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Dearomative [3 + 2] cycloaddition reaction of nitrobenzothiophenes with nonstabilized azomethine ylides†

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A highly diastereoselective dearomative [3 + 2] 1,3-dipolar cycloaddition reaction of nitrobenzothiophenes with an *in situ*-generated nonstabilized azomethine ylides has been developed. The transformation provides a series of functionalized fused tricyclic benzo[4,5]thieno[2,3-*c*]pyrroles in good yields (up to 92%) under mild reaction conditions. In addition, a gram-scale experiment and the synthetic transformation of the cycloadduct further highlighted the synthetic utility. The relative configurations of the typical products were clearly confirmed by X-ray crystallography.

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The dearomative cycloaddition reactions are a powerful synthetic strategy to obtain valuable structural motifs which exist in numerous biologically active natural products, pharmaceutical agents, and also in synthetic and materials building blocks.¹ Among them, indole substrates gained more and more research interest to develop effective methods for the construction of indole-based skeletons and their functionalization *via* dearomative transformation.² Because the unique properties of indole ring systems are ubiquitous in biologically active alkaloids,³ the range of methodologies that have been explored to access dearomatized indole heterocycles is extremely extensive. In contrast to the dearomative reactions of indole substrates, the analogous benzothiophenes derivatives have been less explored.⁴ In addition, the benzo[*b*]thiophene derivatives that have found widespread application are frequently found in many bioactive compounds, pharmaceuticals, and as synthetic building blocks.⁵ Therefore, the development of efficient synthetic method to realize the dearomatization of benzo[*b*]thiophenes for the construction of diverse functionalized heteroarenes molecules continues to be an important and highly desirable in the organic synthetic community.

On the other hand, 1,3-dipolar cycloaddition of azomethine ylides with electron deficient dipolarophiles that have a wide

range of applications in organic synthesis, is a useful and facile synthetic process for five or six membered heterocyclic rings in one step.⁶ Especially, nonstabilized azomethine ylides generated *in situ* are highly active intermediates,⁷ with electron-deficient benzoheterocycles, including 2-nitroindoles or 3-nitroindoles (Scheme 1a)⁸ and benzo[*b*]thiophene 1,1-dioxides (Scheme 1b)⁹ as robust electrophiles to construct various polycyclic heterocyclic skeletons *via* the dearomative [3 + 2] 1,3-dipolar cycloaddition reaction in the simple way. However, 3- and 2-nitrobenzothiophenes have been uncovered as electrophiles for the dearomative 1,3-dipolar cycloaddition reactions with nonstabilized azomethine ylides to provide S-containing polyheterocyclic compounds. Enormous efforts have been devoted to the development of ever more efficient synthetic

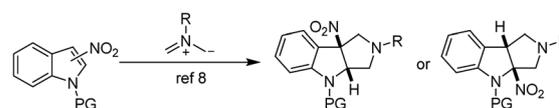
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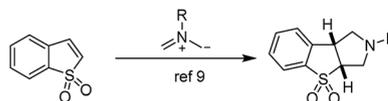
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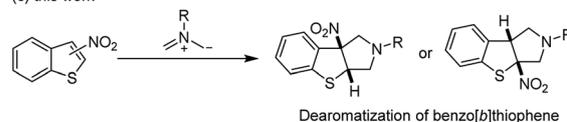
(a) Dearomatization of 3-nitroindoles with nonstabilized azomethine ylides



(b) Dearomatization of benzo[*b*]thiophene 1,1-dioxide with nonstabilized azomethine ylides



(c) this work



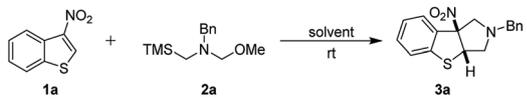
Scheme 1 Dearomative cycloaddition reaction of electron-deficient heteroarenes with nonstabilized azomethine ylides.



methods for the construction and direct functionalization of these heteroaromatic compounds. Herein, we describe a dearomative [3 + 2] cycloaddition reaction of 3-nitrobenzothiophenes with nonstabilized azomethine ylides without metal catalysts under mild reaction conditions, providing a convenient and efficient access to functionalized fused tricyclic benzo[4,5]thieno[2,3-*c*]pyrroles derivatives bearing two contiguous stereocenters. Additionally, we also successfully extended this new protocol to 2-nitrobenzothiophene and 2-nitrobenzofuran for the corresponding dearomatization products.

Initially, we chose 3-nitrobenzothiophene **1a** and *N*-(methoxymethyl)-*N*-(trimethylsilyl-methyl)-benzyl-amine **2a** which generated *in situ* nonstabilized azomethine ylide in the presence of trifluoroacetic acid (TFA) as model substrates to optimize the reaction conditions. As the results are shown in Table 1. To our delight, the cycloaddition reaction proceeded smoothly and the desired [3 + 2] cycloadduct **3a** was obtained in 90% yield with in high diastereoselective CH₂Cl₂ (entry 1). Moreover, the yield could not be further improved when the reaction time was prolonged (entry 2). The yields were decreased (5–81%) when we employed other organic solvents (entries 3–10). In order to further improve the yield, the reaction was performed at 40 °C in CH₂Cl₂. However, the yield of the product decreased to 72% (entry 11), which the possible reason may be that the nonstabilized azomethine ylide was unstable at high temperature that resulted in unexpected side reactions. When the amount of trifluoroacetic acid was loaded to 1.2 equiv., the reaction does not improve the yield of product **3a**

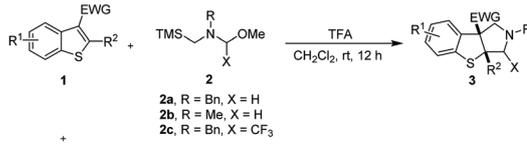
Table 1 Optimization of reaction conditions^a



Entry	Solvent	Time	Yield of 3a ^b (%)
1	CH ₂ Cl ₂	12	90
2	CH ₂ Cl ₂	24	90
3	CHCl ₃	24	81
4	DCE	24	80
5	EtOAc	24	<5
6	CH ₃ CN	24	<5
7	Toluene	24	<5
8	THF	24	22
9	Et ₂ O	24	20
10	Dioxane	24	73
11 ^c	CH ₂ Cl ₂	12	72
12 ^d	CH ₂ Cl ₂	12	90
13 ^e	CH ₂ Cl ₂	24	62
14	CH ₂ Cl ₂	6	64

^a Unless noted otherwise, reactions were performed with 3-nitrobenzothiophene **1a** (0.1 mmol) and **2a** (0.12 mmol), TFA (0.1 mmol, 1 equiv.) in solvent (1.0 mL) at rt. ^b Yield of the isolated product and dr >20 : 1 by ¹H NMR analysis. ^c The reaction was performed at 40 °C. ^d 1.2 equiv. TFA were used. ^e 0.5 equiv. TFA were used.

Table 2 Substrate scope and limitations of the [3 + 2] cycloaddition^a

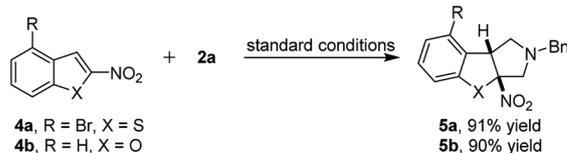


Entry	R ¹	R ²	Substrate	Yield ^b (%)
1	H	H	2a	3a , 90
2	5-Me	H	2a	3b , 92
3	4-Cl	H	2a	3c , 90
4 ^c	5-Cl	H	2a	3d , 91
5	4-Br	H	2a	3e , 92
6	5-Br	H	2a	3f , 88
7	6-Br	H	2a	3g , 87
8	7-Br	H	2a	3h , 89
9	H	H	2b	3i , 84
10	4-Cl	H	2b	3j , 86
11	5-Cl	H	2b	3k , 85
12	4-Br	H	2b	3l , 82
13	5-Br	H	2b	3m , 83
14	6-Br	H	2b	3n , 81
15	7-Br	H	2b	3o , 84
16	H	H	2c	3p , 0
17 ^d	H	H	2a	3q , 0
18	H	Me	2a	3r , 0

^a Unless noted otherwise, reactions were performed with 3-nitrobenzothiophene **1** (0.1 mmol), **2** (0.12 mmol), TFA (0.1 mmol, 1 equiv.) in CH₂Cl₂ (1.0 mL) at rt for 12 h, EWG = NO₂. ^b Yield of the isolated product and dr >20 : 1 by ¹H NMR analysis. ^c The relative configuration of **3d** was determined by X-ray analysis. The other products were assigned by analogy. ^d EWG = CN.

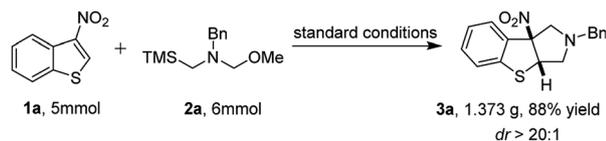
(entry 12). Lowering the amount of trifluoroacetic acid led to a decreased yield despite with a prolonged reaction time (entry 13). In addition, the yield of the product **3a** was 64% when the reaction was carried out for 6 h (entry 14) (Table 1).

With the optimized conditions in hand, we set out to investigate the scope and limitation of 3-nitrobenzothiophenes **1** with nonstabilized azomethine ylides *via* dearomative [3 + 2] cycloaddition reaction to provide fused tricyclic benzo[4,5]thieno[2,3-*c*]pyrroles. The representative results are summarized in Table 2. Under the optimized conditions, the dearomative [3 + 2] cycloaddition reactions were tolerated all the screening various 3-nitrobenzothiophenes **1**, regardless of the different positions and electronic properties of substituents into the aryl ring of 3-nitrobenzothiophenes when the 3-



Scheme 2 Dearomative cycloaddition reaction of 2-nitrobenzothiophene and 2-nitrobenzofuran with nonstabilized azomethine ylide.



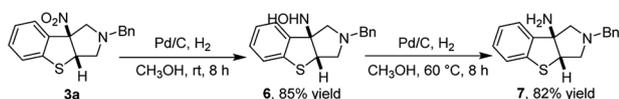


Scheme 3 Scaled-up version of synthesis of fused tricyclic benzo[4,5]thieno[2,3-c]pyrrole.

nitrobenzothiophenes **1** reacted smoothly with the precursor of nonstabilized azomethine ylides **2a** or **2b**. The reaction afforded the corresponding products **3** (**3a–o**) in high isolated yields with excellent diastereoselectivities (>20 : 1 dr). In addition, the relative configuration of product **3d** was determined unambiguously as (3*S*,8*S*) or (3*R*,8*R*) *via* single-crystal X-ray diffraction analysis (CCDC 2006826†).¹² For its structural details, see the ESI.†¹⁰ The other products were assigned by analogy. However, when the **2c** substrate reacts with 3-nitrobenzothiophene **1a** and 3-cyanobenzothiophene **1q** reacts with *N*-(methoxymethyl)-*N*-(trimethylsilyl-methyl)-benzyl-amine **2a** under the standard conditions (entries 16 and 17). These reactions didn't work. These reactions revealed that the compounds **2c** and **1q** had significantly lower reactivity. Subsequently, when we tried the reaction of 3-2-methyl-3-nitrobenzothiophene **1r** with *N*-(methoxymethyl)-*N*-(trimethylsilyl-methyl)-benzyl-amine **2a** under the standard conditions (entry 18). Unfortunately, it was observed that the reaction did not take place. The possible reason may be due to the increased steric hindrance at the C2-position of the 2-methyl-3-nitrobenzothiophene, inhibiting the cycloaddition reaction.

Having proven the effectiveness of our protocol for dearomative [3 + 2] cycloaddition of 3-nitrobenzothiophenes with nonstabilized azomethine ylides. Then, we next turned our attention to dearomative annulation of other heteroaromatic ring bearing nitro group to confirm the practicability of the methodology (Scheme 2). The results show that the 2-nitrobenzothiophene and 2-nitrobenzofuran proved to be well compatible with the dearomative [3 + 2] cycloaddition reaction and underwent the transformation successfully to provide the expected products in the 91% and 90% yield, respectively.

Moreover, in order to highlight the synthetic utility of our methodology, a gram scale experiment between 5 mmol of 3-nitrobenzothiophene **1a** and 6 mmol of *N*-(methoxymethyl)-*N*-(trimethylsilyl-methyl)-benzyl-amine **2a** proceeded smoothly under the standard conditions and offered compound **3a** (1.373 g) in 88% yield with dr >20 : 1 (Scheme 3). Subsequently, the attempt to reduce the nitro group and remove the benzyl group of **3a** through Pd/C-catalyzed hydrogenation. However, the benzyl group was not removed,^{11a} while the nitro group on the quaternary carbon center in **3a** was reduced to give an NHOH



Scheme 4 Transformations of product **3a**.

intermediate **6** in 85% yield at room temperature.^{11b} Next, Pd/C-catalyzed hydrogenation of the NHOH intermediate **6** was successfully conducted at 60 °C to give a free amine **7** in 82% yield (Scheme 4).¹¹

In conclusion, we have successfully developed an efficient dearomative [3 + 2] cycloaddition reaction of nitrobenzothiophenes with nonstabilized azomethine ylides generated *in situ*. The functionalized fused tricyclic benzo[4,5]thieno[2,3-c]pyrroles frameworks were efficiently constructed in high yields (up to 92%) with excellent diastereoselectivities (>20 : 1 dr) under mild reaction condition without metal catalyst. The potential synthetic utility and practicality of the approach were also highlighted by the gram-scale experiment and the synthetic transformation of the product into other polycyclic heterocyclic compounds. The further application of this strategy is presently under bioactive investigation in our laboratory.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

- For reviews, see: (a) C.-X. Zhuo, W. Zhang and S.-L. You, Catalytic Asymmetric Dearomatization Reactions, *Angew. Chem., Int. Ed.*, 2012, **51**, 12662; (b) W. C. Wertjes, E. H. Southgate and D. Sarlah, Recent advances in chemical dearomatization of nonactivated arenes, *Chem. Soc. Rev.*, 2018, **47**, 7996; (c) C. Li, S. S. Ragab, G. Liu and W. Tang, Enantioselective formation of quaternary carbon stereocenters in natural product synthesis: a recent update, *Nat. Prod. Rep.*, 2020, **37**, 276; (d) C. Zheng and S.-L. You, Catalytic asymmetric dearomatization (CADA) reaction-enabled total synthesis of indole-based natural products, *Nat. Prod. Rep.*, 2019, **36**, 1589.
- For selected examples, see: (a) K. Liu, W. Song, Y. Deng, H. Yang, C. Song, T. Abdelilah, S. Wang, H. Cong, S. Tang and A. Lei, Electrooxidation enables highly regioselective dearomative annulation of indole and benzofuran derivatives, *Nat. Commun.*, 2020, **11**, 3; (b) J.-Q. Zhang, F. Tong, B.-B. Sun, W.-T. Fan, J.-B. Chen, D. Hu and X.-W. Wang, Pd-Catalyzed Asymmetric Dearomative Cycloaddition for Construction of Optically Active Pyrroloindoline and Cyclopentaindoline Derivatives: Access to 3-Aminopyrroloindolines, *J. Org. Chem.*, 2018, **83**, 2882; (c) L. Birbaum, L. Gillard, H. Gerard, H. Oulyadi, G. Vincent, X. Moreau, M. De Paolis and I. Chataigner, Dearomatization of 3-Nitroindoles with Highly gamma-Functionalized Allenates in Formal (3 + 2) Cycloadditions, *Chem.-Eur. J.*, 2019, **25**, 13688; (d) J.-J. Suo, J. Du,



- Y.-J. Jiang, D. Chen, C.-H. Ding and X.-L. Hou, Diastereo- and enantioselective palladium-catalyzed dearomative 4 + 2 cycloaddition of 3-nitroindoles, *Chin. Chem. Lett.*, 2019, **30**, 1512; (e) P. V. Santhini, S. A. Babu, A. R. Krishnan, E. Suresh and J. John, Heteroannulation of 3-Nitroindoles and 3-Nitrobenzo[*b*]thiophenes: A Multicomponent Approach toward Pyrrole-Fused Heterocycles, *Org. Lett.*, 2017, **19**, 2458; (f) Y. S. Gee, D. J. Rivinoja, S. M. Wales, M. G. Gardiner, J. H. Ryan and C. J. T. Hyland, Pd-Catalyzed Dearomative 3 + 2 Cycloaddition of 3-Nitroindoles with 2-Vinylcyclopropane-1,1-dicarboxylates, *J. Org. Chem.*, 2017, **82**, 13517; (g) D.-F. Yue, J.-R. Zhao, X.-Z. Chen, Y. Zhou, X.-M. Zhang, X.-Y. Xu and W.-C. Yuan, Multiple Hydrogen-Bonding Bifunctional Thiourea-Catalyzed Asymmetric Dearomative 4 + 2 Annulation of 3-Nitroindoles: Highly Enantioselective Access to Hydrocarbazole Skeletons, *Org. Lett.*, 2017, **19**, 4508; (h) X. Zhao, X. Liu, H. Mei, J. Guo, L. Lin and X. Feng, Asymmetric Dearomatization of Indoles through a Michael/Friedel-Crafts-Type Cascade To Construct Polycyclic Spiroindolines, *Angew. Chem., Int. Ed.*, 2015, **54**, 4032; (i) Y.-C. Zhang, J.-J. Zhao, F. Jiang, S.-B. Sun and F. Shi, Organocatalytic Asymmetric Arylative Dearomatization of 2,3-Disubstituted Indoles Enabled by Tandem Reactions, *Angew. Chem., Int. Ed.*, 2014, **53**, 13912; (j) W. Shao, H. Li, C. Liu, C.-J. Liu and S.-L. You, Copper-Catalyzed Intermolecular Asymmetric Propargylic Dearomatization of Indoles, *Angew. Chem., Int. Ed.*, 2015, **54**, 7684; (k) C. Liu, Q. Yin, L.-X. Dai and S.-L. You, Synthesis of pyrroloindolines and furoindolines via cascade dearomatization of indole derivatives with carbenium ion, *Chem. Commun.*, 2015, **51**, 5971.
- 3 (a) M. Bandini and A. Eichholzer, Catalytic Functionalization of Indoles in a New Dimension, *Angew. Chem., Int. Ed.*, 2009, **48**, 9608; (b) N. R. Ball-Jones, J. J. Badillo and A. K. Franz, Strategies for the enantioselective synthesis of spirooxindoles, *Org. Biomol. Chem.*, 2012, **10**, 5165; (c) J. Ling, D. Mara, B. Roure, M. Laugeois and M. R. Vitale, Copper(I)-Catalyzed Dearomative (3 + 2) Cycloaddition of 3-Nitroindoles with Propargylic Nucleophiles: An Access to Cyclopenta[*b*]indolines, *J. Org. Chem.*, 2020, **85**, 3838.
- 4 For selected examples, see: (a) J.-R. Zhuo, B.-X. Quan, J.-Q. Zhao, M.-L. Zhang, Y.-Z. Chen, X.-M. Zhang and W.-C. Yuan, Base-mediated 4 + 2 annulation of electron-deficient nitrobenzoheterocycles and alpha,alphadicyanoalkenes in water: Facile access to structurally diverse functionalized dibenzoheterocyclic compounds, *Tetrahedron*, 2020, **76**, 131115; (b) X.-J. Zhou, J.-Q. Zhao, X.-M. Chen, J.-R. Zhuo, Y.-P. Zhang, Y.-Z. Chen, X.-M. Zhang, X.-Y. Xu and W.-C. Yuan, Organocatalyzed Asymmetric Dearomative Aza-Michael/Michael Addition Cascade of 2-Nitrobenzofurans and 2-Nitrobenzothiophenes with 2-Aminochalcones, *J. Org. Chem.*, 2019, **84**, 4381; (c) J.-Q. Zhao, L. Yang, Y. You, Z.-H. Wang, K.-X. Xie, X.-M. Zhang, X.-Y. Xu and W.-C. Yuan, Phosphine-catalyzed dearomative (3 + 2) annulation of 2-nitrobenzofurans and nitrobenzothiophenes with allenates, *Org. Biomol. Chem.*, 2019, **17**, 5294; (d) D.-F. Yue, J.-Q. Zhao, Y.-Z. Chen, X.-M. Zhang, X.-Y. Xu and W.-C. Yuan, Zinc-Catalyzed Enantioselective Dearomative 3 + 2 Cycloaddition Reaction of 3-Nitrobenzothiophenes and 3-Nitrothieno-2,3-*b*-yridine with 3-Isothiocyanato Oxindoles, *Adv. Synth. Catal.*, 2018, **360**, 1420; (e) H. Wang, Q. Hu, M. Wang and C. Guo, Enantioselective 4 + 2 Annulation to the Concise Synthesis of Chiral Dihydrocarbazoles, *Science*, 2020, **23**, 100840; (f) P. V. Santhini, A. R. Krishnan, S. A. Babu, B. S. Simethy, G. Das, V. K. Praveen, S. Varughese and J. John, One-Pot MCR-Oxidation Approach toward Indole-Fused Heteroacenes, *J. Org. Chem.*, 2017, **82**, 10537; (g) Y. Li, F. Tur, R. P. Nielsen, H. Jiang, F. Jensen and K. A. Jorgensen, Enantioselective Formal 4 + 2 Cycloadditions to 3-Nitroindoles by Trienamine Catalysis: Synthesis of Chiral Dihydrocarbazoles, *Angew. Chem., Int. Ed.*, 2016, **55**, 1020; (h) X.-M. Chen, C.-W. Lei, D.-F. Yue, J.-Q. Zhao, Z.-H. Wang, X.-M. Zhang, X.-Y. Xu and W.-C. Yuan, Organocatalytic Asymmetric Dearomatization of 3-Nitroindoles and 3-Nitrobenzothiophenes via Thiol-Triggered Diastereo- and Enantioselective Double Michael Addition Reaction, *Org. Lett.*, 2019, **21**, 5452; (i) D. Cao, A. Ying, H. Mo, D. Chen, G. Chen, Z. Wang and J. Yang, 4 + 2 Annulation of 3-Nitroindoles with Alkylidene Malononitriles: Entry to Substituted Carbazol-4-amine Derivatives, *J. Org. Chem.*, 2018, **83**, 12568.
- 5 For selected examples, see: (a) S.-M. Wen, C.-H. Lin, C.-C. Chen and M.-J. Wu, Efficient synthesis of 3-benzoyl Benzo[*b*]thiophenes and raloxifene via Mercury(II)-Catalyzed cyclization of 2-alkynylphenyl alkyl sulfoxides, *Tetrahedron*, 2018, **74**, 2493; (b) W. E. Noland, H. V. Kumar, Y. Reddi, C. J. Cramer, A. V. Novikov, H. Kim, Y. Zhu, Y. C. Chin, Y. Zhou, P. Radakovic, A. Uprety, J. Xie and G. C. Flick, Diels-Alder/Ene Reactivities of 2-(1'-Cycloalkenyl)thiophenes and 2-(1'-Cycloalkenyl)benzo[*b*]thiophenes with N-Phenylmaleimides: Role of Cycloalkene Ring Size on Benzothiophene and Dibenzothiophene Product Distributions, *J. Org. Chem.*, 2020, **85**, 5265; (c) M. Zhang, H. Xu, C. Peng, H. Huang, S. Bo, J. Liu, X. Liu, Z. Zhen and L. Qiu, Novel NLO-phores containing dihexyl amino benzo[*b*]thiophene exhibiting good transparency and enhanced electro-optical activity dagger, *RSC Adv.*, 2014, **4**, 15870; (d) C. Viglianisi, L. Di Pietro, V. Meoni, R. Amorati and S. Menichetti, From simple phenols to potent chain-breaking antioxidants by transposition of benzo-1,4-oxathiines to benzo[*b*]thiophenes, *Arkivoc*, 2019, 65.
- 6 For reviews, see: (a) R. Narayan, M. Potowski, Z.-J. Jia, A. P. Antonchick and H. Wadmann, Catalytic Enantioselective 1,3-Dipolar Cycloadditions of Azomethine Ylides for Biology-Oriented Synthesis, *Acc. Chem. Res.*, 2014, **47**, 1296; (b) C. Najera, J. M. Sansano and M. Yus, 1,3-Dipolar cycloadditions of azomethine imines, *Org. Biomol. Chem.*, 2015, **13**, 8596; (c) K. Martina, S. Tagliapietra, V. V. Veselov and G. Cravotto, Green Protocols in Heterocycle Syntheses via 1,3-Dipolar



- Cycloadditions, *Front. Chem.*, 2019, 7, 1; (d) T. Hashimoto and K. Maruoka, Recent Advances of Catalytic Asymmetric 1,3-Dipolar Cycloadditions, *Chem. Rev.*, 2015, 115, 5366; (e) M. S. Singh, S. Chowdhury and S. Koley, Progress in 1,3-dipolar cycloadditions in the recent decade: an update to strategic development towards the arsenal of organic synthesis, *Tetrahedron*, 2016, 72, 1603.
- 7 For selected examples, see: (a) K.-K. Wang, Y.-L. Li, Z.-Y. Wang, M.-W. Hu, T.-T. Qiu and B.-K. Zhu, Cross 1,3-dipolar cycloadditions of C,N-cyclic azomethine imines with an N-benzyl azomethine ylide: facile access to fused tricyclic 1,2,4-hexahydrotriazines, *Org. Biomol. Chem.*, 2019, 17, 244; (b) S.-n. Li, B. Yu, J. Liu, H.-l. Li and R. Na, Bronsted Acid or Lewis Acid Catalyzed 3 + 3 Cycloaddition of Azomethine Imines with N-Benzyl Azomethine Ylide: A Facile Access to Bicyclic N-Heterocycles, *Synlett*, 2016, 27, 282; (c) K.-K. Wang, Y.-L. Li, Z.-Y. Wang, X. Ma, Y.-L. Mei, S.-S. Zhang and R. Chen, Formal [3 + 2] cycloaddition of azomethine ylides generated in situ with unactivated cyclic imines: A facile approach to tricyclic imidazolines derivatives, *J. Heterocycl. Chem.*, 2020, 57, 1456; (d) E. M. Buev, V. S. Moshkin and V. Y. Sosnovskikh, Nonstabilized Azomethine Ylides in the Mannich Reaction: Synthesis of 3,3-Disubstituted Pyrrolidines, Including Oxindole Alkaloids, *J. Org. Chem.*, 2017, 82, 12827; (e) E. M. Buev, V. S. Moshkin and V. Y. Sosnovskikh, Reagents for Storage and Regeneration of Nonstabilized Azomethine Ylides: Spiroanthraceneoxazolidines, *Org. Lett.*, 2016, 18, 1764; (f) A. M. D'Souza, N. Spiccia, J. Basutto, P. Jokisz, L. S. M. Wong, A. G. Meyer, A. B. Holmes, J. M. White and J. H. Ryan, 1,3-Dipolar Cycloaddition-Decarboxylation Reactions of an Azomethine Ylide with Isatoic Anhydrides: Formation of Novel Benzodiazepinones, *Org. Lett.*, 2011, 13, 486; (g) V. S. Moshkin, E. M. Buev and V. Y. Sosnovskikh, Nonstabilized azomethine ylides as reagents for alkylaminomethylation of aromatic ketones via 5-aryloxazolidines, *Tetrahedron Lett.*, 2015, 56, 5278.
- 8 (a) S. Roy, T. L. S. Kishbaugh, J. P. Jasinski and G. W. Gribble, 1,3-Dipolar cycloaddition of 2- and 3-nitroindoles with azomethine ylides. A new approach to pyrrolo-3,4-*b*-indoles, *Tetrahedron Lett.*, 2007, 48, 1313; (b) S. Lee, S. Diab, P. Queval, M. Sebban, I. Chataigner and S. R. Piettre, Aromatic C=C Bonds as Dipolarophiles: Facile Reactions of Uncomplexed Electron-Deficient Benzene Derivatives and Other Aromatic Rings with a Non-Stabilized Azomethine Ylide, *Chem.-Eur. J.*, 2013, 19, 7181.
- 9 K.-K. Wang, Y.-L. Li, G.-Y. Ma, M.-H. Yi and B.-K. Zhu, Highly Efficient and Diastereoselective Construction of Tricyclic Pyrrolidine-Fused Benzo[*b*]thiophene 1,1-dioxide Derivatives via 1,3-Dipolar [3 + 2] Cycloaddition, *J. Heterocycl. Chem.*, 2019, 56, 2274.
- 10 For more details, see the ESI†
- 11 (a) J.-Y. Guo, Z.-Y. Zhang, T. Guan, L.-W. Mao, Q. Ban, K. Zhao and T.-P. Loh, Photoredox-catalyzed stereoselective alkylation of enamides with N-hydroxyphthalimide esters via decarboxylative cross-coupling reactions, *Chem. Sci.*, 2019, 10, 8792; (b) G.-Y. Ran, P. Wang, W. Du and Y.-C. Chen, α -Regioselective [3 + 2] annulations with Morita-Baylis-Hillman carbonates of isatins and 2-nitro-1,3-enynes, *Org. Chem. Front.*, 2016, 3, 861; (c) Z. Wang, D.-C. Wang, M.-S. Xie, G.-R. Qu and H.-M. Guo, Enantioselective Synthesis of Fused Polycyclic Tropanes via Dearomative 3 + 2 Cycloaddition Reactions of 2-Nitrobenzofurans, *Org. Lett.*, 2020, 22, 164; (d) H. Wang, J. Zhang, Y. Tu and J. Zhang, Phosphine-Catalyzed Enantioselective Dearomative 3 + 2 -Cycloaddition of 3-Nitroindoles and 2-Nitrobenzofurans, *Angew. Chem., Int. Ed.*, 2019, 58, 5422.
- 12 CCDC 2006826† for 3d contains the supplementary crystallographic data for this paper.

