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Lewis Acid-Catalyzed Intramolecular [3+2] Cross Cycloadditions of Aziridine 2,2-Diesters with Conjugated Dienes for Construction of Aza-[n.2.1] Skeletons

Yizhou Zhan, Tao Liu, Jun Ren, Zhongwen Wang*

Abstract: A novel Lewis acid-catalyzed [3+2]IMCC between aziridine 2,2-diesters and conjugated dienes has been developed. The [3+2]IMCC is the first regiospecific IMCC of intramolecular 1,3-dipolar cycloadditions of azomethine ylides with carbon-carbon double bonds, and supplies a general and efficient strategy for construction of structurally complex and diverse aza-[n.2.1] skeletons. The [3+2]IMCC could be carried out under mild conditions and in gram scale. More importantly, 3-alkyl-substituted aziridines were also successful. The excellent structural diversity, the facile operation and the versatile post-modifications will support the applications of the [3+2]IMCC in natural products synthesis and drugs discovery.

General and highly efficient construction of structurally diverse and complex polycyclic skeletons in biologically important natural products is quite important for both organic synthesis and drug discovery. Bridged aza-[n.2.1] skeletons broadly exist in bioactive natural products and synthetic molecules (Figure 1),^[1] and are important building blocks and catalysts in organic synthesis.^[2] However, general and highly efficient synthetic approaches to these structurally diverse and complex bridged skeletons are quite limited. Most of the reported methods have been developed aiming at one specific skeleton. For example, while aza-Diels-Alder [4+2] cycloaddition can afford a highly efficient construction of the 2-aza-[2.2.1]heptane,^[2] it's quite difficult to be applied to other structurally diverse aza-[n.2.1] skeletons. Thus, developing a new general and highly efficient strategy to construct those skeletons is highly desirable.

From the structural point of view, a pyrrolidine ring is embedded in the bridged aza-[n.2.1] skeleton. 1,3-Dipolar cycloaddition of azomethine ylide with carbon-carbon double bond is a general strategy for efficient construction of the pyrrolidine ring.^[3] Besides the formal [3+2] cycloaddition through C-N bond cleavage,^[4] aziridine is often used as a precursor of azomethine ylide (through C-C bond cleavage under photolysis or thermal conditions) to participate in the 1,3-dipolar cycloadditions which have been successfully applied to natural products synthesis.^[3,4b,5]



Figure 1. Representative natural products and synthetic molecules with aza-[n.2.1] skeletons.

However, whether from the point of view of the theory, or from the synthetic applications, regulation of the regioselectivity is generally a real challenge in various types of intramolecular cycloadditions among which type I 1,3-dipolar cycloaddition of azomethine ylide with carbon-carbon double bond (carboncarbon double bond was connected to the carbon atom of azomethine ylide) is one of the representatives (Scheme 1). Most of the type I intramolecular 1,3-dipolar cycloadditions give fused [n.3.0] skeletons via IMPC (IntraMolecular Parallel Cycloaddition) instead of bridged [n.2.1] ones via IMCC (IntraMolecular Cross Cycloaddition).^[6,7] Only two examples with carbon-carbon double bonds were reported to afford [3+2]IMCC cycloadducts, but with lower regioselectivities.^[6a,6b] The IMPC regioselectivities of azomethine ylides are inherently attributed to the intramolecular nature of the reactions.^[3k] Effort to switch the regioselectivity to IMCC was failed,^[8a] and theoretical calculations also indicate that the [3+2]IMPC is much more preferred both kinetically and thermodynamically.^[8b,8c]

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Scheme 1. Regioselectivities of Type I Intramolecular 1,3-Dipolar Cycloadditions of Azomethine Ylides with Carbon-carbon Double Bonds.

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As the 1,3-dipolar cycloadditions of aziridines with carboncarbon double bonds were generally carried out under harsh conditions (under photolysis or high temperature conditions), aiming to develop a more mild method, by using the donoracceptor design principle of cyclopropane [donor: electrondonating group (EWG); acceptor: electron-withdrawing groups (EWGs)] in combination with Lewis acids (LAs),^[9] Johnson et al developed an intermolecular ZnCl₂-promoted [3+2] cycloaddition of aziridine 2,2-diesters with carbon-carbon double bonds (Scheme 2, a).^[10a,10b] Recently, several other groups reported related cycloadditions with various dienophiles.^[10] In these intermolecular examples, besides the two geminal EWG groups, an aryl group in the 3-position of aziridine is necessary as a donor to further activate the carbon-carbon bond. Several [3+2]IMPC of EWG-substituted aziridines with carbon-carbon double bonds have been developed, in most of which the EWG is placed in the internal position to be connected to the carbon-carbon double bond moiety (Scheme 2, b).^[5] Garner et al reported one example with an external EWG, in which the carbon-carbon double bond was mono-substituted and a [3+2]IMPC product was obtained under thermal condition (Scheme 2, c).^[5g] We have recently developed the IMCC and IMPC strategy of cyclopropanes.[11] Following our design principle in cyclopropane system (Scheme 2, d),^[11g] we envisaged to place two geminal ester groups in the external position and introduced an additional carbon-carbon double bond (as a conjugated diene) as an activating group, a regioselectivity-switching group and a group for further functionalization in future applications (Scheme 2, e). We herein report our recent results.



Scheme 2. [3+2] Cycloadditions of EWG-activated Aziridines with Carboncarbon Double Bonds.

We prepared 1a as a model substrate to optimize the reaction conditions for the [3+2]IMCC reaction (Scheme 3). Various LAs and solvents (see in the supporting materials) were screened and we found that the [3+2]IMCC cycloadduct 2a could be obtained under most of the reaction conditions at room temperature, and Sc(OTf)₃ or SnCl₄ in DCM (dichloromethane) with addition of 4Å molecular sieves was selected as the optimal condition. It should be noted that p-TsOH (Bronsted acid) also worked well to give 2a (81% NMR yield). The structure of 2a was unambiguously confirmed by NMR spectroscopy and X-ray crystallography analysis.^[12] This reaction could also be carried out in gram scale. It should also be noted that 2a was also obtained under thermal condition (60 °C) in toluene without addition of LAs (31% NMR yield). The above results are quite different from what Garner et al (Scheme 2, b) reported^[5g] and fully illustrate the necessity of the introduction of the additional vinyl group for the switch of the regioselectivity. The above result was also different from the intermolecular result reported by Zhang et al.[10]



 a Reaction conditions: Sc(OTf)₃ (0.1 equiv.), 4 Å MS, DCM (0.03 M), Ar, r.t. b 1a (1 g), Sc(OTf)₃ (0.05 equiv.), 4 Å MS, DCM (0.03 M), Ar, r.t. c 0.05 equiv. of Sc(OTf)₃ was used. d 0.2 equiv. of Sc(OTf)₃ was used. e 0.1 equiv. of SnCl₄ was used. f 0.2 equiv. of SnCl₄ was used.

Scheme 3. [3+2]IMCC of 3-Arylaziridine-2,2-diesters^a.

Scopes and limitations of the [3+2]IMCC were then investigated under the optimal reaction conditions. We first explored the [3+2]IMCC of 3-arylaziridine 2,2-diesters. Most of the substrates reacted smoothly to afford the desired products in excellent yields (Scheme 3). [3+2]IMCC of **1a-1k** afforded 2-aza-[2.2.1]heptane cycloadducts. Substrate **1c** with electron-donating group (MeO) was relatively unstable but was with high reactivity. Substrates **1d** and **1e** with electron-withdrawing groups (NO₂, CN) were more stable but the reactivity was relatively low. Three substrates with different ester groups (**1f-1h**) gave desired

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products in excellent yields. Three substrates with variously substituted tosyl (1i-1k) also gave desired products in excellent yields. It should be noted that substrates without an additional vinyl group (1I and 1m) also worked well although the reaction time was prolonged and the yields decreased. This is similar to our previously reported results on cyclopropanes,^[111]] but is quite different from the intermolecular results reported by Zhang el al in which no reaction happened with 1-methylstryrene.^[13] Examples with lengthened linkers could also work to afford respectively [3.2.1]-cycloadduct **2n** and [4.2.1]-cycloadduct **2o** in moderate yields.

We then explored the [3+2]IMCC of 3-alkylaziridine 2,2diesters. To our great delight, quite different from the intermolecular [3+2] cycloadditions of aziridine 2,2-diesters with various dienophiles in which 3-aryl groups were necessary as donors for the activation of carbon-carbon bonds of aziridines, most of the substrates herein reacted smoothly to afford the desired products in excellent yields (Scheme 4). Reactions of 1p gave a mixture of two inseparable isomers (2p and 2p'), which was different from those of the aryl-linked examples (1a-1k). 2p and 2p' were obtained via [3+2]IMCC of the internal and external carbon-carbon double bonds respectively. [3+2]IMCC of 1q-1s were successfully carried out to afford 2q-2s respectively. While 2q and 2r contained a [3.2.1] skeleton, 2s and 2t contained a [4.2.1] one.



Scheme 4. [3+2]IMCC of 3-Alkylaziridine-2,2-diesters *.

Several post-modifications of the [3+2]IMCC cycloadducts have been carried out to preliminarily explore the potential applications of the developed strategy (Scheme 5). The removal of the *p*-nitrobenzenesulfonyl group of **2**j was carried out to afford **3**^[7c] and subsequent benzylation of which gave **4**. Oxidation of the vinyl group at the bridgehead of **2a** gave aldehyde **5** or 1,2-diol **6** (with an excellent stereoselectivity).^[12] Krapcho dealkoxycarbonylation of **2a** afforded **7** with an excellent stereoselectivity, which might be further developed for conformationally rigid amino acid drugs.^[14]



Scheme 5. Post-modifications of [3+2]IMCC Cycloadducts.

In conclusion, we have successfully developed LA-catalyzed [3+2]IMCC of aziridine 2,2-diesters with conjugated dienes. The [3+2]IMCC supplied a general and efficient strategy for construction of structurally complex and diverse aza-[n.2.1] skeletons. With introduction of a conjugated vinyl group, this [3+2]IMCC represents the first regiospecific IMCC of intramolecular 1,3-dipolar cycloaddition of azomethine ylides with carbon-carbon double bonds. More importantly, 3-alkyl-substituted aziridines were also successful, which makes the strategy possess an excellent structural diversity. The excellent structural diversity, the facile operation and the versatile post-modifications are also the features of the [3+2]IMCC. We strongly believe that this strategy will be widely applied to synthesis of natural products and discovery of new drugs and catalysts.

Acknowledgements

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Keywords: aziridine • cycloaddition • bridged ring • mediumsized ring • regioselectivity

 Daphniphyllum alkaloids: a) J. Kobayashi, T. Kubota, *Nat. Prod. Rep.* 2009, *26*, 936; Lyconadin A: b) J. i. Kobayashi, Y. Hirasawa, N. Yoshida, H. Morita, *J. Org. Chem.* 2001, *66*, 5901; Azaprophen: c) F. I. Carroll, P. Abraham, K. Parham, R. C. Griffith, A. Ahmad, M. M. Richard, F. N. Padilla, J. M. Witkin, P. K. Chiang, *J. Med. Chem.* 1987, *30*, 805; Aphanorphine: d) N. Gulavita, A. Hori, Y. Shimizu, P. Laszlo, J. Clardy, *Tetrahedron, Lett.* 1988, *29*, 4381; Fastigiatine: e) R. V. Gerard, D. B. Maclean, R. Fagianni, C. J. Lock, *Can. J. Chem.* 1986, *64*, 943; Sarain A: f) G. Cimino, G. Scognamiglio, A. Spinella, E. Trivellone, *J. Nat. Prod.* 1990, *53*, 1519; Gelsemium alkaloids: g) H. Lin, S. J. Danishefsky, *Angew. Chem.* 2003, *115*, 38; *Angew. Chem. Int. Ed.* 2003, *42*, 36; h) M. Kitajima, *J. Nat. Med.* 2007, *61*, 14; Securinega alkaloids: i) S. M. Weinreb, *Nat. Prod. Rep.*

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- a) D. Blondet, C. Morin, *Heterocycles* **1982**, *19*, 2155; b) R. Singh, R. Vince, *Chem. Rev.* **2012**, *112*, 4642; c) E. Wojaczynska, J. Wojaczynski, K. Kleniewska, M. Dorsz, T. K. Olszewski, *Org. Biomol. Chem.* **2015**, *13*, 6116.
- Some reviews on 1,3-dipolar cycloadditions of azomethine ylides: a) R. [3] Huisgen, In 1,3-Dipolar Cycloaddition Chemistry; A. Padwa, Ed.; Wiley: New York, 1984; Vol. 1, pp 1-177; b) K. V. Gothelf, K. A. Jorgensen, Chem. Rev. 1998, 98, 863; c) L. M. Harwood, R. J. Vickers, In The Chemistry of Heterocyclic Compounds: Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry toward Heterocycles and Natural Products; A. Padwa, W. H. Pearson, Ed.; Wiley and Sons: New York, 2002; Vol. 59, pp 169-252; d) C. Najera, J. M. Sansano, Curr. Org. Chem. 2003, 7, 1105; e) G. Pandey, P. Banerjee, S. R. Gadre, Chem. Rev. 2006, 106, 4484; f) T. M. V. D. Pinho e Melo, Eur. J. Org. Chem. 2006, 2006, 2873; g) M. Bonin, A. Chauveau, L. Micouin, Synlett 2006, 2349; h) H. Pellissier, Tetrahedron. 2007, 63, 3235; i) G. S. Singh, M. D'hooghe, N. De Kimpe, Chem. Rev. 2007, 107, 2080; j) G. Pandey, D. Dey, S. K. Tiwari, Tetrahedron Lett. 2017, 58, 699; A general review on intramolecular 1,3-dipolar cycloadditions of azomethine ylides: k) I. Coldham, R. Hufton, Chem. Rev. 2005, 105, 2765; Some other reviews on intramolecular 1,3-dipolar cycloadditions of azomethine ylides: I) A. Padwa, Angew. Chem. 1976, 88, 131; Angew. Chem. Int. Ed. 1976, 15, 123; m) Aziridines and Epoxides in Organic Synthesis; A. K. Yudin, Ed.; WILEY-VCH Verlag GmbH & Co. KGaA: Weinheim, 2006; n) V. Nair, T. D. Suja, Tetrahedron 2007, 63, 12247; o) A. J. M. Burrell, I. Coldham, Curr. Org. Synth. 2010, 7, 312.
- [4] Reviews on formal [3+2] cycloadditions of aziridines. General reviews: a)
 A. L. Cardoso, T. M. V. D. Pinho e Melo, *Eur. J. Org. Chem.* 2012, 6479;
 b) J. Feng, J. Zhang, *ACS Catalysis* 2016, *6*, 6651; Some other related reviews: c) D. Tanner, *Angew. Chem.* 1994, *106*, 625; *Angew. Chem. Int. Ed.* 1994, *33*, 599; d) W. McCoull, F. A. Davis, *Synthesis* 2000, 1347; e)
 J. B. Sweeney, *Chem. Soc. Rev.* 2002, *31*, 247; f) X. E. Hu, *Tetrahedron* 2004, *60*, 2701; g) A. Padwa, S. S. Murphree, *ARKIVOC* 2006, 6; h) T. L. Church, Y. D. Y. L. Getzler, C. M. Byrne, G. W. Coates, *Chem. Commun.* 2007, 657; i) D. Agrawal, V. K. Yadav, *Chem. Commun.* 2008, 6471; j) P. Dauban, G. Malik, *Angew. Chem.* 2009, *121*, 9188; *Angew. Chem. Int. Ed.* 2009, *48*, 9026; k) S. H. Krake, S. C. Bergmeier, *Tetrahedron* 2010, *66*, 7337; l) P. Lu, *Tetrahedron* 2010, *66*, 2549; i) H. Ohno, *Chem. Rev.* 2014, *114*, 7784; m) N. R. O'Connor, J. L. Wood, B. M. Stoltz, *Israel J. Chem.* 2016, *56*, 431.
- [5] Type I intramolecular 1,3-dipolar cycloadditions of aziridines with carbon-carbon multiple bonds: a) P. DeShong, D. A. Kell, D. R. Sidler, J. Org. Chem. 1985, 50, 2309; b) S. Takano, Y. Iwabuchi, K. Ogasawara, J. Am. Chem. Soc. 1987, 109, 5523; c) S. Takano, Y. Iwabuchi, K. Ogasawara, Chem. Commun. 1988, 1204; d) S. Takano, Y. Iwabuchi, K. Ogasawara, Heterocycles 1989, 29, 1473; e) J. Sisko, S. M. Weinreb, J. Org. Chem. 1991, 56, 3210; f) B. R. Henke, A. J. Kouklis, C. H. Heathcock, J. Org. Chem. 1992, 57, 7056; g) O. Dogan, P. P. Garner, Turk. J. Chem. 2000, 24, 59; h) M. A. Kuznetsov, A. S. Pan'kova, V. V. Voronin, N. A. Vlasenko, Chem. Heterocycl. Compd. 2012, 47, 1353; Type II intramolecular 1,3-dipolar cycloadditions of aziridines with carbon-carbon multiple bonds: i) P. Garner, P. B. Cox, J. T. Anderson, J. Protasiewicz, R. Zaniewski, J. Org. Chem. 1997, 62, 493.
- [6] Limited examples of Type I [3+2]IMCC of azomethine ylides were reported. With carbon-carbon double bonds: a) W. Eberbach, H. Fritzb, I. Heinzea, P. von Laera, P. Link, *Tetrahedron Lett.* **1986**, *27*, 4003; b) S. Kanemasa, K. Doi, E. Wada, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2866; With carbonyls: c) M. S. Novikov, I. V. Voznyi, A. F. Khlebnikov, J. Kopf, R. R. Kostikov, *J. Chem. Soc., Perkin Trans.* **1 2002**, 1628; d) I. Voznyi, M. S. Novikov, A. F. Khlebnikov, J. Kopf, R. R. Kostikov, *Russ. J. Org. Chem.* **2004**, *40*, 199; e) A. P. Kadina, A. F. Khlebnikov, M. S. Novikov, P. J. Perez, D. S. Yufit, *Org. Biomol. Chem.* **2012**, *10*, 5582.
- [7] The regioselectivity of most of the formal [3+2] cycloadditions of aziridines (through C-N bond cleavage) were similar to those of the 1,3-dipolar cycloaddition, except the only example developed by Bergmeier et al.: a) D. J. Lapinsky, S. C. Bergmeier, *Tetrahedron* 2002, *58*, 7109; b) S. C.

Bergmeier, S. J. Katz, J. Huang, H. McPherson, P. J. Donoghue, D. D. Reed, *Tetrahedron Lett.* **2004**, *45*, 5011; c) A. B. Pulipaka, S. C. Bergmeier, *J. Org. Chem.* **2008**, *73*, 1462.

- [8] a) I. Kim, H. Na, K. R. Kim, S. G. Kim, G. H. Lee, *Synlett* **2008**, 2069; b) S. Maiti, T. M. Lakshmykanth, S. K. Panja, R. Mukhopadhyay, A. Datta, C. Bandyopadhyay, *J. Heterocycl. Chem.* **2011**, 763; c) M. Hamzehloueian, S. Yeganegi, Y. Sarrafi, K. Alimohammadi, M. Sadatshahabi, *J. Serb. Chem. Soc.* **2014**, *79*, 911.
- [9] a) H.-U. Reissig, R. Zimmer, *Chem. Rev.* 2003, *103*, 1151; b) M. Yu, B. L. Pagenkopf, *Tetrahedron* 2005, *61*, 321; c) C. A. Carson, M. A. Kerr, *Chem. Soc. Rev.* 2009, *38*, 3051; d) F. De Simone, J. Waser, *Synthesis* 2009, 3353; e) M. J. Campbell, J. S. Johnson, A. T. Parsons, P. D. Pohlhaus, S. D. Sanders, *J. Org. Chem.* 2010, *75*, 6317; f) M. Y. Mel'nikov, E. M. Budynina, O. A. Ivanova, I. V. Trushkov, *Mendeleev Commun.* 2011, *21*, 293; g) M. A. Cavitt, L. H. Phun, S. France, *Chem. Soc. Rev.* 2014, *43*, 804; h) T. F. Schneider, J. Kaschel, D. B. Werz, *Angew. Chem.* 2014, *126*, 5608; *Angew. Chem. Int. Ed.* 2014, *53*, 5504; i) H. K. Grover, M. R. Emmett, M. A. Kerr, *Org. Biomol. Chem.* 2015, *13*, 655.
- LA-promoted [3+2] cycloadditions of 2,2-di-EWGs-substituted aziridines: [10] a) M. Vaultier, R. Carrie, Tetrahedron, Lett. 1978, 19, 1195; b) P. D. Pohlhaus, R. K. Bowman, J. S. Johnson, J. Am. Chem. Soc. 2004, 126, 2294; Other examples with or without promotion of LAs. With carboncarbon double bonds (Enol ethers, enamines and styrenes): c) T. Schirmeister, Liebigs Ann. 1997, 1895; d) L. Li, X. Wu, J. Zhang, Chem. Commun. 2011, 47, 5049; e) H. Liu, C. Zheng, S. You, Chin. J. Chem. 2014, 32, 709; f) H. Liu, C. Zheng, S. L. You, J. Org. Chem. 2014, 79, 1047; g) A. S. Pankova, M. A. Kuznetsov, Tetrahedron Lett. 2014, 55, 2499; h) A. Ghosh, A. K. Pandey, P. Banerjee, J. Org. Chem. 2015, 80, 7235; i) B. Wang, M. Liang, J. Tang, Y. Deng, J. Zhao, H. Sun, C. H. Tung, J. Jia, Z. Xu, Org. Lett. 2016, 18, 4614; j) L. Liao, B. Zhou, Y. Xia, X. Liu, L. Lin, X. Feng, ACS Catal. 2017, 7, 3934; With other dienophiles: k) G. Mloston, K. Urbaniak, Helv. Chim. Acta 2002, 85, 2056; I) X. Wu, L. Li, J. Zhang, Chem. Commun. 2011, 47, 7824; m) L. Li, J. Zhang, Org. Lett. 2011, 13, 5940; n) Z. Jiang, J. Wang, P. Lu, Y. Wang, Tetrahedron. 2011, 67, 9609; o) J. Zhang, X. Wu, Synthesis. 2012, 44, 2147; p) T. Soeta, Y. Miyamoto, S. Fujinami, Y. Ukaji, Tetrahedron. 2014, 70, 6623; q) R. A. Craig, II, N. R. O'Connor, A. F. G. Goldberg, B. M. Stoltz. Chem. Eur. J. 2014, 20, 4806; r) Y. Liao, X. Liu, Y. Zhang, Y. Xu, Y. Xia, L. Lin, X. Feng, Chem. Sci. 2016, 7, 3775; s) J. Zhang, X. Wu, W. Zhou, H. Wu, Chem. Commun. 2017, 53, 5661.
- Account: d) Z. Wang, Synlett 2012, 23, 2311; IMCC/IMPC examples of [11] cyclopropanes: e) S. Xing, W. Pan, C. Liu, J. Ren, Z. Wang, Angew. Chem. 2010, 122, 3283; Angew. Chem. Int. Ed. 2010, 49, 3215; f) B. Hu, S. Xing, J. Ren, Z. Wang, Tetrahedron 2010, 66, 5671; g) S. Xing, Y. Li, Z. Li, C. Liu, J. Ren, Z. Wang, Angew. Chem. 2011, 123, 12813; Angew. Chem. Int. Ed. 2011, 50, 12605; h) Y. Bai, W. Tao, J. Ren, Z. Wang, Angew. Chem. 2012, 124, 4188; Angew. Chem. Int. Ed. 2012, 51, 4112; i) Z. Wang, J. Ren, Z. Wang, Org. Lett. 2013, 15, 5682; j) W. Zhu, J. Fang, Y. Liu, J. Ren, Z. Wang, Angew. Chem. 2013, 125, 2086; Angew. Chem. Int. Ed. 2013, 52, 2032; k) J. Ren, J. Bao, W. Ma, Z. Wang, Synlett 2014, 25, 2260; I) W. Zhu, J. Ren, Z. Wang, Eur. J. Org. Chem. 2014, 2014, 3561; m) W. Ma, J. Fang, J. Ren, Z. Wang, Org. Lett. 2015, 17, 4180; n) Z. Wang, S. Chen, J. Ren, Z. Wang, Org. Lett. 2015, 17, 4184; o) J. Zhang, S. Xing, J. Ren, S. Jiang, Z. Wang, Org. Lett. 2015, 17, 218; p) C. Zhang, J. Tian, J. Ren, Z. Wang, Chem. Eur. J. 2017, 23, 1231.
- [12] CCDC 1485700 (2a), 1556291 (2s) and 1556290 (6) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [13] L. Li, Doctoral Thesis: Study on the Selective Carbon-carbon Bond Cleavage and Transformation of Aziridines Derivates Catalyzed by Lewis Acid, East China Normal University, 2012.
- [14] I. V. Komarov, A. O. Grigorenko, A. V. Turov, V. P. Khilya, *Russ. Chem. Rev.* 2004, 73, 785.

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Entry for the Table of Contents (Please choose one layout) Layout 1: COMMUNICATION Text for Table of Contents Author(s), Corresponding Author(s)* Page No. – Page No. Title ((Insert TOC Graphic here)) Layout 2: COMMUNICATION Yizhou Zhan, Tao Liu, Jun Ren, Zhongwen Wang* .CO₂R [3+2]IMCC Page No. – Page No. CO₂R CO₂R Lewis acids °CO₂R Lewis Acid-Catalyzed Intramolecular [3+2] Cross Cycloadditions of aza-[n,2,1] Aziridine 2,2-Diesters with [3+2]IMCC of aziridine 2,2-diesters with conjugated dienes has been **Conjugated Dienes for Construction** successfully developed. The [3+2]IMCC is the first regiospecific IMCC of of Aza-[n.2.1] Skeletons intramolecular 1,3-dipolar cycloadditions of azomethine ylides with carbon-carbon double bonds, and supplies a general and efficient strategy for construction of structurally complex and diverse aza-[n.2.1] skeletons.