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CESIUM FLUORIDE INDUCED DESILYLATION REACTION OF IMMONIUM SALTS DERIVED FROM VINYLOGOUS AMIDES

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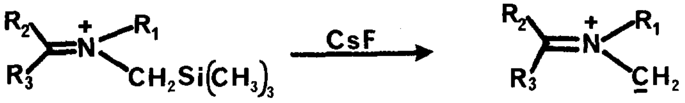
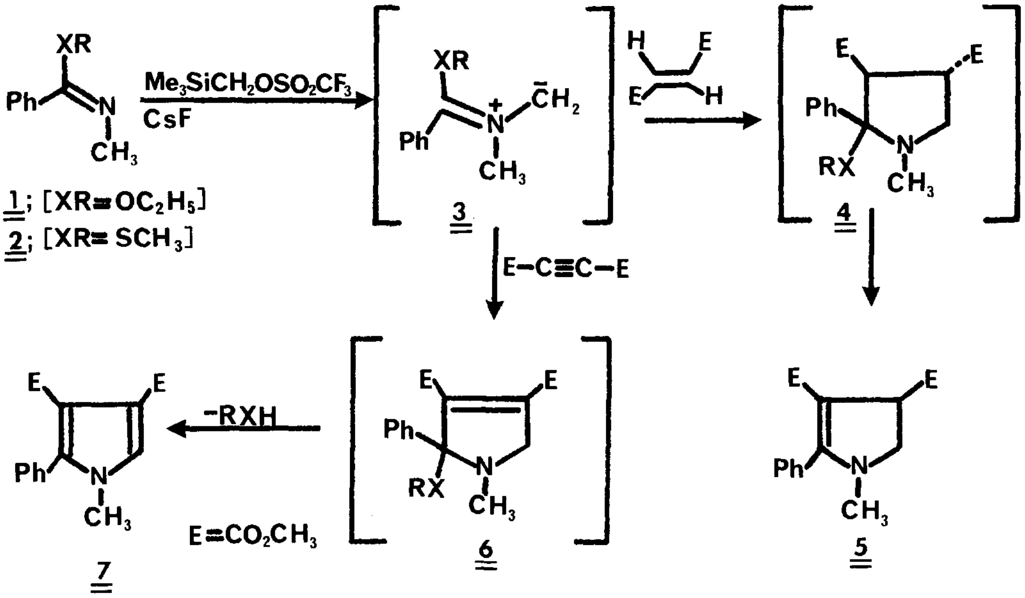
Abstract: The cesium fluoride induced desilylation reaction of immonium salts derived from amides, thioamides and vinylogous amides provides access to reactive azomethine ylides in synthetically useful yields.

Reactions involving the thermal and photochemical cleavage of aziridines to azomethine ylides and their subsequent 1,3-dipolar additions to reactive carbon-carbon multiple bonds are well known.[1-7] Azomethine ylides react most rapidly with electron deficient alkenes, since such a pair of addends possesses a narrow dipole HOMO-dipolarophile LUMO gap.[8,9] Although ring opening of aziridines to azomethine ylides works well when the substituent groups are capable of stabilizing the dipole centers, the ring cleavage fails completely when simple alkyl substituents are used. An alternate route to nonstabilized azomethine ylides involves desilylation of an appropriately substituted immonium cation.[10-12] The fluoride induced desilylation has become a useful tool for the generation of nucleophilic carbon species.[13,14] The research described herein was aimed at demonstrating the usefulness of amides and vinylogous amides as azomethine ylide equivalents.

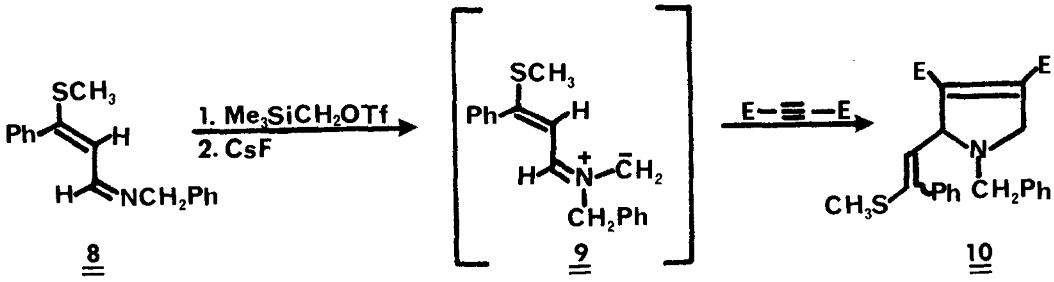


Alkylation of imidate 1 with trimethylsilylmethyltriflate (25^{o}C,3h,DME) followed by cesium fluoride desilylation of the resulting salt afforded azomethine ylide 3.[15] Cycloaddition of this transient species with dimethyl fumarate produced dihydropyrrole 5 in 45% yield. The initially formed cycloadduct 4 readily loses a molecule of methanol under the reaction conditions to give 5. Similarly, treatment of 1 with

$Me_3SiCH_2OSO_2CF_3$, CsF and dimethyl acetylenedicarboxylate produced pyrrole 7 in 48% yield. An alternative route to 7 begins with N-alkylation of thioimidate 2 with $Me_3SiCH_2OSO_2CF_3$. The crude salt is stirred with dimethyl acetylenedicarboxylate annd anhydrous CsF to effect 1,3-dipolar cycloaddition. Loss of methyl mercaptan from the initial cycloadduct 6 afforded pyrrole 7 in 74% yield.

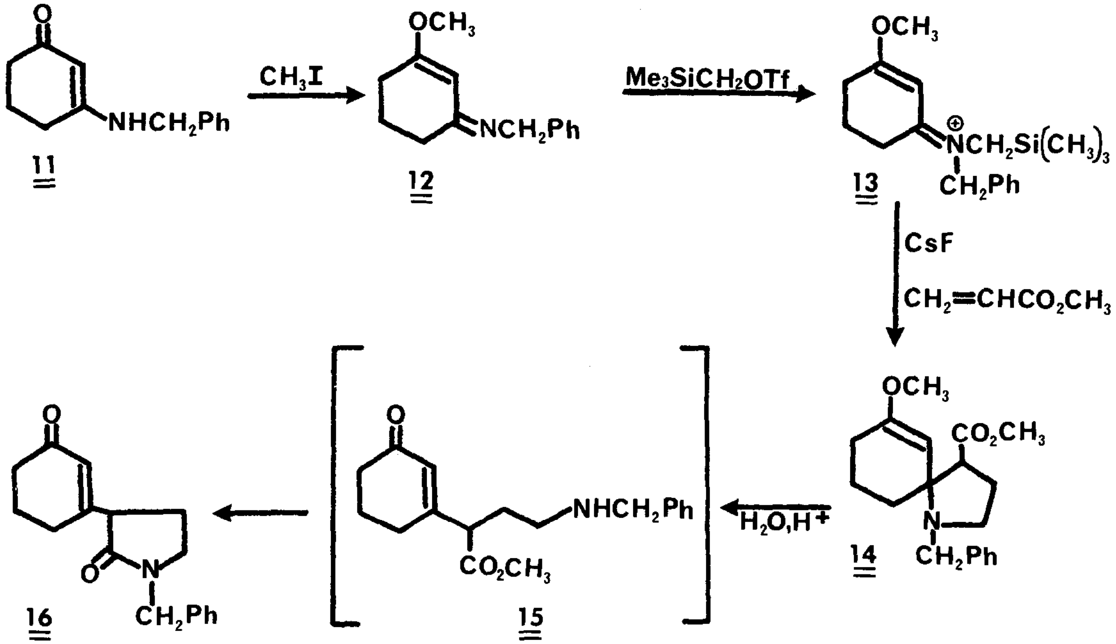


Generation of intermediates have azomethine ylide reactivity was also achieved by the reaction of vinylogous amides or thioamides with methyl iodide followed by treatment of the resulting imine with $Me_3SiCH_2OSO_2CF_3$, CsF and an appropriate trapping reagent. It is noteworthy that azomethine ylide 9 undergoes cycloaddition with dimethylacetylene



dicarboxylate to give 10[16] (36%) even though 9 could undergo a 1,5-electrocyclization reaction.[17]

Treatment of 2-benzylaminocyclohexenone (11) with methyl iodide followed by reaction with trimethylsilylmethyltriflate gave immonium salt 13 in good yield. The crude salt was dissolved in DME and was stirred with methyl acrylate and anhydrous cesium fluoride to effect the 1,3-dipolar cycloaddition.[18] After stirring for 3 hr, an 85% yield of cycloadduct 14 could be isolated. Hydrolysis of the enol ether afforded lactam 16 as the exclusive product.[19] This conversion probably involves the initial formation of a ring opened intermediate (i.e. 15) which subsequently cyclizes under the reaction conditions. Through this series of reactions, enamide 11 was converted into 16 in 75% overall yield.



In summary, the cesium fluoride induced desilylation reaction of immonium salts derived from amides, thioamides and vinylogous amides provides access to reactive azomethine ylides in synthetically useful yields. This method allows access to nonstabilized azomethine ylides and is currently being used in our laboratory to synthesize a number of alkaloids possessing the pyrroline ring.

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*Alexander von Humboldt Senior Scientist, 1983-1984; University of Wurzburg.

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(16) NMR **10** (90 MHz,CDCl$_3$) δ 2.20 (*s*, 3H), 3.30 (*d*, 1H, J=12.0 Hz), 3.35 (*dd*, 1H, J=14.0 and 6.0 Hz), 3.71 (*s*, 3H), 3.82 (*dd*, 1H, J=14.0 and 6.0 Hz), 3.85 (*s*, 3H), 3.90 (*d*, 1H, J=12.0 Hz), 4.58 (*m*, 1H), 5.40 (*d*, 1H, J=10.0 Hz) and 7.4 (*m*, 10H).

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(18) Structure **14** was a 1:1 mixture of both possible diastereomers.

(19) Structure **16** was independently synthesized by treating 2-ethoxycyclohexenone with the anion derived from N-benzyl γ-lactam.

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