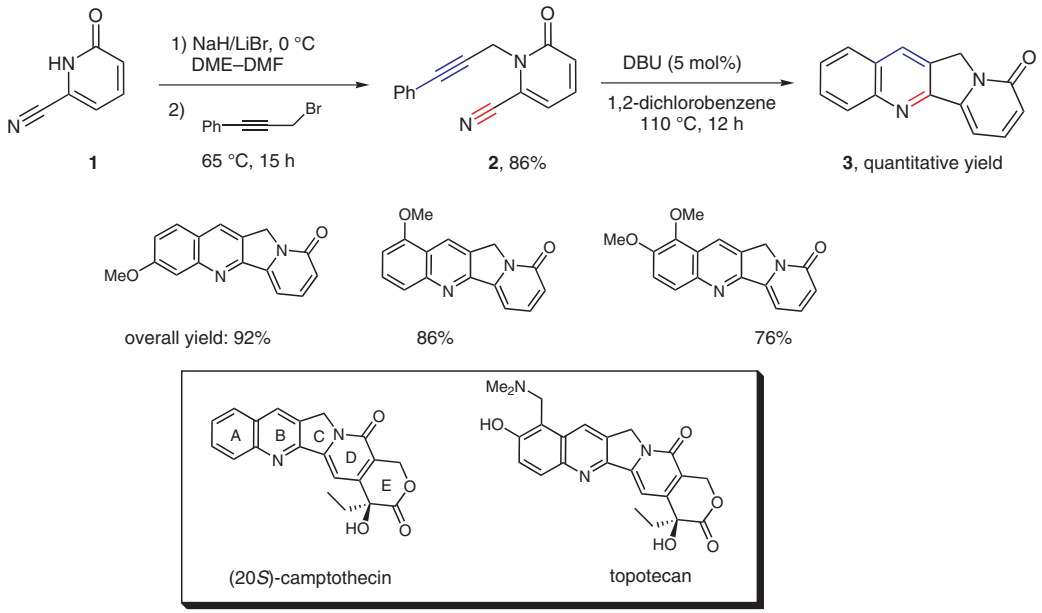
Synthesis of Tetracyclic ABCD Ring Cores of Camptothecins



Significance: A concise synthetic sequence has been developed for the parent and substituted ABCD ring cores of the camptothecin family of alkaloids. This two-step synthesis starts by N-alkylation of the 2-pyridone **1** with 3-bromo-1-phenylpropyne (Curran's protocol: D. P. Curran and coworkers *Tetrahedron Lett.* **1995**, *36*, 8917-8920) to give **2**, followed by DBU-induced cyclization, presumably involving an intramolecular hetero-Diels–Alder reaction, to produce the target tetracyclics **3** in good overall yield. The scope and limitations of this method were not sufficiently investigated.

Comment: Considerable effort has been expended on the synthesis of the antitumor camptothecin alkaloids (see review below). In comparison with previous radical cyclization and other intramolecular Diels–Alder approaches involving multisteps from easily available starting materials (e.g., W. R. Bowman et al. *J. Chem. Soc., Perkin Trans. 1*, **2002**, 58-68; J. M. D. Fortunak et al. *Tetrahedron Lett.* **1996**, *37*, 5679-5682), the new method establishes a short process for the formation of the parent and substituted ABCD ring cores of the camptothecins with respectable yields in the cyclization step. This heteroannulation strategy may have wider application.

Review: W. Du *Tetrahedron* **2003**, *59*, 8649-8687.

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Category
Synthesis of Heterocycles

Key words
1,6-dihydro-6-oxo-2-pyridinecarbonitrile
intramolecular Diels–Alder reaction
camptothecins