



HAL
open science

A strategy for improving the efficiency of boronic acid catalysis in the synthesis of amides

Fatima Almetwali, Jacques Rouden, Jérôme Blanchet

► **To cite this version:**

Fatima Almetwali, Jacques Rouden, Jérôme Blanchet. A strategy for improving the efficiency of boronic acid catalysis in the synthesis of amides. *European Journal of Organic Chemistry*, 2023, 26 (45), pp.e202300720. 10.1002/ejoc.202300720 . hal-04229362

HAL Id: hal-04229362

<https://hal.science/hal-04229362v1>

Submitted on 5 Oct 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

A Strategy for Improving the Efficiency of Boronic Acid Catalysis in the Synthesis of Amides.

Dr. Fatima Almetwali^[a], Prof. Jacques Rouden^[a], Dr. Jérôme Blanchet^{*[a]}

[a] Dr Jérôme Blanchet

Normandie Univ, LCMT UMR 6507, ENSICAEN, UNICAEN, CNRS, 6 Bd. du Maréchal Juin, 14050 Caen, France.

jerome.blanchet@ensicaen.fr

<https://www.lcmt.ensicaen.fr/groupe-jacques-rouden-2/>

Supporting information for this article is given via a link at the end of the document.

Abstract: This study outlines the development of novel boronic acids as catalysts for the direct synthesis of amides from carboxylic acids and amines. The Lewis acidity of the boronic acids was estimated by means of computational techniques, and the observed increase in catalytic activity was corroborated by kinetic data derived from a model reaction. Our investigations led to the discovery of a set of ortho-(sulfonyloxy)benzeneboronic acids that compared favorably with the established state-of-the-art. These newly developed catalysts demonstrated efficacy in the coupling of aliphatic, aromatic, and heteroaromatic acids, as well as primary and secondary amines.

Introduction

The significance of amide synthesis in the industry is a topic that is scarcely disputed as numerous top-selling pharmaceutical drugs contain this specific functional group. However, the present industrial standard for direct amide synthesis continues to rely on the stoichiometric activation of carboxylic acids, resulting in unwanted waste and purification expenses. Recent progress in the field has shown promising developments, particularly with boron and group (IV) metal catalysts.^[1] Nonetheless, apart from boric acid catalysis, the usefulness of boron catalysts for the industry has yet to be fully established.^[2] One important topic is the continued pursuit of more efficient boronic acid catalysts. Notable advancements in this area have been made by various groups^[3], resulting in the discovery of highly efficient boronic acid derivatives (Figure 1) when combined with a water exclusion setup, such as Dean-Stark, Soxhlet, or molecular sieves.

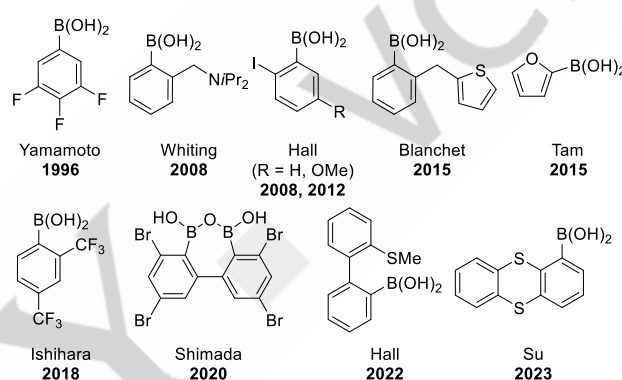
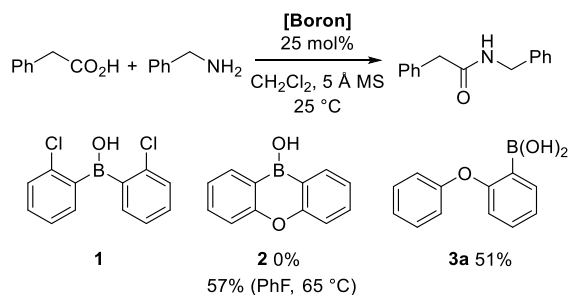


Figure 1. Boronic acid catalysts in amidation reactions.

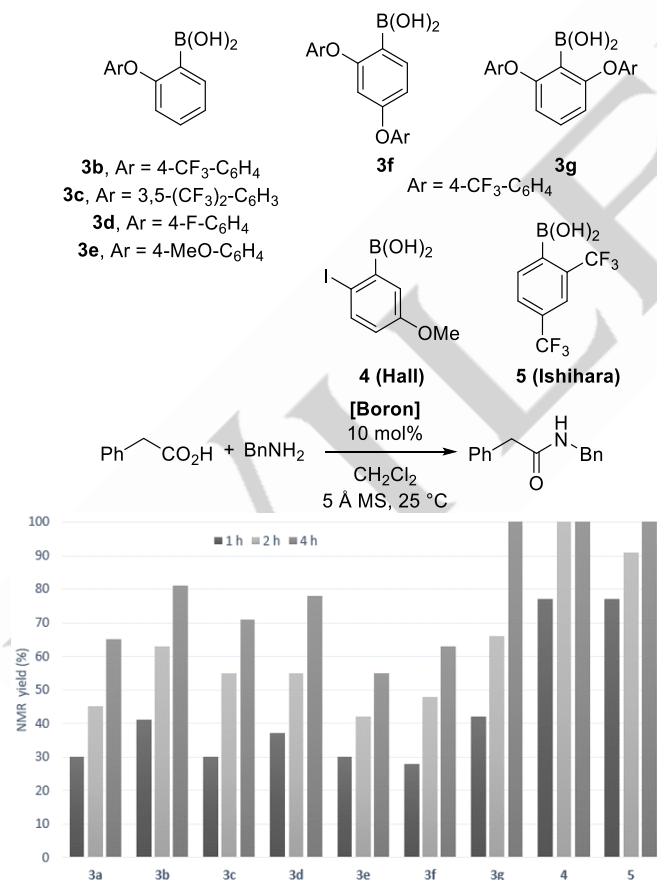
In a recent report, our research group detailed the successful application of boronic acid **1** as a catalyst for the mild synthesis of peptides.^[4] Our initial hypothesis regarding the role of boronic species in the catalytic cycle was subsequently scrutinized by Whiting, leading to a more nuanced understanding of the activation of carboxylic acids by a boronic acid active species.^[5] Our initial findings were supported by the discovery of cyclic boronic acid **2**, which exhibited moderate efficacy at 65 °C. Interestingly, no proto-deborylation or amidation was observed at 25 °C, as shown in Scheme 1. However, ¹¹B NMR spectroscopic analysis indicated that proto-deborylation of **2** to **3a** is indeed occurring at 65 °C, with a recorded conversion of 20% after 0.5 h, and 100% after 6 h (see SI pS3-S6). Consistent with Whiting's findings, the active catalyst was re-designated as 2-phenoxybenzene boronic acid **3a**, which gave a 51% yield at 25 °C (Scheme 1). Building on these outcomes, we sought to explore the potential of 2-aryloxybenzene boronic acids **3b-g** as catalysts in amide synthesis, with the aim of improving the catalytic efficiency of such compounds.



Scheme 1. Initial results.

Results and Discussion

To monitor the conversion of the reaction, ^1H NMR spectroscopy was employed, with tetrachloroethane as an internal standard (Scheme 2). The investigation of monosubstituted 2-aryloxybenzene boronic acids **3a-3e** revealed that increasing the electron depletion of the aryl substituent significantly enhanced the rate of the reaction, with a maximum efficiency attained by a trifluoromethyl substituent in the para position (**3b**). The addition of an extra trifluoromethyl group (**3c**) or an electron-donating methoxy group (**3e**) was found to decrease the efficiency of the reaction (Scheme 2).

Scheme 2. 2-Aryloxybenzene boronic acids tested in this study and efficiency in amide synthesis.^a

Unexpectedly, a reduction in performance was observed upon the introduction of a second aryloxy group in the para position relative to the boron atom (**3f**). Intriguingly, the incorporation of an additional aryloxy group in the second ortho position with 2,6-disubstituted **3g** resulted in complete conversion within 4 h, achieving the fastest reaction rate observed for 2-aryloxybenzene boronic acids so far. This outcome sharply contrasts with previous investigations where *ortho* disubstitution consistently led to decreased reactivity (for further details see boronic acids **6-9** in the supporting information).^[3f,6]

Unfortunately, comparative experiments carried out with the state-of-the-art catalysts **4**^[3c] and **5**^[3f] demonstrated that the desired enhancement had not yet been achieved. While full conversion was attained with **4** after merely two hours, a moderate 66% conversion was obtained with **3g** over the same duration (for detailed kinetic data, see the supporting information). To further enhance the catalyst's efficacy, we endeavored to exploit strategies that decrease the electron density at the boron center to promote higher Lewis acidity. In this perspective, Whiting has previously reported that the stoichiometric use of 2-nitrobenzeneboronic acid displayed a moderate efficiency in refluxing fluorobenzene.^[7] Although aryl boronic acids are established catalyst in numerous chemical processes, the intrinsic Lewis acidity of such compounds has only recently been examined using water as a Lewis base.^[8] A general Lewis acid scaling method relies on theoretical calculation of the fluorine ion affinity (FIA).^[9] The Hammett parameter of trifluoromethane sulfonate group ($\sigma_p = 0.53$, $\sigma_m = 0.56$) led us to expect sulfonate substituted boronic acids to display interesting Lewis acidity. Hence, the Lewis acidity of boronic acids **3** and **5**, as well as the anticipated sulfonate derivatives **10-12** (figure 2), has been estimated by DFT calculation at the $\omega\text{WB97XD/6-31++(d,p)}$ level of theory (Table 1).^[10]

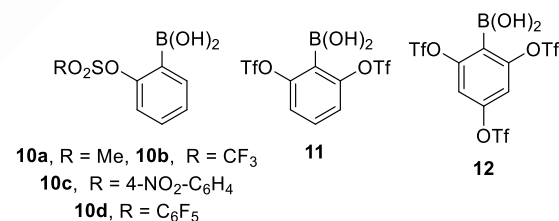
Figure 2. Boronic acids **10-12**.

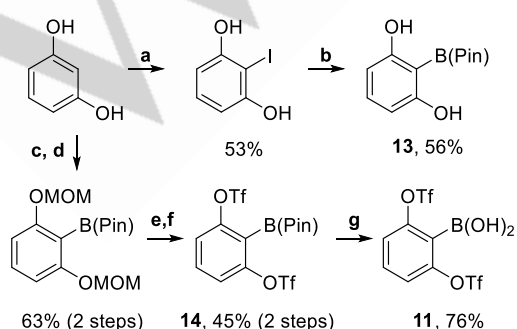
Table 1. FIA estimation and quantitative scale for Lewis acidity for boronic acids.

Boronic acid	FIA _{COF₂} ^[a]	pF ^[b]	Boronic acid	FIA _{COF₂} ^[a]	pF ^[b]
3b	239.8	5.73	10a	240.5	5.97
3c	259.6	6.20	10b	250.7	5.99
3d	227.7	5.44	10c	277.7	6.64
3e	213.2	5.10	10d	292.3	6.99
3f	272.3	6.51	11	279.3	6.68
3g	272.7	6.52	12	309.5	7.40
5	269.9	6.45			

^[a]The fluoride ion affinity (FIA in kJ.mol⁻¹) of a given boronic acid A is estimated by the -ΔH of the following reaction LA + F⁻ ⇌ [LAF]⁻ using COF₂/COF₃⁻ anchor at the ωWB97XD/6-31++(d,p) level of theory. ^[b]The corresponding pF⁻ value corresponds to pF⁻ = FIA/10 (in kcal.mol⁻¹), according to Christe.^[11]

Notably, calculations revealed that aryl boronic acids **10-12**, substituted with at least one sulfonate groups, exhibit a Lewis acidity range (240.5-309.5 kJ.mol⁻¹) that encompasses the ones of boronic acids **3g** (272.7 kJ.mol⁻¹) and **5** (269.9 kJ.mol⁻¹). This observation prompted us to synthesize **10-12** and evaluate their catalytic properties. Compounds **10a-d** were easily synthesized in two steps from commercially available 2-hydroxybenzene boronic acid pinacol ester. It should be noted that the deprotection of the pinacol ester required some optimization, with electrophilic oxidative conditions (NaIO₄)^[12] yielding boronic acids **10** with variable yields (30-83%) depending on the substrate's nature (see the supporting information).

The synthesis of boronic acid **11** required a more complex strategy (Scheme 3). Initially, a protection group-free approach was designed via the regioselective monoiodination of resorcinol, followed by an iodine-to-lithium exchange to obtain 2,6-dihydroxybenzene boronic pinacol ester **13**. While relatively straightforward, an impractical 30% yield from resorcinol was obtained despite efforts to mitigate polyiodination and a capricious lithium-iodine exchange/borylation sequence. It is worth noting that the latter step required a large excess of *n*BuLi (6 equivalents), presumably to enhance the solubility of the highly polar intermediate lithium trisanion.



Reaction conditions: (a) NaHCO₃, THF, H₂O then I₂. (b) *n*BuLi, TMEDA, THF, -78 °C then *i*PrOB(Pin) 5 equiv. -60 °C. (c) NaH, DMF, MOMCl, 90%. (d) *n*BuLi,

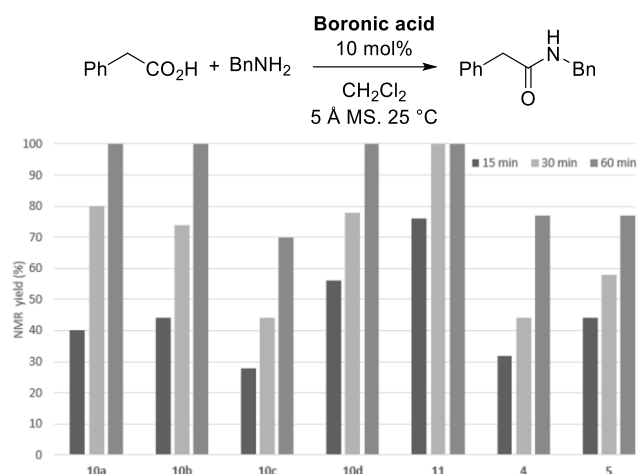
THF, 0 °C then *i*PrOB(Pin), 85%. (e) TFA, CH₂Cl₂. (f) DIPEA, Tf₂O, CH₂Cl₂. (g) NaIO₄, 1M HCl, THF:H₂O.

Scheme 3. Synthesis of boronic acid **11**.

To address the challenge of regioselectivity, a directed ortho metalation was investigated. Initial attempts to selectively demethylate the 2,6-dimethoxybenzene boronic acid pinacol ester resulted in uncontrolled protodeborylation. However, the use of methoxymethyl ether protecting groups proved more effective, allowing for selective borylation and mild deprotection conditions, resulting in a global yield of pinacol ester **14** of 30% from resorcinol. Targeted boronic acid **11** was obtained through the deprotection of the pinacol ester **14**. Unfortunately, **12** remained elusive as uncontrolled polymerization or protodeborylation prevented its synthesis.

The boronic acids **10a-d** and **11** were then evaluated for their ability to catalyze the coupling of benzylamine with phenylacetic acid, and compared to reference catalysts **4** and **5** using similar reaction conditions. Interestingly, all the tested boronic acids resulted in significantly faster reactions that reached completion within an hour or less, except for **10c** [X = SO₂(4-NO₂-C₆H₄)]. Importantly, kinetic data for the tested boronic acids compared favorably to reference compounds **4** and **5**. For instance, the amide synthesis catalyzed by **11** was completed after just 30 minutes (Scheme 4), compared to 2 hours for **4** and 4 hours for **5** (Scheme 2). Upon examination of the para-substituted regioisomer of **10a**, a decrease in catalytic efficiency was observed, underscoring the importance of the *ortho*-substitution (data not shown, see the supporting information).

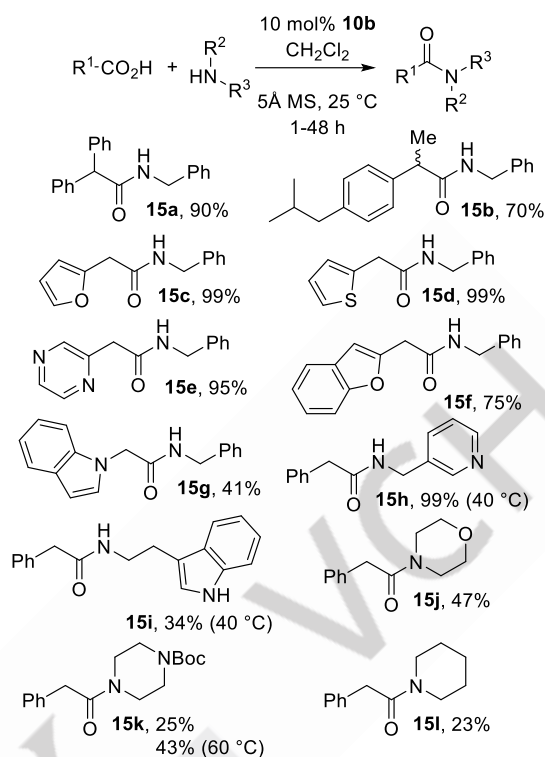
Although a direct correlation at this stage of the investigation cannot be firmly established, it is noteworthy that an increase in the Lewis acidity of the boronic acid resulted in enhanced reaction rates. Notably, boronic acids **10a** and **10b** demonstrated comparable efficiency (Scheme 4) and possessed similar FIA (240.5 and 250.7 kJ.mol⁻¹ respectively). In contrast, compound **11**, with two *ortho*-substituents and a higher FIA of 279.3 kJ.mol⁻¹, exhibited approximately twice the reaction rate compared to **10a** and **10b**. Despite boronic acid **10d** having the highest calculated FIA among the tested compounds (292.3 kJ.mol⁻¹, it remained less effective than compound **11**. This disparity was attributed to the absence of a second *ortho*-substituent in **10d**. The unexpected lower efficiency observed for compound **10c** lacks a clear explanation and is tentatively ascribed to unproductive intermolecular interactions with the nitro group.



Scheme 4. 2-Sulfonatobenzene boronic acids as catalysts in amidation Reactions.^a Reaction conditions: boronic acid (10 mol%), BnNH₂, PhCH₂CO₂H (1.1 equiv), 5 Å MS in dichloromethane, under an Ar atmosphere, 25 °C.

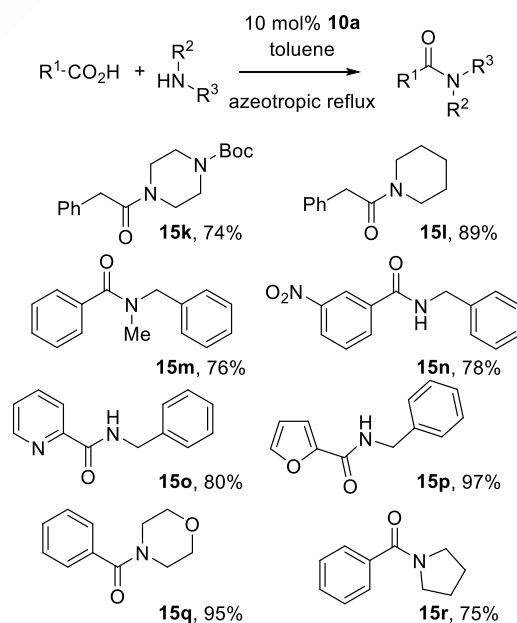
While the synthesis of **10d** required the use of an expensive sulfonyl chloride derivative, the efficiency of compound **11** was found to be variable due to its sensitivity to protodeborylation. Thus, boronic acids **10a** and **10b** were identified as stable, efficient and readily available catalysts for amide synthesis, therefore we proceeded to investigate their scope and limitations. Our methodology was successfully applied to the synthesis of a broad range of amides, including α -substituted carboxylic acids for **15a** (90%) and **15b** (70%), indicating a degree of tolerance to steric hindrance. Comparatively, **15a** was reported in 2023 with only 58% yield using a thianthrene catalyst in refluxing dichloromethane.^[3] Additionally, heterocycles such as furan, thiophene, pyrazine, and benzofuran were well-tolerated, as exemplified by the synthesis of **15c-f** with high yields. Notably, 3-picolylamine produced **15h** in 99% isolated yield, albeit at a slightly increased temperature, possibly due to the Lewis-basic pyridine.

The modest yields of **15g** and **15i** indole-containing derivatives (34-41%) were attributed to the low solubility of the starting materials in the reaction medium. The use of secondary amines as substrates proved to be more challenging, resulting in moderate yields for **15j-15l** (23-47%, Scheme 5). Increasing the reaction temperature to 60 °C for Boc-protected piperazine marginally improved the yield obtained at 20 °C.



Scheme 5. Scope of the amide synthesis in the presence of molecular sieves.

In sharp contrast, when **10b** was used and reaction conditions were changed to refluxing toluene using a Dean-Stark device to trap water irreversibly, amidation involving secondary amines such as piperazine or piperidine delivered good yields of 74-89% (**15k** and **15l**, Scheme 6).



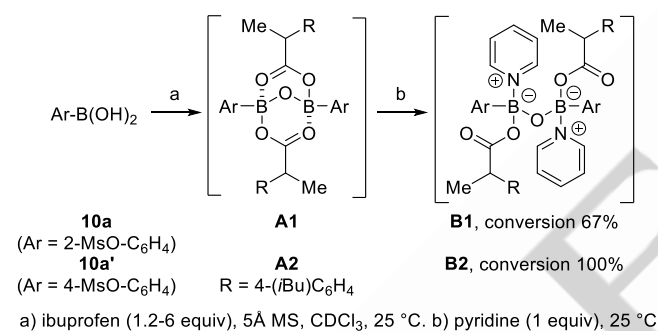
Scheme 6. Challenging substrates using Dean-Stark reaction conditions.

Aryl and heteroaryl carboxylic acids are known to be reluctant to low-temperature catalysis or in refluxing toluene, regardless of the electron density of the aromatic ring. However, good yields were

obtained with electron-poor 3-nitrobenzoic acid (**15n**, 78%) or picolinic acid (**15o**, 80%), as well as with electron-rich furoic acid (**15p**, 97%). Furthermore, tertiary amides were successfully obtained from benzoic acid in yields of 95% (**15q**) and 75% (**15r**). Significantly, a recently disclosed thianthrene catalyst yielded only 38% for **15q** under identical reaction conditions.^[3]

To explore the possibility of any degradation pathway involving the non-selective nucleophilic addition of the amine to the methanesulfonate group of boronic acid **10b**, a control experiment was conducted. In this experiment, boronic acid **10b** and 2 equivalents of benzylamine were stirred at 115 °C, with the absence of a potentially productive amidation pathway. After 24 hours, ¹H NMR analysis indicated that approximately 50% of boronic acid **10b** remained while the rest had essentially transformed into phenyl methanesulfonate due to the cleavage of the boron-carbon bond. This suggests that the sulfonate group is inert in the reported reaction conditions (see supporting information).

The early stage of the reaction was investigated through ¹H, ¹¹B and ¹³C NMR monitoring, which confirmed the formation of a dimeric intermediate previously reported by Whiting (Scheme 7).^[5]



Scheme 7. Investigating ortho substitution hindrance.

Interesting differences were observed upon comparison of the regioisomers boronic acids **10a** (*ortho*) and **10a'** (*para*). Specifically, **10a'** demonstrated a reduced inclination to generate the reactive intermediate, requiring a larger excess of ibuprofen (6 equivalents) compared to **10a**, which only required a small excess (1.2 equivalents). Upon introduction of pyridine to both intermediates, a significant difference in favor of the *ortho*-substituted boronic acid **10a** was observed. This observation suggests the mitigation of unproductive coordination at the boron center, in line with recent findings by Ishihara.^[3f]

Conclusion

In summary, we have developed a series of original boronic acids for the catalysis of direct amide synthesis from various amines and carboxylic acids. While a first group of aryloxybenzene boronic acids served as a preliminary template for further improvement, kinetic data associated with Lewis acidity estimation using DFT allowed us to uncover a second group of sulfonatobenzene boronic acids that compared favorably with the established state of the art for the coupling of phenylacetic acid

and benzylamine.^[13] The scope of two boronic acids **10a** and **10b** was investigated, revealing good efficiency for a set of amines and carboxylic acids.

Experimental section

Dry solvents were obtained from a double-cartridge solvent purification system. Thin layer chromatographies were performed on silica gel 60 F254 plates. ¹H NMR spectra were recorded on BRUKER Avance III (500 MHz) and BRUKER NEO (600 MHz) spectrometers. ¹H NMR spectral data were recorded as follows: chemical shift in ppm from internal tetramethylsilane. The residual solvent protons (in ¹H NMR) were used as internal standards (CDCl₃ at 7.26 ppm, CD₃CN at 1.94 ppm, and DMSO-*d*₆ at 2.50 ppm). ¹³C NMR chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (CDCl₃ at 77.16 ppm, CD₃CN at 1.32 and 118.26 ppm, and DMSO-*d*₆ at 39.52 ppm). Because of their low intensity (resulting from quadrupolar coupling), ¹³C signals of the carbon bearing the boronic acid group were generally not observed. High-resolution mass spectra (APCI analyzer) were recorded using either atmospheric solids analysis probe (ASAP) or electrospray ionization (ESI) techniques. Infrared spectra were obtained with frequencies expressed in cm⁻¹. Molecular sieves were purchased from Sigma-Aldrich (5Å-233676, powder, undried, reference is no more available and 4Å-688363, powder, activated) and were activated using a Kugelrohr distillation instrument under 1 mbar vacuum at 250 °C for 2 hours.

General procedure for the amide synthesis procedure.

25 °C amidation: In a dry flask under argon, carboxylic acid (0.55 mmol, 1.1 equiv.), boronic acid **10b** (14 mg, 0.05 mmol, 10 mol%), and 1 g of freshly activated 5Å molecular sieves were introduced. Then 7 mL of dry CH₂Cl₂ (0.07 M) were added, and the mixture was stirred vigorously for 15 minutes at 25 °C. Next, amine (0.50 mmol) was added and the mixture was stirred under argon. The reaction was monitored by ¹H NMR. Then, the reaction mixture was filtered through a 1 cm celite pad and washed with EtOAc and CH₂Cl₂. Evaporation of volatiles gave a residue that was purified by flash silica-gel column chromatography to afford the corresponding pure amide.

Amidation using Dean-Stark apparatus: To a dry flask charged with carboxylic acid (0.55 mmol, 1.1 equiv), boronic acid **10a** (11 mg, 0.05 mmol, 10 mol%), dry toluene (3.5 mL) and amine (0.5 mmol, 1 equiv). The resulting suspension was stirred under azeotropic reflux. Upon completion, volatiles were evaporated and the pure amide was isolated upon purification using flash silica-gel column chromatography.

Supporting Information

The authors have cited additional references within the Supporting Information.^[14–31]

Acknowledgements

The authors acknowledge the financial support of the French Agence Nationale de la Recherche through the Project GLUE-BOCA (Grant No. ANR-18-CE07-0046). This work was supported by the excellence laboratory LabEx SYNORG (ANR-11-LABX-0029), the Conseil Régional de Normandie and the European FEDER funding.

Keywords: amide • catalysis • boronic acid • lewis acid • FIA

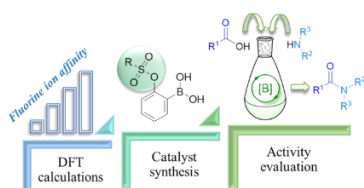
References

- [1] For boron catalyst other than boronic acids, see : (a) P. V. Ramachandran, H. J. Hamann, *Org. Lett.* **2021**, *23*, 2938–2942. (b) M. T. Sabatini, L. T. Boulton, T. D. Sheppard, *Science Adv.* **2017**, *3*, e1701028. (c) T. Maki, K. Ishihara, H. Yamamoto, *Org. Lett.* **2006**, *8*, 1431–1434. (d) H. Noda, M. Furutachi, Y. Asada, M. Shibasaki, N. Kumagai, *Nature Chem.* **2017**, *9*, 571–577. (e) D. N. Sawant, D. B. Bagal, S. Ogawa, K. Selvam, S. Saito, *Org. Lett.* **2018**, *20*, 4397–4400. For group IV metals based catalyst see (f) C. L. Allen, A. R. Chhatwal, J. M. J. Williams, *Chem. Commun.* **2011**, *48*, 666–668. (g) H. Lundberg, F. Tinnis, H. Adolfsson, *Chem – Eur. J.* **2012**, *18*, 3822–3826. (h) F. de Azambuja, T. N. Parac-Vogt, *ACS Catal.* **2019**, *9*, 10245–10252.
- [2] (a) J. Magano, *Org. Process Res. Dev.* **2022**, *26*, 1562–1689. For recent reviews see (b) X. Wang, *Nature Catalysis* **2019**, *2*, 98–102. (c) M. T. Sabatini, L. T. Boulton, H. F. Sneddon, T. D. A Sheppard, *Nature Catalysis* **2019**, *2*, 10–17. (d) M. Todorovic, D. M. Perrin, *Peptide Science* **2020**, *112* (6), e24210.
- [3] (a) K. Ishihara, S. Ohara, H. Yamamoto, *J. Org. Chem.* **1996**, *61*, 4196–4197. (b) K. Arnold, A. S. Batsanov, B. Davies, A. Whiting, *Green Chem.* **2008**, *10*, 124–134. (c) N. Gernigon, R. M. Al-Zoubi, D. G. Hall, *J. Org. Chem.* **2012**, *77*, 8386–8400. (d) T. Mohy El Dine, W. Erb, Y. Berhault, J. Rouden, J. Blanchet, *J. Org. Chem.* **2015**, *80*, 4532–4544. (e) E. K. W. Tam, Rita, L. Y. Liu, A. Chen, *Eur. J. Org. Chem.* **2015**, 1100–1107. (f) K. Wang, Y. Lu, K. Ishihara, *Chem. Commun.* **2018**, *54*, 5410–5413. (g) M. Koshizuka, K. Makino, N. Shimada, *Org. Lett.* **2020**, *22*, 8658–8664. (h) J. Zhou, M. Paladino, D. G. Hall, *Eur. J. Org. Chem.* **2022**, e202201050. (i) B. Pan, D.-M. Huang, H.-T. Sun, S.-N. Song, X.-B. Su, *J. Org. Chem.* **2023**, *88*, 2832–2840. (j) for a review see: P. Huy, B. Zoller, *Nachr. Chem.* **2019**, *67*, 51–54.
- [4] T. Mohy El Dine, J. Rouden, J. Blanchet, *Chem. Commun.* **2015**, *51*, 16084–16087.
- [5] S. Arkhipenko, M. T. Sabatini, A. S. Batsanov, V. Karaluka, T. D. Sheppard, H. S. Rzepa, A. Whiting, *Chem. Sci.* **2018**, *9*, 1058–1072.
- [6] (a) R. M. Al-Zoubi *PhD Thesis, University of Alberta, Canada*, **2011**, 65. (b) R. M. Al-Zoubi, O. Marion, D. G. Hall, *Angew. Chem. Inter. Ed.* **2008**, *47*, 2876–2879.
- [7] S. Liu, Y. Yang, X. Liu, F. K. Ferdousi, A. S. Batsanov, A. Whiting, *Eur. J. Org. Chem.* **2013**, 5692–5700.
- [8] J. Jian, R. Hammink, C. J. McKenzie, F. M. Bickelhaupt, J. Poater, J. Mecinović, *Chem.–Eur. J.* **2022**, *28*, e202104044.
- [9] P. Erdmann, J. Leitner, J. Schwarz, L. Greb, *ChemPhysChem* **2020**, *21*, 987–994.
- [10] Gaussian 09, Revision E.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford CT, **2013**.
- [11] K. O. Christe, D. A. Dixon, D. McLemore, W. W. Wilson, J. A. Sheehy, J. A. Boatz, *J. Fluor. Chem.* **2000**, *101*, 151–153.
- [12] (a) S. J. Coutts, J. Adams, D. Krolikowski, R. J. Snow, *Tetrahedron Lett.* **1994**, *35*, 5109–5112. (b) H. Nakamura, M. Fujiwara, Y. A Yamamoto, *Bull. Chem. Soc. J.* **2000**, *73*, 231–235.
- [13] While the correlation between Lewis acidity and catalytic ability has served as a valuable guide in our pursuit of enhancing catalyst design, it is crucial to recognize that catalyst activity can be subject to various secondary interactions, impeded by steric repulsion, or even nullified by catalyst decomposition. Consequently, any inference drawn regarding the relationship between FIA (Fluorine Ion Affinity) and reaction rate should be treated with careful consideration.
- [14] K. Ishihara, Q. Gao, H. Yamamoto, *J. Org. Chem.* **1993**, *58*, 6917–6919.
- [15] J. W. Lockner, D. D. Dixon, R. Risgaard, P. S. Baran, *Org. Lett.* **2011**, *13*, 5628–5631.
- [16] L. F. Tietze, T. Hungerland, A. Düfert, I. Objartel, D. Stalke, *Chem. Eur. J.* **2012**, *18*, 3286–3291.
- [17] R. M. Al-Zoubi. *PhD Thesis*. University of Alberta Canada. **2011**, p 65.
- [18] K. Wang, Y. Lu, K. Ishihara. *Chem. Commun.* **2018**, *54*, 5410–5413.
- [19] Y. Sumida, T. Kato, T. Hosoya, *Org. Lett.* **2013**, *15*, 2806–2809.
- [20] (a) S. Yamada, M. Kawasaki, M. Fujihara, M. Watanabe, Y. Takamura, M. Takioku, H. Nishioka, Y. Takeuchi, M. Makishima, T. Motoyama, S. Ito, H. Tokiwa, S. Nakano, H. Kakuta, *J. Med. Chem.* **2019**, *62*, 8809–8818. (b) A. C. Donnelly, J. R. Mays, J. A. Burlison, J. T. Nelson, G. Vielhauer, J. Holzbeierlein, B. S. J. Blagg, *J. Org. Chem.* **2008**, *73*, 8901–8920.
- [21] (a) T. Hamura, T. Hosoya, H. Yamaguchi, Y. Kuriyama, M. Tanabe, M. Miyamoto, Y. Yasui, T. Matsumoto, K. Suzuki, *Helv. Chim. Acta* **2002**, *85*, 3589–3604. (b) J. Shi, H. Xu, D. Qiu, J. He, Y. Li, *J. Am. Chem. Soc.* **2017**, *139*, 623–626.
- [22] (a) A. Takagi, T. Ikawa, K. Saito, S. Masuda, T. Ito, S. Akai, *Org. Biomol. Chem.* **2013**, *11*, 8145–8150. (b) T. Ikawa, R. Yamamoto, A. Takagi, T. Ito, K. Shimizu, M. Goto, Y. Hamashima, S. Akai, *Adv. Syn. Catal.* **2015**, *357*, 2287–2300.
- [23] J. Sun, M. T. Perfetti, W. L. Santos, *J. Org. Chem.* **2011**, *76*, 3571–3575.
- [24] S. P. A. Hinkes, C. D. P. Klein, *Org. Lett.* **2019**, *21*, 3048–3052.
- [25] T. Mohy El Dine, W. Erb, Y. Berhault, J. Rouden, J. Blanchet, *J. Org. Chem.* **2015**, *80*, 4532–4544.
- [26] N. Gernigon, R. M. Al-Zoubi, D. G. Hall, *J. Org. Chem.* **2012**, *77*, 8386–8400.

- [27] M. P. Cassidy, J. Raushel, V. V. Fokin, *Angew. Chem., Int. Ed.* **2006**, *45*, 3154–3157.
- [28] D. C. Braddock, P. D. Lickiss, B. C. Rowley, D. Pugh, T. Purnomo, G. Santhakumar, S. J. Fussell, *Org. Lett.* **2018**, *20*, 950–953.
- [29] D. F. J. Hamstra, D. C. Lenstra, T. J. Koenders, F. P. J. T. Rutjes, J. Mecinović, *Org. Biomol. Chem.* **2017**, *15*, 6426–6432.
- [30] Sawant, D. N.; Bagal, D. B.; Ogawa, S.; Selvam, K.; Saito, S. *Org. Lett.* **2018**, *20*, 4397–4400.
- [31] D. Leow, *Org. Lett.* **2014**, *16*, 5812–5815.

WILEY-VCH

Entry for the Table of Contents



Novel boronic acids have been developed for the catalysed amide synthesis. Lewis acidity estimation using DFT, associated with collected kinetic data, allowed to uncover *ortho*-(sulfonyloxy)benzeneboronic acids that compared favourably with the established state-of-the-art boronic acids. Efficient coupling of aliphatic, aromatic, and heteroaromatic carboxylic acids as well as primary and secondary amines were obtained.