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Rapid Synthesis of Psychoplastogenic Tropane Alkaloids
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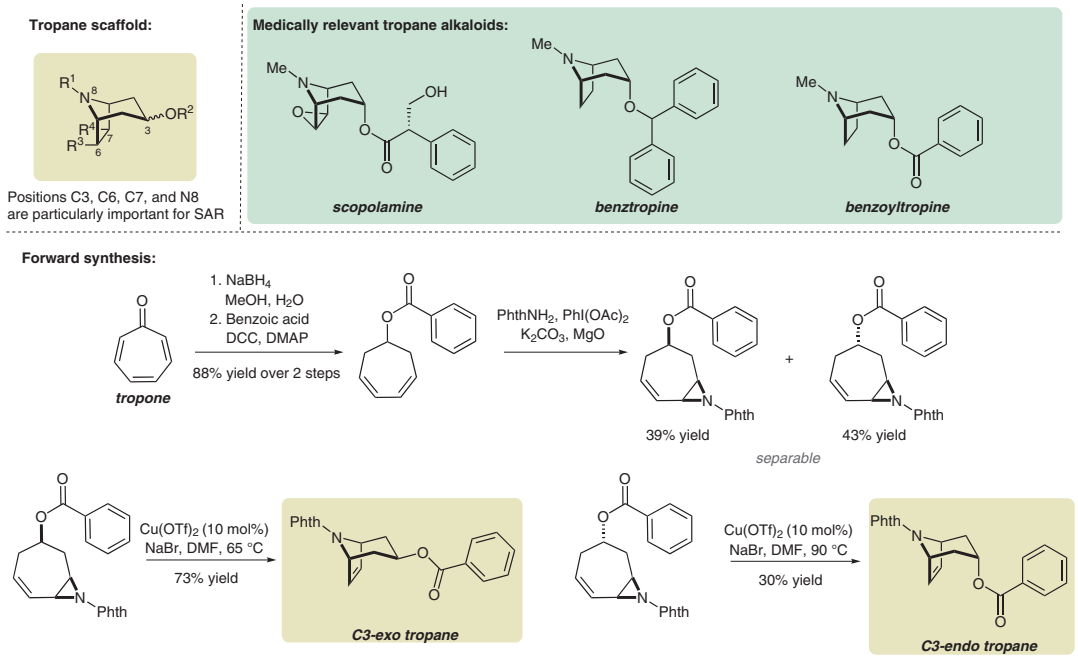
# A New Approach to the Tropane Alkaloids Enables Late-Stage Diversification




**Significance:** Tropane is a highly relevant scaffold in drug development, as evidenced by its presence in prescription medications such as the motion sickness drug scopolamine and the movement disorder drug benztropine. The Olson group is particularly interested in these compounds as non-serotonergic psychoplastogens, capable of inducing neuroplasticity without triggering hallucinations. Prior synthetic efforts on this scaffold have not produced syntheses amenable to late-stage diversification at the highly relevant N8, C3, C6, or C7 position. In this work, Olson and co-workers present a synthesis of tropane alkaloids capable of diversification at these positions.

**Comment:** Reduction and esterification of commercially available tropone afforded a symmetric diene, which was subsequently aziridinated in a 1:1 diastereomeric ratio. The diastereomers were separated and the tropane core was assembled in a $S_N2'/S_N2$ cascade. Thus, a rapid synthesis of both C3-endo and C3-exo tropanes was accomplished, with synthetic handles allowing for the diversification of the N8, C3, C6, and C7 position. The Olson group then leveraged this strategy to accomplish the synthesis of several known tropane alkaloids, including the first total syntheses of the natural product benzoyltropine. Benzoyltropine was also identified as a non-serotonergic, non-deliriant compound capable of inducing neuroplasticity.

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