Synthesis of Azabicyclo[3.1.1]heptane Derivatives from Cyclobutanones

Significance: Reported is the synthesis of a variety of 2-alkyl-2-azabicyclo[3.1.1]heptane-1-carbonitriles via a Dynamic Addition–Intramolecular Substitution Sequence.

Comment: The syntheses of azabicyclo[3.1.1] derivatives of type 4 and 5 are not well represented in literature. The route utilizes a modification of the previously reported route described by Radchenko et al. (J. Org. Chem. 2009, 74, 5541). The key intermediate 3 was prepared on >100 mmol scale. Furthermore, the current route provides access to compounds not previously described by Radchenko (R variation).