

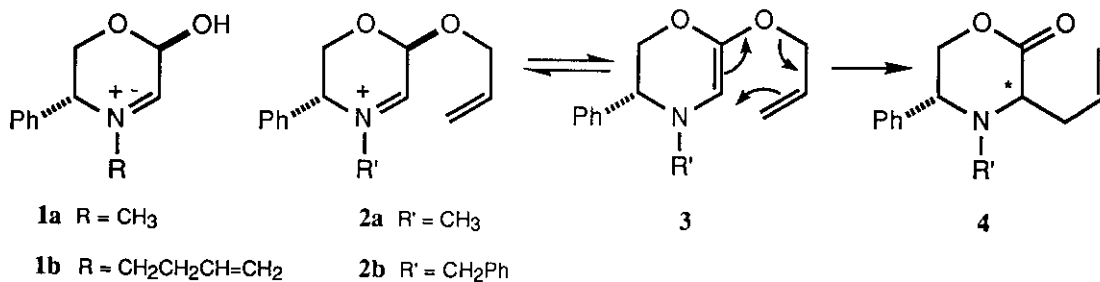
**MECHANISTIC INVESTIGATION OF AN INTRAMOLECULAR
REARRANGEMENT IN A HETEROCYCLIC ALLYLOXY IMINIUM
COMPOUND**

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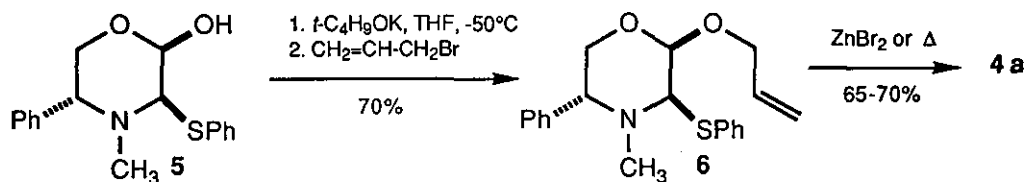
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Abstract - A new rearrangement involving an ene iminium system derived from a homochiral 2-allyloxy-3-phenylthiomorpholine is reported.

Claisen rearrangements have found widespread use for the stereoselective transformation of organic molecules.¹ The increasing attention being devoted to the application of this process in heterocyclic chemistry is focusing principally in aromatic compounds.² Our interest in the synthetic potential of chiral glycine cation equivalents (**1a**) and (**1b**) which have been used respectively in the enantioselective syntheses of acyclic³ and cyclic⁴ α -amino acids led us to investigate the reactivity of iminium ions (**2**). These substrates are well suited for a transformation into the allyloxyenamines (**3**) *via* the classical⁵ enamine-iminium ion tautomerism. [3,3]-Sigmatropic rearrangements of compounds (**3**) would thus give access to lactones (**4**) which are precursors of unsaturated α -amino acids.

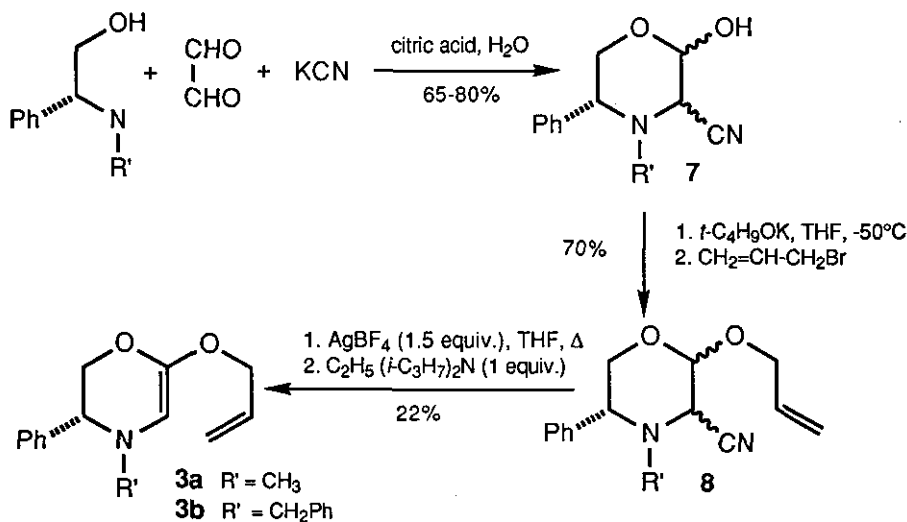


Amino thio ether (6) was synthesized from the chiral tetrahydrooxazine (5):⁶



Refluxing a THF solution of compound (6) in the presence of zinc bromide (1 equiv.)⁷ afforded lactone (4a) (yield: 65%); comparison of its ^1H nmr spectrum with previous data⁸ showed that this lactone was formed with a 70% diastereoselectivity in favor of the *trans* isomer.

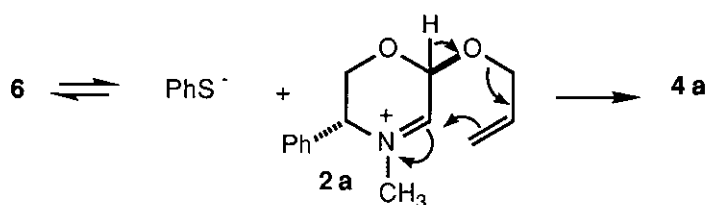
As regards the mechanism of the formation of the lactone (4a) from morpholine derivative (6), it is clear that iminium ion (2a) is involved since amino thio ethers are well-known precursors of such ions. However this transformation may not necessarily imply the enamine (3a) as an intermediate. In order to see to it that this really occurs, enamines (3a)⁹ and (3b)¹⁰ were synthesized as depicted on the following scheme: ¹¹



Unexpectedly, none of these enamines (3a,b) yielded the corresponding Claisen-rearranged lactones. These compounds remain unchanged whatever the experimental conditions: refluxing in toluene solution with or without a transition metal catalyst¹³ ($\text{PdCl}_2(\text{CH}_3\text{CN})_2$) or a Lewis acid catalyst¹⁴ (ZnBr_2).

Claisen rearrangements of acyclic allyloxyenamines were observed by Barluenga *et al.*,¹⁵ however our substrates actually show an extra enol ether moiety and, in view of the very intricate effects of substituents on Claisen rearrangements,¹⁶ it would be hazardous to rationalize the lack of reactivity of enamines (3).

Therefore it appears that an enamine is not implied during the 6 → 4a transformation. It could be assumed that the iminium ion (2a) resulting from (6) undergoes an ene-iminium rearrangement as shown below :



The major isomer produced by this reaction, that is *trans* (4a), corresponds to an axial attack onto the C=N⁺ double bond of compound (2a). The same *anti* attack in relation to the phenyl group was already observed for the ene-iminium cyclization of substrate (1b); it could be noted that (1b) and (2a) essentially differ by the position of the tethered unsaturated chain.

References and notes

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7. In the absence of ZnBr₂, with a protracted reaction time, the amino thio ether (6) gave the same ratio of *cis* and *trans* lactones (4a) (yield: 70%). It has been checked that no epimerization took place when either *cis* or *trans* (4a) were separately treated with zinc bromide.

8. ^1H Nmr signals (200 MHz, CDCl_3 solution) of the N- CH_3 moiety appear respectively at 2.16 and 2.30 ppm respectively for *cis* and *trans* (**4a**) (see ref.3).
9. ^1H Nmr (200 MHz, CDCl_3): 2.87 (s, 3H), 3.65 (d, $J = 11.7$, 1H), 4.1-4.3 (m, 3H), 4.61 (dd, $J = 3.8$ and 11.7 Hz, 1H), 5.10 (s, 1H), 5.2-5.4 (m, 2H), 5.9-6.0 (m, 1H), 7.2-7.4 (m, 5H). ^{13}C Nmr (50 MHz, CDCl_3): 33.1, 62.1, 62.7, 69.4, 94.8, 118.1, 126.6, 128.2, 128.8, 133.5, 138.2, 164.6.
10. ^1H Nmr (200 MHz, CDCl_3): 3.39 (d, $J = 14.7$ Hz, 1H), 3.62 (d, $J = 9.8$ Hz, 1H), 4.2-4.3 (m, 3H), 4.44 (dd, $J = 3.7$ and 11.7 Hz, 1H), 5.20 (s, 1H), 5.25-5.5 (m, 2H), 5.56 (d, $J = 14.7$ Hz, 1H), 5.9-6.1 (m, 1H), 7.2-7.4 (m, 10H). ^{13}C Nmr (50 MHz, CDCl_3): 47.2, 58.4, 63.3, 69.7, 95.0, 118.3, 127.1, 127.8, 128.4, 128.6, 126.8, 129.0, 133.8, 136.2, 138.4, 164.8.
11. The key-step of this sequence is the treatment¹² of the amino nitrile (**8**) with AgBF_4 followed by a tertiary amine-mediated deprotonation of the resulting iminium ion.
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