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Aza-[2,3] Sigmatropic Rearrangement of Phosphoramides

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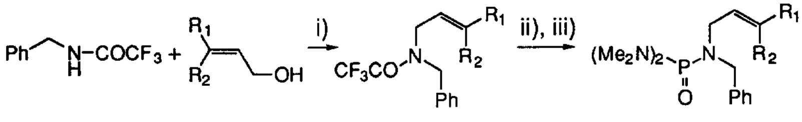
Abstract: The aza-[2,3] sigmatropic rearrangement was realized by using a phosphoramide group as a stabilization group of the carbanion. Not only (*E*)-substituted alkene, but also (*Z*)-, and trisubstituted alkene can be used as substrates. © 1997 Elsevier Science Ltd.

The [2,3] sigmatropic rearrangement, particularly the oxy-[2,3] sigmatropic rearrangement, has been studied with regard to its stereochemical course and in view of its modern synthetic application to preparation of highly functionalized derivatives.[1] However, there are few examples of the aza counterpart, in which substrates employed are such as allylbenzylamines and alkynylbenzylamines. It is known that the [1,2] rearrangement is prone to take place rather than the [2,3] rearrangement in these systems.[2] There are only three prior reports of true examples of this reaction, two of which involved the use of cyclic substrates 1-benzyl-4-vinyl-2-azetidinone and vinyl aziridines, which are highly strained because they have three- and four-membered rings.[3] However, there have been unsuccessful examples in the case of acyclic variants which do not possess this driving force.[2] The third example was reported by Anderson and Smith last year.[4] They showed the [2,3] rearrangement of an acyclic substrate by use of a *t*-butoxycarbonyl group (Boc) as a protecting group and a stabilization group of the carbanion. We expected that phosphoramide could also stabilize a carbanion, and as a result, rearrangement would proceed. The phosphoramides were known to give dipole stabilized carbanion.[5] Here we report an aza-[2,3] sigmatropic rearrangement of phosphoramides.

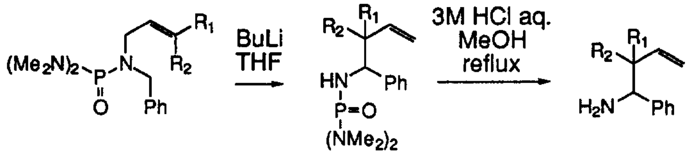
The substrates were synthesized as shown below.[6] The N-crotyl, and N-prenyl trifluoroamides were prepared by the modified Mitsunobu reaction reported by Ito and Tsunoda.[7] After hydrolysis of trifluoroacetamides, amines were converted to the corresponding phosphoramides **1a**, **1a'**, and **1b**.



1a R_1=Me, R_2=H
1a' R_1=H, R_2=Me
1b R_1=R_2=Me

i) PBu_3, 1,1'-(azodicarbonyl)dipiperidine, benzene ii) 1 M KOH aq., MeOH
iii) $(Me_2N)_2P(O)Cl$, Et_3N, THF

When phosphoramide **1a** was treated with BuLi (1.2 equiv) in THF at 0 °C for 2 h, aza-[2,3] sigmatropic rearrangement product **2a** was obtained in 90% yield as a 1:1 mixture of diastereomers. No [1,2] rearrangement product was observed in ^{1}H NMR of the crude mixture. The product **2a** could be hydrolyzed in refluxing aqueous 3 M HCl-MeOH quantitatively to give amine **3a**. During hydrolysis, the ratio of the diastereomers was not changed. Not only (*E*)-substituted alkene **1a**, but also (*Z*)-substituted alkene **1a'** gave [2,3] rearrangement product **2a** in 90% yield. The diaseteomer ratio was also 1:1. This result is remarkable, because the Boc protected (Z)-crotyl benzyl amine is reported to give an elimination product with no [2,3]-sigmatropic rearrangement product.[4] The trisubstituted substrate **1b** also afforded [2,3]-sigmatropic rearrangement product **2b**. After hydrolysis, amine **3b**[8] was obtained in 40% yield (2 steps).



1a R_1=Me, R_2=H
1a' R_1=H, R_2=Me
1b R_1=R_2=Me

2a R_1=Me, R_2=H
2b R_1=R_2=Me

3a R_1=Me, R_2=H
3b R_1=R_2=Me

In summary, the aza-[2,3] sigmatropic rearrangement of phosphoramides was achieved. The phosphoramide group effectively assists this rearrangement *regardless* of the substitution pattern of the alkenes.

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