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LETTERS

A new stereoselective access to *N*-benzyl *trans*-propargylic aziridines

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Abstract

The metallation of 3-trimethylsilyl-1-chloroprop-2-yne and the subsequent reaction with *N*-benzyl imines affords stereospecifically *trans* propargylic aziridines with good to excellent yields. © 1999 Elsevier Science Ltd. All rights reserved.

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We have recently disclosed a new stereoselective access to *trans* propargylic oxiranes by condensation of the 3-chloro-1-trimethylsilyl zincioallene **2** onto aldehydes and subsequent ring closure.[1] We have now examined the reaction of this zincioallene with imines, in order to obtain propargylic aziridines. This class of compounds has been prepared previously by the reaction of nitrenes or nitrene equivalents with enynes[2,3] or from the corresponding propargylic epoxides in a two-step reaction.[4] Very recently, the condensation of propargylic sulfonium ylides[5] onto imines has been described, as well as a preparation of optically pure aziridines from aminoacids.[6]

As starting materials we chose the *N*-benzyl imines derived from the corresponding carbonyl compounds by a well-known procedure (aldehyde or ketone and benzylamine in dichloromethane in the presence of 4 Å molecular sieves). We were very pleased to see that the zincioallene **2**, prepared from 3-trimethylsilyl propargyl chloride[7] by the method we have described recently,[1] reacts smoothly with these *N*-benzylimines to directly afford in one step the corresponding propargylic aziridines in good yield (Scheme 1).

In the case of *N*-benzylimines derived from aldehydes, the stereoselectivity of this reaction was excellent: only the corresponding *trans* aziridines were obtained. Our results are reported in Table 1.

It should be noted that in contrast to the case of aldehydes, the reaction leads directly to the aziridines by a cyclization of the first-produced propargylic chloroamine. It is not still clear whether this ring-

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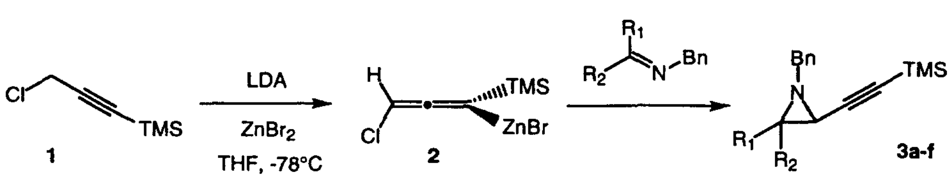
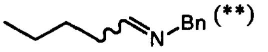
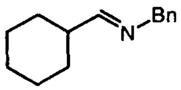
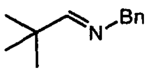
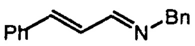
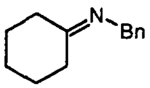


Scheme 1.

Table 1
Reaction of zincioallene **2** with *N*-benzylimines

Entry	N-Benzylimine	Aziridine	*anti* / *syn* ratio*	Yield (%)
1	 (**)	**3a**	> 98 / 2	50
2		**3b**	> 98 / 2	67
3		**3c**	> 98 / 2	13***
4		**3d**	> 98 / 2	73
5		**3e**	> 98 / 2	65
6		**3f**		40

* Based on the observed coupling constants for the two aziridinyl protons by ^{1}H NMR.

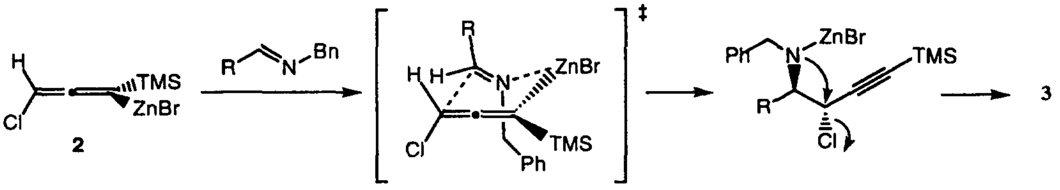
** As a mixture of two isomers in a 60 / 40 ratio.

*** In the presence of BF_3-Et_2O (2 eq.): 50 % yield by ^{1}H NMR.

closure occurs from the formed zinc amide, as depicted in Scheme 1, or through the chloroamine upon hydrolysis.

From a chemical point of view, these *N*-benzylimines were found to be much less reactive than the corresponding aldehydes, as the reaction with aldehydes occurs at −78°C,[1] whereas no reaction with *N*-benzyl imines was observed below 0°C. As can be seen in Table 1, the zincioallene **2** reacted with all *N*-benzyl imines we tried with an equally excellent diastereoselectivity to afford only the *trans* aziridines, as shown by ^{1}H NMR on the basis of the measurement of the coupling constants between the two aziridinyl protons.[8] The reaction of propargylic organometallics (Grignard reagents,[9–11] aluminium,[11,12] titanium[12] or zinc[10,11,13] reagents) with imines have already been studied. Among these reagents, it has been shown that propargylic zinc reagents react with *N*-alkyl imines with a high level of diastereoselectivity.[10,13] This stereoselectivity can be explained in our case by the possible chelate-type transition state depicted on Scheme 2.

Interestingly, it should be noted that this diastereoselectivity does not depend on the configuration of the starting imine, as either purely *E* imines (entries 2–6) or a mixture of *E* and *Z* isomers (entry 1) led

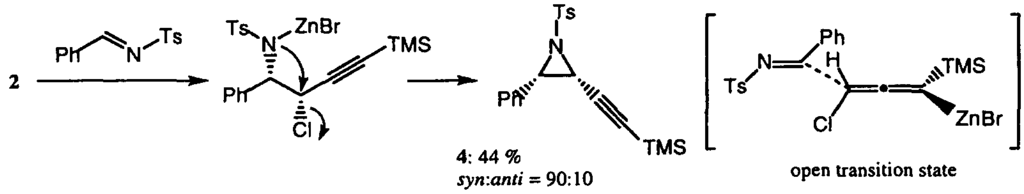


Scheme 2.

only to the *trans* aziridine. However, despite all our efforts, the reaction of zincioallene **2** with *n*-butyl *N*-benzyl imine gave the corresponding aziridine **3a** only in a 50% yield. This aziridine could perhaps be produced from the reaction of **2** with the *E* imine, the *Z* imine giving some side products. Alternatively, a possible base-catalyzed *E* to *Z* equilibration could also be envisioned.

This type of transition state could also explain the lack of reactivity of *N*-benzyl-*tert*-butylimine (entry 3), probably due to the greater steric hindrance: no reaction was observed with **2** in the absence of a Lewis acid. Addition of BF_3–Et_2O to the reaction mixture led to the formation of the aziridine **3c** in fair yield (50% based on ^{1}H NMR). Unfortunately, this aziridine was found to be very sensitive and difficult to purify by flash-chromatography. We also observed no reaction with the *N*-α-methylbenzylimines derived from benzaldehyde and cyclohexylcarboxaldehyde. These imines presumably show a lower reactivity than the corresponding *N*-benzylimines, due to the higher steric hindrance around the nitrogen atom, and unfortunately the zincioallene **2** is not stable at temperatures higher than 10°C.

We then turned to the use of other imines. No reaction was observed with *N*-trityl imines or with N-PMP imines. On the other hand, reaction of zincioallene **2** with phenyl *N*-tosyl imine led to the corresponding *N*-tosyl aziridine **4** in moderate yield and with an excellent stereoselectivity (*syn*:*anti*=90:10 from ^{1}H NMR). This divergent stereoselectivity (compared to the one observed in the case of *N*-benzyl imines) can be interpreted through an open transition state, as depicted in Scheme 3.



Scheme 3.

The reaction of zincioallene **2** with other *N*-sulfonylimines is currently under investigation. Further results will be reported in due course.

Acknowledgements

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8. *Typical procedure*: To a mixture of zinc bromide (10 mmol) and compound **1** (5 mmol) in THF (20 mL) was added dropwise at –78°C a freshly prepared solution of LDA (10 mmol) in THF (7 mL). After stirring for 30 min, the *N*-benzylimine was added and the temperature was allowed to warm gradually to 0°C overnight. After usual workup the corresponding aziridine was purified by flash-chromatography. The coupling constants between the two aziridinyl protons was found to be between 2.8 and 3.4 Hz by ^{1}H NMR.
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