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# One-pot Stereoselective Syntheses of 2-Acylaziridines and 2-Acylpyrrolidines from *N*-(Propargylic)hydroxylamines

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**Abstract:** A stereoselective direct transformation of *N*-(propargylic)hydroxylamines into *cis*-2-acylaziridines was realized by the combined use of AgBF<sub>4</sub> and CuCl. Copper salts were confirmed to promote the transformation of the

intermediary 4-isoxazolines to 2-acylaziridines. Both 3-aryl and 3-alkyl substituted 2-acylaziridines could be prepared by this method. Furthermore, subsequent 1,3-dipolar cycloaddition of azomethine ylides generated in situ from the intermediary 2-acylaziridines with maleimides was achieved by one-

pot procedure to afford the corresponding 2-acylpyrrolidines consisting of an octahydropyrrolo[3,4-*c*]pyrrole skeleton stereoselectively.

**Keywords:** 2-acylaziridine • 2-acylpyrrolidine • 4-isoxazoline • rearrangement • azomethine ylide

## Introduction

2-Acylaziridines are versatile synthetic intermediates for a wide range of important nitrogen-containing chemicals, for example via ring-opening reactions,<sup>[1]</sup> and some of them have biological activities.<sup>[2]</sup> General procedure to prepare 2-acylaziridines includes metal catalyzed addition of nitrene to alkenes,<sup>[3]</sup> metal catalyzed carbene addition to imine functions,<sup>[4]</sup> Micheal addition-elimination of hydroxylamine and hydrazine derivatives to enones,<sup>[5]</sup> ring-closure of 2-azido-3-hydroxy ketones,<sup>[6]</sup> and nucleophilic reaction of amines to  $\alpha,\beta$ -dibromoketones.<sup>[7]</sup> Although *trans*-2-acylaziridines could be readily prepared, stereoselective synthesis of *cis*-2-acylaziridines is rather difficult. Only a few methods for preparation of *cis*-3-alkyl substituted 2-acylaziridines were reported.<sup>[4a,b,d]</sup> Baldwin rearrangement of 4-isoxazolines was known to afford 2-acylaziridines, however, the reaction conditions were drastic and the diastereoselectivity was not always good.<sup>[8]</sup> Although cobalt-mediated rearrangement of 4-isoxazolines also gave the corresponding 2-acylaziridines, stereoselectivity was not so high.<sup>[8i]</sup>

Recently, we have reported a one-pot reaction consisting of an enantioselective nucleophilic addition of alkynylzinc reagents to nitrones and a subsequent cyclization to give the corresponding 4-isoxazolines with high enantioselectivity.<sup>[9]</sup> In order to prepare 4-isoxazolines more efficiently, the cyclization of *N*-(propargylic)hydroxylamines to 4-isoxazolines was investigated in the presence of a metal salt, and AgBF<sub>4</sub> was found to be a catalyst of choice for the cyclization.<sup>[10]</sup> During the investigation of the metal catalyzed ring closure of *N*-(propargylic)hydroxylamines, *cis*-2-acylaziridines were found to be produced diastereoselectively in the presence of a copper salt at rt. Herein, we wish to report the details about one-pot preparation of 2-acylaziridines from *N*-(propargylic)hydroxylamines via ring closure to 4-isoxazolines and the successive Baldwin rearrangement in the presence of AgBF<sub>4</sub> and a copper salt.<sup>[11]</sup> Furthermore, one-pot stereoselective synthesis of 2-acylpyrrolidines via 1,3-dipolar cycloaddition of azomethine ylides generated from the 2-acylaziridines is also described.

## Results and Discussion

The cyclization of *N*-benzyl-*N*-(1,3-diphenylprop-2-ynyl)hydroxylamine (**1a**) was examined in the presence of various kinds of metal salts without an amine, and it was found that AgBF<sub>4</sub> was a good catalyst for cyclization to 4-isoxazolines.<sup>[10]</sup> During the survey of metal salts, it was found that not only 4-isoxazoline **2a** but also a *cis*-2-acylaziridine **3a**<sup>[8i,12]</sup> was produced with complete diastereoselectivity when CuCl was used in CH<sub>2</sub>Cl<sub>2</sub> at rt (Table 1, Entry 1). Then, direct transformation of **1a** to 2-acylaziridine **3a** was intensively investigated and the results were summarized in Table 1.

The reaction by the use of 1.0 equiv of CuCl<sub>2</sub> or CuI was messy and the 2-acylaziridine **3a** was not obtained (Entries 2 and 3). The use of cationic copper salts afforded the *cis*-2-acylaziridine **3a** as a major product (Entries 4–7), however, the chemical yield was not high. By monitoring the reaction using TLC, it was observed that the 4-isoxazoline was once produced and gradually consumed. In order to promote the cyclization step to 4-isoxazoline, *N*-

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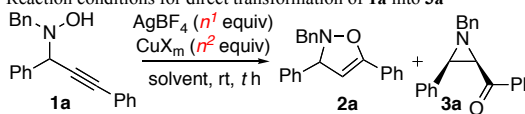
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Recently, microwave-assisted rearrangement was reported, however, the methods was limited to 3-aryl substituted acylaziridines.<sup>[8m]</sup>

(propargylic)hydroxylamine was firstly treated with 0.1 equiv AgBF<sub>4</sub> for 7 h and then CuCl was added to the reaction mixture: The chemical yield of **3a** was improved (Entry 8). The treatment with AgBF<sub>4</sub> together with CuCl further increased the yield of **3a** (Entry 9). By the use of 0.2 equiv of AgBF<sub>4</sub> and 1.0 equiv of CuCl, the reaction proceeded rather smoothly to afford **3a** in more than 80% yield (Entries 10 and 11). Solvent effect was examined in the reaction using 0.2 equiv of AgBF<sub>4</sub> and 1.0 equiv of CuCl, and CH<sub>2</sub>Cl<sub>2</sub> was found to be best among the examined solvents (Entries 11–16). Although combination of 0.2 equiv of AgBF<sub>4</sub> and 1.0 equiv of several cationic copper salts were examined, the reactions were not so clean and resulted in decrease of the chemical yields of **3a** (Entries 17–20).

In order to explore the possibilities reducing the amount of copper salt, the reaction using 0.2 equiv of CuCl with 0.2 equiv of AgBF<sub>4</sub> was carried out: The transformation proceeded a little sluggishly to afford **3a**, but still in comparably good yield (Entries 21 and 22). In the present one-pot reaction, the active copper species was presumed to be CuBF<sub>4</sub> accompanied with generation of AgCl. Then the reaction in the presence of only 0.2 equiv of CuBF<sub>4</sub>(CH<sub>3</sub>CN)<sub>2</sub> was again examined to give the *cis*-2-acylaziridine **3a** in good yield (Entry 23), although the use of 1.0 equiv of CuBF<sub>4</sub>(CH<sub>3</sub>CN)<sub>4</sub> made the reaction rather complicated (Entry 6). Further addition of AgCl slightly decreased the yield (Entry 24). The use of 0.2 equiv of CuOTf(C<sub>6</sub>H<sub>6</sub>)<sub>0.5</sub> was also effective to give **3a** in good yield (Entry 25). Consequently, the combined use of 0.2 equiv of AgBF<sub>4</sub> and 1.0 equiv of CuCl was the best for the sequential cyclization and Baldwin rearrangement.

Table 1. Reaction conditions for direct transformation of **1a** into **3a**



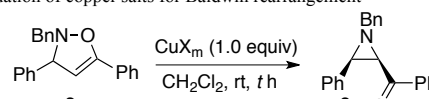
Entry	n <sup>1</sup> / equiv	CuX <sub>m</sub>	n <sup>2</sup> / equiv	solvent	t / h	<b>2a</b> / %	<b>3a</b> / %
1	0	CuCl	1.0	CH <sub>2</sub> Cl <sub>2</sub>	41	16	2 <sup>[a]</sup>
2	0	CuCl <sub>2</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	44	--	--
3	0	CuI	1.0	CH <sub>2</sub> Cl <sub>2</sub>	44	--	-- <sup>[b]</sup>
4	0	CuOTf(C <sub>6</sub> H <sub>6</sub> ) <sub>0.5</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	17	23	58
5	0	Cu(OTf) <sub>2</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	48	--	45
6	0	CuBF <sub>4</sub> (CH <sub>3</sub> CN) <sub>4</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	7	--	45
7	0	Cu(BF <sub>4</sub> ) <sub>2</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	25	--	48
8 <sup>[c]</sup>	0.1	CuCl	1.0	CH <sub>2</sub> Cl <sub>2</sub>	41	24	53
9	0.1	CuCl	1.0	CH <sub>2</sub> Cl <sub>2</sub>	8	32	61
10	0.2	CuCl	1.0	CH <sub>2</sub> Cl <sub>2</sub>	8	13	84
11	0.2	CuCl	1.0	CH <sub>2</sub> Cl <sub>2</sub>	20	4	88
12	0.2	CuCl	1.0	MeCN	20	24	-- <sup>[a]</sup>
13	0.2	CuCl	1.0	MeOH	20	12	21
14	0.2	CuCl	1.0	THF	20	23	47
15	0.2	CuCl	1.0	Et <sub>2</sub> O	20	22	6 <sup>[a]</sup>
16	0.2	CuCl	1.0	toluene	20	28	13 <sup>[a]</sup>
17	0.2	CuOTf(C <sub>6</sub> H <sub>6</sub> ) <sub>0.5</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	7	--	35
18	0.2	Cu(OTf) <sub>2</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	8	--	13
19	0.2	CuBF <sub>4</sub> (CH <sub>3</sub> CN) <sub>4</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	8	--	42
20	0.2	Cu(BF <sub>4</sub> ) <sub>2</sub>	1.0	CH <sub>2</sub> Cl <sub>2</sub>	8	10	42
21	0.2	CuCl	0.2	CH <sub>2</sub> Cl <sub>2</sub>	8	10	58
22	0.2	CuCl	0.2	CH <sub>2</sub> Cl <sub>2</sub>	23	--	82
23	0	CuBF <sub>4</sub> (CH <sub>3</sub> CN) <sub>4</sub>	0.2	CH <sub>2</sub> Cl <sub>2</sub>	23	--	74
24	0.2 <sup>[d]</sup>	CuBF <sub>4</sub> (CH <sub>3</sub> CN) <sub>4</sub>	0.2	CH <sub>2</sub> Cl <sub>2</sub>	23	--	65
25	0	CuOTf(C <sub>6</sub> H <sub>6</sub> ) <sub>0.5</sub>	0.2	CH <sub>2</sub> Cl <sub>2</sub>	41	--	78

[a] The hydroxylamine **1a** was recovered in 69% (Entry 1), 32% (Entry 12), 65% (Entry 15), and 7% (Entry 16) yields, respectively. [b] Most of the hydroxylamine **1a** was recovered. [c] The hydroxylamine **1a** was firstly treated with AgBF<sub>4</sub> for 7 h, and then CuCl was added to the resulting reaction mixture. [d] 0.2 Equiv of AgCl was used instead of AgBF<sub>4</sub>.

Toward the rearrangement from 4-isoxazoline to 2-acylaziridine, evaluation of copper salts was separately performed, that is, the 4-isoxazoline **2a** was treated with copper salts as shown in the Table 2.

Although the reaction was rather sluggish when only CuCl was used, addition of AgBF<sub>4</sub> again promoted the rearrangement (Entries 1 and 2). Cationic Cu(I) salts, especially CuOTf(C<sub>6</sub>H<sub>6</sub>)<sub>0.5</sub>, were found to be effective as a promoter for this rearrangement (Entries 3 and 5), whereas Cu(II) salts were not effective (Entries 4 and 6).

Table 2. Evaluation of copper salts for Baldwin rearrangement

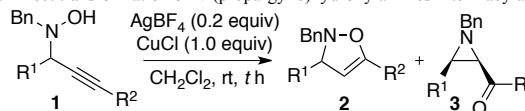


Entry	CuX <sub>m</sub>	t / h	Yield / %
1	CuCl	41	23 <sup>[a]</sup>
2 <sup>[b]</sup>	CuCl	18	89
3	CuOTf(C <sub>6</sub> H <sub>6</sub> ) <sub>0.5</sub>	4	81
4	Cu(OTf) <sub>2</sub>	41	3
5	CuBF <sub>4</sub> (CH <sub>3</sub> CN) <sub>4</sub>	22	71
6	Cu(BF <sub>4</sub> ) <sub>2</sub>	41	45

[a] The 4-isoxazoline **2a** was recovered in 68% yield. [b] In addition to CuCl, 0.2 equiv of AgBF<sub>4</sub> was also added to the reaction.

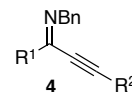
The one-pot cyclization-rearrangement was applied to several *N*-(propargylic)hydroxylamines **1** bearing aromatic and/or aliphatic substituents by the treatment with AgBF<sub>4</sub> (0.2 equiv) and CuCl (1.0 equiv). As listed in Table 3, the corresponding *cis*-acylaziridines **3** were produced stereoselectively.<sup>[12]</sup> A *cis*-2-heptanoyl-3-phenylaziridine **3b** was obtained in reasonable chemical yield (Entry 2). In the case of 2-pivaloylaziridine **3c**, a small amount of *trans*-isomer was furnished (Entry 3). Although transformation of propyl-substituted hydroxylamine **1d** was not so clean and a small amount of the corresponding *trans*-isomer and a dehydrated imine **4d** were formed, *cis*-2-benzoyl-3-propylaziridine **3d** was predominantly produced (Entry 4). In the case of cyclohexyl-substituted *N*-(propargylic)hydroxylamine **1e**, increase of the amount of AgBF<sub>4</sub> could improve the chemical yield (Entries 5 and 6). The reaction of a hydroxylamine **1f**, in which both R<sup>1</sup> and R<sup>2</sup> were alkyl groups, afforded *cis*-2-acylaziridine **3f** stereoselectively (Entry 7).

Table 3. Direct transformation of *N*-(propargylic)hydroxylamines into 2-acylaziridines



Entry	R <sup>1</sup>	R <sup>2</sup>		t / h	<b>2a</b> / %	<b>3a</b> / %
1	Ph	Ph	<b>a</b>	20	4	88
2	Ph	<i>n</i> Hex	<b>b</b>	27	--	63
3	Ph	<i>t</i> Bu	<b>c</b>	24	--	72 <sup>[a]</sup>
4	<i>n</i> Pr	Ph	<b>d</b>	41	--	49 <sup>[a,b]</sup>
5	<i>c</i> Hex	Ph	<b>e</b>	25	14	64
6 <sup>[c]</sup>				24	7	76
7	Me	<i>n</i> Hex	<b>f</b>	23	--	58

[a] The corresponding *trans*-isomer of **3** was obtained in 6% (Entry 3) and 10% (Entry 4) yields, respectively. [b] An imine, 1-phenyl-*N*-(1-phenylhex-1-yn-3-ylidene)methanamine (**4d**), was obtained in 28% yield. [c] The amount of AgBF<sub>4</sub> was 0.3 equiv.



In the case of Co<sub>2</sub>(CO)<sub>8</sub> (0.5 equiv) mediated rearrangement of 4-isoxazoline, a radical pathway was proposed to give 2.8/1 mixture of *cis/trans*-2-acylaziridines starting from **1a**.<sup>[81]</sup> When **1a** was treated with 1.0 equiv of CuOTf(C<sub>6</sub>H<sub>6</sub>)<sub>0.5</sub> under a similar conditions (in ClCH<sub>2</sub>CH<sub>2</sub>Cl at 80 °C for 0.5 h), **3a** was obtained in 80% yield and the diastereoselectivity was still high (**3a**/*trans*-isomer = 20/1, determined by <sup>1</sup>H NMR spectrum of the crude products), different from the result of the reaction catalyzed by Co<sub>2</sub>(CO)<sub>8</sub>. Furthermore, addition of galvinoxyl free radical did not affect the reaction from

**2a** to **3a** (according to Entry 3 in Table 2) as a radical inhibitor. These facts might suggest that a radical pathway might be ruled out. Although the precise reaction mechanism of the present rearrangement is not yet clear, [1,3]-sigmatropic rearrangement proposed for original Baldwin rearrangement without metal salts is a probable pathway to afford the *cis*-2-acylaziridine (Figure 1).<sup>[8c,d,f]</sup> The reaction might be activated by coordination of nitrogen to copper resulting in weakening the N–O bond (Figure 1).

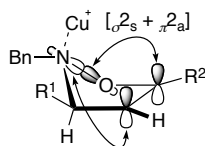


Figure 1. [1,3]-Sigmatropic rearrangement proposed for the present transformation

2-Acylaziridines are well-known to generate azomethine ylides via thermal ring-opening, which proceeds through a conrotatory C–C bond-breaking process according to the Woodward–Hoffmann rules. Following 1,3-dipolar cycloaddition of the generated azomethine ylides with electron-deficient olefins afforded 2-acylpyrrolidine skeletons,<sup>[13,14]</sup> some of which were bioactive.<sup>[15]</sup> For example, the cycloaddition of azomethine ylides generated from *cis*- and/or *trans*-2-benzoylaziridines with *N*-phenylmaleimide gave a diastereomeric mixture of pyrrolidines depends on the reaction conditions.<sup>[14d,e]</sup> However, *cis*-2-acylaziridines were not so easy to be prepared and related cycloaddition of azomethine ylides derived from 2-acylaziridines with various substituents including aliphatic groups at C3 position was scarcely reported. Now, we could prepare 2-acylaziridines possessing aromatic and/or aliphatic substituents in a *cis*-selective manner. Therefore, we investigated 1,3-dipolar cycloaddition of azomethine ylides generated in situ from the 2-acylaziridines via one-pot procedure starting from *N*-(propargylic)hydroxylamines **1**.

After treatment of *N*-(propargylic)hydroxylamines **1a** with 0.2 equiv of AgBF<sub>4</sub> and 1.0 equiv of CuCl for 24 h at rt in CH<sub>2</sub>Cl<sub>2</sub>, *N*-methylmaleimide (**5A**) was added to the reaction mixture. When the reaction was carried out at rt, the desired product was not obtained. However, the expected 1,3-dipolar cycloaddition proceeded at 75 °C in ClCH<sub>2</sub>CH<sub>2</sub>Cl, after exchanging the solvent from CH<sub>2</sub>Cl<sub>2</sub>, to give a 2-acylpyrrolidine **6aA** consisting of an octahydropyrrolo[3,4-*c*]pyrrole skeleton diastereoselectively in 33% yield (Table 4, Entry 1). Cycloaddition to *N*-benzylmaleimide (**5B**) afforded the corresponding cycloadduct **6aB** in a similar chemical yield (Entry 2). Due to easy handling of *N*-benzylmaleimide (**5B**) and its product **6aB** especially for their relatively high solubility, 1,3-dipolar cycloaddition was further examined using **5B**. When the reaction temperature was increased, the chemical yield was improved (Entry 3). The cycloadduct **6aB** was obtained in 60% yield when cycloaddition was carried out at 145 °C in xylene (Entry 4). When the reaction was performed under more condensed conditions, the chemical yield was further improved up to 85% yield (Entry 5).

One-pot synthesis of substituted pyrrolidines was then investigated starting from *N*-(propargylic)hydroxylamines **1** possessing not only aromatic but also aliphatic substituents. Phenyl-substituted pyrrolidines **6bB** and **6cB** (R<sup>1</sup> = Ph) were obtained in ca 60% yields with complete diastereoselectivity (Entries 6 and 7). It was revealed that 1,3-dipolar cycloaddition of azomethine ylides via 2-acylaziridines **3d–f** bearing an aliphatic substituent at C3 position (R<sup>1</sup> = alkyl) afforded the corresponding pyrrolidines stereoselectively although total chemical yields were not good enough (Entries 8–11). In the case of 5-cylohexyl-substituted pyrrolidines **6eA** and **6eB**, chemical yields were still over 50%

yields after 3 step-reaction consisting of ring-closure, Baldwin rearrangement, and 1,3-dipolar cycloaddition (Entries 9 and 10).

Table 4. One-pot preparation of 2-acylpyrrolidines from *N*-(propargylic)hydroxylamines

Entry	R <sup>1</sup>	R <sup>2</sup>	R	t <sup>1</sup> / h	solvent	T / °C	t <sup>2</sup> / h	<b>6</b>	Yield / %
1	Ph	Ph	Me	24	ClCH <sub>2</sub> CH <sub>2</sub> Cl <sup>[a]</sup>	75	24	<b>6aA</b>	33
2	Ph	Ph	Bn	24	ClCH <sub>2</sub> CH <sub>2</sub> Cl <sup>[a]</sup>	75	24	<b>6aB</b>	32
3				24	toluene <sup>[b]</sup>	110	6		53
4				27	xylene <sup>[a]</sup>	145	1		60
5				24	xylene <sup>[b]</sup>	145	2		85
6	Ph	<i>n</i> Hex	Bn	31	xylene <sup>[b]</sup>	145	3	<b>6bB</b>	56
7	Ph	<i>t</i> Bu	Bn	31	xylene <sup>[b]</sup>	145	1	<b>6cB</b>	66
8	<i>n</i> Pr	Ph	Bn	48	xylene <sup>[b]</sup>	145	2	<b>6dB</b>	39
9 <sup>[c]</sup>	<i>c</i> Hex	Ph	Me	27	xylene <sup>[b]</sup>	145	3	<b>6eA</b>	52
10 <sup>[c]</sup>	<i>c</i> Hex	Ph	Bn	27	xylene <sup>[b]</sup>	145	3	<b>6eB</b>	53
11	Me	<i>n</i> Hex	Bn	24	xylene <sup>[b]</sup>	145	1.5	<b>6fB</b>	27

[a] Concentration was 0.06 mmol mL<sup>-1</sup>. [b] Concentration was 0.25 mmol mL<sup>-1</sup>. [c] Amount of AgBF<sub>4</sub> was 0.3 equiv.

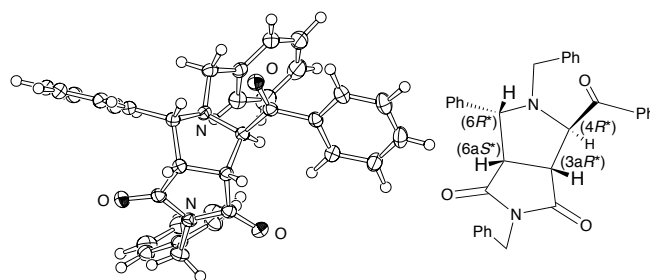


Figure 2. X-ray structure of **6aB**

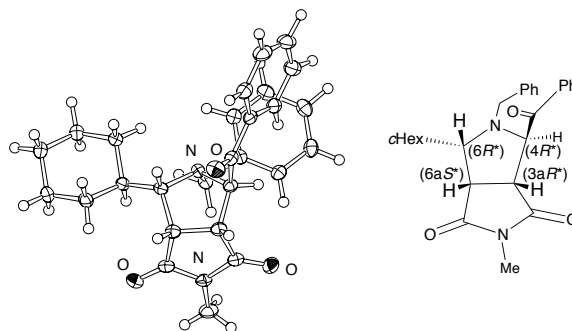
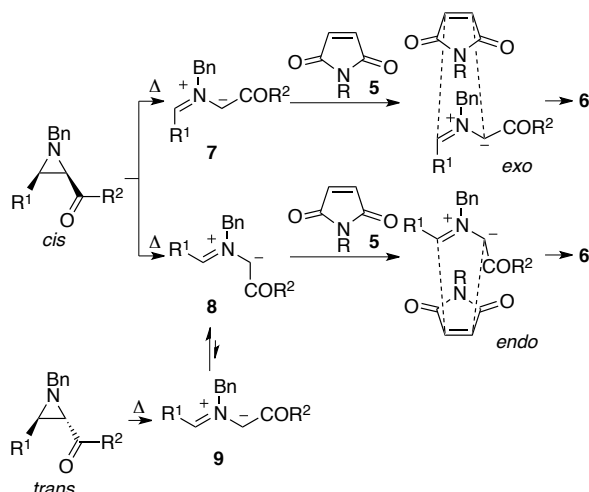


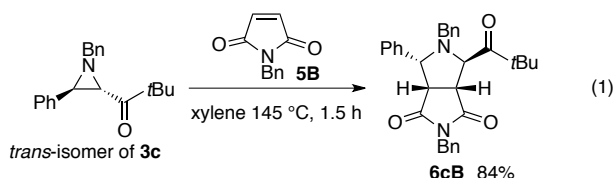
Figure 3. X-ray structure of **6eA**

Relative stereochemistry of the product **6aB** and **6eA** was determined to be 3a*R*\*,4*R*\*,6*R*\*,6a*S*\* by X-ray crystallographic analyses of their single crystals (Figures 2 and 3). The stereochemistry of other cycloadducts was tentatively assigned to be also 3a*R*\*,4*R*\*,6*R*\*,6a*S*\*, since the coupling constants *J*<sub>3a-4</sub> and *J*<sub>6-6a</sub> between the methine protons in their <sup>1</sup>H NMR spectra were in accordance with those of **6aB** and **6eA**, the stereochemistry of which was determined by X-ray crystallography. Based on this assignment, 1,3-dipolar cycloaddition was considered to proceed via *exo*-mode with *S*-shaped azomethine ylide **7** and/or *endo*-mode with *S*-shaped azomethine ylide **8** regardless of R<sup>1</sup>, whether it is an aromatic or aliphatic substituent (Scheme 1).<sup>[16]</sup> In the case of pyrrolidines **6cB** and **6dB**, the products were isolated as single diastereomers although the intermediary *cis*-2-acylaziridines might be contaminated with their *trans*-isomers as observed in Table 3 (Entries 3 and 4). We confirmed that 1,3-dipolar cycloaddition of

the isolated *trans*-isomer of **3c** with **5B** gave **6cB** stereoselectively at 145 °C in xylene in 84% yield (eq. 1).<sup>[17]</sup> These results suggested existence of the equilibrium between *W*-dipole **9**, which might be favorable than *U*-dipole,<sup>[18]</sup> and *S*-dipole **7** and/or **8** under high temperature even in the case of 3-alkyl substituted 2-acylaziridine **3d**.<sup>[19]</sup> Therefore, the *trans*-2-acylaziridine also afforded **6** via 1,3-dipolar cycloaddition through *S*-dipole **7** and/or **8**.



Scheme 1. Proposed pathway of 1,3-dipolar cycloaddition



## Conclusion

As described above, a direct transformation of *N*-(propargylic)hydroxylamines into *cis*-2-acylaziridines has been developed. Furthermore, one-pot stereoselective preparation of 2-acylpyrrolidine consisting of an octahydropyrrolo[3,4-*c*]pyrrole skeleton was achieved via 1,3-dipolar cycloaddition of azomethine ylides, generated in situ by thermal ring-opening of the intermediary 2-acylaziridines, in the presence of maleimides. The present methods would be quite useful for the synthesis of a wide range of nitrogen containing biologically active compounds because *cis*-2-acylaziridines and 2-acylpyrrolidines are versatile synthons for such chemicals.

## Experimental Section

**General Remarks:** The <sup>1</sup>H NMR spectra were recorded on a JEOL ECS 400 NMR (400 MHz) spectrometer in CDCl<sub>3</sub> and the chemical shifts were determined in the δ-scale relative to TMS (δ = 0 ppm) as an internal standard. The <sup>13</sup>C NMR spectra were measured on a JEOL ECS 400 NMR (100 MHz) spectrometer in CDCl<sub>3</sub> and the chemical shifts were determined in the δ-scale relative to CDCl<sub>3</sub> (δ = 77.0 ppm) as an internal standard. The IR spectra were performed on a JASCO FT/IR-230 spectrometer. All measurements for X-ray crystallographic analyses were made on a Rigaku/MSC Mercury diffractometer with graphite monochromated Mo-Kα radiation. Elemental analyses were carried out on a Yanaco CHN Corder MT-5 elemental analyzer. The MS spectra were recorded with JEOL JMS-SX102A and JMS-700 mass spectrometers. All solvents were distilled and stored over drying agents. Merck silica gel 60 PF254 (Art. 7749) and Cica silica gel 60N spherical neutral (37563-84) were used for thin-layer chromatography (TLC) and flash column chromatography, respectively. All of the melting points were determined with a micro melting apparatus (Yanagimoto-Seisakusho) and are uncorrected.

**Representative procedure of direct transformation of *N*-(propargylic)hydroxylamine **1a** to 2-acylaziridine **3a** (Table 3, Entry 1):** A mixture of *N*-(propargylic)hydroxylamine **1a** (219 mg, 0.7 mmol), AgBF<sub>4</sub> (27 mg, 0.14 mmol) and CuCl (69 mg, 0.7 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was stirred at rt under an argon atmosphere. After 20 h, the mixture was filtered through a pad of Celite and the solvent was removed under reduced pressure. The residue was purified by preparative TLC (hexane/AcOEt = 5/1) to give *cis*-2-acylaziridine **3a** (193 mg, 88% yield) and 4-isoxazoline **2a**<sup>[20]</sup> (9 mg, 4% yield).

In a similar manner, 2-acylaziridines **3b–3f** were prepared from the corresponding *N*-(propargylic)hydroxylamines **1b–1f**, respectively.

[(2*R*\*,3*R*\*)-1-Benzyl-3-phenylaziridin-2-yl](phenyl)methanone (**3a**):<sup>[18]</sup> *R*<sub>f</sub> = 0.35 (hexane/AcOEt = 5/1); a solid; m.p. 94–96 °C (from EtOH/hexane); <sup>1</sup>H NMR δ 3.22 (d, 1H, *J* = 6.9 Hz), 3.30 (d, 1H, *J* = 6.9 Hz), 3.71 (d, 1H, *J* = 14.0 Hz), 3.93 (d, 1H, *J* = 14.0 Hz), 7.01–7.40 (m, 13H), 7.77 (d, 2H, *J* = 6.4 Hz); <sup>13</sup>C NMR δ 49.6, 51.0, 63.5, 127.0, 127.2, 127.4, 127.7, 127.8, 127.9, 128.2, 132.8, 134.8, 136.7, 137.7, 192.9; IR (KBr) 3027, 1681, 1495, 1449, 1355, 1223, 1056, 935, 747, 737, 707, 696 cm<sup>-1</sup>.

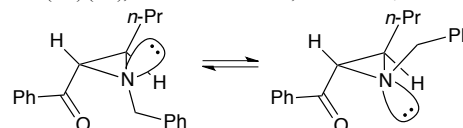
1-[(2*R*\*,3*R*\*)-1-Benzyl-3-phenylaziridin-2-yl]heptan-1-one (**3b**): *R*<sub>f</sub> = 0.45 (hexane/AcOEt = 5/1); an oil; <sup>1</sup>H NMR δ 0.80 (t, 3H, *J* = 7.4 Hz), 0.88–1.30 (m, 8H), 1.88 (ddd, 1H, *J* = 17.4, 8.2, 6.4 Hz), 2.20 (ddd, 1H, *J* = 17.4, 8.2, 6.4 Hz), 2.64 (d, 1H, *J* = 7.0 Hz), 3.14 (d, 1H, *J* = 7.0 Hz), 3.69 (d, 1H, *J* = 13.8 Hz), 3.78 (d, 1H, *J* = 13.8 Hz), 7.18–7.43 (m, 10H); <sup>13</sup>C NMR δ 14.0, 22.3, 22.8, 28.5, 31.4, 40.7, 48.6, 52.4, 64.0, 127.36, 127.43, 127.8, 128.10, 128.14, 128.4, 135.3 138.0, 207.4; IR (neat) 3062, 3031, 2928, 2857, 1699, 1604, 1496, 1454, 1376, 1204, 1067, 1029, 738, 699 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) (*M*<sup>+</sup>), Found: *m/z* 321.2087; Calcd for C<sub>22</sub>H<sub>27</sub>NO: 321.2093.

1-[(2*R*\*,3*R*\*)-1-Benzyl-3-phenylaziridin-2-yl]-2,2-dimethylpropan-1-one (**3c**): *R*<sub>f</sub> = 0.45 (hexane/AcOEt = 5/1); a solid; m.p. 85–88 °C (from EtOH/hexane); <sup>1</sup>H NMR δ 0.96 (s, 9H), 3.05 (d, 1H, *J* = 6.8 Hz), 3.12 (d, 1H, *J* = 6.8 Hz), 3.67 (d, 1H, *J* = 14.0 Hz), 3.94 (d, 1H, *J* = 14.0 Hz), 7.19–7.41 (m, 10H); <sup>13</sup>C NMR δ 25.7, 43.2, 49.4, 50.0, 63.4, 126.8, 127.1, 127.4, 127.5, 128.1, 134.9, 137.7, 206.6; IR (KBr) 3027, 2973, 1703, 1604, 1495, 1455, 1378, 1312, 1265, 1091, 1027, 840, 758, 732 cm<sup>-1</sup>; Found: C, 81.81; H, 7.79; N, 4.79%; Calcd for C<sub>20</sub>H<sub>23</sub>NO: C, 81.87; H, 7.90; N, 4.77%.

1-[(2*S*\*,3*R*\*)-1-Benzyl-3-phenylaziridin-2-yl]-2,2-dimethylpropan-1-one (*trans*-isomer of **3c**): *R*<sub>f</sub> = 0.50 (hexane/AcOEt = 5/1); an oil; <sup>1</sup>H NMR δ 1.04 (s, 9H), 3.15 (d, 1H, *J* = 2.5 Hz), 3.37 (d, 1H, *J* = 2.5 Hz), 3.93 (d, 1H, *J* = 13.8 Hz), 4.20 (d, 1H, *J* = 13.8 Hz), 7.19–7.41 (m, 10H); <sup>13</sup>C NMR δ 25.7, 44.6, 45.9, 49.7, 54.0, 126.3, 126.9, 128.2, 128.4, 128.5, 138.9, 139.3, 210.2; IR (neat) 3038, 2966, 1683, 1541, 1507, 1457, 1395, 1362, 1073, 752, 698 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) (*M*<sup>+</sup>), Found: *m/z* 293.1774; Calcd for C<sub>20</sub>H<sub>23</sub>NO: 293.1780.

[(2*R*\*,3*R*\*)-1-Benzyl-3-propylaziridin-2-yl](phenyl)methanone (**3d**): *R*<sub>f</sub> = 0.40 (hexane/AcOEt = 4/1); an oil; <sup>1</sup>H NMR δ 0.80 (t, 3H, *J* = 7.3 Hz), 1.18–1.52 (m, 4H), 2.21 (q, 1H, *J* = 6.4 Hz), 3.08 (d, 1H, *J* = 6.9 Hz), 3.61 (d, 1H, *J* = 13.7 Hz), 3.77 (d, 1H, *J* = 13.7 Hz), 7.22–7.56 (m, 8H), 8.00 (d, 2H, *J* = 8.2 Hz); <sup>13</sup>C NMR δ 13.7, 20.6, 29.6, 47.4, 48.9, 64.1, 127.1, 128.0, 128.1, 128.3, 128.5, 133.1, 137.3, 137.9, 195.2; IR (neat) 3059, 2954, 2869, 1673, 1596, 1578, 1496, 1449, 1389, 1361, 1228, 1067, 1020, 930, 737, 700, 661 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) (*M*<sup>+</sup>), Found: *m/z* 279.1621; Calcd for C<sub>19</sub>H<sub>21</sub>NO: 279.1623.

[(2*S*\*,3*R*\*)-1-Benzyl-3-propylaziridin-2-yl](phenyl)methanone (*trans*-isomer of **3d**): *R*<sub>f</sub> = 0.45 (hexane/AcOEt = 4/1); an oil; NMR showed the presence of two isomers (ratio = 3.5/1), which might be a sort of diastereomers in equilibrium as depicted below.<sup>21</sup> Major isomer: <sup>1</sup>H NMR δ 0.86 (t, 3H, *J* = 7.3 Hz), 1.30–1.37 (m, 2H), 1.48–1.56 (m, 2H), 2.59 (dt, 1H, *J* = 2.7, 6.0 Hz), 3.40 (d, 1H, *J* = 2.7 Hz), 3.78 (d, 1H, *J* = 13.3 Hz), 3.86 (d, 1H, *J* = 13.3 Hz), 7.18–7.59 (m, 8H), 7.92–7.95 (m, 2H); <sup>13</sup>C NMR δ 13.8, 20.4, 34.9, 44.2, 48.1, 55.3, 126.9, 128.2, 128.3, 128.5, 128.6, 133.1, 138.4, 139.1, 196.1; Minor isomer: <sup>1</sup>H NMR δ 0.99 (t, 3H, *J* = 7.3 Hz), 1.47–1.91 (m, 4H), 2.66 (dt, 1H, *J* = 2.7, 7.4 Hz), 2.87 (d, 1H, *J* = 2.7 Hz), 3.72 (d, 1H, *J* = 14.2 Hz), 4.10 (d, 1H, *J* = 14.2 Hz), 7.18–7.59 (m, 8H), 7.92–7.95 (m, 2H); <sup>13</sup>C NMR δ 14.0, 21.5, 28.0, 47.6, 48.3, 127.6, 128.1, 128.4, 128.5, 133.0, 138.9, 196.6 (Three signals might be overlapped with those of major isomer); IR (neat) 3061, 2959, 2929, 2871, 1667, 1538, 1449, 1379, 1265, 1070, 1026, 695 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) (*M*<sup>+</sup>), Found: *m/z* 279.1627; Calcd for C<sub>19</sub>H<sub>21</sub>NO: 279.1623.



1-Phenyl-*N*-(1-phenylhex-1-yn-3-ylidene)methanamine (**4d**): *R*<sub>f</sub> = 0.20 (hexane/AcOEt = 5/1); a solid; m.p. 77–78 °C (from AcOEt/hexane); <sup>1</sup>H NMR δ 0.93 (t, 3H, *J* = 7.3 Hz), 1.57–1.68 (m, 2H), 2.55 (t, 2H, *J* = 7.8 Hz), 5.31 (s, 2H), 7.23–7.31 (m, 6H), 7.37–7.40 (m, 2H), 7.44 (d, 2H, *J* = 7.8 Hz); <sup>13</sup>C NMR δ 13.7, 18.8, 32.4, 66.6, 82.9, 104.2, 121.5, 128.3, 128.5, 128.6, 129.3, 131.0, 133.9, 134.0; IR (KBr) 3058, 2955, 2870, 1517, 1485, 1438, 1303, 1250, 1176, 1164, 935, 759 cm<sup>-1</sup>; HRMS (FAB<sup>+</sup>) (*M*<sup>+</sup> + H), Found: *m/z* 262.1592; Calcd for C<sub>19</sub>H<sub>20</sub>N: 262.1596.

[(2*R*\*,3*R*\*)-1-Benzyl-3-cyclohexylaziridin-2-yl](phenyl)methanone (**3e**): *R*<sub>f</sub> = 0.40 (hexane/AcOEt = 5/1); a solid; m.p. 113–115 °C (from hexane/EtOH); <sup>1</sup>H NMR δ 0.92–1.26 (m, 6H), 1.40–1.76 (m, 5H), 1.96 (dd, 1H, *J* = 8.7, 6.9 Hz), 3.10 (d, 1H, *J* = 6.9 Hz), 3.60 (d, 1H, *J* = 13.7 Hz), 3.73 (d, 1H, *J* = 13.7 Hz), 7.23–7.58 (m, 8H), 8.01 (d, 2H, *J* = 7.3 Hz); <sup>13</sup>C NMR δ 25.27, 25.29, 26.0, 30.2, 31.2, 35.5, 47.3, 55.1, 64.5, 127.1, 128.0, 128.17, 128.19, 128.4, 132.9, 137.3, 137.8, 195.0; IR (KBr) 3031, 2924, 2849, 1683, 1598, 1448, 1225, 1049, 1023, 915, 738, 688 cm<sup>-1</sup>; Found: C, 82.72; H, 7.89; N, 4.38%; Calcd for C<sub>22</sub>H<sub>25</sub>NO: C, 82.41; H, 7.94; N, 4.42%.

1-[(2*R*\*,3*R*\*)-1-Benzyl-3-methylaziridin-2-yl]heptan-1-one (**3f**):  $R_f = 0.45$  (hexane/AcOEt = 4/1); an oil;  $^1\text{H NMR } \delta$  0.86 (t, 3H,  $J = 5.5$  Hz), 1.19 (d, 3H,  $J = 5.5$  Hz), 1.19–1.30 (m, 6H), 1.46–1.56 (m, 2H), 2.05 (dq, 1H,  $J = 6.9, 5.5$  Hz), 2.32 (d, 1H,  $J = 6.9$  Hz), 2.38–2.53 (m, 2H), 3.43 (d, 1H,  $J = 13.7$  Hz), 3.69 (d, 1H,  $J = 13.7$  Hz), 7.21–7.36 (m, 5H);  $^{13}\text{C NMR } \delta$  13.3, 14.0, 22.4, 23.5, 28.9, 31.5, 42.3, 43.4, 49.1, 63.9, 127.1, 127.8, 128.3, 138.2, 207.8; IR (neat) 3030, 2956, 2928, 2858, 1699, 1496, 1454, 1413, 1354, 1142, 1121, 1073, 1030, 733, 698  $\text{cm}^{-1}$ ; HRMS ( $\text{E}^+$ ) ( $\text{M}^+$ ): Found:  $m/z$  259.1937; Calcd for  $\text{C}_{17}\text{H}_{25}\text{NO}$ : 259.1936.

**Representative procedure of one-pot synthesis of 2-acylpyrrolidine 6aB starting from *N*-(propargylic)hydroxylamine 1a (Table 4, Entry 5):** A mixture of *N*-(propargylic)hydroxylamine **1a** (157 mg, 0.5 mmol),  $\text{AgBF}_4$  (19 mg, 0.1 mmol) and  $\text{CuCl}$  (50 mg, 0.5 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was stirred at rt under an argon atmosphere. After 24 h, *N*-benzylmaleimide (**5B**) (112 mg, 0.6 mmol) in xylene (2 mL) was added to the reaction mixture and  $\text{CH}_2\text{Cl}_2$  was evaporated under the reduced pressure. The resulting mixture in xylene was heated at 145 °C for 2 h and cooled to rt. The insoluble substance was filtered off through a pad of Celite and the solvent was removed under reduced pressure. The residue was purified by preparative TLC (hexane/Et<sub>2</sub>O = 1/1) to give **6aB** (215 mg, 85% yield).

In a similar manner, other 2-acylpyrrolidines **6aA**, **6eA**, and **6bB–6fB** were prepared from the corresponding *N*-(propargylic)hydroxylamines **1a–1f**, respectively.

(3*aR*\*,4*R*\*,6*R*\*,6*aS*\*)-4-Benzoyl-5-benzyl-2-methyl-6-phenyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6aA**):  $R_f = 0.30$  (hexane/Et<sub>2</sub>O = 1/1); a solid; m.p. 164–165 °C (from AcOEt/hexane);  $^1\text{H NMR } \delta$  2.94 (s, 3H), 3.24 (d, 1H,  $J = 7.8$  Hz), 3.63 (d, 1H,  $J = 13.7$  Hz), 3.70 (dd, 1H,  $J = 9.6, 7.8$  Hz), 3.77 (d, 1H,  $J = 13.7$  Hz), 5.15 (d, 1H,  $J = 9.6$  Hz), 5.24 (s, 1H), 7.04–7.12 (m, 2H), 7.19–7.22 (m, 3H), 7.29–7.41 (m, 7H), 7.56 (t, 1H,  $J = 7.3$  Hz), 7.80 (dd, 2H,  $J = 8.3, 0.9$  Hz);  $^{13}\text{C NMR } \delta$  25.0, 48.5, 50.2, 51.1, 62.4, 68.2, 127.2, 128.1, 128.30, 128.31, 128.4, 128.6, 128.7, 133.8, 135.0, 137.8, 137.9, 175.7, 177.3, 200.7; IR (KBr) 3031, 2876, 1773, 1697, 1668, 1591, 1494, 1434, 1381, 1323, 1284, 1230, 1115, 1069, 1001, 870, 755, 731, 697  $\text{cm}^{-1}$ ; Found: C, 76.25; H, 5.82; N, 6.57%; Calcd for  $\text{C}_{27}\text{H}_{24}\text{N}_2\text{O}_3$ : C, 76.39; H, 5.70; N, 6.60%.

(3*aR*\*,4*R*\*,6*R*\*,6*aS*\*)-4-Benzoyl-2,5-dibenzyl-6-phenyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6aB**):  $R_f = 0.35$  (hexane/Et<sub>2</sub>O = 1/1); a solid; m.p. 165–166 °C (from AcOEt/hexane);  $^1\text{H NMR } \delta$  3.28 (d, 1H,  $J = 7.8$  Hz), 3.56 (d, 1H,  $J = 13.7$  Hz), 3.62 (dd, 1H,  $J = 9.6, 7.8$  Hz), 3.67 (d, 1H,  $J = 13.7$  Hz), 4.56 (d, 1H,  $J = 13.8$  Hz), 4.65 (d, 1H,  $J = 13.8$  Hz), 5.11 (d, 1H,  $J = 9.6$  Hz), 5.19 (s, 1H), 6.93–6.97 (m, 2H), 7.02–7.12 (m, 2H), 7.13–7.27 (m, 6H), 7.37–7.46 (m, 7H), 7.55 (t, 1H,  $J = 7.3$  Hz), 7.83 (d, 2H,  $J = 7.8$  Hz);  $^{13}\text{C NMR } \delta$  42.6, 48.0, 49.9, 50.5, 62.6, 68.0, 127.1, 127.8, 128.0, 128.1, 128.3, 128.35, 128.40, 128.5, 128.7, 129.4, 133.7, 135.0, 135.8, 136.9, 138.0, 175.0, 177.3, 200.3; IR (KBr) 3030, 2878, 1772, 1702, 1579, 1494, 1453, 1422, 1396, 1339, 1235, 1175, 1136, 1027, 989, 727, 699  $\text{cm}^{-1}$ ; Found: C, 79.25; H, 5.65; N, 5.63%; Calcd for  $\text{C}_{33}\text{H}_{28}\text{N}_2\text{O}_3$ : C, 79.18; H, 5.64; N, 5.60%. Crystal data:  $\text{C}_{33}\text{H}_{28}\text{N}_2\text{O}_3$ ,  $M_r = 500.60$ , monoclinic,  $P2_1/n$ ,  $a = 11.7284(8)$ ,  $b = 9.1475(5)$ ,  $c = 24.016(2)$  Å,  $V = 2528.7(3)$  Å<sup>3</sup>,  $\beta = 101.057(2)^\circ$ ,  $Z = 4$ ,  $D_{\text{calcd}} = 1.315$  g  $\text{cm}^{-3}$ ,  $R = 0.065$  ( $R_w = 0.070$ ) for 5599 reflections with  $I > 3.00\sigma(I)$  and 343 variable parameters. Crystallographic data for **6aB** have been deposited with Cambridge Crystallographic Data Centre as supplementary publication No. CCDC 913503.

(3*aR*\*,4*R*\*,6*R*\*,6*aS*\*)-2,5-Dibenzyl-4-heptanoyl-6-phenyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6bB**):  $R_f = 0.30$  (hexane/AcOEt = 3/1); an oil;  $^1\text{H NMR } \delta$  1.00–1.31 (m, 5H), 1.52–1.71 (m, 6H), 1.95–2.05 (m, 2H), 3.16 (d, 1H,  $J = 13.3$  Hz), 3.40–3.43 (m, 2H), 3.54 (d, 1H,  $J = 6.8$  Hz), 3.70 (d, 1H,  $J = 13.3$  Hz), 4.68 (d, 1H,  $J = 13.7$  Hz), 4.75 (d, 1H,  $J = 13.7$  Hz), 4.85 (s, 1H), 6.86 (d, 2H,  $J = 6.8$  Hz), 7.16–7.30 (m, 6H), 7.35 (t, 2H,  $J = 7.3$  Hz), 7.42–7.47 (m, 3H), 7.51 (d, 2H,  $J = 7.4$  Hz);  $^{13}\text{C NMR } \delta$  14.0, 22.4, 23.0, 28.7, 31.5, 42.1, 42.7, 47.2, 49.8, 51.0, 66.5, 68.1, 127.4, 127.9, 128.11, 128.13, 128.50, 128.54, 128.6, 129.5, 135.8, 136.7, 138.0, 175.0, 177.1, 212.7; IR (neat) 3063, 3032, 2929, 2857, 1775, 1713, 1604, 1585, 1495, 1454, 1433, 1398, 1347, 1290, 1215, 1173, 1144, 1074, 1029, 921, 882, 832, 754, 699  $\text{cm}^{-1}$ ; HRMS ( $\text{FAB}^+$ ) ( $\text{M}^+ + \text{H}$ ): Found:  $m/z$  509.2808; Calcd for  $\text{C}_{33}\text{H}_{37}\text{N}_2\text{O}_3$ : 509.2804.

(3*aR*\*,4*R*\*,6*R*\*,6*aS*\*)-2,5-Dibenzyl-4-phenyl-6-pivaloyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6cB**):  $R_f = 0.35$  (hexane/Et<sub>2</sub>O = 1/1); a solid; m.p. 133–134 °C (from AcOEt/hexane);  $^1\text{H NMR } \delta$  0.99 (s, 9H), 3.11 (d, 1H,  $J = 8.2$  Hz), 3.37 (d, 1H,  $J = 15.1$  Hz), 3.55 (dd, 1H,  $J = 9.6, 8.2$  Hz), 3.68 (d, 1H,  $J = 15.1$  Hz), 4.55 (d, 1H,  $J = 13.7$  Hz), 4.62 (d, 1H,  $J = 13.7$  Hz), 4.83 (s, 1H), 5.27 (d, 1H,  $J = 9.6$  Hz), 6.96–7.29 (m, 10H), 7.35–7.41 (m, 3H), 7.43–7.46 (m, 2H);  $^{13}\text{C NMR } \delta$  26.0, 42.6, 44.9, 48.3, 49.3, 50.4, 61.7, 68.4, 126.9, 127.2, 128.0, 128.1, 128.4, 128.5, 129.5, 135.8, 137.3, 138.2, 175.0, 177.0, 217.8; IR (KBr) 3037, 2977, 1774, 1702, 1493, 1477, 1436, 1394, 1343, 1215, 1172, 1136, 1062, 988, 878, 778, 753, 730, 701  $\text{cm}^{-1}$ ; Found: C, 77.35; H, 6.80; N, 5.79%; Calcd for  $\text{C}_{31}\text{H}_{32}\text{N}_2\text{O}_3$ : C, 77.47; H, 6.71; N, 5.83%.

(3*aR*\*,4*R*\*,6*S*\*,6*aS*\*)-4-Benzoyl-2,5-dibenzyl-6-propyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6dB**):  $R_f = 0.30$  (hexane/AcOEt = 4/1); a solid; m.p. 146–147 °C (from AcOEt/hexane);  $^1\text{H NMR } \delta$  0.93 (t, 3H,  $J = 6.9$  Hz), 1.33–1.42 (m, 2H), 1.67–1.81 (m, 2H), 3.25 (d, 1H,  $J = 7.8$  Hz), 3.38 (t, 1H,  $J = 7.8$  Hz), 3.71 (d, 1H,  $J = 14.2$  Hz), 3.87–3.96 (m, 1H), 3.94 (d, 1H,  $J = 14.2$  Hz), 4.69 (d, 1H,  $J = 14.2$  Hz), 4.76 (d, 1H,  $J = 14.2$  Hz), 4.88 (s, 1H), 6.92 (d, 2H,  $J = 6.0$  Hz), 7.09–7.18 (m, 3H), 7.29–7.44 (m, 7H), 7.52 (t, 1H,  $J = 7.3$  Hz), 7.84 (d, 2H,  $J = 8.2$  Hz);  $^{13}\text{C NMR } \delta$  14.4, 19.7, 31.8, 42.6, 47.1, 47.4, 50.8, 63.6, 65.0, 127.0, 127.9, 128.0, 128.4, 128.5, 128.56, 128.64, 128.7, 133.6, 134.9, 135.6, 138.8, 176.2, 177.8, 199.7; IR (KBr) 2960, 2869, 1772, 1702, 1541, 1506, 1490, 1428, 1398, 1340, 1238, 1185, 1135, 1000, 724, 702  $\text{cm}^{-1}$ ; Found: C, 77.15; H, 6.62; N, 5.96%; Calcd for  $\text{C}_{30}\text{H}_{30}\text{N}_2\text{O}_3$ : C, 77.23; H, 6.48; N, 6.00%.

(3*aR*\*,4*R*\*,6*S*\*,6*aS*\*)-4-Benzoyl-5-benzyl-6-cyclohexyl-2-methyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6eA**):  $R_f = 0.40$  (hexane/Et<sub>2</sub>O = 1/1); a solid. m.p. 142–

143 °C (from AcOEt/hexane);  $^1\text{H NMR } \delta$  1.11–1.37 (m, 5H), 1.66–1.78 (m, 4H), 1.94–2.04 (m, 1H), 2.08–2.15 (m, 1H), 3.04 (s, 3H), 3.41–3.53 (m, 4H), 3.85 (d, 1H,  $J = 13.3$  Hz), 4.97 (s, 1H), 7.10–7.14 (m, 2H), 7.21–7.27 (m, 5H), 7.43–7.49 (m, 3H);  $^{13}\text{C NMR } \delta$  25.3, 26.2, 26.4, 26.5, 29.5, 30.0, 36.1, 47.2, 47.3, 52.2, 65.4, 69.2, 127.5, 128.3, 128.56, 128.65, 129.2, 133.1, 134.8, 137.8, 178.0, 179.0, 198.2; IR (KBr) 2922, 2851, 1769, 1697, 1593, 1432, 1381, 1337, 1277, 1230, 1189, 1131, 1094, 1048, 752, 730, 694  $\text{cm}^{-1}$ ; Found: C, 75.26; H, 7.11; N, 6.53%; Calcd for  $\text{C}_{27}\text{H}_{30}\text{N}_2\text{O}_3$ : C, 75.32; H, 7.02; N, 6.51%. Crystal data:  $\text{C}_{27}\text{H}_{30}\text{N}_2\text{O}_3$ ,  $M_r = 430.55$ , monoclinic,  $P2_1/c$ ,  $a = 8.4348(7)$ ,  $b = 21.818(2)$ ,  $c = 12.635(1)$  Å,  $V = 2231.4(3)$  Å<sup>3</sup>,  $\beta = 106.338(2)^\circ$ ,  $Z = 4$ ,  $D_{\text{calcd}} = 1.281$  g  $\text{cm}^{-3}$ ,  $R = 0.051$  ( $R_w = 0.066$ ) for 3690 reflections with  $I > 3.00\sigma(I)$  and 289 variable parameters. Crystallographic data for **6eA** have been deposited with Cambridge Crystallographic Data Centre as supplementary publication No. CCDC 913504.

(3*aR*\*,4*R*\*,6*S*\*,6*aS*\*)-4-Benzoyl-2,5-benzyl-6-cyclohexyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6eB**):  $R_f = 0.40$  (hexane/Et<sub>2</sub>O = 1/1); a solid; m.p. 161–162 °C (from AcOEt/hexane);  $^1\text{H NMR } \delta$  1.01–1.31 (m, 5H), 1.62–1.71 (m, 4H), 1.88–1.96 (m, 1H), 1.98–2.15 (m, 1H), 3.16 (d, 1H,  $J = 12.8$  Hz), 3.39–3.43 (m, 2H), 3.52–3.55 (m, 1H), 3.70 (d, 1H,  $J = 12.8$  Hz), 3.77 (d, 1H,  $J = 12.8$  Hz), 4.74 (d, 1H,  $J = 13.8$  Hz), 4.85 (s, 1H), 6.87 (d, 2H,  $J = 6.4$  Hz), 7.16–7.31 (m, 6H), 7.33 (t, 2H,  $J = 7.8$  Hz), 7.41–7.48 (m, 1H), 7.46 (d, 2H,  $J = 7.3$  Hz), 7.51 (d, 2H,  $J = 7.4$  Hz);  $^{13}\text{C NMR } \delta$  26.2, 26.3, 26.4, 29.6, 30.0, 36.0, 43.0, 47.2, 47.3, 51.8, 65.8, 69.2, 127.3, 128.2, 128.35, 128.41, 128.6, 128.7, 129.0, 129.5, 133.1, 134.75, 134.83, 138.0, 177.4, 178.6, 197.9; IR (KBr) 3038, 2933, 2853, 1774, 1705, 1673, 1577, 1494, 1396, 1343, 1227, 1172, 1142, 1073, 732, 704  $\text{cm}^{-1}$ ; Found: C, 78.25; H, 6.78; N, 5.55%; Calcd for  $\text{C}_{33}\text{H}_{34}\text{N}_2\text{O}_3$ : C, 78.23; H, 6.76; N, 5.53%.

(3*aR*\*,4*R*\*,6*S*\*,6*aS*\*)-2,5-Dibenzyl-4-heptanoyl-6-methyltetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2*H*,3*aH*)-dione (**6fB**):  $R_f = 0.35$  (hexane/Et<sub>2</sub>O = 1/1); an oil;  $^1\text{H NMR } \delta$  0.87 (t, 3H,  $J = 6.9$  Hz), 1.14 (d, 3H,  $J = 6.4$  Hz), 1.13–1.27 (m, 6H), 1.40–1.45 (m, 2H), 2.15 (td, 1H,  $J = 7.4, 17.4$  Hz), 2.30 (td, 1H,  $J = 7.8, 17.4$  Hz), 3.04 (d, 1H,  $J = 7.8$  Hz), 3.24 (t, 1H,  $J = 7.8$  Hz), 3.58 (d, 1H,  $J = 13.8$  Hz), 3.82–3.89 (m, 1H), 3.84 (d, 1H,  $J = 13.8$  Hz), 3.98 (s, 1H), 4.67 (d, 1H,  $J = 14.2$  Hz), 4.72 (d, 1H,  $J = 14.2$  Hz), 7.00–7.02 (m, 2H), 7.18–7.42 (m, 8H);  $^{13}\text{C NMR } \delta$  14.0, 15.7, 22.3, 23.1, 28.7, 31.4, 41.4, 42.5, 46.5, 48.1, 50.8, 57.9, 68.2, 127.2, 127.9, 128.0, 128.39, 128.41, 128.5, 135.6, 138.4, 176.2, 177.5, 211.9; IR (neat) 3038, 2929, 2857, 1774, 1708, 1496, 1455, 1432, 1397, 1345, 1178, 1078, 732, 700  $\text{cm}^{-1}$ ; HRMS ( $\text{FAB}^+$ ) ( $\text{M}^+ + \text{H}$ ): Found:  $m/z$  447.2640; Calcd for  $\text{C}_{38}\text{H}_{35}\text{N}_2\text{O}_3$ : 447.2648.

**1,3-Dipolar cycloaddition of azomethine ylide generated from *trans*-isomer of 3c:** A mixture of *trans*-isomer of **3c** (26 mg, 0.09 mmol) and *N*-benzylmaleimide (**5B**) (20 mg, 0.11 mmol) in xylene (0.9 mL) was heated at 145 °C for 1.5 h and cooled to rt. The solvent was removed under reduced pressure. The residue was purified by preparative TLC (hexane/AcOEt = 5/1) to give **6cB** (36 mg, 84% yield).

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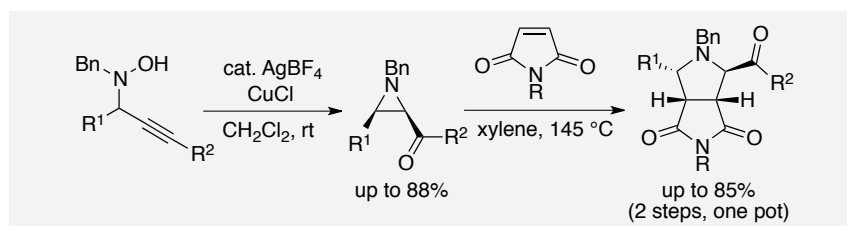
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#### One-pot Stereoselective Syntheses of 2-Acylaziridines and 2- Acylpyrrolidines from *N*- (Propargylic)hydroxylamines



A stereoselective direct transformation of *N*-(propargylic)hydroxylamines into *cis*-2-acylaziridines was realized by the combined use of  $\text{AgBF}_4$  and  $\text{CuCl}$ . The subsequent 1,3-dipolar cycloaddition of azomethine ylides generated in situ from the

intermediary 2-acylaziridines with maleimides was achieved by one-pot procedure to afford the corresponding 2-acylpyrrolidines consisting of an octahydropyrrolo[3,4-*c*]pyrrole skeleton stereoselectively.