

INTRAMOLECULAR PHOTOCYCLOADDITION AND RETRO-MANNICH FRAGMENTATION OF ACYCLIC TERTIARY VINYLOGOUS AMIDES

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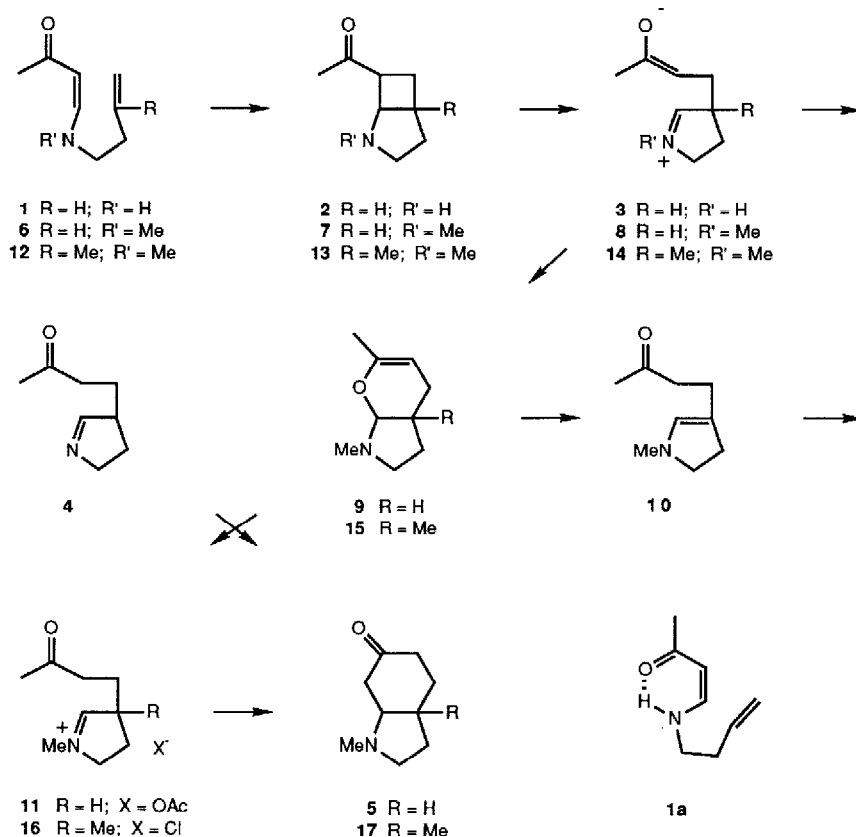
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Abstract. *The intramolecular photocycloaddition/fragmentation of tertiary vinylogous amides, in which stabilization of the chromophore by intramolecular hydrogen bonding is not possible, and the selective conversion of the derived zwitterionic intermediate to either ketoenamine, aminal or ketoiminium products is described.*

We have recently introduced a new method for the construction of nitrogen-containing ring systems, **1** → **5**.² Intramolecular photocycloaddition of vinylogous amide **1**,³ followed by retro-Mannich fragmentation of the derived photoadduct **2**, leads to the formation of the zwitterionic species **3**, which undergoes proton transfer to generate the neutral ketoimine, **4**. This reaction sequence concludes with Mannich closure of **4** to provide the perhydroindole, **5**. Secondary vinylogous amide photosubstrate **1** can be rigidly held in a six-membered ring by an intramolecular hydrogen bond, as shown in **1a**, which is an essential feature of the related de Mayo reaction of acyclic β-diketones.⁴ We report herein the successful photocycloaddition and fragmentation of tertiary vinylogous amides, **6** and **12**, in which neither the stabilization of the chromophore by intramolecular hydrogen bonding, nor the conversion of the zwitterionic intermediates to a neutral ketoimine by proton transfer, is possible, and the selective formation of either ketoenamine, bicyclic aminal, or ketoiminium products, respectively.

The requisite photosubstrates **6** and **12** were prepared in 80-90% yield by condensation of the appropriate homoallylic amine with 4-chloro-3-buten-2-one (Et₃N, CH₂Cl₂, 25°C).⁵ Irradiation of **6** (26 mM in acetonitrile, medium-pressure Hg lamp, Pyrex filter) led to the formation of mixtures of bicyclic aminal **9** and enamine **10** in 70% distilled yield (b.p. 0.5 85-90°C). When the reaction was carried out at 0°C, the major product was bicyclic aminal **9** (ratio of **9/10**: 6/1), while the major product at room temperature was enamine **10** (ratio of **9/10**: 1/3.5). We attribute this difference in product distribution to the relative rates of isomerization of aminal **9** to ketoenamine **10** at 0°C and 25°C, respectively, as **9** is converted to ketoenamine **10** in 88% yield on exposure to wet acetonitrile at 25°C. Treatment of **10** with glacial acetic acid at 25°C led to the formation, in 95% yield, of the desired iminium salt **11**, a key intermediate in our recently reported synthesis of nitrogen-containing ring systems.² The intermediacy of ketoenamine **10** was precluded with photosubstrate **12** (R=Me). Irradiation of **12** in benzene or acetonitrile solution at 25°C led to the formation of **15** in 82% yield. Treatment of **15** with triethylammonium hydrochloride in acetonitrile gave ketoiminium **16** in 75% yield, which had previously been cyclized to give **17**.^{2,6} Alternatively, irradiation of **12** in the presence of 1.3 equiv triethylammonium hydrochloride at 25°C provided **16** directly in 80% yield.

These results demonstrate the broad potential utility of the photocycloaddition/fragmentation of *acyclic* tertiary vinylogous amides for the construction of diverse nitrogen-containing ring systems. Further studies directed towards the application of this methodology to the synthesis of naturally occurring nitrogen-containing ring systems are currently in progress in our laboratory.⁷



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