Organic LETTERS
Letter
pubs.acs.org/OrgLett

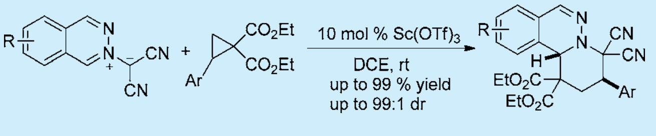
Sc(OTf)$_3$-Catalyzed [3 + 3] Cycloaddition of Cyclopropane 1,1-Diesters with Phthalazinium Dicyanomethanides

Honglei Liu, Chunhao Yuan, Yang Wu, Yumei Xiao, and Hongchao Guo*

Department of Applied Chemistry, China Agricultural University, Beijing 100193, P. R. China

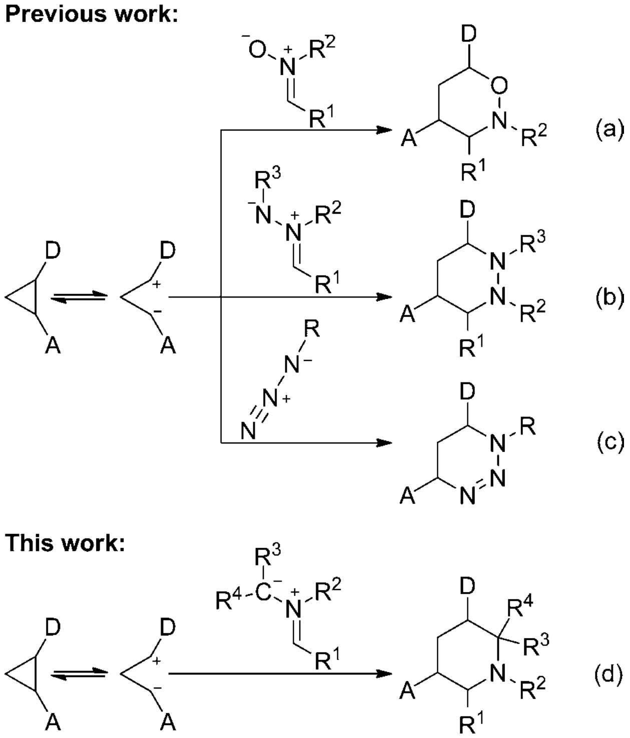
Supporting Information

ABSTRACT: The Sc(OTf)$_3$-catalyzed diastereoselective [3 + 3] cycloaddition of phthalazinium dicyanomethanides with cyclopropane 1,1-diesters proceeded smoothly under mild reaction conditions, affording a variety of 3,4-dihydro-1*H*-pyrido[2,1-*a*]phthalazine derivatives in up to 99% yields with excellent diastereoselectivities.



The cycloaddition reactions of donor−acceptor cyclopropanes (DA cyclopropanes) with various dipoles have emerged as one of the most important tools for synthesis of a variety of carbo- and heterocyclic compounds,[1] as well as the total synthesis of many natural products.[1d,h,i,k] Among various cycloadditions of DA cyclopropanes, [3 + 3] cycloaddition constitutes an interesting and important class of reactions, which provides a rapid access to six-membered cyclic scaffolds.[2−8] Generally, [3 + 3] cycloaddition occurs via a stepwise reaction of a stable 1,3-dipole with reactive 1,3-dipolar species generated in situ from DA cyclopropanes in the presence of Lewis acid catalyst. Since Kerr reported seminal [3 + 3]-cycloaddition of DA cyclopropanes with nitrones in 2003,[2] the search for a stable 1,3-dipole with suitable reactivity for developing [3 + 3] cycloaddition of DA cyclopropanes has attracted much attention. However, the scope and type of 1,3-dipoles used for [3 + 3] cycloaddition of DA cyclopropanes are still quite limited, although these reactions have been studied for more than 10 years. Most research has been focused on [3 + 3]-cycloaddition involving nitrones (Scheme 1a), and many successful examples have been achieved, giving achiral and chiral 1,2-oxazinane derivatives.[3] Until 2008, Charette expanded the scope of 1,3-dipoles to azomethine imines and developed [3 + 3] cycloadditions of azomethine imines with D−A cyclopropanes to afford a hexahydropyridazine scaffold (Scheme 1b).[4] Afterward, in 2013, Tang reported its enantioselective variant by using a chiral trisoxazoline ligand, providing the chiral dihydroquinoline derivatives with high enantioselectivity.[5] Most recently, using azides as 1,3-dipoles, Xu developed a TiCl$_4$-promoted [3 + 3] cycloaddition of cyclopropane 1,1-diesters for the synthesis of highly functionalized triazinines, which could be easily converted to biologically important azetidines by simple thermolysis (Scheme 1c).[6] To the best of our knowledge, the C−N−C type of azomethine ylides has never been investigated in the [3 + 3] cycloaddition of DA cyclopropane. Herein, using phthalazinium dicyanomethanides[9] as a 1,3-dipole, we report Sc(OTf)$_3$-catalyzed [3 + 3] cycloaddition of cyclopropane 1,1-diesters for the synthesis of pharmaceutically interesting 3,4-dihydro-1*H*-pyrido[2,1-*a*]phthalazine derivatives with excellent diastereoselectivities (Scheme 1d).[10]

Scheme 1. Cycloaddition Reactions of Donor−Acceptor Cyclopropanes with Stable 1,3-Dipoles



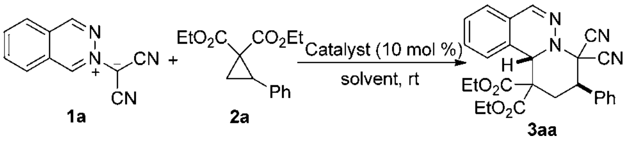
In our initial investigation, the reaction of cyclopropane 1,1-diester **2a** with phthalazinium dicyanomethanide **1a** was chosen as the model reaction. In the presence of 10 mol % of the Lewis acid catalyst, the reaction was performed in 1,2-dichloroethane (DCE) at rt. Various Lewis acids had been screened. Unfortunately, only a trace of [3 + 3] cycloaddition product

Received: July 13, 2015
Published: August 14, 2015

DOI: 10.1021/acs.orglett.5b02003
Org. Lett. 2015, 17, 4220−4223

was observed with the use of Lewis acids such as Yb(OTf)$_3$, Ni(ClO$_4$)$_2$·6H$_2$O, Zn(OTf)$_2$, ZnCl$_2$, Zn(OAc)$_2$, Cu(OTf)$_2$, and CuOTf. In contrast, AlCl$_3$ displayed moderate catalytic activity, affording the [3 + 3] cycloaddition product **3aa** as a single diastereomer in 45% yield. To our delight, Sc(OTf)$_3$ showed remarkable catalytic capability. In the presence of 10 mol % of Sc(OTf)$_3$, the reaction of phthalazinium dicyanomethanide **1a** with cyclopropane 1,1-diester **2a** worked efficiently in DCE at rt for 6 h, giving the [3 + 3] cycloadduct **3aa** as a single diastereomer in 99% yield (entry 2). The product's structure has unambiguously been established by NMR spectra and X-ray crystallography of **3aa** (Table 1).[11] Strangely, subsequent investigation of solvent effects indicated that the halogenated solvents such as dichloromethane (DCM) and chloroform were detrimental to the reaction, leading to moderate yields (43% and 47%) (entries 3–4), but other solvents such as toluene, THF, and methanol afforded the products in decent yields (81–90%) (entries 5–7). The catalyst Sc(OTf)$_3$ is quite efficient. Using 5 mol % of the catalyst loading, the [3 + 3] cycloadduct could be obtained in 88% yield, albeit requiring a longer reaction time (entry 8). Even by using 1 mol % of catalyst, the product **3aa** was still obtained in 65% yield (entry 9).

Table 1. Screening of the Reaction Conditions[a]

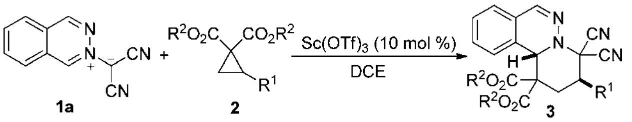


entry	catalyst	solvent	t/h	yield/%[b]
1	AlCl$_3$	DCE	12	45
2	Sc(OTf)$_3$	DCE	6	99
3	Sc(OTf)$_3$	DCM	24	43
4	Sc(OTf)$_3$	CHCl$_3$	24	47
5	Sc(OTf)$_3$	toluene	24	90
6	Sc(OTf)$_3$	THF	72	85
7	Sc(OTf)$_3$	MeOH	24	81
8[c]	Sc(OTf)$_3$	DCE	12	88
9[d]	Sc(OTf)$_3$	DCE	24	65

[a] Unless otherwise stated, reactions of **1a** (0.2 mmol), **2a** (0.22 mmol), and the catalyst (0.02 mmol) were carried out in 4 mL of solvent at rt. [b] Isolated yield. [c] 5 mol % catalyst was used. [d] 1 mol % catalyst was used.

Under the optimal reaction conditions (using 10 mol % Sc(OTf)$_3$ as the catalyst in DCE at rt), we explored the [3 + 3] cycloaddition reaction of phthalazinium dicyanomethanide **1a** with various cyclopropane 1,1-diesters **2** (Table 2). Good to excellent yields (85–96%) were acquired using those cyclopropane 1,1-diesters containing an electron-donating-group-substituted aryl (entries 2–8). Substrates bearing fluoro, chloro, and bromo at the 4-position of the aryl displayed similar reactivity (entries 11, 14, 16), but substrates bearing fluoro, chloro, and bromo at the 2- or 3-position of the aryl showed poor activities and required a higher reaction temperature (40 °C) to furnish the products in moderate yields (entries 9–10, 12–13, 15). Further attempts to improve the yields of halo-aryl substituted substrates by performing reactions at higher temperature or with a higher concentration of the substrates did not work, leading to a messy mixture. It seems that the steric effect has a significant influence on the reactivity of the cyclopropane 1,1-diesters. The naphthyl substituted cyclopropane 1,1-diester was well tolerated in the [3 + 3] annulation reaction with phthalazinium dicyanomethanide **1a**, providing the corresponding product **3aq** in 94% yield (entry 17). Displacing the ethyl ester of cyclopropanes with methyl ester did not influence the reactivity, leading to the corresponding product **3ar** in 86% yield (entry 18).

Table 2. Scope of Cyclopropane 1,1-Diesters[a]

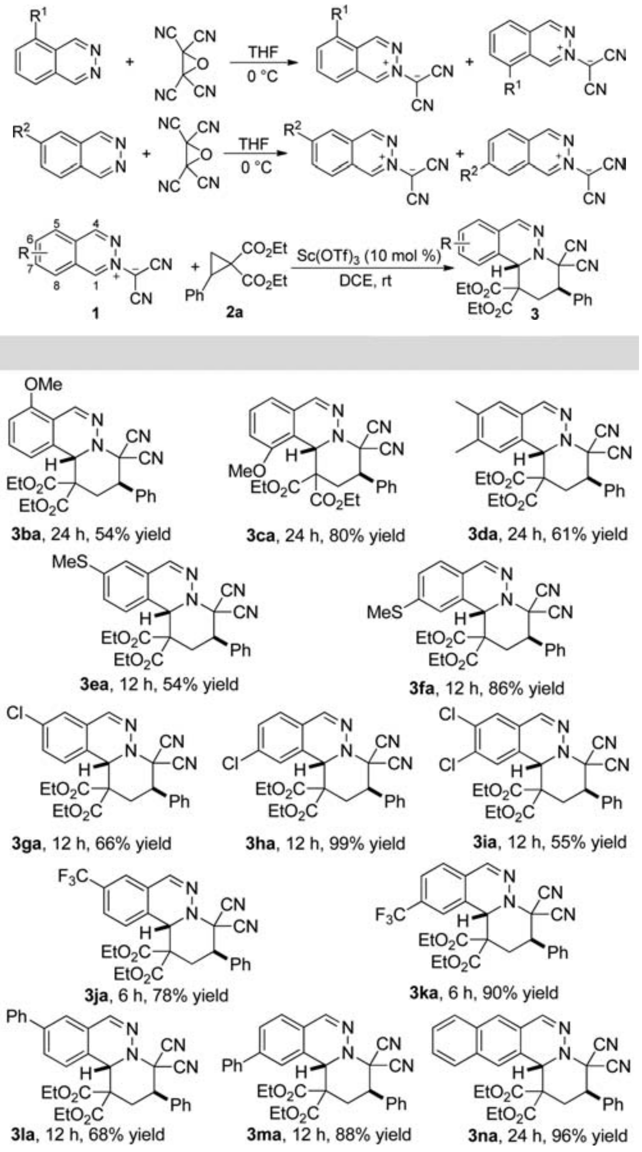


entry	R^1	R^2	t/°C	t/h	3	yield/%[b]
1	Ph (**2a**)	Et	25	6	**3aa**	99
2	2-MeC$_6$H$_4$ (**2b**)	Et	25	24	**3ab**	86
3	3-MeC$_6$H$_4$ (**2c**)	Et	25	24	**3ac**	92
4	4-MeC$_6$H$_4$ (**2d**)	Et	25	24	**3ad**	96
5	2,4-Me$_2$C$_6$H$_3$ (**2e**)	Et	25	24	**3ae**	85
6	4-^{t}BuC$_6$H$_4$ (**2f**)	Et	25	24	**3af**	91
7	4-OMeC$_6$H$_4$ (**2g**)	Et	25	12	**3ag**	96
8	4-OEtC$_6$H$_4$ (**2h**)	Et	25	12	**3ah**	93
9	2-FC$_6$H$_4$ (**2i**)	Et	40	12	**3ai**	31
10	3-FC$_6$H$_4$ (**2j**)	Et	40	12	**3aj**	42
11	4-FC$_6$H$_4$ (**2k**)	Et	25	48	**3ak**	88
12	2-ClC$_6$H$_4$ (**2l**)	Et	40	12	**3al**	35
13	3-ClC$_6$H$_4$ (**2m**)	Et	40	12	**3am**	62
14	4-ClC$_6$H$_4$ (**2n**)	Et	25	48	**3an**	95
15	3-BrC$_6$H$_4$ (**2o**)	Et	40	12	**3ao**	71
16	4-BrC$_6$H$_4$ (**2p**)	Et	25	48	**3ap**	97
17	2-naphthyl (**2q**)	Et	25	24	**3aq**	94
18	Ph (**2r**)	Me	25	24	**3ar**	86

[a] Reactions of **1a** (0.2 mmol), **2** (0.22 mmol), and Sc(OTf)$_3$ (0.02 mmol) were carried out in 4 mL of DCE at room temperature. [b] Isolated yields.

Next, the scope of the phthalazinium dicyanomethanides was investigated (Table 3). Phthalazinium dicyanomethanides were prepared by reaction of phthalazine or phthalazine derivative with TCNEO.[9m,12] For nonsymmetric substituted phthalazines, since there are two nitrogen atoms, both of which can attack tetracyanoethylene oxide, two positional isomeric phthalazinium-2-dicyanomethanide derivatives were formed in nearly quantitative total yield (Table 3). These two isomers could not be separated by flash column chromatography; thus, the mixture of two isomeric substrates was used for [3 + 3] cycloaddition with DA cyclopropane. Fortunately, the mixture of [3 + 3] cycloaddition products from these two isomeric substrates could be separated by using flash column chromatography. The cycloaddition yields were calculated on the basis of HPLC analysis of two isomeric substrates. Several phthalazinium dicyanomethanides **1** were examined under standard reaction conditions. These substrates underwent the reaction with cyclopropane 1,1-diester **2a** to afford the corresponding products (**3ba**–**3na**) as a single diastereoisomer in moderate to excellent yields (Table 3). The reactions were tolerant of various phthalazinium dicyanomethanides with electron-donating or -withdrawing groups. It was observed that the substitution pattern of substituents on the phthalazine ring has remarkable influence on the reactivity. 7-Position substituted phthalazinium dicyanomethanides carried out the cycloaddition with cyclopropane 1,1-diester **2a** to give the [3 + 3] cycloadducts **3fa**, **3ha**, **3ka**, and **3ma** in 86–99% yield. In contrast, other position substituted substrates led to the

Table 3. Scope of Phthalazinium Dicyanomethanides[a,b]



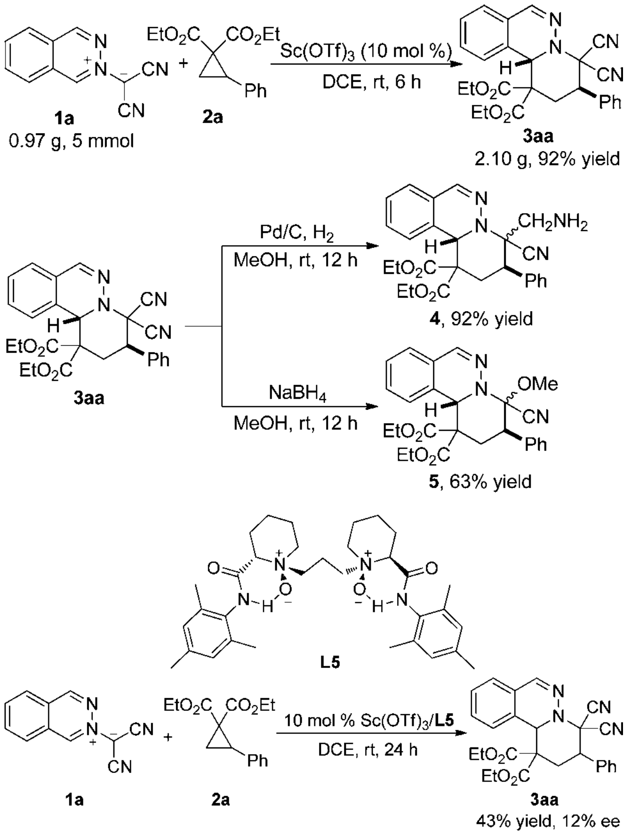
3ba, 24 h, 54% yield
3ca, 24 h, 80% yield
3da, 24 h, 61% yield
3ea, 12 h, 54% yield
3fa, 12 h, 86% yield
3ga, 12 h, 66% yield
3ha, 12 h, 99% yield
3ia, 12 h, 55% yield
3ja, 6 h, 78% yield
3ka, 6 h, 90% yield
3la, 12 h, 68% yield
3ma, 12 h, 88% yield
3na, 24 h, 96% yield

[a] Reactions of **1** (0.2 mmol), **2a** (0.22 mmol), and Sc(OTf)$_3$ (0.02 mmol) were carried out in 4 mL of DCE at rt. [b] Isolated yields.

corresponding products in moderate yields. The benzo[*g*]-phthalazine-derived dicyanomethanide also worked under the reaction conditions, affording the product **3na** in 96% yield.

The present reaction is quite robust, allowing it to be performed on the gram scale. As shown in Scheme 2, using 10 mol % of Sc(OTf)$_3$, phthalazinium dicyanomethanide **1a** (0.97 g, 5 mmol) reacted with cyclopropane 1,1-diester **2a** to give the [3 + 3] cycloaddtion product **3aa** in 92% yield (2.10 g). It indicated that the reaction could be a practical tool for the synthesis of 3,4-dihydro-1*H*-pyrido[2,1-*a*]phthalazine derivatives. Interestingly, through treatment of the product **3aa** with H$_2$/Pd/C, one of two cyano groups was reduced to an amine, affording the derivative **4** in 92% yield. On the other hand, by treatment of **3aa** with NaBH$_4$ in methanol at rt for 12 h, one of two cyano groups was transformed into the MeO group, giving the product **5** in 63% yield (Scheme 2). To achieve an asymmetric variant of the present reaction, several chiral ligands, such as the Pybox ligand, Trost ligand, and *N,N*′-dioxide ligands, had been screened (see Supporting Information for details). Unfortunately, the catalytic activity of Sc(OTf)$_3$ was significantly weakened after its complexation with a chiral ligand. In the presence of the Pybox or Trost ligand and Sc(OTf)$_3$, the desired product could not be obtained. Although Sc(OTf)$_3$/*N,N*′-dioxide can promote this reaction, a moderate yield and poor enantioselectivity could only be obtained. In the presence of **L5**, up to 12% ee was achieved (Scheme 2).

Scheme 2. Gram-Scale Synthesis and Further Transformations of the Cycloadduct



In summary, we have developed a Sc(OTf)$_3$-catalyzed diastereoselective [3 + 3] cycloaddition of phthalazinium dicyanomethanides with DA cyclopropanes, providing access to 3,4-dihydro-1*H*-pyrido[2,1-*a*]phthalazine derivatives in up to 99% yields with excellent diastereoselectivities. A variety of cyclopropane 1,1-diesters and phthalazinium dicyanomethanides are compatible with the mild reaction conditions. This reaction provides an efficient method for constructing diverse and complex heterocyclic compounds. Further research on cycloaddition reactions between two different 1,3-dipoles is in progress.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02003.

Experimental procedure, characterization data, NMR spectra (PDF)
CIF file of **3aa** (CIF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: hchguo@cau.edu.cn.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work is supported by the NSFC (21172253 and 21372256).

REFERENCES

(1) For reviews about donor−acceptor cyclopropanes, see: (a) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151. (b) Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321. (c) De Simone, F.; Waser, J. *Synthesis* **2009**, *2009*, 3353. (d) Carson, C. A.; Kerr, M. A. *Chem. Soc. Rev.* **2009**, *38*, 3051. (e) Campbell, M. J.; Johnson, J. S.; Parsons, A. T.; Pohlhaus, P. D.; Sanders, S. D. *J. Org. Chem.* **2010**, *75*, 6317. (f) Lebold, T. P.; Kerr, M. *Pure Appl. Chem.* **2010**, *82*, 1797. (g) Melnikov, M. Ya.; Budynina, E. M.; Ivanova, O. A.; Trushkov, I. V. *Mendeleev Commun.* **2011**, *21*, 293. (h) Lu, B. L.; Dai, L. Z.; Shi, M. *Chem. Soc. Rev.* **2012**, *41*, 3318. (i) Tang, P.; Qin, Y. *Synthesis* **2012**, *44*, 2969. (j) Wang, Z. *Synlett* **2012**, *23*, 2311. (k) Waser, J. *Top. Heterocycl. Chem.* **2013**, *32*, 225. (l) Cavitt, M. A.; Phun, L. H.; France, S. *Chem. Soc. Rev.* **2014**, *43*, 804. (m) Schneider, T. F.; Kaschel, J.; Werz, D. B. *Angew. Chem., Int. Ed.* **2014**, *53*, 5504. (n) De Nanteuil, F.; De Simone, F.; Frei, R.; Benfatti, F.; Serrano, E.; Waser, J. *Chem. Commun.* **2014**, *50*, 10912. (o) Liao, S. H.; Sun, X. L.; Tang, Y. *Acc. Chem. Res.* **2014**, *47*, 2260. (p) Grover, H. K.; Emmett, M. R.; Kerr, M. A. *Org. Biomol. Chem.* **2015**, *13*, 655.

(2) Young, I. S.; Kerr, M. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3023.

(3) For successful examples of [3 + 3]-cycloaddition of DA cyclopropanes with nitrones, see: (a) Ganton, M. D.; Kerr, M. A. *J. Org. Chem.* **2004**, *69*, 8554. (b) Young, I. S.; Kerr, M. A. *Org. Lett.* **2004**, *6*, 139. (c) Sibi, M. P.; Ma, Z.; Jasperse, C. P. *J. Am. Chem. Soc.* **2005**, *127*, 5764. (d) Lebold, T. P.; Carson, C. A.; Kerr, M. A. *Synlett* **2006**, 364. (e) Kang, Y.-B.; Sun, X.-L.; Tang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3918. (f) Sapeta, K.; Kerr, M. A. *J. Org. Chem.* **2007**, *72*, 8597. (g) Karadeolian, A.; Kerr, M. A. *J. Org. Chem.* **2007**, *72*, 10251. (h) Young, I. S.; Kerr, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 1465. (i) Johansen, M. B.; Kerr, M. A. *Org. Lett.* **2008**, *10*, 3497. (j) Dias, D. A.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 3694. (k) Ding, Q.; Wang, Z.; Wu, J. *Tetrahedron Lett.* **2009**, *50*, 198. (l) Wu, L.; Shi, M. *Chem. - Eur. J.* **2010**, *16*, 1149. (m) Zhang, Y.; Liu, F.; Zhang, J. *Chem. - Eur. J.* **2010**, *16*, 6146. (n) Humenny, W. J.; Kyriacou, P.; Sapeta, K.; Karadeolian, A.; Kerr, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 11088. (o) Yang, H.-B.; Shi, M. *Org. Biomol. Chem.* **2012**, *10*, 8236. (p) Hardman, A. M.; So, S. S.; Mattson, A. E. *Org. Biomol. Chem.* **2013**, *11*, 5793. (q) Gorbacheva, E. O.; Tabolin, A. A.; Novikov, R. A.; Khomutova, Y. A.; Nelyubina, Y. V.; Tomilov, Y. V.; Ioffe, S. L. *Org. Lett.* **2013**, *15*, 350. (r) Mikhaylov, A. A.; Novikov, R. A.; Khomutova, Yu. A.; Arkhipov, D. E.; Korlyukov, A. A.; Tabolin, A. A.; Tomilov, Yu. V.; Ioffe, S. L. *Synlett* **2014**, *25*, 2275. (s) Tabolin, A. A.; Novikov, R. A.; Khomutova, Y. A.; Zharov, A. A.; Stashina, G. A.; Nelyubina, Y. V.; Tomilov, Y. V.; Ioffe, S. L. *Tetrahedron Lett.* **2015**, *56*, 2102. (t) Braun, C. M.; Congdon, E. A.; Nolin, K. A. *J. Org. Chem.* **2015**, *80*, 1979.

(4) Perreault, C.; Goudreau, S. R.; Zimmer, L. E.; Charette, A. B. *Org. Lett.* **2008**, *10*, 689.

(5) Zhou, Y.-Y.; Li, J.; Ling, L.; Liao, S.-H.; Sun, X.-L.; Li, Y.-X.; Wang, L.-J.; Tang, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 1452.

(6) Zhang, H.-H.; Luo, Y.-C.; Wang, H.-P.; Chen, W.; Xu, P.-F. *Org. Lett.* **2014**, *16*, 4896.

(7) For [3 + 3] cycloaddition reactions of donor−acceptor cyclopropanes with reactive dipolar species formed in situ, see: (a) Sapeta, K.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 2081. (b) Lebold, T. P.; Leduc, A. B.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 3770. (c) Leduc, A. B.; Lebold, T. P.; Kerr, M. A. *J. Org. Chem.* **2009**, *74*, 8414. (d) Grover, H. K.; Lebold, T. P.; Kerr, M. A. *Org. Lett.* **2011**, *13*, 220. (e) Sathishkannan, G.; Srinivasan, K. *Chem. Commun.* **2014**, *50*, 4062. (f) Talukdar, R.; Tiwari, D. P.; Saha, A.; Ghorai, M. K. *Org. Lett.* **2014**, *16*, 3954. (g) Wang, H. P.; Zhang, H.-H.; Hu, X.-Q.; Xu, P. F.; Luo, Y.-C. *Eur. J. Org. Chem.* **2015**, *2015*, 3486.

(8) For [3 + 3] cycloaddition reactions through dimerization of donor−acceptor cyclopropanes, see: (a) Ivanova, O. A.; Budynina, E. M.; Chagarovskiy, A. O.; Trushkov, I. V.; Melnikov, M. Y. *J. Org. Chem.* **2011**, *76*, 8852. (b) Novikov, R. A.; Korolev, V. A.; Timofeev, V. P.; Tomilov, Y. V. *Tetrahedron Lett.* **2011**, *52*, 4996.

(9) For cycloaddition reactions with phthalazinium dicyanomethanides as 1,3-dipoles, see: (a) Sustmann, R.; Trill, H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 838. (b) Sustmann, R. *Pure Appl. Chem.* **1974**, *40*, 569. (c) Matsumoto, K.; Uchida, T. *J. Chem. Soc., Perkin Trans. 1* **1981**, 73. (d) Bergsträßer, U.; Hoffmann, A.; Regitz, M. *Tetrahedron Lett.* **1992**, *33*, 1049. (e) Butler, R. N.; Coyne, A. G.; McArdle, P.; Cunningham, D.; Burke, L. A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1391. (f) Butler, R. N.; Coyne, A. G.; Burke, L. A. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1781. (g) Butler, R. N.; Coyne, A. G.; Cunningham, W. J.; Burke, L. A. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1807. (h) Butler, R. N.; Coyne, A. G.; Cunningham, W. J.; Moloney, E. M.; Burke, L. A. *Helv. Chim. Acta* **2005**, *88*, 1611. (i) Butler, R. N.; Coyne, A. G.; Moloney, E. M. *Tetrahedron Lett.* **2007**, *48*, 3501. (j) Butler, R. N.; Coyne, A. G.; McArdle, P.; Sibley, L. M.; Burke, L. A. *Tetrahedron Lett.* **2007**, *48*, 6684. (k) Beare, K. D.; Yuen, A. K. L.; Masters, A. F.; Maschmeyer, T.; McErlean, C. S. P. *Chem. Commun.* **2013**, *49*, 8347. (l) Butler, R. N.; Coyne, A. G.; Cunningham, W. J.; Moloney, E. M. *J. Org. Chem.* **2013**, *78*, 3276. (m) Yuan, C. H.; Liu, H. L.; Gao, Z. Z.; Zhou, L. J.; Feng, Y. L.; Xiao, Y. M.; Guo, H. C. *Org. Lett.* **2015**, *17*, 26.

(10) (a) Ruebsam, F.; Sun, Z. X.; Ayida, B. K.; Webber, S. E.; Zhou, Y. F.; Zhao, Q.; Kissinger, C. R.; Showalter, R. E.; Shah, A. M.; Tsan, M.; Patel, R.; Lebrun, L. A.; Kamran, R.; Sergeeva, M. V.; Bartkowski, D. M.; Nolan, T. G.; Norris, D. A.; Kirkovsky, L. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5002. (b) Yu, H. J.; Fang, Y.; Lu, X.; Liu, Y. J.; Zhang, H. B. *Chem. Biol. Drug Des.* **2014**, *83*, 89.

(11) Crystallographic data for **3aa** has been deposited with the Cambridge Crystallographic Data Centre as deposition number CCDC 1409180. 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.

(12) Fernández, N.; Carrillo, L.; Vicario, J. L.; Badía, D.; Reyes, E. *Chem. Commun.* **2011**, *47*, 12313.

DOI: 10.1021/acs.orglett.5b02003
Org. Lett. 2015, 17, 4220−4223