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**A metal-free, catalytic route to the activation of  $C(sp^3)$ –H bonds in *N*-protected dialkylpyrroles to diazodicarboxylates is reported using  $HB(C_6F_5)_2$  as the optimized catalyst. These reactions tolerate aryl and alkyl substituents on the pyrrole *N*-atom as well as variation in the azodicarboxylates giving rise to 41 examples. These reactions were also performed on a gram scale and conversion to the corresponding amino-esters is demonstrated. A DFT computation study reveals that the Lewis acid adduct of azodicarboxylates generates a Lewis acidic *N*-atom capable of hydride abstraction from dimethylpyrrole, ultimately effecting  $C(sp^3)$ –H functionalization.**

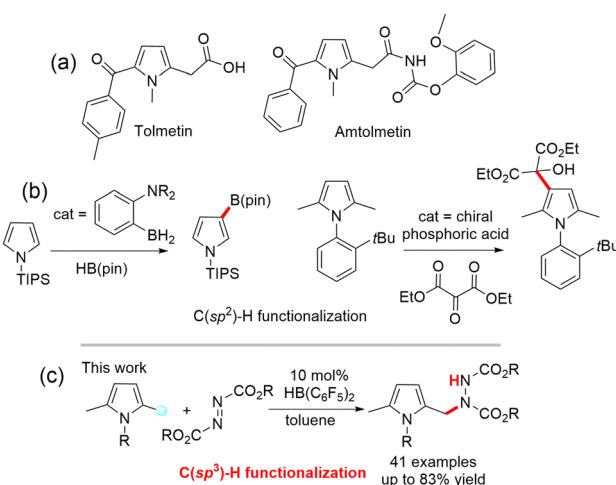
Pyrrole is a privileged aromatic heterocycle that is found in chlorophyll, heme, vitamin B<sub>12</sub>, and bile acids. Naturally occurring and synthetic molecules incorporating pyrrole units have been shown to exhibit a broad range of biological and pharmacological activities.<sup>1</sup> For example, over 20 synthetic pyrrole derivatives are commercially marketed drugs as such species exhibit anti-psychotic, anti-anxiolytic, anti-cancer, anti-bacterial, anti-fungal, anti-malarial, anti-inflammatory, and anti-hyperlipidemic behavior (Fig. 1a).<sup>1a,1b</sup>

Synthetic efforts to derivatize pyrroles have led to the development of a wide variety of transition metal catalyzed processes.<sup>2</sup> These protocols allow the incorporation of a wide range of functional groups, typically leading to substitution at N or at the  $C(sp^2)$  atoms at the C-2 or C-3 positions. These methods have been reviewed.<sup>2b–e</sup> Alternatively main group species are known to mediate the derivatization of *N*-protected pyrroles.<sup>3</sup> For example, Lewis acid mediated Friedel-Crafts methods readily provide substitution again at  $sp^2$  carbons, where the steric demands of

the *N*-protecting group can be used to direct substitution to either the C-2 or C-3 positions.<sup>3</sup>

In 2010, we showed that *N*-alkylpyrroles participate in frustrated Lewis pair (FLP) alkyne-addition reactions, leading to C–C bond formation at the  $C(sp^2)$  atoms at the C-3 position.<sup>4</sup> Several years later, in a seminal finding, Fontaine and coworkers<sup>5</sup> exploited intramolecular N/B FLPs to effect borylation of *N*-methylpyrrole, thiophene and furan derivatives, again at the C-2 or C-3 positions depending on the other substituents (Fig. 1b). Subsequently, Shi and coworkers used  $BBR_3$  to direct  $C(sp^2)$ –H borylation of indoles at the C-7 or C-4 positions and other (hetero)arenes.<sup>6</sup> More recently, Tan *et al.* elegantly used chiral phosphoric acid catalysts to functionalize *N*-protected-pyrroles at the C-3 position, affording axially chiral arylpyrroles (Fig. 1b).<sup>7</sup>

In contemplating alternative strategies for the functionalization of pyrroles, we considered activation of the  $C(sp^3)$ –H bonds of substituents at the C-2 position. While the majority of the activation strategies for unactivated  $C(sp^3)$ –H bonds have been



**Fig. 1** (a) Representative pyrrole-derived drugs. (b) Metal free  $C(sp^2)$ –H functionalization of *N*-protected pyrroles. (c) This work –  $C(sp^3)$ –H functionalization of *N*-protected pyrroles with azodicarboxylates.

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achieved using transition-metal catalysts,<sup>8</sup> we noted that boranes have been used as catalysts to promote C–C and C–heteroatom bond formation.<sup>9</sup> For example, Wang and coworkers achieved C(sp<sup>3</sup>)–H alkylation of tertiary amines with electron-deficient olefins using B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> as the catalyst.<sup>10</sup> In another recent breakthrough, Lin *et al.*<sup>11</sup> used frustrated radical pairs (FRPs) to functionalize the C(sp<sup>3</sup>)–H bonds of various organic substrates, affording aminoxylated products. Nonetheless, to our knowledge, C(sp<sup>3</sup>)–H bond activation of pyrrole derivatives is not known. Herein, we develop a protocol for the C(sp<sup>3</sup>)–H bond functionalization of the methyl groups of *N*-protected methylpyrroles with azodicarboxylates using Piers' borane HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> as the catalyst (Fig. 1c).

Our investigation began with the reaction of *N*-phenylpyrrole **1a** and commercially available dibenzyl azodicarboxylate **2a** in toluene. In the presence of 10 mol% Al(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>, this gave mixtures of C(sp<sup>2</sup>)–H and C(sp<sup>3</sup>)–H activation products, with poor regioselectivity at 60 °C (Table 1, entry 1). In the presence of B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> and HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>, the selectivity for the C(sp<sup>3</sup>)–H functionalization product **3a** improved (Table 1, entries 2 and 3). Using HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> as the catalyst, product **3a** was obtained in 47% yield at 60 °C. Altering the reactant ratio of **1a**:**2a** to 1.5:1 afforded product **3a** in 61% yield with a 13% yield of the C(sp<sup>2</sup>)–H functionalization product **4a** (Table 1, entries 3–6), while further variations of the solvent, temperature and catalyst loading did not increase the yield (Table 1, entries 7–12).

Using the optimized reaction conditions, the substrate scope for C(sp<sup>3</sup>)–H functionalization of *N*-protected dialkylpyrroles with azodicarboxylates was examined. Firstly, the reactions of a series of *N*-arylpolyrroles with **2a** in toluene were investigated. In the presence of 10 mol% HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>, *para*-substituted *N*-arylpolyrroles with electron-donating or electron-withdrawing substituents on the phenyl ring (Fig. 2, R = C<sub>6</sub>H<sub>5</sub> **1a**, 4-FC<sub>6</sub>H<sub>4</sub> **1b**, 4-ClC<sub>6</sub>H<sub>4</sub> **1c**,

Table 1 Optimized reaction conditions for C–H functionalization

Entry <sup>a</sup>	Cat.	<b>1a</b> : <b>2a</b>	Solvent	T (°C)	Yield (%) <b>3a</b> <sup>b</sup>	Yield (%) <b>4a</b> <sup>b</sup>
1	Al(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub>	1.0:1.5	Toluene	60	21	22
2	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub>	1.0:1.5	Toluene	60	43	6
3	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.0:1.5	Toluene	60	47	6
4	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.0:1.0	Toluene	60	47	12
5	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.5:1.0	Toluene	60	61	13
6	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	2.0:1.0	Toluene	60	55	13
7	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.5:1.0	Benzene	60	57	14
8	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.5:1.0	p-Xylene	60	52	10
9	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.5:1.0	PhF	60	39	19
10	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.5:1.0	Toluene	45	47	11
11	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.5:1.0	Toluene	80	52	12
12 <sup>c</sup>	HB(C <sub>6</sub> F <sub>5</sub> ) <sub>2</sub>	1.5:1.0	Toluene	60	23	26

<sup>a</sup> Unless otherwise noted, all reactions were performed using 10 mol% catalyst, **1a** and **2a** in solvent (2.0 mL) under argon for 12 h. <sup>b</sup> Isolated yield after chromatography. <sup>c</sup> 5 mol% catalyst.

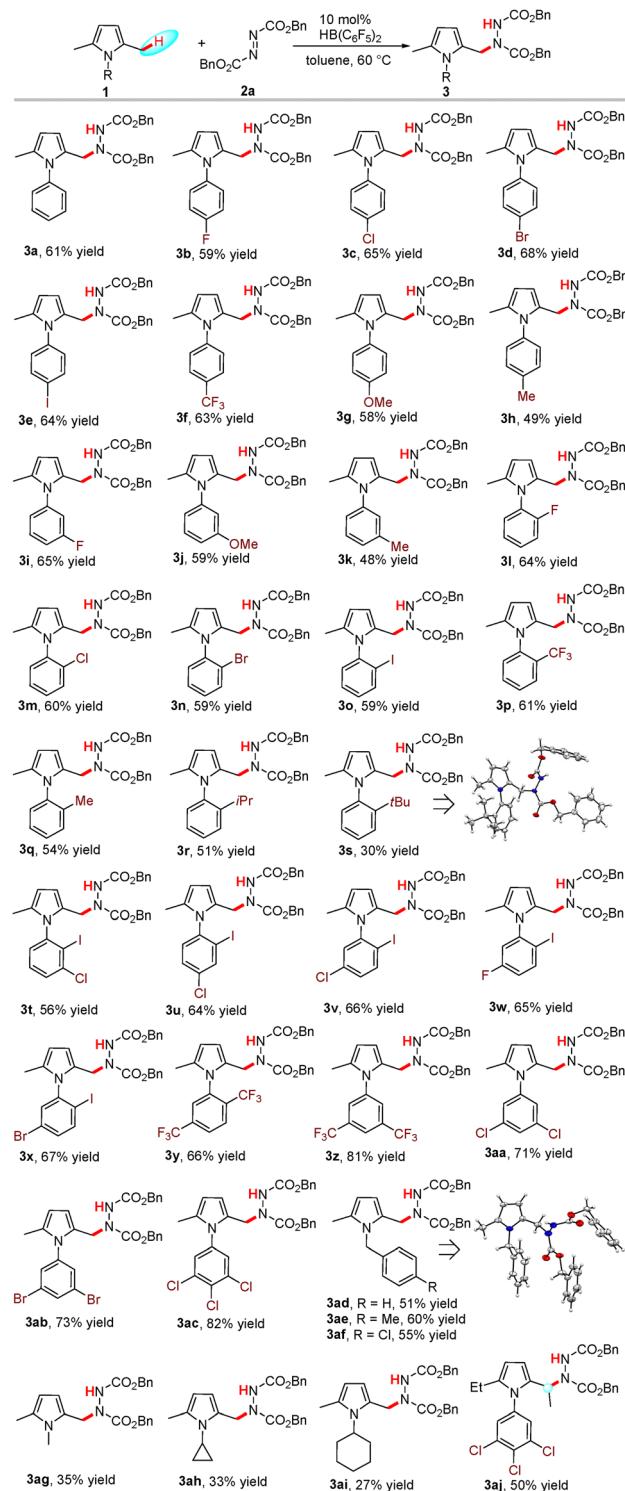


Fig. 2 Scope of *N*-protected dialkylpyrroles. Reaction conditions: a solution of **1** (0.3 mmol), dibenzyl azodicarboxylate **2a** (0.2 mmol) and HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> (10 mol%) in toluene (2.0 mL) was stirred at 60 °C for 1–2 h in argon.

4-BrC<sub>6</sub>H<sub>4</sub> **1d**, 4-IC<sub>6</sub>H<sub>4</sub> **1e**, 4-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub> **1f**, 4-MeOC<sub>6</sub>H<sub>4</sub> **1g**, 4-MeC<sub>6</sub>H<sub>4</sub> **1h**) reacted smoothly with **2a** to provide the corresponding products **3a**–**3h** in 49–68% yields. Similarly, *meta*-substituted *N*-arylpolyrroles bearing differing functional groups (Fig. 2, R = 3-FC<sub>6</sub>H<sub>4</sub> **1i**, 3-MeOC<sub>6</sub>H<sub>4</sub> **1j**, 3-MeC<sub>6</sub>H<sub>4</sub> **1k**) were tolerated, affording **3i**–**3k**



in 48–65% yields. *ortho*-Substituted *N*-arylpyrroles (Fig. 2, R = 2-FC<sub>6</sub>H<sub>4</sub> **1l**, 2-ClC<sub>6</sub>H<sub>4</sub> **1m**, 2-BrC<sub>6</sub>H<sub>4</sub> **1n**, 2-iC<sub>6</sub>H<sub>4</sub> **1o**, 2-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub> **1p**, 2-MeC<sub>6</sub>H<sub>4</sub> **1q**, 2-*i*PrC<sub>6</sub>H<sub>4</sub> **1r**, 2-*t*BuC<sub>6</sub>H<sub>4</sub> **1s**) were also suitable substrates, affording the C(sp<sup>3</sup>)-H functionalization products **3l–3s** in 30–64% yields. The identity of **3s** was confirmed by X-ray crystallography (see the SI).<sup>12</sup>

In addition, *N*-arylpyrroles with 2 or 3 substituents on the phenyl ring (Fig. 2, R = 2-I,3-ClC<sub>6</sub>H<sub>3</sub> **1t**, 2-I,4-ClC<sub>6</sub>H<sub>3</sub> **1u**, 2-I,5-ClC<sub>6</sub>H<sub>3</sub> **1v**, 2-I,5-FC<sub>6</sub>H<sub>3</sub> **1w**, 2-I,5-BrC<sub>6</sub>H<sub>3</sub> **1x**, 2,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub> **1y**, 3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub> **1z**, 3,5-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub> **1aa**, 3,5-Br<sub>2</sub>C<sub>6</sub>H<sub>3</sub> **1ab**, 3,4,5-Cl<sub>3</sub>C<sub>6</sub>H<sub>2</sub> **1ac**) were also successfully converted to the C(sp<sup>3</sup>)-H functionalized products **3t–3ac** in 56–82% yields. The reactions of *N*-benzylpyrroles (Fig. 2, R = CH<sub>2</sub>Ph **1ad**, CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Me **1ae**, CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Cl **1af**) provided products **3ad–3af** in 51–60% yields. The nature of **3ad** was also confirmed by X-ray analysis (see the SI).<sup>12</sup> Moreover, alkylpyrroles (Fig. 2, R = Me **1ag**, C<sub>3</sub>H<sub>5</sub> **1ah**, C<sub>6</sub>H<sub>11</sub> **1ai**) also reacted with **2a**, giving the products **3ag–3ai**, albeit in somewhat reduced yields of 27–35%. Furthermore, changing the pyrrole substituents to Et groups, as in **1aj**, afforded **3aj** in 50% yield, while the reaction of the dissymmetric pyrrole 2-Me-5-Ph-*N*-(C<sub>6</sub>H<sub>2</sub>Cl<sub>3</sub>)-pyrrole **1ak** with **2a** gave the C(sp<sup>2</sup>)-H amination product **4ak** in 55% yield (see the SI).

Efforts to identify by-products were undertaken. Even on doubling the reaction scale for all reactions, most by-products were not unambiguously identifiable although the C(sp<sup>2</sup>)-H amination products **4ah** and **4ai** were observed in 10 and 11% yields, respectively, while the double C(sp<sup>2</sup>)-H amination product **4ag'** was observed in 9% yield (see the SI).

The reaction also tolerated variations in the azodicarboxylates. Thus, the reaction of the commercially available (RO<sub>2</sub>CN)<sub>2</sub> (Fig. 3, R = CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Cl **2b**, Et **2c**, *i*Pr **2d**) with **1ac** proceeded smoothly to give products **3ak–3am** in 43–83% yields. In contrast, the use of **2e** (R = *t*Bu) gave only a 19% yield of **3an** (Fig. 3). We note that this diazo-species is known to react with boranes to liberate CO<sub>2</sub> and isobutylene.<sup>13</sup> Notably, 4-phenyl-1,2,4-triazoline-3,5-dione **2f** also reacted smoothly with **1ac**, affording the desired product **3ao** in 40% yield.

The scalability of this protocol to gram-scale reactions was demonstrated. Thus, using over 2 grams of **1ac** with **2a** in the presence of 10 mol% HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> afforded 2.35 g of **3ac** in an

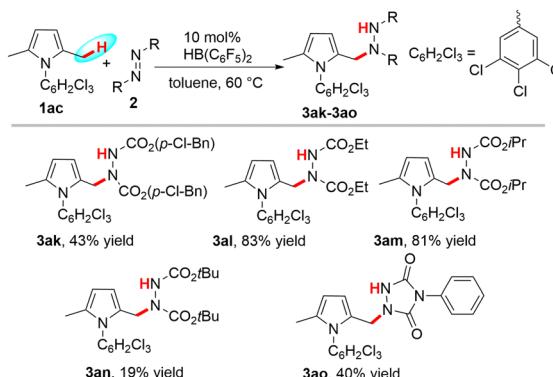


Fig. 3 Scope of azodicarboxylates. Reaction conditions: a solution of **1ac** (0.3 mmol), dibenzyl azodicarboxylate **2** (0.2 mmol) and HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> (10 mol%) in toluene (2.0 mL) was stirred at 60 °C for 1–2 h in argon.

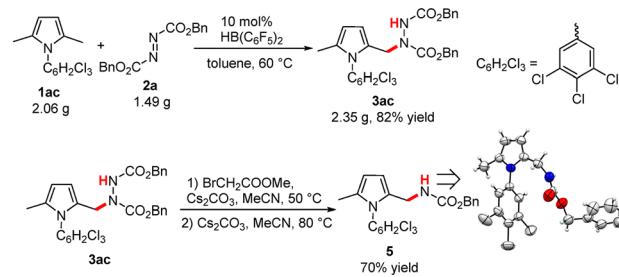


Fig. 4 Scale-up synthesis and synthetic transformation.

overall yield of 82% (Fig. 4). In addition, **3ac** was reacted with bromoacetate and Cs<sub>2</sub>CO<sub>3</sub> using the method of Magnus *et al.*,<sup>14</sup> affording C<sub>4</sub>H<sub>2</sub>Me(CH<sub>2</sub>NH(CO<sub>2</sub>CH<sub>2</sub>Ph)N(C<sub>6</sub>H<sub>2</sub>Cl<sub>3</sub>) **5** in 70% yield (Fig. 4). This carbamate ester was characterized by X-ray crystallography (see the SI).<sup>12</sup>

The mechanism of these reactions was established *via* a computational study using density functional theory (DFT) computations at the PW6B95-D3/def2-QZVP + COSMO-RS//TPSS-D3/def2-TZVP + COSMO level of theory.<sup>15</sup> As B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> and HB(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub> showed similar reactivity, B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> was used in the calculations to avoid the complexity associated with the dimerization equilibrium of Piers' borane in solution. The initial interaction of B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> with the carbonyl fragment of azodicarboxylate **2c** enhances the Lewis acidity of the remote N-atom, allowing it to abstract hydride from methylpyrrole **1a** over a free energy barrier of 22.5 kcal mol<sup>-1</sup> (**TS1**). This generates the transient ion pair **1a**<sup>+</sup> and **2cBH**<sup>-</sup> (Fig. 5), which reacts exothermically to form a new C–N bond. The release of borane is slightly endergonic, allowing the catalytic reaction to continue, consistent with both experimental conditions and the improved catalysis for (C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>BH, where the slightly reduced Lewis acidity presumably accelerates the Lewis acid release. Regarding the role of the N-Lewis acid, we note that such species have been pioneered by Gandelman,<sup>16</sup> although we<sup>17</sup> and others<sup>18</sup> have described related diazo-derived Lewis acid systems.

In conclusion, we have reported a metal-free, catalytic and scalable protocol for the functionalization of C(sp<sup>3</sup>)-H bonds in

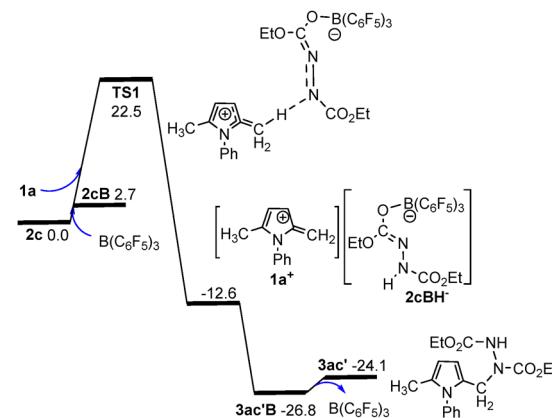


Fig. 5 DFT computed mechanism (in kcal mol<sup>-1</sup>, at 298 K and 1 M concentration) for C(sp<sup>3</sup>)-H functionalization of *N*-Ph-dimethylpyrrole to azodicarboxylates.



N-protected dimethylpyrroles with azodicarboxylates. The resulting diazo-pyrrole derivatives can be converted to the corresponding amino-esters. A mechanistic study showed that the Lewis acid adduct of the azodicarboxylate generates a Lewis acidic N-atom capable of hydride abstraction from the C(sp<sup>3</sup>) carbon on the pyrrole. We are continuing to study metal-free avenues for C–H functionalization and Lewis acid applications in organic synthesis.

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## Conflicts of interest

There are no conflicts to declare.

## Data availability

The data that support this study are available in the SI of this article.

Experimental and spectral data are available as SI See DOI:

<https://doi.org/10.1039/d5cc03254g>

3s: CCDC 2434837; 3ad: CCDC 2434838 and 5: CCDC 2434839 contain the supplementary crystallographic data for this paper.<sup>19–21</sup>

## Notes and references

- (a) B. H. Ganesh, A. G. Raj, B. Aruchamy, P. Nanjan, C. Drago and P. Raman, *ChemMedChem*, 2024, **19**, e202300447; (b) T. Biswas, R. K. Mittal, V. Sharma, Kanupriya and I. Mishra, *Med. Chem.*, 2024, **20**, 369–384; (c) B. S. Manya, M. R. P. Kumar, K. Rajagopal, A. M. Hassan, S. O. Rab, M. A. Alshehri and T. B. Emran, *Chem. Biodiversity*, 2024, **21**, e202400534.
- (a) A. M. Wagner and M. S. Sanford, *Org. Lett.*, 2011, **13**, 288–291; (b) M. K. Hunjan, S. Panday, A. Gupta, J. Bhaumik, P. Das and J. K. Laha, *Chem. Rec.*, 2021, **21**, 715–780; (c) K. Pedretty, K. Tillett, W. Tsuei and J. M. Lopchuk, *Prog. Heterocycl. Chem.*, 2021, vol. 32, pp. 193–240; (d) B. Prabagar and Z. Shi, *Recent Advances in C–H Functionalization of Five-Membered Heterocycles with Single Heteroatoms*, John Wiley & Sons, Inc., 2023; (e) J. W. Campbell, M. J. Cotnam, F. R. Annan, J. W. Hilborn and A. Thompson, *Chem. Commun.*, 2024, **60**, 11385–11414.
- S. Rej and N. Chatani, *Angew. Chem., Int. Ed.*, 2022, **61**, e202209539.
- M. A. Dureen, C. C. Brown and D. W. Stephan, *Organometallics*, 2010, **29**, 6422–6432.
- (a) M. A. Legare, M. A. Courtemanche, E. Rochette and F. G. Fontaine, *Science*, 2015, **349**, 513–516; (b) S. K. Bose and T. B. Marder, *Science*, 2015, **349**, 473–474; (c) J. Legare Lavergne, A. Jayaraman, L. C. Misal Castro, E. Rochette and F.-G. Fontaine, *J. Am. Chem. Soc.*, 2017, **139**, 14714–14723.
- J. Lv, X. Chen, X.-S. Xue, B. Zhao, Y. Liang, M. Wang, L. Jin, Y. Yuan, Y. Han, Y. Zhao, Y. Lu, J. Zhao, W.-Y. Sun, K. N. Houk and Z. Shi, *Nature*, 2019, **575**, 336–340.
- L. Zhang, S. H. Xiang, J. J. Wang, J. Xiao, J. Q. Wang and B. Tan, *Nat. Commun.*, 2019, **10**, 566.
- (a) J. He, M. Wasa, K. S. L. Chan, Q. Shao and J.-Q. Yu, *Chem. Rev.*, 2016, **117**, 8754–8786; (b) B. Liu, A. M. Romine, C. Z. Rubel, K. M. Engle and B. F. Shi, *Chem. Rev.*, 2021, **121**, 14957–15074; (c) Y. Yang, W. Gao, Y. Wang, X. Wang, F. Cao, T. Shi and Z. Wang, *ACS Catal.*, 2021, **11**, 967–984; (d) K. P. Bryliakov, *ACS Catal.*, 2023, **13**, 10770–10795; (e) M. Sadeghi, *ACS Catal.*, 2024, **14**, 15356–15373.
- (a) S. Basak, L. Winfrey, B. A. Kustiana, R. L. Melen, L. C. Morrill and A. P. Pulis, *Chem. Soc. Rev.*, 2021, **50**, 3720–3737; (b) G. Kumar, S. Roy and I. Chatterjee, *Org. Biomol. Chem.*, 2021, **19**, 1230–1267; (c) A. Dasgupta, E. Richards and R. L. Melen, *ACS Catal.*, 2021, **12**, 442–452; (d) J. Guo, M. Yan and D. W. Stephan, *Org. Chem. Front.*, 2024, **11**, 2375–2396; (e) T. Liu, *Org. Chem. Front.*, 2025, **12**, 2481–2498; (f) B. Rao and R. Kinjo, *Chem. – Asian J.*, 2018, **13**, 1279–1292.
- X.-Y. Zhou, Y.-B. Shao, R.-T. Guo, Y.-L. Zhang, X.-S. Xue and X.-C. Wang, *ACS Catal.*, 2024, **14**, 8041–8049.
- Z. Lu, M. Ju, Y. Wang, J. M. Meinhardt, J. I. Martinez Alvarado, E. Villemure, J. A. Terrett and S. Lin, *Nature*, 2023, **619**, 514–520.
- The X-ray data have been deposited in the CCDC 2434837 (3s), 2434838 (3ad) and 2434839 (5).
- Z. Hussain, Y. A. Luo, Y. Wu, Z. W. Qu, S. Grimme and D. W. Stephan, *J. Am. Chem. Soc.*, 2023, **145**, 7101–7106.
- P. Magnus, N. Garizi, K. A. Seibert and A. Ornholt, *Org. Lett.*, 2009, **11**, 5646–5648.
- (a) A. Klamt and G. Schüürmann, *J. Chem. Soc. Perkin Trans. 2*, 1993, 799–805; (b) K. Eichkorn, F. Weigend, O. Treutler and R. Ahlrichs, *Theor. Chem. Acc.*, 1997, **97**, 119–124; (c) F. Weigend, M. Häser, H. Patzelt and R. Ahlrichs, *Chem. Phys. Lett.*, 1998, **294**, 143–152; (d) F. Eckert and A. Klamt, *AIChE J.*, 2002, **48**, 369–385; (e) J. Tao, J. P. Perdew, V. N. Staroverov and G. E. Scuseria, *Phys. Rev. Lett.*, 2003, **91**, 146401; (f) F. Weigend, F. Furche and R. Ahlrichs, *J. Chem. Phys.*, 2003, **119**, 12753–12762; (g) P. Deglmann, K. May, F. Furche and R. Ahlrichs, *Chem. Phys. Lett.*, 2004, **384**, 103–107; (h) F. Weigend and R. Ahlrichs, *Phys. Chem. Chem. Phys.*, 2005, **7**, 3297–3305; (i) Y. Zhao and D. G. Truhlar, *J. Phys. Chem. A*, 2005, **109**, 5656–5667; (j) F. Weigend, *Phys. Chem. Chem. Phys.*, 2006, **8**, 1057–1065; (k) S. Grimme, J. Antony, S. Ehrlich and H. Krieg, *J. Chem. Phys.*, 2010, **132**, 154104–154119; (l) S. Grimme, S. Ehrlich and L. Goerigk, *J. Comput. Chem.*, 2011, **32**, 1456–1465; (m) S. Grimme, *Chem. – Eur. J.*, 2012, **18**, 9955–9964; (n) F. Eckert and A. Klamt, COSMOtherm, Version C3.0, Release 16.01, COSMOlogic GmbH & Co., Leverkusen, Germany, 2015; (o) TURBOMOLE V7.4, 2019, a development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989–2007, TURBOMOLE GmbH, since 2007; available from <https://www.turbomole.com>, 2019.
- (a) Y. Tulchinsky, S. Kozuch, P. Saha, M. Botoshansky, L. J. W. Shimon and M. Gandelman, *Chem. Sci.*, 2014, **5**, 1305–1311; (b) Y. Tulchinsky, S. Kozuch, P. Saha, A. Mauda, G. Nisnevich, M. Botoshansky, L. J. W. Shimon and M. Gandelman, *Chem. – Eur. J.*, 2015, **21**, 7099–7110; (c) A. Pogoreltsev, Y. Tulchinsky, N. Fridman and M. Gandelman, *J. Am. Chem. Soc.*, 2017, **139**, 4062–4067; (d) I. Avigdori, A. Pogoreltsev, A. Kaushanski, N. Fridman and M. Gandelman, *Angew. Chem., Int. Ed.*, 2020, **59**, 23476–23479.
- (a) A. E. Waked, R. O. Memar and D. W. Stephan, *Angew. Chem., Int. Ed.*, 2018, **57**, 11934–11938; (b) J. Zhou, L. L. Liu, L. Cao and D. W. Stephan, *Chem. Commun.*, 2018, **54**, 4390–4393; (c) J. L. Zhou, L. L. Liu, L. Cao and D. W. Stephan, *Angew. Chem., Int. Ed.*, 2018, **57**, 3322–3326.
- E. Habraken, A. Jupp and J. Slootweg, *Synlett*, 2019, 875–884.
- J. Guo, M. Yan, L. Xiao, J. Li, Z.-W. Qu, S. Grimme and D. W. Stephan, CCDC 2434837: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/ccdc.csd.cc2mqn45](https://doi.org/10.5517/ccdc.csd.cc2mqn45).
- J. Guo, M. Yan, L. Xiao, J. Li, Z.-W. Qu, S. Grimme and D. W. Stephan, CCDC 2434838: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/cede.csd.cc2mqn56](https://doi.org/10.5517/cede.csd.cc2mqn56).
- J. Guo, M. Yan, L. Xiao, J. Li, Z.-W. Qu, S. Grimme and D. W. Stephan, CCDC 2434839: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/cede.csd.cc2mqn67](https://doi.org/10.5517/cede.csd.cc2mqn67).

