A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

GDCh

Chemie

www.angewandte.org

Accepted Article

Title: Oxidation of Alkynyl Boronates to Carboxylic Acids, Esters and Amides

Authors: Wanxiang Zhao, Chenchen Li, Pei Zhao, Ruoling Li, and Bing Zhang

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.202000988
Angew. Chem. 10.1002/ange.202000988

Link to VoR: http://dx.doi.org/10.1002/anie.202000988
http://dx.doi.org/10.1002/ange.202000988

WILEY-VCH

10.1002/anie.202000988

WILEY-VCH

Oxidation of Alkynyl Boronates to Carboxylic Acids, Esters and Amides

Chenchen Li, Pei Zhao, Ruoling Li, Bing Zhang, and Wanxiang Zhao*

ABSTRACT: A general efficient protocol was developed for the synthesis of carboxylic acids, esters, and amides via oxidation of alkynyl boronates, generated directly from terminal alkynes. This protocol represents the first example of C(sp)–B bond oxidation. This approach displays a broad substrate scope, including aryl and alkyl alkynes, and exhibits excellent functional group tolerance. Water, primary and secondary alcohols, and amines are suitable nucleophiles for this transformations. Notably, amino acids and peptides can be used as nucleophiles, providing an efficient method for the synthesis and modification of peptides. The practicability of this methodology was further highlighted by the preparation of pharmaceutical molecules.

The use of C–B bonds to forge carbon–carbon and carbon–heteroatom bonds is an ongoing synthetic endeavor, with extensive applications in synthetic chemistry and pharmaceutical production, as well as in natural product synthesis.[1] The oxidation of C(sp^3)–B bonds to C–O bonds is credited as being the first transformation of organoboron compounds, which was discovered accidentally by Franlkand when he attempted to prepare BEt_3 from $B(OEt)_3$ and $ZnEt_2$.[2] The discovery of hydroboration of alkenes by Brown tremendously accelerated the development of C(sp^3)–B bond oxidation, making it a text-book reaction.[3] Likewise, C(sp^2)–B bond oxidation to carbonyl compounds or phenols has been well-established due to the abundance of vinyl or aryl boronic esters.[4] However, to the best of our knowledge, the oxidation of C(sp)–B bonds (Figure 1a) is yet to be reported, and is addressed in this study.

From a mechanistic perspective, we envision that alkynyl boronate **I**[5] could undergo an alkynyl B→O migration to generate boron ynolate **II** under oxidative conditions, analogous to C(sp^3)–B and C(sp^2)–B bond oxidation.[3,4] Subsequently, the hydrolysis of intermediate **II** forms ynol **III**, which then tautomerizes to ketene **IV**.[6] Ultimately, nucleophilic addition to ketene **IV** delivers product **V**.[7] The overall conversion is the oxidation of alkynyl boronates to carboxylic acids or their derivatives via a ketene intermediate, in the presence of nucleophiles and an oxidant (Figure 1b). In addition, the alkynyl boronates can be readily prepared from terminal alkynes.[8] Therefore, the realization of this unprecedented C(sp)–B bond oxidation would offer a complement to the existing protocols for the synthesis of carboxylic acids, esters, and amides from terminal alkynes.[9] It is expected to find applications in organic synthesis, medicinal chemistry, and materials science due to the carboxyl being one of the most prevalent and important functional groups in biologically active molecules, natural products (i.e., mycophenolic acid, Figure 1c) and drugs (i.e., ibuprofen, and lyrica, Figure 1c), and serves as a synthetically valuable building block in modern synthetic organic chemistry.[10]

The C(sp)–B bond oxidation of alkynyl boronates presents daunting challenges: (1) the C–C triple bond oxidation would be competitive, which typically generates 1,2-diketones[11] that could undergo further oxidation to form anhydrides and results in triple bond cleavage.[12] (2) The protodeboronation of alkynyl boronates becomes an issue when water or alcohol are used as nucleophiles,[13] and the terminal alkynes generated from protodeboronation would likely be oxidized to carboxylic acids or their derivatives. For instance, the groups of Che and Wong, Lee, Saá and Esteruelas have demonstrated elegant transiton-metal catalyzed oxidation of terminal alkynes for the synthesis of amides, esters, and carboxylic acids.[9c-f] Consequently, the choice of oxidant is vital for the success of C(sp)–B bond oxidation of alkynyl boronates. Herein, we report the first example of C(sp)–B bond oxidation using inexpensive and commercially

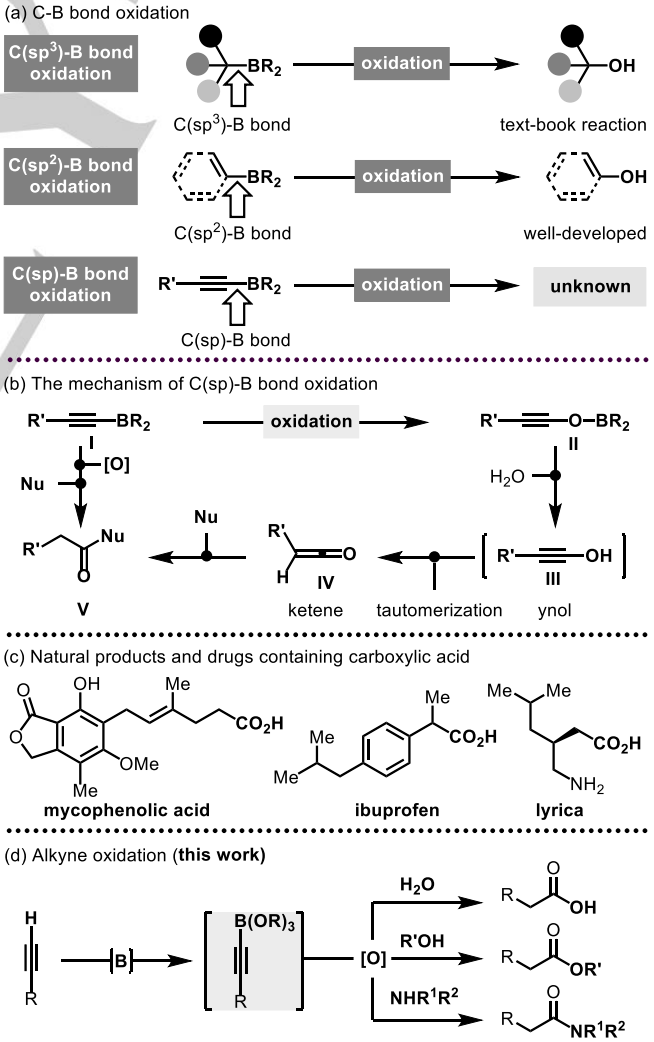


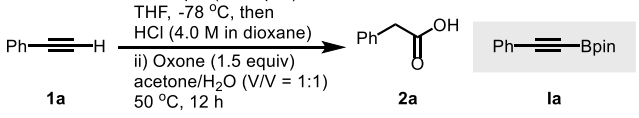
Figure 1. (a) C–B Bond Oxidation. (b) C(sp)–B Bond Oxidation Mechanism. (c) Carboxylic Acids in Natural Products and Drugs. (d) Alkyne Oxidation.

[a] C. Li, P. Zhao, R. Li, B. Zhang, Prof. Dr. W. Zhao
State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha, Hunan 410082, P. R. China
E-mail: zhaowanxiang@hnu.edu.cn

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

10.1002/anie.202000988

Table 1. Optimization of Reaction Conditions[a]



1a **2a** **Ia**

Entry	change from standard conditions	yield[b] (%)
1	none	99 (93[c])
2	H_2O_2/NaOH instead of Oxone	0
3	*m*-CPBA instead of Oxone	90
4	1,4-dioxane instead of acetone	57
5	DMF instead of acetone	64
6	THF instead of acetone	72
7	MeCN instead of acetone	98
8	1.0 equiv Oxone instead of 1.5 equiv	80
9	2.0 equiv Oxone instead of 1.5 equiv	83
10	rt instead of 50 °C	76
11	40 °C instead of 50 °C	88
12	60 °C instead of 50 °C	94

[a] Standard conditions: i) **1a** (1.0 mmol), ^{n}BuLi (1.2 equiv), -78 °C, 1 h; ^{i}PrOBpin (1.2 equiv), -78 °C, 2 h, then HCl (1.5 equiv, 4.0 M in dioxane); ii) Oxone (1.5 equiv), acetone/H_2O (V/V=1:1), 50 °C, 12 h. [b] The yields were determined by ^{1}H NMR with CH_2Br_2 as an internal standard. [c] Isolated yield. *m*-CPBA = 3-chloroperoxybenzoic acid.

available Oxone as the oxidant for the synthesis of carboxylic acids, esters, and amides.

We initiated our investigation using phenylacetylene **1a** as the model substrate, which reacted with ^{i}PrOBpin in the presence of *n*-butyllithium to generate alkynyl boronate **Ia**, which was subjected to subsequent oxidation without purification. After careful evaluation of all the reaction parameters, we found that the treatment of **Ia** with Oxone in a mixture of acetone/H_2O (1:1) at 50 °C gave the best result, affording the desired phenylacetic acid **2a** in 99% yield (Table 1, entry 1). Surprisingly, no carboxyl acid was obtained when **Ia** was treated with hydrogen peroxide (H_2O_2), a frequently used oxidant for C(sp^3)–B and C(sp^2)–B bond oxidation, and instead the deboronation product **1a** was obtained (entry 2). The use of 3-chloroperoxybenzoic acid (*m*-CPBA) as an oxidant provided a slightly lower yield (entry 3). Solvents other than acetone, such as 1,4-dioxane, DMF, and THF gave inferior results (entries 4-6), although acetonitrile delivered the desired product in 98% yield (entry 7). Intriguingly, more, or less than 1.5 equivalents of Oxone had deleterious effects on the yield (entries 8-9). Moreover, as shown in entries 10-12, reaction temperatures higher or lower than 50 °C had a detrimental impact as well.

With the optimal reaction conditions in hand, we next studied the generality of the alkyne substrate for this oxidation reaction. As shown from the results compiled in Table 2, a wide range of aryl acetylenes with various substituents at different positions were suitable for this oxidation process, providing a diverse set of carboxyl acids with good to excellent efficiency. The reaction is amenable to both electron-withdrawing and electron-donating groups. Various functional groups, including fluoride (**2e**), chloride (**2f**), ester (**2g**), nitrile (**2h**), trifluoromethyl (**2i**), internal alkyne (**2j**), and sulfamide (**2l**) were all tolerated. It is worth mentioning that the C–C double bond remains intact under the oxidative conditions, to furnish the product **2k** in a moderate yield. Other aromatic rings, such as naphthalene (**2q**), anthracene (**2r**), phenanthrene(**2s**), and fluorene (**2t**), all reacted smoothly to afford the corresponding carboxylic acids in good yields. In addition, numerous heterocycles, including thiophene (**2u**), benzofuran (**2v**), indole (**2w**), and carbazole (**2x**), can be incorporated into the products. Diyne **1y**-**aa** also successfully participated in the oxidation to deliver the corresponding dicarboxylic acids (**2y**-**aa**). Notably, the acid **2aa** with a BINOL-skeleton may have potential applications in the synthesis of catalysts and ligands. Particularly noteworthy, 1,3,5-triethynylbenzene was found to be tolerated, allowing for the formation of tricarboxylic acid **2ab** in a reasonable yield.

We next turned our attention to the alkyl terminal alkynes (Table 2). To our delight, a series of alkyl terminal alkynes reacted smoothly under our standard reaction conditions (**2ac**-**2ao**). Importantly, the considerably sterically hindered *t*-butyl group (**2ae**) was compatible. Additionally, functional groups, such as cyclopropyl (**2af**)**,** ether (**2ag**), chloride (**2ah**), nitrile (**2ai**), and alkyne (**2aj**-**ak**) were applicable, affording carboxylic acids amenable of further downstream diversification. Interestingly, N- and O-tethered 1,6-diynes were reactive under optimized conditions to provide dicarboxylic acids in moderate to good yields (**2al** and **2am**). We were especially intrigued to find that the terminal alkynes derived from (+)-menthol and estradiol were competent substrates to afford the corresponding products **2an** and **2ao** in 48% and 73% yield, respectively.

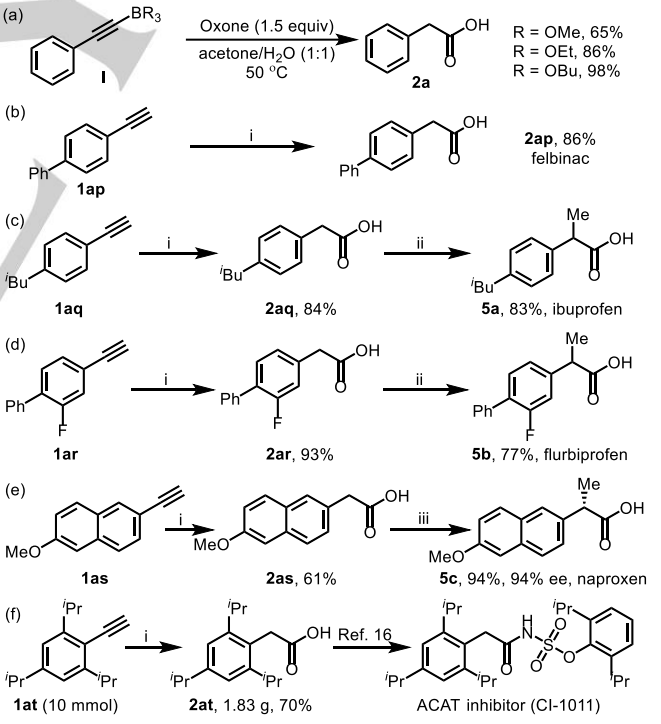
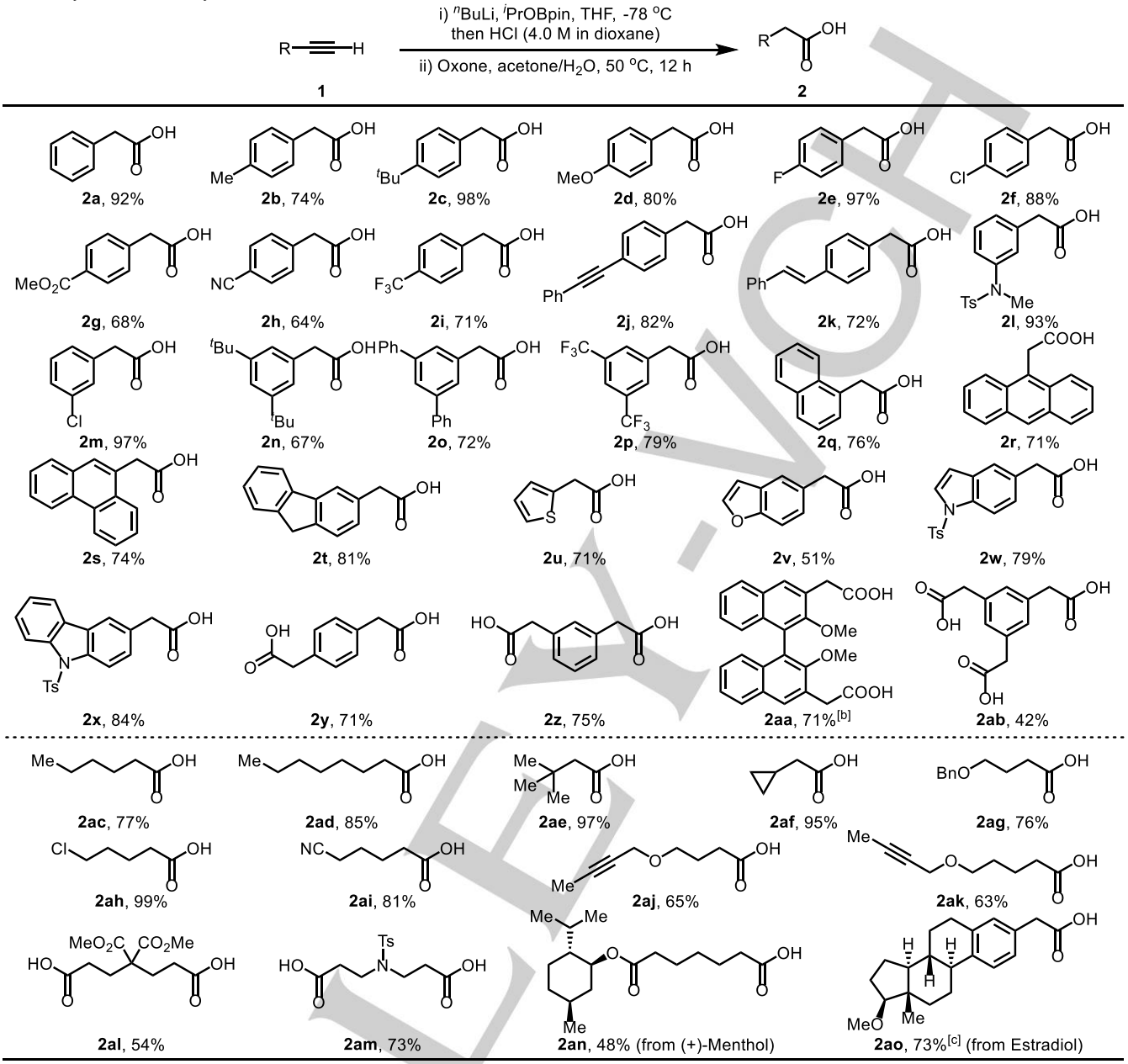


Figure 2. Synthesis of drug molecules (a: felbinac; b: ibuprofen; c: flurbiprofen; d: naproxen; e: ACAT inhibitor). Reaction conditions: i) **1** (1.0 mmol), ^{n}BuLi (1.2 equiv), -78 °C, 1 h; ^{i}PrOBpin (1.2 equiv), -78 °C, 2 h, then HCl (1.5 equiv, 4.0 M in dioxane); then Oxone (1.5 equiv), acetone/H_2O (V/V=1:1), 50 °C, 12 h. ii) LHMDS (4.0 equiv), MeI (4.0 equiv), THF, rt. iii) ^{n}BuLi (4.0 equiv), MeI (4.0 equiv), (*R*,*R*)-Koga amine (1.03 equiv), THF, -78 °C.

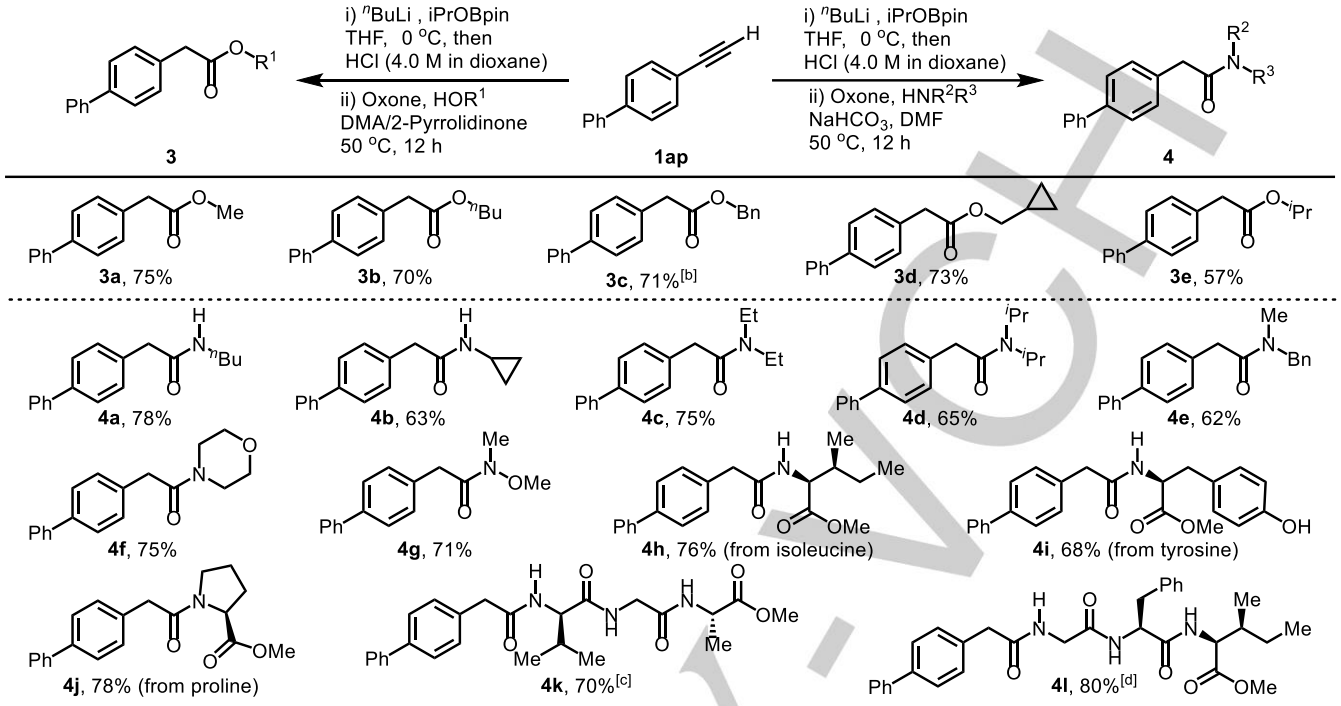
Table 2. Synthesis of Carboxylic Acids[a]



[a] Standard conditions: i) **1a** (5.0 mmol), ^{n}BuLi (1.2 equiv), -78 °C, 1 h; ^{i}PrOBpin (1.2 equiv), -78 °C, 2 h, then HCl (1.5 equiv, 4.0 M in dioxane) ; ii) Oxone (1.5 equiv), acetone/H_2O (V/V=1:1), 50 °C, 12 h; isolated yields. [b] **1aa** (1.0 mmol). [c] **1ao** (0.5 mmol).

Encouraged by the success of water serving as a nucleophile, we investigated the applicability of the protocol to alcohol and amine nucleophiles given the synthetic values of their adducts (ester and amide). Under the standard conditions, unfortunately, the reaction with a representative alcohol[14] and amine resulted in low yields due to protodeboronation. However, a brief survey of several solvents established that a mixture of DMA and 2-pyrrolidinone was the most efficient for ester formation, while a combination of DMF and $NaHCO_3$ provided the best results when amine nucleophiles were employed. As summarized in Table 3, a number of primary and secondary alcohols were suitable nucleophiles for this oxidation (**3a**-**e**). In sharp contrast, when a tertiary alcohol such as *tert*-butanol was employed, the reaction gave the ester product in a low yield, and instead produced carboxylic acid **2ap**. It is intriguing to note that both primary and secondary amines also reacted smoothly to produce amides in good yields. Gratifyingly, N-methoxymethylamine was successfully transferred to form Weinreb amide **4g** in 71% yield, which is a useful building block for ketone/aldehydesynthesis. The most remarkable feature of this process is probably the ability to employ a range of amino acids, such as isoleucine, tyrosine, and proline, as well as peptides as the nucleophiles to give the corresponding amides and peptides in high yields (**4h**-**l**), thus providing a convenient approach for the synthesis and modification of peptides.

Table 3. Synthesis of Esters and Amides[a]



[a] Reaction conditions for ester formation: i) **1ap** (1.0 mmol), ^{n}BuLi (1.2 equiv), 0 °C, 1 h; ^{i}PrOBpin (1.2 equiv), 0 °C, 2 h, then HCl (1.5 equiv, 4.0 M in dioxane); ii) Oxone (3.0 equiv), alcohol (2.0 mL), DMA/2-pyrrolidinone (V/V=1:1), 50 °C, 12 h. Reaction conditions for amide formation: i) **1ap** (1.0 mmol), ^{n}BuLi (1.2 equiv), 0 °C, 1 h; ^{i}PrOBpin (1.2 equiv), 0 °C, 2 h; ii) Oxone (1.5 equiv), amine (15 equiv), $NaHCO_3$ (4.5 equiv), DMF, 50 °C, 12 h, isolated yields. [b] BnOH (3.0 mL). [c] **1ap** (0.3 mmol), $NaHCO_3$ (20 equiv) and ammonium trifluoroacetate (15 equiv) instead of free amine were used. [d] **1ap** (0.2 mmol).

As a further demonstration of the robustness and practicability of this protocol, other alkynyl boronates generated from $B(OMe)_3$, $B(OEt)_3$, and $B(OBu)_3$ were treated with the standard reaction conditions, and all proceeded smoothly to furnish the product **2a,** albeit with lower efficiency compared with the alkynyl boronate made from ^{i}PrOBpin (Figure 2a). The application of this method was then highlighted by the synthesis of several nonsteroidal anti-inflammatory drugs (NSAID) of the arylacetic acid family (Figure 2b-f). Under our conditions, commercial 4-ethynylbiphenyl was directly converted to felbinac **2ap** in 86% yield, which is used to treat muscle inflammation and arthritis. Furthermore, the successful oxidation of terminal alkynes **1aq**-**as** to the corresponding arylacetic acids **2aq**-**as** and subsequent methylation, provided an efficient entry to ibuprofen **5a**, flurbiprofen **5b**, and (*S*)-naproxen **5c**,[15] which are well known pain or fever reducers. It should also be noted that the utility of this methodology was additionally demonstrated through a gram-scale reaction of **1at** to yield 1.86 g of **2at**, which is a key intermediate for the synthesis of an ACAT inhibitor (CI-1011).[16]

In summary, we have developed a robust method for the synthesis of carboxylic acids, esters, and amides via oxidation of alkynyl boronates in the presence of inexpensive Oxone. This protocol exhibits high efficiency and excellent functional-group tolerance. The reaction proceeded with a broad range of aryl and alkyl terminal alkynes, and tolerated various nucleophiles, including water, primary and secondary alcohols, and amines. Furthermore, the amenability of peptides is particularly attractive from the perspective of late-stage functionalization. The practicability of this methodology was demonstrated by the preparation of several pharmaceutical molecules. More importantly, this transformation represents the first example of C(sp)–B bond oxidation used for the synthesis of carboxylic acids and their derivatives, and preliminary mechanistic studies have revealed that the mechanism might involve a ketene intermediate generated from a boron ynolate,[17] which would enable this strategy to open up a new avenue for the development of boron ynolate and ketene chemistry.

Acknowledgements

Financial support from the National Natural Science Foundation of China (Grant No. 21702056, 21971059), the National Program for Thousand Young Talents of China and the Fundamental Research Funds for the Central Universities are greatly appreciated.

Conflict of interest

The authors declare no competing financial interests.

Keywords: alkynes • boron • carboxylic acids • oxidation • synthetic method

[1] For selected reviews, see: a) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457-2483; b) D. V. Partyka, *Chem. Rev.* **2011**, *111*, 1529-1595; c) D. G. Hall, *Boronic Acids: Preparation and*

Applications in Organic Synthesis, Medicine and Materials, Vol. 1 and 2, 2nd ed., Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, **2011**. d) A. Coca, *Boron reagents in synthesis*, *Vol. 1236*, American Chemical Society, Washington, DC, **2016**, pp. 1–25; e) D. Leonori, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2015**, *54*, 1082-1096; *Angew. Chem.* **2015**, *127*, 1096-1111; f) C. Sandford, V. K. Aggarwal, *Chem. Commun.* **2017**, *53*, 5481-5494.

[2] E. Frankland, B. F. Duppa, *Justus Liebigs Ann. Chem.* **1860**, *115*, 319-322.

[3] a) H. C. Brown, B. C. S. Rao, *J. Am. Chem. Soc.* **1956**, *78*, 5694-5695; b) H. C. Brown, *Organic syntheses via boranes*, Wiley, **1975**.

[4] For selected examples, see: a) Y. Q. Zou, J. R. Chen, X. P. Liu, L. Q. Lu, R. L. Davis, K. A. Jørgensen, W. J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 784-788; *Angew. Chem.* **2012**, *124*, 808-812; b) S. P. Pitre, C. D. McTiernan, H. Ismaili, J. C. Scaiano, *J. Am. Chem. Soc.* **2013**, *135*, 13286-13289; c) T. C. Stephens, G. Pattison, *Org. Lett.* **2017**, *19*, 3498-3501; d) C. Zhu, R. Wang, J. R. Falck, *Org. Lett.* **2012**, *14*, 3494-3497; e) L. E. Longobardi, A. Fürstner, *Chem. Eur. J.* **2019**, *25*, 10063-10068.

[5] Selected examples for transformations of alkynyl boronate, see: a) M. Suginome, M. Shirakura, A. Yamamoto, *J. Am. Chem. Soc.* **2006**, *128*, 14438-14439; b) A. L. Auvinet, J. P. A. Harrity, *Angew. Chem. Int. Ed.* **2011**, *50*, 2769-2772; *Angew. Chem.* **2011**, *123*, 2821-2824; c) D. A. Mundal, K. E. Lutz, R. J. Thomson, *J. Am. Chem. Soc.* **2012**, *134*, 5782-5785; d) H. Wang, C. Grohmann, C. Nimphius, F. Glorius, *J. Am. Chem. Soc.* **2012**, *134*, 19592-19595; e) M. Nogami, K. Hirano, M. Kanai, C. Wang, T. Saito, K. Miyamoto, A. Muranaka, M. Uchiyama, *J. Am. Chem. Soc.* **2017**, *139*, 12358-12361; f) Y. Jiang, A. B. Diagne, R. J. Thomson, S. E. Schaus, *J. Am. Chem. Soc.* **2017**, *139*, 1998-2005; g) E. E. Lin, J.-Q. Wu, F. Schäfers, X.-X. Su, K.-F. Wang, J.-L. Li, Y. Chen, X. Zhao, H. Ti, Q. Li, T.-M. Ou, F. Glorius, H. Wang, *Commun. Chem.* **2019**, *2*, 34; h) W. X. Lv, Z. Li, E. Lin, J. L. Li, D. H. Tan, Y. H. Cai, Q. Li, H. Wang, *Chem. Eur. J.* **2019**, *25*, 4058-4061; i) W.-X. Fan, J.-L. Li, W.-X. Lv, L. Yang, Q. Li, H. Wang, *Chem. Commun.* **2020**, *56*, 82-85.

[6] P. J. Stang, *Acc. Chem. Res.* **1991**, *24*, 304-310.

[7] M. K. Louie, J. S. Francisco, M. Verdicchio, S. J. Klippenstein, A. Sinha, *J. Phys. Chem. A* **2015**, *119*, 4347-4357.

[8] a) H. C. Brown, N. G. Bhat, M. Srebnik, *Tetrahedron Lett.* **1988**, *29*, 2631-2634; b) L. Deloux, E. Skrzypczak-Jankun, B. V. Cheesman, M. Srebnik, M. Sabat, *J. Am. Chem. Soc.* **1994**, *116*, 10302-10303; c) C.-I. Lee, J. Zhou, O. V. Ozerov, *J. Am. Chem. Soc.* **2013**, *135*, 3560-3566; d) R. J. Procter, M. Uzelac, J. Cid, P. J. Rushworth, M. J. Ingleson, *ACS Catal.* **2019,** *9*, 5760−5771; e) E. A. Romero, R. Jazzar, G. Bertrand, *Chem. Sci.* **2017**, *8*, 165-168.

[9] a) S. H. Cho, E. J. Yoo, I. Bae, S. Chang, *J. Am. Chem. Soc.* **2005**, *127*, 16046-16047; b) M. P. Cassidy, J. Raushel, V. V. Fokin, *Angew. Chem. Int. Ed.* **2006**, *45*, 3154-3157; c) W.-K. Chan, C.-M. Ho, M.-K. Wong, C.-M. Che, *J. Am. Chem. Soc.* **2006**, *128*, 14796-14797; d) I. Kim, C. Lee, *Angew. Chem. Int. Ed.* **2013**, *52*, 10023-10026; *Angew. Chem.* **2013**, *125*, 10207-10210; e) M. Zeng, S. B. Herzon, *J. Org. Chem.* **2015**, *80*, 8604-8618; f) A. Álvarez-Pérez, M. A. Esteruelas, S. Izquierdo, J. A. Varela, C. Saá, *Org. Lett.* **2019**, *21*, 5346-5350.

[10] a) L. J. Gooßen, N. Rodríguez, K. Gooßen, *Angew. Chem. Int. Ed.* **2008**, *47*, 3100-3120; *Angew. Chem.* **2008**, *120*, 3144-3164; b) N. Rodriguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030-5048; c) C. Min, D. Seidel, *Chem. Soc. Rev.* **2017**, *46*, 5889-5902.

[11] a) Z. Wan, C. D. Jones, D. Mitchell, J. Y. Pu, T. Y. Zhang, *J. Org. Chem.* **2006**, *71*, 826-828; b) W. Ren, Y. Xia, S.-J. Ji, Y. Zhang, X. Wan, J. Zhao, *Org. Lett.* **2009**, *11*, 1841-1844; c) C. Zhang, N. Jiao, *J. Am. Chem. Soc.* **2009**, *132*, 28-29; d) C.-F. Xu, M. Xu, Y.-X. Jia, C.-Y. Li, *Org. Lett.* **2011**, *13*, 1556-1559; e) M. E. Jung, G. Deng, *Org. Lett.* **2014**, *16*, 2142-2145; f) Y. Miao, A. Dupe, C. Bruneau, C. Fischmeister, *Eur. J. Org. Chem.* **2014**, *2014*, 5071-5077.

[12] a) A. Wang, H. Jiang, *J. Am. Chem. Soc.* **2008**, *130*, 5030-5031; b) D. Yang, F. Chen, Z.-M. Dong, D.-W. Zhang, *J. Org. Chem.* **2004**, *69*, 2221-2223; c) G. Urgoitia, R. SanMartin, M. T. Herrero, E. Domínguez, *ACS Catal.* **2017**, *7*, 3050-3060; d) S. Kolle, S. Batra, *Org. Biomol. Chem.* **2016**, *14*, 11048-11060.

[13] a) H. C. Brown, N .G. Bhat, M. Srebnik, *Tetrahedron Lett.* **1988**, *29*, 2631-2634; b) H. E. Ho, N. Asao, Y. Yamamoto, T. Jin, *Org. Lett.* **2014**, *16*, 4670-4673; c) A. J. J. Lennox, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **2012**, *134*, 7431-7441. The solution of **Ia** in acetone and H_2O (1:1) stirred at 50 °C for 12h resulted in full conversion to phenylacetylene.

[14] The carboxylic acid was obtained when phenol was employed as a nucleophile.

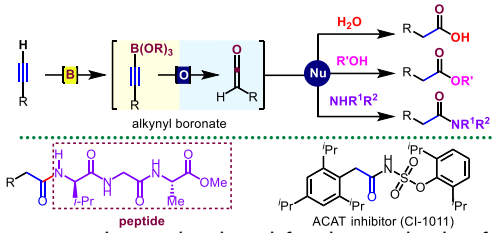
[15] C. E. Stivala, A. Zakarian, *J. Am. Chem. Soc.* **2011**, *133*, 11936-11939.

[16] G. J. Dozeman, P. J. Fiore, T. P. Puls, J. C. Walker, *Org. Process Res. Dev.* **1997**, *1*, 137-148.

[17] See more details about mechanistic studies in Supporting Information.

10.1002/anie.202000988

COMMUNICATION



A general efficient protocol was developed for the synthesis of carboxylic acids, esters, and amides via oxidation of alkynyl boronates, generated directly from terminal alkynes. This protocol represents the first example of C(sp)–B bond oxidation. This approach displays a broad substrate scope, including aryl and alkyl alkynes, and exhibits excellent functional group tolerance. Water, primary and secondary alcohols, and amines are suitable nucleophiles for this transformations. Notably, amino acids and peptides can be used as nucleophiles, providing an efficient method for the synthesis and modification of peptides. The practicability of this methodology was further highlighted by the preparation of pharmaceutical molecules.

*C. Li, P. Zhao, R. Li, B. Zhang, W. Zhao**

Page No. – Page No.

Oxidation of Alkynyl Boronates to Carboxylic Acids, Esters and Amides