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# Gold-catalyzed [4+3]- and [4+2]-annulations of 3-en-1-ynamides with isoxazoles *via* novel $6\pi$ -electrocyclizations of 3-azahepta trienyl cations†

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New gold-catalyzed [4+3]-annulations of 3-en-1-ynamides with isoxazoles afford 4*H*-azepines efficiently; this process involves  $6\pi$  electrocyclizations of gold-stabilized 3-azaheptatrienyl cations. In the presence of  $\text{Zn}(\text{OTf})_2$ , the resulting 4*H*-azepines undergo skeletal rearrangement to furnish substituted pyridine derivatives. We subsequently develop new catalytic [4+2]-annulations between the same 3-en-1-ynamides and isoxazoles to deliver substituted pyridine products using  $\text{Au}(\text{I})/\text{Zn}(\text{II})$  catalysts. This work reports the first success of the  $6\pi$  electrocyclizations of heptatrienyl cations that are unprecedented in literature reports.

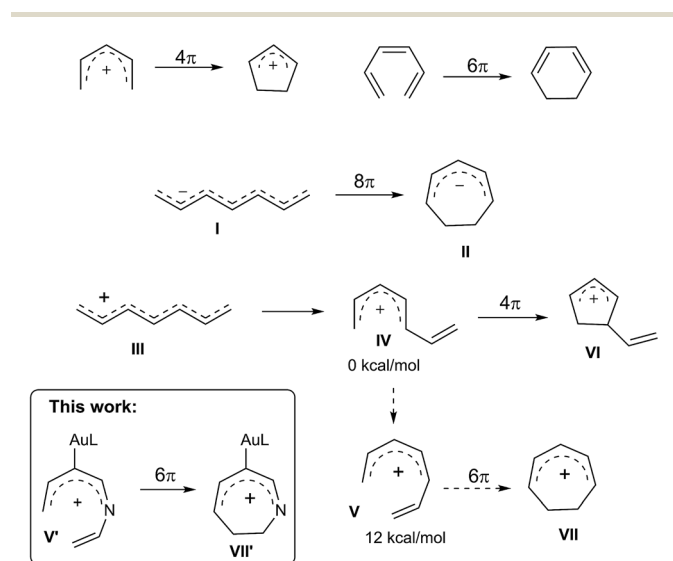
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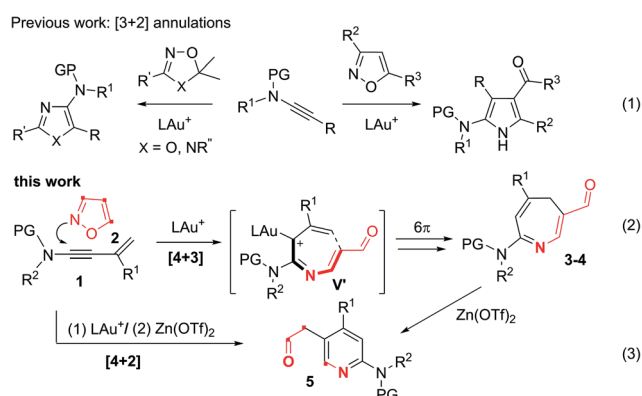
## Introduction

Electrocyclizations of acyclic conjugated  $\pi$ -motifs are powerful tools to access five-, six- and seven-membered carbocycles;<sup>1</sup> prominent examples include Nazarov cyclizations of penta-dienyl cations<sup>2</sup> and  $6\pi$  electrocyclizations of trienes,<sup>3</sup> which have found widespread applications in organic synthesis.

In the context of seven-carbon  $\pi$ -motifs, heptatrienyl anions **I** undergo facile  $8\pi$  electrocyclizations *via* rapid interconversions among various anion configurations (Scheme 1).<sup>4</sup> In contrast, heptatrienyl cations **III**<sup>5</sup> exclusively undergo Nazarov reactions because of the difficulties of forming all  $\sigma$ -*cis* configured cations **V** that have a high energy state.<sup>5b</sup> 1-Aza- and 1-oxaheptatrienyl cations<sup>6</sup> were also reported to follow Nazarov cyclizations. The realization of a  $6\pi$  electrocyclization of conjugated seven-membered cations is formidable but challenging. This work reveals the first success of such seven-membered cyclizations of gold-stabilized 3-azaheptatrienyl cations **V'** to form azacyclic products **3–4** *via* a new C–C bond formation.



Scheme 1 Electrocyclizations of conjugated  $\pi$ -motifs.



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The advent of gold catalysis has inspired new annulations between alkynes and poor nucleophiles.<sup>7</sup> N–O containing nucleophiles serve as useful building blocks to construct valuable azacyclic frameworks.<sup>7</sup> Ye and Hashmi reported interesting [3+2]-annulations of isoxazoles or benzisoxazoles with electron-

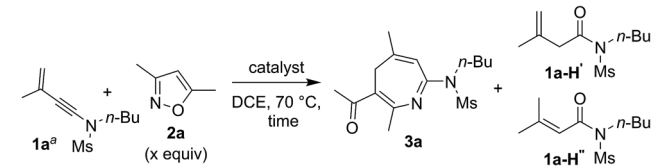


rich ynamides, yielding substituted pyrrole derivatives through aza-Nazarov cyclizations of the key intermediate [eqn (1)].<sup>7,8</sup> These [3+2]-annulations were extensively expanded to other N–O heterocycles including benzisoxazoles, 1,2,4-oxadiazoles, 1,4,2-dioxazoles and 4,5-dihydro-1,2,4-oxadiazoles, yielding additional five-membered azacycles as depicted in [eqn (1)].<sup>9</sup> Here, we report two distinct [4+3]- and [4+2]-annulations between 3-en-1-ynamides and isoxazoles using varied catalysts. An Au(I) catalyst alone delivers 4*H*-azepines 3–4 through 6π electrocyclizations of intermediates **V'** [eqn (2)] whereas a combined action of Au(I)/Zn(II) on the same reactants furnishes highly functionalized pyridines 5 [eqn (3)]. With our convenient synthesis, the synthetic utility of new 4*H*-azepines 3–4 is also reported.<sup>10</sup>

## Results and discussion

We examined the reactions of 3-methyl-3-en-1-ynamide **1a** with 3,5-dimethylisoxazole **2a** using various gold catalysts. Heating this mixture (**1a/2a** = 1 : 2 ratio) in hot DCE with 5 mol% LAuCl/AgNTf<sub>2</sub> [L = *p*-(*t*-Bu)<sub>2</sub>(*o*-biphenyl)] and IPr afforded a [4+3]-annulation product, 4*H*-azepine **3a**, in 64% and 75% yields respectively (Table 1, entries 1–2). Under these conditions, a low loading (1.2 equiv.) of 3,5-dimethylisoxazole **2a** gave **3a** in a decreased yield, *ca.* 62% (entry 3). With a 10 mol% catalyst, IPrAuCl/AgNTf<sub>2</sub> gave a clean reaction, yielding desired **3a** up to 91% (entry 4). We tested other phosphine ligands such as PPh<sub>3</sub> and P(OPh)<sub>3</sub>, yielding desired **3a** in satisfactory yields (78–81%, entries 5–6). Other counter anions such as OTf<sup>−</sup> and SbF<sub>6</sub><sup>−</sup> were also effective in producing **3a** in 85–88% yields (entries 7–8). AgNTf<sub>2</sub> alone was not active at all (entry 9).

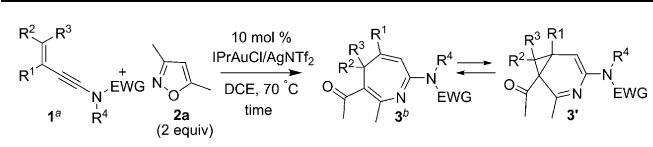
Table 1 [4+3]-Annulations over various gold catalysts



Entry	Catalyst [mol%]	x	Time [h]		Yield <sup>b</sup> [%]		
			1	2	1a	3a	1a-H'/1a-H'' <sup>a</sup>
1 <sup>c</sup>	LAuCl/AgNTf <sub>2</sub> [5]	2	3	20	64	—	
2 <sup>d</sup>	IPrAuCl/AgNTf <sub>2</sub> [5]	2	7	12	75	7 [2.5 : 1]	
3	IPrAuCl/AgNTf <sub>2</sub> [5]	1.2	7	23	62	5 [1 : 1]	
4	IPrAuCl/AgNTf <sub>2</sub> [10]	2	3	—	91	Trace	
5	PPh <sub>3</sub> AuCl/AgNTf <sub>2</sub> [10]	2	3.5	—	81	5 [1.25 : 1]	
6	[PhO] <sub>3</sub> PAuCl/AgNTf <sub>2</sub> [10]	2	3.5	—	78	13 [1.1 : 1]	
7	IPrAuCl/AgSbF <sub>6</sub> [10]	2	2.5	—	85	6 [1.4 : 1]	
8	IPrAuCl/AgOTf [10]	2	2	—	88	Trace	
9	AgNTf <sub>2</sub> [10]	2	15	33	—	11	

<sup>a</sup> [**1a**] = 0.15 M. <sup>b</sup> Product yields are reported after separation from a silica column. <sup>c</sup> L = *p*-(*t*-Bu)<sub>2</sub>(*o*-biphenyl). <sup>d</sup> IPr = 1,3-bis(diisopropylphenyl)-imidazol-2-ylidene. Ms = methanesulfonyl, DCE = 1,2-dichloroethane, and Tf = trifluoromethanesulfonyl.

Table 2 [4+3]-Annulations with various 3-en-1-ynamides



(1) R<sup>4</sup>, EWG = CH<sub>3</sub>, Ts (**3b**, 3 h, 84%, **x-ray**)  
 (2) R<sup>4</sup>, EWG = *c*-Pr, Ts (**3c**, 7 h, 86%)  
 (3) R<sup>4</sup>, EWG = Bn, Ts (**3d**, 4.5 h, 87%)  
 (4) R<sup>4</sup>, EWG = *n*-Bu, *n*-BuSO<sub>2</sub> (**3e**, 6 h, 90%)

(5) (**3f**, 22 h, 64%)

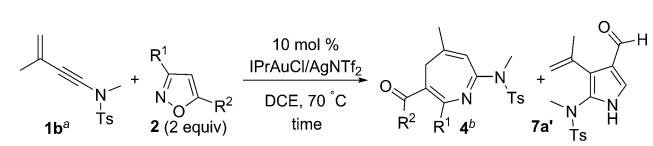
(6) R<sup>1</sup> = *i*-Pr (**3g**, 4 h, 74%)  
 (7) R<sup>1</sup> = *c*-Pr (**3h**, 2 h, 79%)  
 (8) R<sup>1</sup> = Ph (**3i**, 2.5 h, 58%)

(9) R<sup>4</sup>, EWG = *n*-Bu, Ms (**3j**, 5 h, 55%, **3j/3j'** = 5:1)  
 (10) R<sup>4</sup>, EWG = CH<sub>3</sub>, Ts (**3k**, 4 h, 68%, **3k/3k'** = 11.1:1)

(11) (**3l**, 2.5 h, 48%, **x-ray**) (**6l**, 43%, *E/Z* = 3.3:1)  
 (12) (**3m**, 14 h, 16%) (**6m**, 73%, **x-ray**)

<sup>a</sup> [**1**] = 0.15 M. <sup>b</sup> Product yields are reported after separation from a silica column. EWG = electron withdrawing group.

Table 3 [4+3]-Annulations with various isoxazoles



Entry	(R <sup>1</sup> , R <sup>2</sup> )	2	Time [h]	Yield [%]	4
(1)	H, H	<b>2b</b>	4	84	<b>4a</b> (X-ray)
				8	<b>7a'</b>
(2)	H, Me	<b>2d</b>	3	75	<b>4b</b>
(3)	Me, H	<b>2c</b>	3	87	<b>4c</b>
(4)	Et, Et	<b>2e</b>	6	85	<b>4d</b>
(5)	<i>n</i> -Bu, <i>n</i> -Bu	<b>2f</b>	7	81	<b>4e</b>
(6)	Me, <i>n</i> -Bu	<b>2g</b>	3	82	<b>4f</b>
(7)	<i>n</i> -Bu, <i>c</i> -Pr	<b>2h</b>	2	77	<b>4g</b>
(8)	Ph, <i>n</i> -Bu	<b>2i</b>	4	69	<b>4h</b>
(9)	Ph, Ph	<b>2j</b>	6.5	61	<b>4i</b>
				30	<b>5i</b> (X-ray)
(10)	Me, Ph	<b>2k</b>	4	71	<b>4j</b>

(15) R<sup>1</sup> = Ph (**5i**)  
 R<sup>1</sup> = Me (**5j**)  
 Yield: 15, Product: **5j**

<sup>a</sup> [**1b**] = 0.15 M. <sup>b</sup> Product yields are reported after separation from a silica column.



Suitable substituents of 3-en-1-ynamides **1** are crucial to achieve  $6\pi$  cyclizations of 3-azaheptatrienyl cations **V'** [eqn (2)]. We tested the reactions on 3-en-1-yne **1b–1m** bearing a C(3)-substituent to circumvent aza-Nazarov cyclizations as reported in Ye's work.<sup>7</sup> Herein, only entries 9 and 10 showed the presence of 3-azanorcaradienes **3'**. We examined these [4+3]-annulations on 3-methyl-3-en-1-ynamides **1b–1e** bearing various sulfonamides NTsR<sup>4</sup> (R<sup>4</sup> = Me, cyclopropyl, benzyl and N(*n*-C<sub>4</sub>H<sub>9</sub>) (-SO<sub>2</sub>Bu)), affording the desired 4*H*-azepines **3b–3e** in high yields (84–90%, Table 2, entries 1–4). Nevertheless, this new annulation becomes less efficient for 3-en-1-ynamide **1f** bearing an oxazolidin-2-one to yield product **3f** in 64% yield (entry 5).

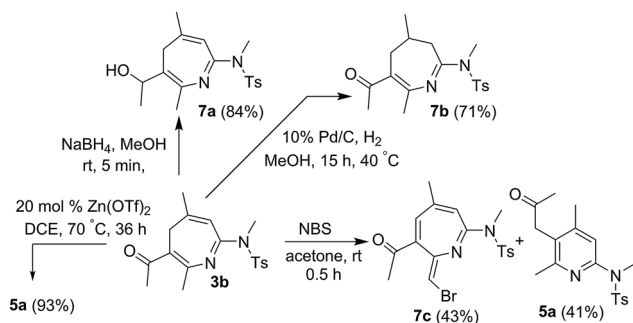
We altered the C(3)-substituents as in substrates **1g–1i**; their resulting products **3g–3h** (R<sup>1</sup> = isopropyl and cyclopropyl) were obtained in 74–79%, and **3i** (R<sup>1</sup> = Ph) with only 58% yield (entries 6–8). Notably, when a long *n*-butyl group was present as in species **1j** and **1k**, their corresponding reactions afforded compounds **3j/3j'** = 5/1 and **3k/3k'** = 11.1 : 1, respectively, in 55% and 68% yields (entries 9–10). For *E*-configured trisubstituted 3-en-1-yne **1l** (R<sup>1</sup> = Me, R<sup>2</sup> = Ph and R<sup>3</sup> = H), 4*H*-azepine **3l**

and pyrrole **6l** were obtained in equal proportions (entry 11). When a cyclohexenyl group was present for alkene as in species **1m**, pyrrole product **6m** was dominant over azepine **3m** (entry 12). Accordingly, preferable 3-en-1-yne comprise a small R<sup>2</sup> or R<sup>3</sup> substituent whereas R<sup>1</sup> must be substituted. Herein, the structures of 4*H*-azepines **3b** and **3l**, and pyrrole species **6m** were confirmed with X-ray diffraction.<sup>11</sup>

Isoxazoles of a wide scope are compatible with these [4+3]-annulations, as depicted in Table 3. The reaction of unsubstituted isoxazole **2b** with model 3-en-1-ynamide **1b** afforded the desired 4*H*-azepine **4a** in 84% yield, together with pyrrole **7a'** in only 8% yield (entry 1). Mono-substituted 3-methyl or 5-methyl isoxazoles **2c** and **2d** are also suitable for these annulations to afford compounds **4b** and **4c** in 75% and 87% yields, respectively (entries 2–3). We prepared additional 3,5-disubstituted isoxazoles **2e–2i** with R<sup>1</sup> = alkyl and phenyl, and R<sup>2</sup> = alkyl; their annulations proceed smoothly to produce desired **4d–4h** in 69–85% yields (entries 4–8). For di-substituted isoxazoles **2j** and **2k** bearing R<sup>2</sup> = Ph, 4*H*-azepines **4i** and **4j** were obtained in 61% and 71% yields respectively, together with their rearrangement products **5i** and **5j** in 15–30% yields (entries 9–10). Compounds **4a** and **5i** were characterized by X-ray diffraction.<sup>11</sup>

Our convenient synthesis of 4*H*-azepines provides new synthetic utilities; several new functionalizations are depicted in Scheme 2. NaBH<sub>4</sub>-reduction of species **3b** delivered an alcohol derivative **7a** in 84% yield. Selective hydrogenation of the same species afforded 2-aza-1,3-dien-5-one **7b** in 71% yield. A final treatment of 4*H*-azepine **3b** with NBS in acetone afforded compound **7c**, of which the molecular structure was determined by <sup>1</sup>H NOE spectra.

The Lewis-catalyzed rearrangement of 4*H*-azepines **3–4** to substituted pyridines **5** [eqn (3)] is unprecedented in 4*H*-azepine chemistry.<sup>10</sup> We undertook such novel [4+2]-annulations



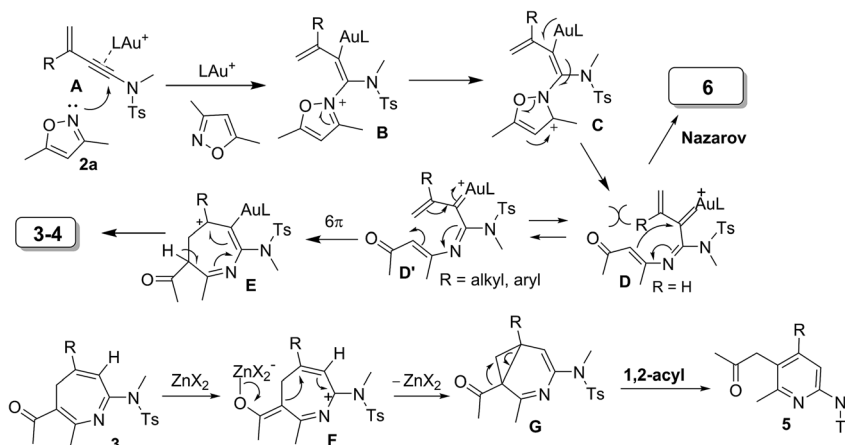
Scheme 2 New functionalization of 4*H*-azepines.

Table 4 [4+2]-Annulations between 3-en-1-ynamides and isoxazoles

Entry	(R <sup>1</sup> , R <sup>2</sup> , EWG)	1	(R <sup>3</sup> , R <sup>4</sup> )	2	Time [h]	Yield [%]	5
(1)	Me, Me, Ts	<b>1b</b>	Me, Me	<b>2a</b>	19	73 (35) <sup>f</sup>	<b>5a</b> (X-ray)
(2)	<i>n</i> -Bu, Me, Ts	<b>1k</b>	Me, Me	<b>2a</b>	33	64	<b>5b</b>
(3)	<i>c</i> -Pr, Me, Ts	<b>1h</b>	Me, Me	<b>2a</b>	20	56	<b>5c</b>
(4)	<i>i</i> -Pr, Me, Ts	<b>1g</b>	Me, Me	<b>2a</b>	15	51	<b>5d</b>
(5)	Me, <i>n</i> -Bu, Ms	<b>1a</b>	Me, Me	<b>2a</b>	28	63	<b>5e</b>
(6)	Me, Me, Ts	<b>1b</b>	<i>n</i> -Bu, <i>n</i> -Bu	<b>2f</b>	19	78	<b>5f</b>
(7)	Me, Me, Ts	<b>1b</b>	Et, Et	<b>2e</b>	16	69	<b>5g</b>
(8)	Me, Me, Ts	<b>1b</b>	<i>n</i> Bu, <i>c</i> -Pr	<b>2h</b>	20	75	<b>5h</b>
(9)	Me, Me, Ts	<b>1b</b>	Ph, Ph	<b>2j</b>	24	80	<b>5i</b> (X-ray)
(10)	Me, Me, Ts	<b>1b</b>	Me, Ph	<b>2k</b>	30	75	<b>5j</b>

<sup>a</sup> [1] = 0.15 M. <sup>b</sup> Product yields are reported after separation from a silica column. <sup>c</sup> The value in parentheses is reported using a mixture of IPrAuCl/AgNTf<sub>2</sub> (10 mol%) and Zn(OTf)<sub>2</sub> (20 mol%) in hot DCE (70 °C, 48 h); **3b** was also isolated in 28% yield.





Scheme 3 A plausible reaction mechanism.

between 3-en-1-ynamides **1** and isoxazoles **2** using Au(I)/Zn(II) in a relay series, as depicted in Table 4. In the reactions of various 3-substituted 3-en-1-ynamides **1** ( $R^1$  = methyl, *n*-butyl, cyclopropyl and isopropyl) with 3,5-dimethylisoxazole **2a**, substituted pyridines **5a–5d** were obtained in satisfactory yields (51–73%, entries 1–4). In entry 1, if the reaction was performed with combined Au(I)/Zn(II) catalysts in a non-relay operation, compounds **5a** and **3b** were isolated in 35% and 28% yields respectively. For 3-en-1-ynamide **1a** bearing a NMs(*n*-butyl), the corresponding product **5e** was obtained in 63% yield (entry 5). We tested the reactions on 3,5-disubstituted isoxazoles **2e–2f** & **2h** bearing all alkyl substituents, producing desired **5f–5h** in good yields (69–78%, entries 6–8). For such disubstituted isoxazoles bearing  $R^4$  = Ph, the reactions afforded the desired pyridine derivatives **5i** and **5j** in 75–80% yields (entries 9–10). The molecular structures of compounds **5a** and **5i** were characterized by X-ray diffraction.<sup>11</sup>

Scheme 3 rationalizes the crucial roles of substituents of 3-en-1-ynamides in the chemoselectivity that relies on two conformational structures **D** versus **D'**. The N-attack of isoxazole at gold- $\pi$ -ynamide **A** is expected to form a gold-carbene **D'**, which can be visualized as a gold-stabilized cycloheptatrienyl cation. Conformation **D** is favorable with  $R$  = H, which prefers aza-Nazarov reactions.<sup>12</sup> When a C(3)-substituent is present ( $R$  = alkyl and aryl), all  $\sigma$ -*cis* configured species **D'** are the preferable geometry to induce novel  $6\pi$  electrocyclizations. This ring closure is expected to proceed through an attack of enamide at the alkenylgold moiety that is also visualized as a gold-stabilized cation. Additional C(4)-substituents render the formation of cations **D'** difficult, thus yielding pyrrole **6** as byproducts. A loss of an acidic proton from seven-membered cations **E** is expected to yield azepines **3–4**. 4*H*-Azepines **3–4** bear an enone conjugated with a triene; this extensive conjugation is very stable to impede a  $6\pi$  electrocyclization of their triene moieties unless a Lewis acid is present. Zn(OTf)<sub>2</sub> likely coordinates with the carbonyl of 4*H*-azepine **3** to generate a 2-azapentadienyl cation **F** bearing a zinc enolate, further enabling an intramolecular cyclization to generate species **G**. A 1,2-acyl shift<sup>14</sup> of species **G** delivers the observed product **5**.<sup>13</sup>

## Conclusions

In summary, this work describes new gold-catalyzed [4+3] annulations<sup>15</sup> of 3-substituted 3-en-1-ynamides with isoxazoles to form 4*H*-azepines. A relay catalysis is also developed with Au(I)/Zn(II) catalysts to achieve [4+2] annulations from the same reactants. The mechanisms of gold-catalyzed [4+3] annulations involve unprecedented  $6\pi$  electrocyclizations of 3-azacycloheptatrienyl cations to form 4*H*-azepines **3–4** efficiently. Control experiments confirm that 4*H*-azepines **3–4** are catalyzed by Zn(OTf)<sub>2</sub> to undergo new rearrangement reactions to form substituted pyridine derivatives.

## Conflicts of interest

The authors declare no conflict of interest.

## Acknowledgements

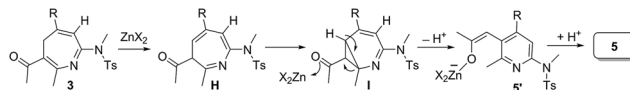
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## Notes and references

- (a) S. Sankararaman, in *Pericyclic Reactions-A Textbook. Reactions, Applications and Theory*, Wiley-VCH, New York, 2005, ch. 6, pp. 393–398; (b) C. M. Beaudry, J. P. Malerich and D. Trauner, *Chem. Rev.*, 2005, **105**, 4757; (c) P. V. R. Schleyer, J. I. Wu, F. P. Cossio and I. Fernandez, *Chem. Soc. Rev.*, 2014, **43**, 4909; (d) M. Bian, L. Li and H. Ding, *Synthesis*, 2017, **49**, 4383; (e) E. C. Taylor and I. J. Turchi, *Chem. Rev.*, 1979, **79**, 181; (f) F. D. Proft, P. K. Chattaraj, P. W. Ayers, M. T. Sucarrat, M. Elango, V. Subramanian, S. Giri and P. Geerlings, *J. Chem. Theory Comput.*, 2008, **4**, 595; (g) N. Jana and G. Driver, *Org. Biomol. Chem.*, 2015, **13**, 9720.
- (a) W. T. Spencer III, T. Vaidya and A. J. Frontier, *Eur. J. Org. Chem.*, 2013, 3621; (b) R. L. Davis and D. L. Tantillo, *Curr. Org. Chem.*, 2010, **14**, 1561; (c) T. N. Grant, C. J. Rieder and



- F. G. West, *Chem. Commun.*, 2009, 5676; (d) M. J. Riveira, L. A. Marsili and M. P. Mischno, *Org. Biomol. Chem.*, 2017, **15**, 9255; (e) N. Shimada, C. Stewart and M. A. Tius, *Tetrahedron*, 2011, **67**, 5851.
- 3 (a) V. A. Guner, K. N. Houk and I. W. Davis, *J. Org. Chem.*, 2004, **69**, 8024; (b) R. V. Essen, D. Frank, H. W. Sunnemann, D. Vidovic, J. Magull and A. D. Meijere, *Chem.–Eur. J.*, 2005, **11**, 6583; (c) N. A. Magomedov, P. L. Ruggiero and Y. Tang, *J. Am. Chem. Soc.*, 2004, **126**, 1624; (d) E. N. Marvell, G. Caple, B. Schatz and W. Pippin, *Tetrahedron*, 1973, **29**, 3781; (e) J. R. Otero, *J. Org. Chem.*, 1999, **64**, 6842; (f) P. E. Tessier, N. Nguyen, M. D. Clay and A. G. Fallis, *Org. Lett.*, 2005, **7**, 767; (g) C. L. Benson and F. G. West, *Org. Lett.*, 2007, **9**, 2545; (h) G. A. Barcan, A. Patel, K. N. Houk and O. Kwon, *Org. Lett.*, 2012, **14**, 5388.
- 4 (a) R. B. Bates, W. H. Delnes, D. A. McCombs and D. E. Potter, *J. Am. Chem. Soc.*, 1969, **91**, 4608; (b) K. Marx and W. Eberbach, *Chem.–Eur. J.*, 2000, **6**, 2063; (c) M. Reisser and G. Mass, *J. Org. Chem.*, 2004, **69**, 4913; (d) T. Hübner, *Dissertation*, University of Freiberg, 1987; (e) A. Arany, D. Bendell, P. W. Groudwater, I. Garnett and M. Nyerges, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2605.
- 5 (a) N. C. Deno, C. U. Pittman and J. O. Turner, *J. Am. Chem. Soc.*, 1965, **87**, 2153; (b) O. N. Faza, C. S. López, R. Alvarez and A. R. de Lera, *Chem.–Eur. J.*, 2009, **15**, 1944.
- 6 D. Alickmann, R. Fröhlich, A. H. Maulitz and E. U. Wurthwein, *Eur. J. Org. Chem.*, 2002, 1523.
- 7 (a) A. H. Zhou, Q. He, C. Shu, Y. F. Yu, S. Liu, T. Zhao, W. Zhang, X. Lu and L. W. Ye, *Chem. Sci.*, 2015, **6**, 1265; (b) X. Y. Xiao, A. H. Zhou, C. Shu, F. Pan, T. Li and L. W. Ye, *Chem.–Asian J.*, 2015, **10**, 1854; (c) W. B. Shen, X. Y. Xiao, Q. Sun, B. Zhou, X. Q. Zhu, J. Z. Yan, X. Lu and L. W. Ye, *Angew. Chem., Int. Ed.*, 2017, **56**, 605; (d) L. Li, T. D. Tan, Y. Q. Zhang, X. Liu and L. W. Ye, *Org. Biomol. Chem.*, 2017, **15**, 8483.
- 8 (a) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2016, **55**, 794; (b) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2016, **55**, 12688.
- 9 (a) Z. Zeng, H. Jin, J. Xie, B. Tian, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Org. Lett.*, 2017, **19**, 1020; (b) M. Chen, N. Sun, H. Chen and Y. Liu, *Chem. Commun.*, 2016, **52**, 6324; (c) W. Xu, G. Wang, N. Sun and Y. Liu, *Org. Lett.*, 2017, **19**, 3307.
- 10 For synthesis of *nH*-azepines ( $n = 2$  or 4), see selected examples: (a) U. Gockel, U. Hartmannsgruber, A. Steigel and J. Sauer, *Tetrahedron Lett.*, 1980, **21**, 599; (b) I. R. Dunkin, A. E. Ayeb and M. A. Lynch, *J. Chem. Soc., Chem. Commun.*, 1994, 1695; (c) K. Satake, R. Okuda, M. Hashimoto, Y. Fujiwara, H. Okamoto, M. Kimura and S. Morosawa, *J. Chem. Soc. Perkin Trans 1*, 1994, 1753; (d) Y. Luo and J. Wu, *Chem. Commun.*, 2011, **47**, 11137.
- 11 Crystallographic data of compounds **3b**, **3l**, **4a**, **5a**, **5i**, and **6m** were deposited in Cambridge Crystallographic Data Center: **3b**: CCDC 1589549, **3l**: CCDC 1589562, **4a**: CCDC 1589561, **5a**: CCDC 1589558, **5i**: CCDC 1589559 and **6m**: CCDC 1589560.†
- 12 For the aza-Nazarov cyclizations, see: (a) D. A. Klumpp, Y. Zhang, M. J. O'Connor, P. M. Esteves and L. S. de Almeida, *Org. Lett.*, 2007, **9**, 3085; (b) Z. X. Ma, S. He, W. Song and R. P. Hsung, *Org. Lett.*, 2012, **14**, 5736; (c) R. L. Sahani and R. S. Liu, *Angew. Chem., Int. Ed.*, 2017, **56**, 12736; (d) S. K. Pawar, R. L. Sahani and R. S. Liu, *Chem.–Eur. J.*, 2015, **21**, 10843; (e) C. Shu, Y. H. Wang, C. H. Shen, P. P. Ruan, X. Lu and L. W. Ye, *Org. Lett.*, 2016, **18**, 3254.
- 13 As suggested by one reviewer, an alternative mechanism is also possible for the Zn(II)-catalyzed rearrangement; this process involves an isomerization of initial species **3** to an unconjugated iminoyl ketone **H**, followed by a  $6\pi$ -cyclization to generate species **I**. A subsequent Zn(II)-catalyzed aromatization of species **I** is expected to yield the final product **5**. In this process, species **H** is relatively higher than **3** in energy, but its feasibility is not excluded.



- 14 (a) S. M. Wang and L. Zhang, *Org. Lett.*, 2006, **8**, 4585; (b) G. Li, G. Zhang and L. Zhang, *J. Am. Chem. Soc.*, 2008, **130**, 3704; (c) S. B. Wagh and R. S. Liu, *Chem. Commun.*, 2015, **51**, 15462; (d) R. Chaudhuri, A. Das, H. Y. Liao and R. S. Liu, *Chem. Commun.*, 2010, **46**, 4601.
- 15 For reviews of gold-catalyzed cycloaddition or annulation reactions of alkynes, see (a) D. J. Gorin, B. D. Sherry and F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351; (b) A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180; (c) F. López and J. L. Mascareñas, *Beilstein J. Org. Chem.*, 2011, **7**, 1075; (d) C. Aubert, L. Fensterbank, P. Garcia, M. Malacria and A. Simonneau, *Chem. Rev.*, 2011, **111**, 1954; (e) D. Garayalde and C. Nevado, *ACS Catal.*, 2012, **2**, 1462; (f) M. E. Muratore, A. Homes, C. Obradors and A. M. Echavarren, *Chem.–Asian J.*, 2014, **9**, 3066.

