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Tertiary Enamide-Promoted Diastereoselective Domino: *N*-Acyliminium Ion Trapping and Nazarov Cyclization

Yongxiang Zheng,‖ Lucile Andna,‖ Olivia Bistri, and Laurence Miesch*

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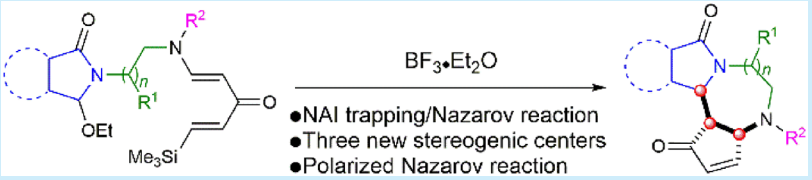

ABSTRACT: *N*-Acyliminium ions generated from enamidyl vinyl ketones provided cyclopentenoid-fused diazepines diastereoselectively using $BF_3{\cdot}Et_2O$ in one pot through a domino *N*-acyliminium ion trapping/Nazarov reaction, simultaneously generating three new stereogenic centers. The particular structural design of the cross-conjugated dienone dictates the torquoselectivity observed in this polarized Nazarov reaction. Various *N*-bridgehead polycyclic scaffolds of putative pharmacological interest were obtained. Cyclic voltammetry was used to support the preferred reaction sequence within this domino reaction.

The *N*-bridgehead unit is a privileged structural motif in numerous biologically active molecules. *N*-Bridgehead diazepines are particularly relevant, displaying interesting pharmacological profiles such as those in (−)-DC-81, a psychoactive drug,[1] Erchinine A and B antimicrobial agents,[2] and the antitumor antibiotic Anthramycin[3] (Figure 1).

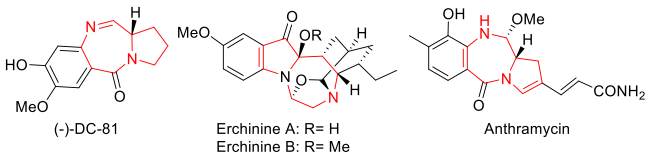

Figure 1. Biologically active *N*-bridgehead diazepines.

Construction of the *N*-bridgehead diazepine unit in polyheterocyclic frameworks usually requires multistep approaches. Tertiary enamides are established as shelf-stable enamine variants[4] and have been revealed to be good nucleophiles toward epoxides,[5] carbonyls,[6] imines,[7] nitrilium ions,[8] activated alkynes,[9] *N*-acyliminium ions (NAI),[10] and preformed carbocations[11] to construct various nitrogen-containing molecules. In this regard, well-designed tertiary enamides may provide an efficient starting point for the synthesis of polyheterocyclic scaffolds involving a *N*-bridgehead backbone. Our aim was to synthesize *N*-bridgehead diazepines fused with cyclopentenones of putative pharmacological interest using enamidyl vinyl ketones.

The Nazarov cyclization, known as a 4π electrocyclization of cross-conjugated dienones, can be considered as one of the most powerful tools to produce cyclopentenones.[12] In particular, to overcome the relatively low reactivity of divinyl ketones and to tune the torquoselectivity of the Nazarov cyclization, these substrates have been activated by adjacent heteroatoms to stabilize the oxyallyl cation.[12c,13] Among those polarized Nazarov cyclizations, nitrogen-substituted cross-conjugated divinyl ketones at the α-position have been frequently investigated.[14] In contrast, Nazarov cyclizations involving dienones substituted with a nitrogen at the β-position are scarce. Cha and Kim reported a Nazarov cyclization of a β-aza-substituted divinyl ketone to achieve the synthesis of the tricyclic core present in cephalotaxine (Scheme 1a).[15] The endocyclic enamine cyclopentenone annulation for the synthesis of cephalotaxine reported by Li and Wang was also rationalized as an unusual Nazarov-type cyclization (Scheme 1b).[16] Recently, we showed that *N*-acyliminium ions (NAI) derived from enamides undergo intramolecular TMSOTf-mediated trapping of the NAI to produce a variety of polyfunctionalized, medium-sized diazaheterocycles.[10] We then anticipated that, in acidic media, NAI precursors tethered with tertiary enamidyl vinyl ketones would offer the possibility of promoting two reactions simultaneously: nucleophilic addition of the enamide to the NAI and subsequent Nazarov reaction (Scheme 1c).

To assess our domino reaction, we synthesized the requisite cross-conjugated dienones **1** by addition of sulfonamides on terminal alkynes by using Triton B[17] or DABCO[18] (see

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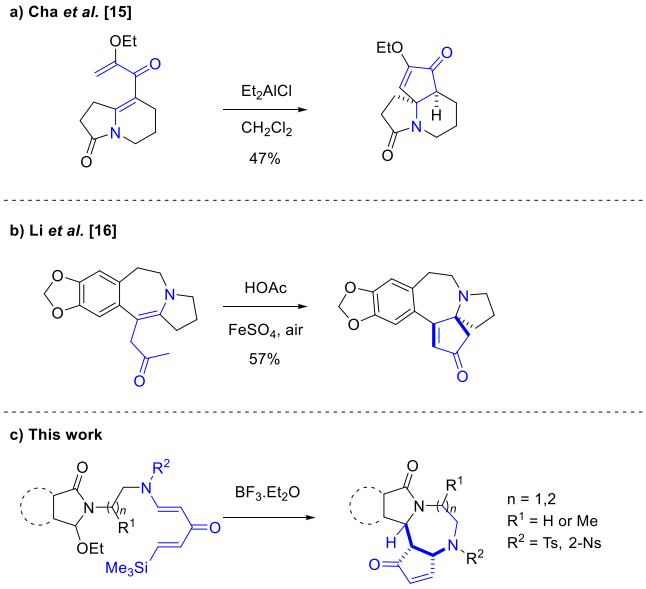
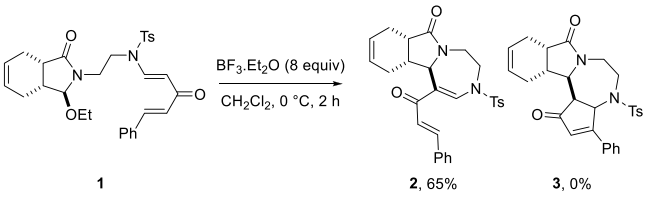
Scheme 1. Nazarov Cyclizations Involving β-Aza-Substituted Cross-Conjugated Divinyl Ketones



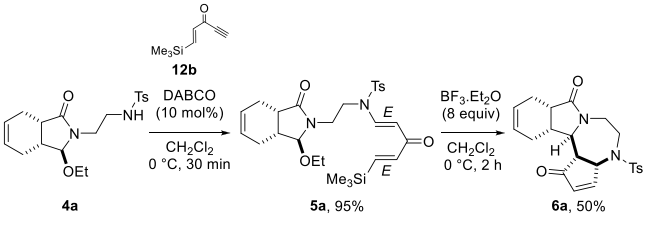
Suporting Information). Having the NAI precursor equipped with the cross-conjugated enamidyl vinyl ketone **1**, we attempted to initiate the domino reaction by using $BF_3{\cdot}Et_2O$ to generate the NAI.[20] With the phenyl substituent, although the trapping of the *N*-acyliminium ion was efficient, the Nazarov reaction did not take place (Scheme 2).

Scheme 2. Nazarov Cyclizations Involving β-Aza-Substituted Cross-Conjugated Divinyl Ketones



We rationalized that a divinyl ketone substituted with a silicon atom would provide an efficient solution to this issue by taking advantage of the β-silicon effect to facilitate the Nazarov reaction.[21] (*E*)-Configured ene-ynone **12b** was obtained from prop-2-yn-1-ol in a six-step reaction sequence with a 37% overall yield (see Supporting Information). The desired (*E*,*E*) cross-conjugated enamidyl vinyl ketone substrate **5a** was obtained by reacting the corresponding tosylsulfonamide **4a** with *E* configured ene-ynone **12b** in the presence of DABCO (Scheme 3). Gratifyingly, using $BF_3{\cdot}Et_2O$, we obtained the desired tetracycle **6a** as a single diastereomer in one pot from

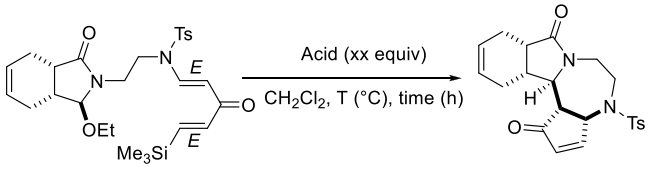
Scheme 3. Domino Cyclization/Nazarov Reaction



N-functionalized alkoxyamide **5a**. The trapping of the *N*-acyliminium ion and the subsequent Nazarov reaction was achieved in 50% yield, and the torquoselectivity was controlled via factors that are challenging to pinpoint owing to the peculiar structure of the cross-conjugated dienone, thus leading stereoselectively to a single aza-polycyclic framework bearing three more stereogenic centers.

Screening of Lewis and Brønsted acids revealed that only a few Lewis acids were able to promote this domino reaction (Table 1, entries 6 to 9). Brønsted acids such as *p*-TsOH,

Table 1. Screening of Lewis and Brønsted Acids



entry	acid (equiv)	temp (°C)	time (h)	yield (%)[a]
1	*p*-TsOH (8)	0 to rt	3	–[b]
2	*p*-TsOH (8)	0 to rt	6	traces
3	TfOH (8)	0	4	–[c]
4	$MeSO_3H$ (8)	0	1	–[c]
5	$BF_3{\cdot}Et_2O$ (8)	−30	2	–[b]
6	$BF_3{\cdot}Et_2O$ (8)	0	2	50
7	$BF_3{\cdot}Et_2O$ (8)	0	6	77
8	$BF_3{\cdot}Et_2O$ (10)	0	6	85
9	TMSOTf (8)	0	4	85
10	$AlCl_3$ (8)	0	6	–[c]
11	$FeCl_3$ (8)	0	2	–[c]
12	$Y(OTf)_3$ (8)	0	6	–[b]

[a]Isolated yields. [b]Starting material **5a** was fully recovered. [c]Degradation observed.

TfOH, $MeSO_3H$ (Table 1, entries 1−2, 3, and 4, respectively) led to either the starting material or degradation. We had more success with $BF_3{\cdot}Et_2O$, although a minimum temperature of 0 °C is required (Table 1, entry 6), and a greater amount of the Lewis acid as well as a longer reaction time have a positive influence on the yield of the reaction (Table 1, entries 7 and 8, respectively). TMSOTf was as effective as $BF_3{\cdot}Et_2O$ and provided the aza-fused polycyclic derivative in similar yields (Table 1, entry 9). Using Lewis acids such as $AlCl_3$, $FeCl_3$, and $Y(OTf)_3$, the outcome for the domino reaction remained the same—degradation or no transformation (Table 1, entries 10, 11, and 12, respectively).

The *N*-bridgehead diazepines bearing a cyclopentenone ring **6a**−**n** were obtained with yields from 41% to 89% through this domino cyclization/Nazarov reaction (Scheme 4). We noticed that this domino reaction was completely diastereoselective, as only one polycyclic diazepine was obtained in each case. The methylated compound **5m** led to a unique aza-fused polycyclic system **6m** bearing four stereogenic centers. The protecting group on the nitrogen moiety of the tertiary enamide was also investigated to facilitate postannulation deprotection; modification of the protecting group showed no influence on the outcome of the reaction. Diazepine **6l** was obtained with a poorer yield than that for compound **6a**. Three methylene units for the spacer length were also allowed, providing an eight-membered fused polycyclic system **6n**. The homologue **5o** with four methylene units did not undergo this domino

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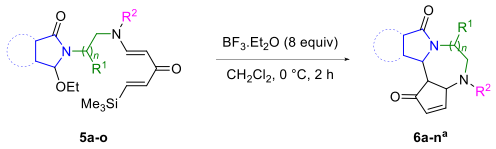
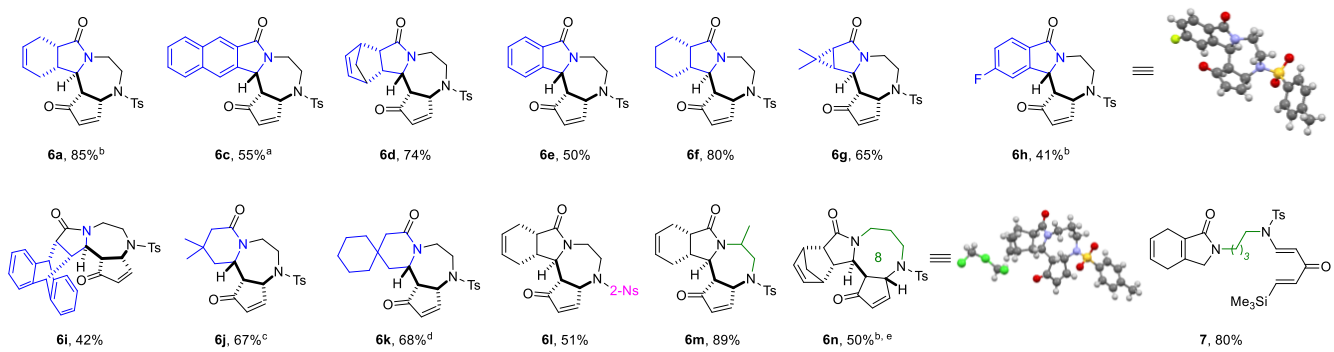
Scheme 4. Substrate Scope for the Domino Reaction



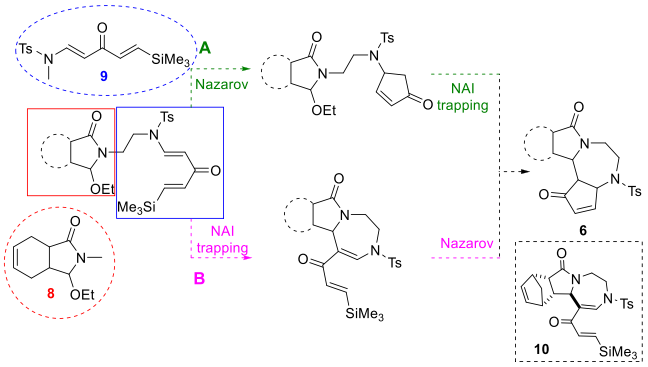


[a]Isolated yields. [b]CCDC deposition numbers for **6a**, **6h**, and **6n** are CCDC 1831780, 2001081, and 2001082, respectively. [c]2 d at rt. [d]3 d at rt. [e]**6n** cocrystallized with one molecule of CH_2Cl_2.

reaction. In this case, elimination of EtOH took place leading to the more stable conjugated alkene **7**.[22] The X-ray structures of compounds **6a**, **6h**, and **6n** corroborated the assigned structures.

Regarding the mechanism involved, the sequence of the reactions was uncertain: Nazarov reaction and subsequent addition on the NAI (Scheme 5, A) or trapping of NAI with

Scheme 5. Two Plausible Pathways for the Domino Reaction



enamide and consecutive Nazarov reaction (Scheme 5, B). Both sequences would lead to the same compound **6**. To gain more insight into the preferred reaction sequence, cyclic voltammetry (CV) was employed to assess the affinity of the Lewis acid for the *N*-acyliminium precursor and for the enamidyl vinyl ketone. For this purpose, two mimics of these moieties were prepared (Scheme 5): **8** for the aminal precursor of the acyliminium and **9** for the enamidyl vinyl ketone.

The latter could be characterized by its reduction peak potential at −1.6 V vs SCE (saturated calomel electrode) in CH_2Cl_2. The CV pattern instantaneously evolved after addition of 1 equiv of $BF_3{\cdot}OEt_2$ with a less cathodic reduction peak at −1.3 V vs SCE (Figure 2 left). However, when adding the Lewis acid in the presence of **8**, no modification of the CV was observed just after addition of $BF_3{\cdot}OEt_2$ (Figure 2 right).

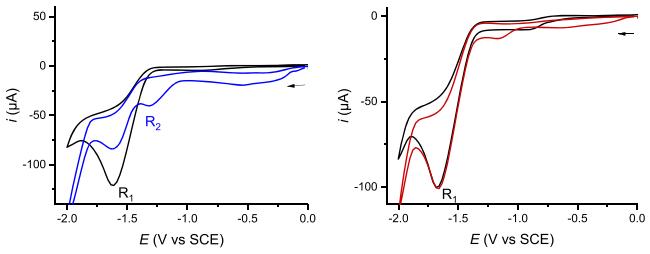


Figure 2. Cyclic voltammetry (CV) performed toward reduction potential of a 4 mM solution in CH_2Cl_2 containing 0.1 M of *n*-Bu_4NBF_4 using a glassy carbon working electrode (d = 3 mm) with a Pt wire as counter-electrode and saturated calomel electrode (SCE) as reference electrode, at a scan rate of 0.1 V s^{-1} at 20 °C. (Left) Black curve: **9** alone. Blue curve: **9** with 1 equiv of $BF_3{\cdot}OEt_2$ at rt. (Right) Black curve: **9** with 1 equiv of **8**. Red curve: **9** with 1 equiv of **8** and 1 equiv of $BF_3{\cdot}OEt_2$ at rt.

This implies that, in the presence of **8**, **9** does not interact with the Lewis acid, consistent with an enhanced affinity of **8** compared to **9**. These results and production of a limited amount of noncyclized dienone **10**, by shortening the reaction time, provide evidence that route B is the more likely mechanistic pathway.

To explain the one-pot formation of fused polycyclic ring system **6a**, the mechanism outlined in Scheme 6 is thus proposed. Regarding the relative stereochemistry and according to the NMR studies and the X-ray structures, two trends were observed. With lactam rings fused to conformationally more flexible rings (compounds **6a**, **6f**, **6i**, **6l**, and **6m**), a *trans* relationship between the lactam proton (H_1) and the two ring junction protons (H_2 and H_3) was observed. Whereas with lactam rings fused to conformationally more rigid cycles, i.e., more conformationally constrained environment (compounds **6c**, **6d**, **6e**, **6h**, **6j**, and **6k**), a *cis* relationship between the lactam proton (H_1) and the two ring junction protons (H_2 and H_3) was observed. Treatment of dienone **5a** with the Lewis acid provides the *N*-acyliminium ion **A**. In this case, the prochiral iminium ion **A** will be attacked from the less hindered side by the tertiary enamide (convex face) leading to iminium

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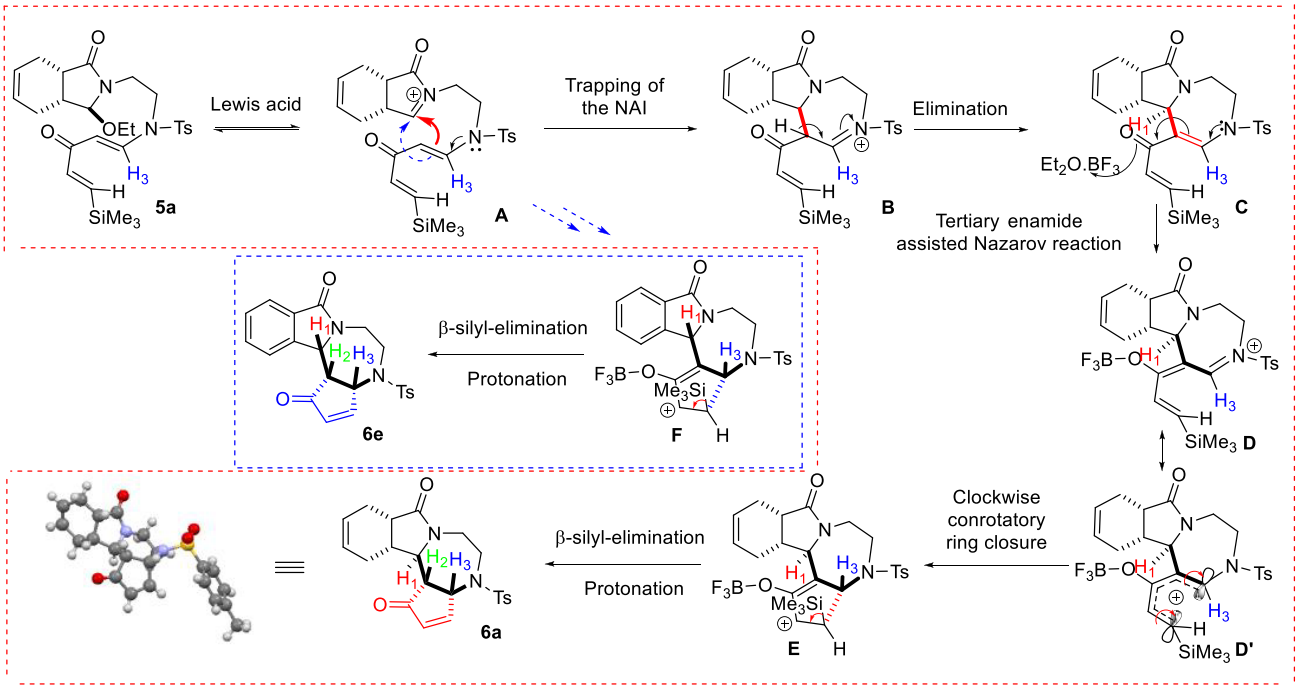
Scheme 6. Plausible Mechanism



ion **B**. After deprotonation, the cross-conjugated dienone **C** undergoes tertiary enamide-assisted Nazarov cyclization.

Indeed, the presence of the nitrogen moiety at the divinyl ketone lowers the energy barrier for the formation of the oxyallyl cation, allowing the Nazarov reaction to take place at 0 °C or rt.[14b,f] Once the stereochemistry of the aminal proton (H_1) is set, clockwise, conrotatory ring closure of **D** pushes down the newly formed five-membered boron enolate **E**. The latter evolves upon *β*-silyl-elimination, and protonation will occur from the less hindered convex face, thus generating the thermodynamically more stable *cis* fused 5−7-membered polycyclic system **6a**.

In the case of divinyl ketone **5e**, the conformationally constrained environment of the lactam will induce an attack from the enamide under the plane of the lactam as drawn, thus pushing the lactam proton H_1 above the plane of the lactam moiety, also pushing down the newly formed 5-membered boron enolate **F**, through a clockwise conrotatory ring closure. Protonation of **F** will occur to generate the thermodynamically more stable *cis* fused 5−7-membered polycyclic system **6e**. Compound **6n** involving an 8-membered ring shows an unusual *cis*−*trans* behavior and would be structurally related to the lactams fused to a flexible ring, but protonation of the enol-boronate occurs from the less hindered side and thus provides a *trans* ring junction because of the presence of the diazocane.

In conclusion, we have shown that NAI generated from tertiary enamidyl vinyl ketones undergo cyclization followed by tertiary enamide-assisted Nazarov cyclization to afford in each case a single diastereomeric polycyclic diazepine bearing a cyclopentenone ring. Torquoselectivity of the domino reaction can be attributed to the particular design of the divinyl ketones involved. Various NAI precursors as well as different chain lengths were accommodated. Electrochemical experiments revealed a higher affinity of the Lewis acid for the aminal part of the substrate than for the divinyl part, thus corroborating the order of the reaction sequence within the domino reaction.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c02251.

Experimental procedure; characterization data; NMR spectra; cyclic voltammetry experiments; X-ray data for **6a**, **6h**, and **6n** (PDF)

Accession Codes

CCDC 1831780 and 2001081−2001082 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Laurence Miesch − *Equipe Synthèse Organique et Phytochimie, Institut de Chimie, 67081 Strasbourg, France*; orcid.org/0000-0002-0369-9908; Email: lmiesch@unistra.fr

Authors

Yongxiang Zheng − *Equipe Synthèse Organique et Phytochimie, Institut de Chimie, 67081 Strasbourg, France*

Lucile Andna − *Equipe Synthèse Organique et Phytochimie, Institut de Chimie, 67081 Strasbourg, France*

Olivia Bistri − *Laboratoire des Biomolécules, LBM, Département de Chimie, École Normale Supérieure, PSL University, Sorbonne Université, 75005 Paris, France*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c02251

Author Contributions

‖Y.Z. and L.A. contributed equally.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Pardo, M.; Tellitu, I.; Domínguez, E. *Tetrahedron* **2010**, *66*, 5811−5818.
(2) Yu, H.-F.; Qin, X.-J.; Ding, C.-F.; Wei, X.; Yang, J.; Luo, J.-R.; Liu, L.; Khan, A.; Zhang, L.-C.; Xia, C.-F.; Luo, X.-D. *Org. Lett.* **2018**, *20*, 4116−4120.
(3) Kaneko, T.; Wong, H.; Doyle, T. W.; Rose, W. C.; Bradner, W. T. *J. Med. Chem.* **1985**, *28*, 388−392.
(4) (a) Wang, M.-X. *Chem. Commun.* **2015**, *51*, 6039−6049 and references therein. (b) Cai, X.; Yang, M.; Guo, H. *Curr. Org. Synth.* **2019**, *16*, 70−97.
(5) (a) Cossey, K. N.; Funk, R. L. *J. Am. Chem. Soc.* **2004**, *126*, 12216−12217. (b) Yang, L.; Zheng, Q.-Y.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *Org. Lett.* **2008**, *10*, 2461−2464. (c) Yang, L.; Wang, D.-X.; Zheng, Q.-Y.; Pan, J.; Huang, Z.-T.; Wang, M.-X. *Org. Biomol. Chem.* **2009**, *7*, 2628−2634.
(6) (a) Yang, L.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *J. Am. Chem. Soc.* **2009**, *131*, 10390−10391. (b) Yang, L.; Lei, C.-H.; Wang, D.-X.; Huang, Z.-T.; Zhu, J.; Wang, M.-X. *Org. Lett.* **2010**, *12*, 3918−3921. (c) Tong, S.; Wang, D.-X.; Zhao, L.; Zhu, J.; Wang, M.-X. *Angew. Chem., Int. Ed.* **2012**, *51*, 4417−4420.
(7) (a) Suga, S.; Nishida, T.; Yamada, D.; Nagaki, A.; Yoshida, J.-I. *J. Am. Chem. Soc.* **2004**, *126*, 14338−14339. (b) Tong, S.; Yang, X.; Wang, D.-X.; Zhao, L.; Zhu, J.; Wang, M.-X. *Tetrahedron* **2012**, *68*, 6492−6497.
(8) (a) Lei, C.-H.; Wang, D.-X.; Zhao, L.; Zhu, J.; Wang, M.-X. *J. Am. Chem. Soc.* **2013**, *135*, 4708−4711. (b) Lei, C.-H.; Wang, D.-X.; Zhao, L.; Zhu, J.; Wang, M.-X. Chem. − Eur. *Chem. - Eur. J.* **2013**, *19*, 16981−16987. (c) Lei, C.-H.; Zhao, L.; Wang, D. X.; Zhu, J.; Wang, M.-X. *Org. Chem. Front.* **2014**, *1*, 909−913.
(9) (a) Harrison, T. J.; Patrick, B. O.; Dake, G. R. *Org. Lett.* **2007**, *9*, 367−370. (b) Nayak, S.; Prabagar, B.; Ghosh, N.; Mallick, R. K.; Sahoo, A. K. *Synthesis* **2017**, *49*, 4261−4271.
(10) Andna, L.; Miesch, L. *Org. Lett.* **2018**, *20*, 3430−3433.
(11) Beltran, F.; Miesch, L. *Org. Lett.* **2019**, *21*, 1569−1573.
(12) (a) Habermas, K. L.; Denmark, S. E.; Jones, T. K. In *Organic Reactions*, Vol. *45*; Paquette, L. A., Ed.; J. Wiley & Sons: 1994; pp 2−158. (b) Pellissier, H. *Tetrahedron* **2005**, *61*, 6479−6517. (c) Frontier, A. J.; Collison, C. *Tetrahedron* **2005**, *61*, 7577−7606. (d) Grant, T. N.; Rieder, C. J.; West, F. G. *Chem. Commun.* **2009**, 5676−5688. (e) Vaidya, T.; Eisenberg, R.; Frontier, A. J. *ChemCatChem* **2011**, *3*, 1531−1548. (f) Spencer, W. T., III; Vaidya, T.; Frontier, A. J. *Eur. J. Org. Chem.* **2013**, *2013*, 3621−3633. (g) Wenz, D. R.; de Alaniz, J. R. *Eur. J. Org. Chem.* **2015**, *2015*, 23−37. (h) Martin, M. C.; Shenje, R.; France, S. *Isr. J. Chem.* **2016**, *56*, 499−511. (i) Vinogradov, M. G.; Turova, O. V.; Zlotin, S. G. *Org. Biomol. Chem.* **2017**, *15*, 8245−8269.
(13) (a) He, W.; Sun, X.; Frontier, A. J. *J. Am. Chem. Soc.* **2003**, *125*, 14278−14279. (b) Liang, G.; Gradl, S. N.; Trauner, D. *Org. Lett.* **2003**, *5*, 4931−4934. (c) Bee, C.; Leclerc, E.; Tius, M. A. *Org. Lett.* **2003**, *5*, 4927−4930. (d) Raja, S.; Ieawsuwan, W.; Korotkov, V.; Rueping, M. *Chem. - Asian J.* **2012**, *7*, 2361−2366. (e) Hutson, G. E.; Türkmen, Y. E.; Rawal, V. H. *J. Am. Chem. Soc.* **2013**, *135*, 4988−4991. (f) Koenig, J. J.; Arndt, T.; Gildemeister, N.; Neudörfl, J.-M.; Breugst, M. *J. Org. Chem.* **2019**, *84*, 7587−7605.
(14) (a) Occhiato, E. G.; Prandi, C.; Ferrali, A.; Guarna, A. *J. Org. Chem.* **2005**, *70*, 4542−4545. (b) Kerr, D. J.; Miletic, M.; Chaplin, J. H.; White, J. M.; Flynn, B. L. *Org. Lett.* **2012**, *14*, 1732−1735. (c) Wu, Y.-K.; Niu, T.; West, F. G. *Chem. Commun.* **2012**, *48*, 9186−9188. (d) Flynn, B. L.; Manchala, N.; Krenske, E. H. *J. Am. Chem. Soc.* **2013**, *135*, 9156−9163. (e) Scarpi, D.; Petrović, M.; Fiser, B.; Gómez-Bengoa, E.; Occhiato, E. G. *Org. Lett.* **2016**, *18*, 3922−3925. (f) Manchala, N.; Law, H. Y. L.; Kerr, D. J.; Volpe, R.; Lepage, R. J.; White, J. M.; Krenske, E. H.; Flynn, B. L. *J. Org. Chem.* **2017**, *82*, 6511−6527. (g) Wang, G.-P.; Chen, M.-Q.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Sci.* **2017**, *8*, 7197−7202. (h) Carlsen, P. N.; Stoutenburg, E. G.; Frontier, A. J. *Synthesis* **2018**, *50*, 1238−1245.
(15) Kim, S.-H.; Cha, J. K. *Synthesis* **2000**, *2000*, 2113−2116.
(16) Li, W.-D. Z.; Wang, Y.-Q. *Org. Lett.* **2003**, *5*, 2931−2934.
(17) Andna, L.; Miesch, L. *Org. Biomol. Chem.* **2019**, *17*, 5688−5692.
(18) Gharpure, S. J.; Prasath, V.; Kumar, V. *Chem. Commun.* **2015**, *51*, 13623−13626.
(19) Koseki, Y.; Fujino, K.; Takeshita, A.; Sato, H.; Nagasaka, T. *Tetrahedron: Asymmetry* **2007**, *18*, 1533−1536.
(20) (a) Speckamp, W. N.; Moolenaar, M. J. *Tetrahedron* **2000**, *56*, 3817−3856. (b) Pyne, S. G.; Au, C. W. G.; Davis, A. S.; Morgan, I. R.; Ritthiwigrom, T.; Yazici, A. *Pure Appl. Chem.* **2008**, *80*, 751−762. (c) Morgan, I. R.; Yazici, A.; Pyne, S. G.; Skelton, B. W. *J. Org. Chem.* **2008**, *73*, 2943−2946. (d) Morgan, I. R.; Yazici, A.; Pyne, S. G. *Tetrahedron* **2008**, *64*, 1409−1419. (e) Wu, P.; Nielsen, T. E. *Chem. Rev.* **2017**, *117*, 7811−7856.
(21) (a) Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642−2645. (b) Miesch, M.; Miesch-Gross, L.; Franck-Neumann, M. *Tetrahedron* **1997**, *53*, 2103−2110. (c) Miesch, M.; Miesch-Gross, L.; Franck-Neumann, M. *Tetrahedron* **1997**, *53*, 2111−2118.
(22) Wijnberg, J. B. P. A.; Schoemaker, H. E.; Speckamp, W. N. *Tetrahedron* **1978**, *34*, 179−187.

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