

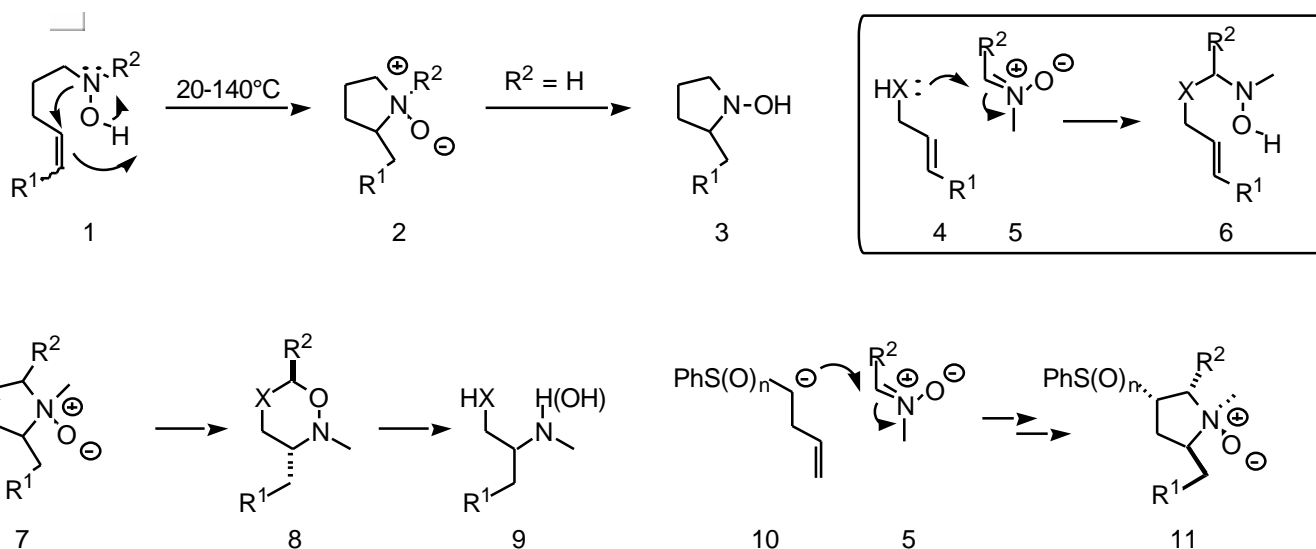
New Aspects of the Reverse-Cope Elimination - a Classic Reaction Goes Backwards

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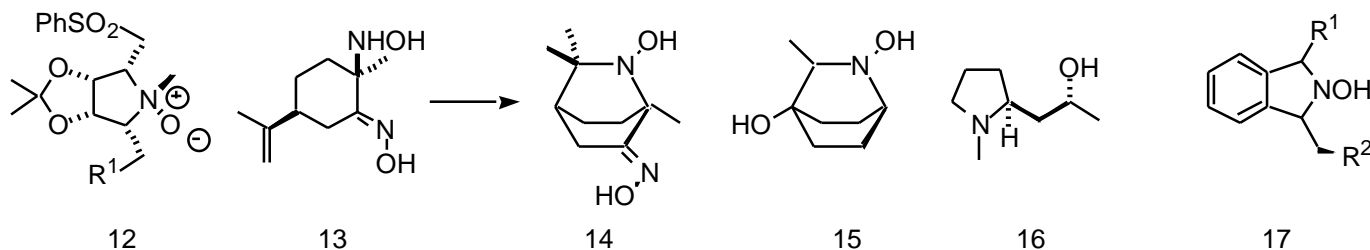
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The reverse-Cope elimination, as the name suggests, is a pericyclic process wherein an unsaturated hydroxylamine **1** undergoes a thermal cyclisation to give pyrrolidine-*N*-oxides **2** and thence the *N*-hydroxypyrrolidines **3** when $R^2 = H$. The initial part of the lecture will feature an outline of our contributions to this area in which we have set up the required hydroxylamines **6** by nucleophilic addition of allylic amines or thiols [**4**; X = NH or S] to nitrones **5**. This has resulted in syntheses of the novel heterocycles **7** and **8**; overall, the method can be used for the amination of an unactivated alkene to give diamines and aminothiols **9**.

Lithiated sulphones and sulfoxides **10** also add smoothly to nitrones **5** leading to pyrrolidine-*N*-oxides **11**, after reverse-Cope cyclisation. The scope and limitations of this methodology will be outlined, along with



suggestions for likely transition state conformations. An alternative strategy, wherein the nitrone and the alkene are contained in the starting material, has resulted in elaboration of the highly functionalized pyrrolidine-*N*-oxides **12**. The constraint of the additional ring doubtless facilitates the cyclisation as it does in the 'transannular' cyclisations of the limonene-derived hydroxylamine **13**, leading to the isoquinuclidine **14**, originally discovered by Tkachev's group.



Our further generalization of this potentially useful method to isoquinuclidines [*eg* **15**] will be described, along with applications of the reverse-Cope method to a stereoselective approach to the Natural pyrrolidine Hygroline **16** and to the dihydroisoindoles **17**, which are potential isoindolene precursors.