

# NaI-catalyzed highly regioselective ring-opening [1 + 2] cycloaddition reaction of cyclopropenes with imines: highly stereoselective synthesis of *cis*-vinylic aziridines

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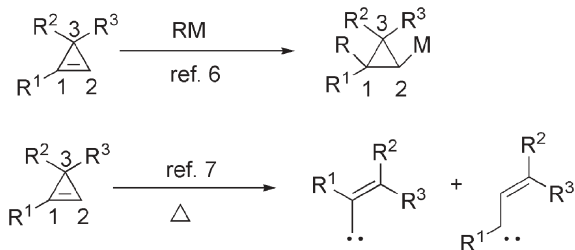
*cis*-Vinylic aziridines were prepared highly stereoselectively via a NaI-catalyzed regioselective ring-opening [1 + 2] cycloaddition reaction of cyclopropenes with imines.

Aziridine, an important synthetic building block, has attracted the attention of many organic chemists due to the general influence of ring strain upon chemical reactivity and the potential of derivatives of these compounds to act as precursors to more elaborate heterocyclic compounds.<sup>1,2</sup> Furthermore, the aziridine structural unit plays an important role in bioactive natural products, which were used as agents for the treatment of cancer and affinity probes of receptors and peptides.<sup>3</sup> Thus, the efficient formation of aziridine in a stereoselective fashion is an important continuing goal in organic synthesis.<sup>4</sup>

Cyclopropenes, highly strained but readily accessible carbocyclic molecules, have been shown to possess unique reactivity in organic synthesis.<sup>5</sup> Two typical reaction modes have been observed in the chemistry of cyclopropenes, *i.e.* nucleophilic addition to the strained C=C bond<sup>6</sup> and ring-opening rearrangement to an allyl carbene<sup>7</sup> (Scheme 1).

Very recently, we have described a novel I<sup>-</sup>- or Br<sup>-</sup>-catalyzed ring-opening coupling reaction of cyclopropenes with organic halides leading efficiently to polyfunctionalized alk-1-enyl halides in a highly stereoselective fashion (eqn. (1), Scheme 2).<sup>8</sup> Based on these results, we were interested in the reaction of cyclopropenes with other electrophiles, which may show different reaction modes. Herein, we wish to report a novel NaI-catalyzed highly stereoselective ring-opening [1 + 2] cycloaddition reaction of cyclopropenes with imines affording vinylic aziridines.

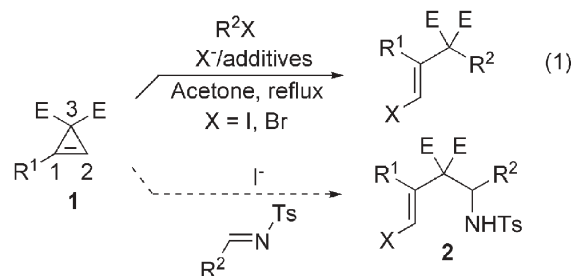
Under similar reaction conditions to those used for the catalytic ring-opening alkylation, the reaction of **1a** with imine **3a** in the presence of Na<sub>2</sub>CO<sub>3</sub> in THF was tested. To our surprise, instead of the expected 1,2-addition-type product **2a**, *cis*-vinylic aziridine **4aa**



Scheme 1 Two principal reaction modes of cyclopropenes.

was formed in 63% yield highly stereoselectively (entry 1, Table 1). Further study indicates that (1) the addition of Na<sub>2</sub>CO<sub>3</sub> is not necessary (entry 2, Table 1); (2) the reaction with 20 mol% NaI afforded **4aa** in the highest yield (compare entries 2–5, Table 1); (3) the reaction catalyzed by LiBr, LiI, or KI yielded **4aa** in much lower yields (entries 6–8, Table 1). The stereochemistry of **4aa** was established by an X-ray diffraction study (Fig. 1).<sup>9</sup> The *trans* isomer was not formed based on the analysis of the <sup>1</sup>H NMR spectrum of the crude reaction mixture.

Some typical results of this reaction are summarized in Table 2. Based on these results it can be concluded that the reaction is general, highly stereoselective, and good-yielding. The C–C bond in the cyclopropenes was cleaved highly regioselectively.



Scheme 2 I<sup>-</sup>- or Br<sup>-</sup>-catalyzed ring-opening coupling reaction of cyclopropenes **1** with organic halides.

Table 1 Coupling reaction of **1a** with **3a** under different reaction conditions<sup>a</sup>

Entry	MI (equiv)	Time/h	Yield of <b>4aa</b> (%)
1	NaI (0.2) <sup>b</sup>	13	63
2	NaI (0.2)	2	65
3	NaI (1.0)	14	62
4	NaI (2.0)	10	43
5	NaI (0.1)	14	54
6	LiBr (0.1)	8	47
7	LiI (0.1)	12	31
8	KI (0.1)	12	20

<sup>a</sup> The reaction was carried out with **1a** and **3a** (2.0 equiv) in the presence of MI in THF. <sup>b</sup> Na<sub>2</sub>CO<sub>3</sub> (1.0 equiv) was added.

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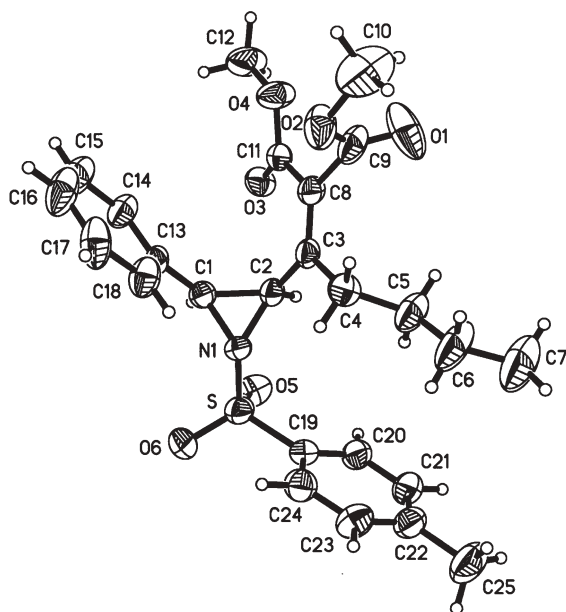
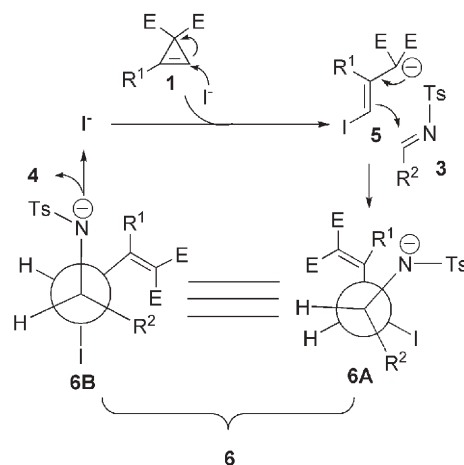


Fig. 1 ORTEP representation of **4aa**.



Scheme 3 A rationale for the NaI-catalyzed ring-opening aziridination reaction of cyclopropenes with imines.

providing an efficient, atom-economic, highly regio- and stereo-selective route to a series of polyfunctionalized vinyl aziridines. Due to the easy availability of both starting materials and functionalities in the final products, this methodology will show its utility in organic synthesis. Further studies on the scope of the reaction and the synthetic application are now being carried out in this laboratory.

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## Notes and references

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Table 2 Ring-opening aziridination reaction of cyclopropenes **1** with imines **3** under conditions A<sup>a</sup>

Entry	<b>1</b> R <sup>1</sup>	<b>3</b> E	<b>3</b> R <sup>2</sup>	Time/ h	Yield of <b>4</b> (%)
1	C <sub>4</sub> H <sub>9</sub>	CO <sub>2</sub> Me ( <b>1a</b> )	Ph ( <b>3a</b> )	2	65 ( <b>4aa</b> )
2	<b>1a</b>		4-NO <sub>2</sub> Ph ( <b>3b</b> )	3	77 ( <b>4ab</b> )
3	C <sub>5</sub> H <sub>11</sub>	CO <sub>2</sub> Me ( <b>1b</b> )	<b>3a</b>	5	71 ( <b>4ba</b> )
4	<b>1b</b>		<b>3b</b>	3.5	71 ( <b>4bb</b> )
5	<b>1b</b>		4-ClC <sub>6</sub> H <sub>4</sub> ( <b>3c</b> )	6.5	58 ( <b>4bc</b> )
6	<b>1b</b>		1-Naphthyl ( <b>3d</b> )	11	75 ( <b>4bd</b> )
7	Ph(CH <sub>2</sub> ) <sub>2</sub>	CO <sub>2</sub> Me ( <b>1c</b> )	<b>3b</b>	4	58 ( <b>4cb</b> )
8	TBSOC <sub>3</sub> H <sub>6</sub>	CO <sub>2</sub> Me ( <b>1d</b> )	<b>3b</b>	2	69 ( <b>4db</b> )
9	PhCH <sub>2</sub>	CO <sub>2</sub> Me ( <b>1e</b> )	<b>3a</b>	3	63 ( <b>4ea</b> )
10	<b>1e</b>		<b>3b</b>	3	76 ( <b>4eb</b> )
11	C <sub>4</sub> H <sub>9</sub>	CO <sub>2</sub> Et ( <b>1f</b> )	<b>3b</b>	2	74 ( <b>4fb</b> )

<sup>a</sup> Conditions A: the reaction was carried out with **1a** and **3a** (1.5–2.0 equiv) in the presence of 20 mol% NaI in 2 mL of THF.

A plausible rationale for this transformation is depicted in Scheme 3. The soft nucleophile I<sup>−</sup> attacked regioselectively the 2-position of cyclopropenes **1** to give a stereodefined allylic carbanion intermediate **5**, which would react with imine **3** to give the possible intermediate **6**. Subsequent intramolecular nucleophilic substitution of **6** would afford **4** and regenerate I<sup>−</sup>. The difference in regioselectivities observed for an imine and an alkyl halide as the electrophile may be explained by the internal delivery of the metal-chelated imine to the remote carbon of the allylic system in **5**.<sup>10</sup>

In conclusion, we have developed a novel NaI-catalyzed ring-opening aziridination reaction of cyclopropenes with imines,

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- 8 S. Ma, J. Zhang, Y. Cai and L. Lu, *J. Am. Chem. Soc.*, 2003, **126**, 13954.
- 9 X-Ray data for compound **4aa**: C<sub>25</sub>H<sub>29</sub>NO<sub>6</sub>S, *M<sub>w</sub>* = 471.55, monoclinic, space group *P2(1)/c*, MoK $\alpha$ , final *R* indices [*I* > 2 $\sigma$ (*I*)], *R*1 = 0.0682, *wR*2 = 0.1607, *a* = 11.211(2), *b* = 8.6072(16), *c* = 26.662(5) Å,  $\alpha$  = 90(2),  $\beta$  = 99.710(4),  $\gamma$  = 90(2)°, *V* = 2535.8(8) Å<sup>3</sup>, *T* = 293(2) K, *Z* = 4, reflections collected/unique: 14986/5885 (*R*<sub>int</sub> = 0.1523), no observation [*I* > 2 $\sigma$ (*I*)] 1636, parameters 319.†
- 10 We thank the referee for this suggestion.

† CCDC 227385. See <http://www.rsc.org/suppdata/cc/b4/b413807d/> for crystallographic data in .cif or other electronic format.