Oxidative β-Halogenation of Alcohols: A Concise and Diastereoselective Approach to Halohydrins

Lingsheng Ai[a]
Weijin Wang[a]
Jialiang Wei[a]
Qing Li[a]
Song Song*[a,b]
Ning Jiao*[a,b]

[a] State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Xue Yuan Rd. 38, Beijing 100191, P. R. of China
ssong@bjmu.edu.cn
jiaoning@pku.edu.cn
[b] State Key Laboratory of Drug Research Shanghai Institute of Materia Medical Chinese Academy of Sciences, Shanghai 201203, P. R. of China

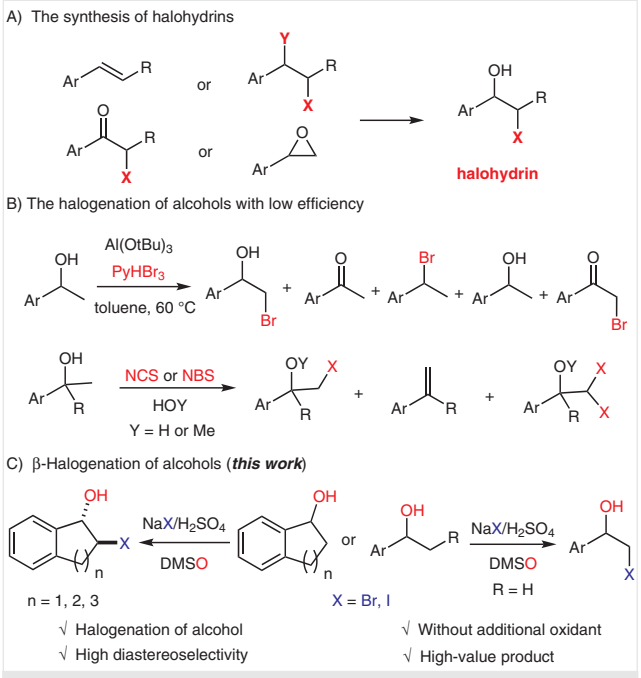
Published as part of the *30 Years SYNLETT – Pearl Anniversary Issue*

Received: 26.08.2018
Accepted after revision: 23.10.2018
Published online: 21.11.2018
DOI: 10.1055/s-0037-1610385; Art ID: st-2018-b0556-l

Abstract β-Halohydrins bearing transformable halo- and hydroxyl groups, are easily converted into various valuable blocks in organic and pharmaceutical synthesis. A diastereoselective β-halogenation of benzylic alcohols was achieved under simple and low-cost conditions, which provided a direct synthesis of β-halohydrins. The simple reaction conditions, easily available reagents, high diastereoselectivities, and additional oxidant-free make this reaction very attractive and practical.

Key words halogenation, alcohols, dimethyl sulfoxide, halohydrins, oxidation

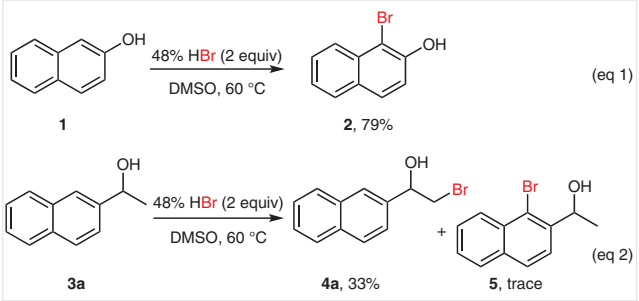
Organohalides are one of the most widespread and important chemicals and are present in more than 4500 natural products,[1] as well as a great number of industrially valuable products such as pharmaceuticals, fire retardants, agrochemicals, and some new materials.[2] In addition, it is no doubt that organohalides with their general reactivity make the chemical synthesis more simple, accessible, and valuable. β-Halohydrins, bearing a hydroxyl and halide functional group, are privileged building blocks in organic synthesis and could be conveniently converted into other significant organic intermediates such as azido alcohols, amino alcohols, and epoxides, all of which are widely used in the synthesis of many highly value-added chemicals.[3] Up to date, halohydrins could be prepared by halohydroxylation of olefins,[4] reduction of haloketones,[5] ring-opening reaction of epoxides,[6] and nucleophilic substitution of benzyl halides[7] (Scheme 1, A). In most cases, the halo atom of halohydrins was introduced by the halo cation such as *N*-halosuccinimides and their analogues which are not good choices for large-scale halogenations because of expensive price and low atomic economy. Inspired by the enzyme-catalyzed aerobic oxidative halogenation in nature,[8] a sophisticated approach by *in situ* generating the halogenating reagent from oxidant and halide salts is widely applied in halogenations[9,10] especially in the oxidative halohydroxylation of olefins which provided a direct approach to halohydrins,[10] although solvent, halide source, acid, oxygen source, and oxidant were required in these approaches.



Scheme 1 The synthesis of halohydrins

The β-halogenation of alcohols[11] provides another direct approach to halohydrins. However, the reported β-halogenation of alcohols with halo cations always delivered mixtures of products (Scheme 1, B).[12] As our continuous development of DMSO-based reactions,[13] we herein reported our success in β-halogenation of alcohols with *in situ* generation of halo cation from sodium halides and DMSO (Scheme 1, C). The magic multiple role of DMSO[14] as solvent, oxidant,[15] stabilizer of halo cations,[10j] and nucleophile[16] successfully enabled this novel transformation. Very importantly and interestingly, the diastereoselectivities of this transformation were very high (>25:1)

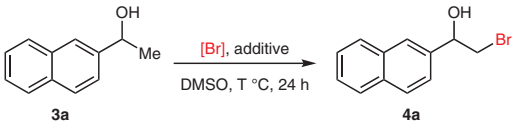
This reaction began with an unexpected bromination. As reported,[12a,17] the combination of aqueous HBr and DMSO showed high efficiency in the aromatic bromination of 2-naphthol **1** to deliver aryl bromide **2** in 79% yield (Scheme 2, eq 1). To our surprise, when changing the substituent of naphthalene from –OH (**1**) to –CH(OH)CH_3(**3a**), the aromatic bromination was totally supressed, and aliphatic bromination at the methyl group occurred to afford bromohydrin **4a** in 33% yield (Scheme 2, eq 2).[18] Due to the importance of the halohydrins, this bromination drew our great interest.



Scheme 2

We then optimized the bromination conditions (Table 1). The reaction did not work when changing aqueous HBr to KBr (Table 1, entry 1). This experiment revealed the acidic conditions were essential for this reaction. When HBr was generated by KBr and H_2SO_4 *in situ*, **4a** could be obtained in 38% yield (Table 1, entry 2). The yield increased to 44% using NaBr instead of KBr (Table 1, entry 3). Other organic acids such as TsOH, MsOH, or TfOH showed lower efficiency than that of H_2SO_4 (Table 1, entries 3–6). The amount of acidic additive influenced the yield strongly. Compound **4a** was obtained in 73% yield when 4 equiv of H_2SO_4were employed (Table 1, entry 9). When the reaction preformed with 1.2 equiv of NaBr, only 46% yield of **4a** was obtained (Table 1, entry 11). Compound **4a** was not detected when the reaction was carried out in other solvents (Table 1, entries 12 and 13). These results indicated that DMSO was indispensable in this bromination.

Table 1 Optimization of the Reaction Conditions[a]



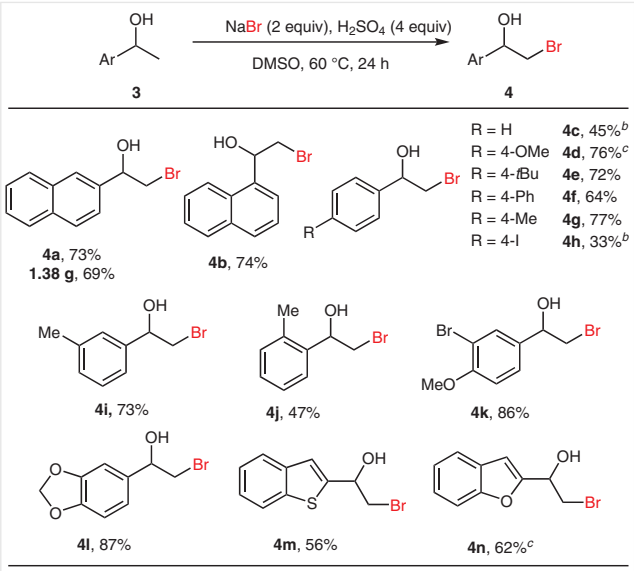
3a 4a

Entry	[Br] (equiv)	Additive (equiv)	Solvent	T (°C)	Yield (%)[b]
1	KBr (2)	–	DMSO	60	0
2	KBr (2)	H_2SO_4 (2)	DMSO	60	38
3	NaBr (2)	H_2SO_4 (2)	DMSO	60	44
4	NaBr (2)	TsOH (2)	DMSO	60	25
5	NaBr (2)	MsOH (2)	DMSO	60	27
6	NaBr (2)	TfOH (2)	DMSO	60	44
7	NaBr (2)	H_2SO_4 (2)	DMSO	40	trace
8	NaBr (2)	H_2SO_4 (4)	DMSO	80	mess
9	NaBr (2)	H_2SO_4 (4)	DMSO	60	73
10	NaBr (2)	H_2SO_4 (8)	DMSO	60	45
11	NaBr (1.2)	H_2SO_4 (4)	DMSO	60	46
12	NaBr (2)	H_2SO_4 (4)	DCE	60	0
13	NaBr (2)	H_2SO_4 (4)	THF	60	0

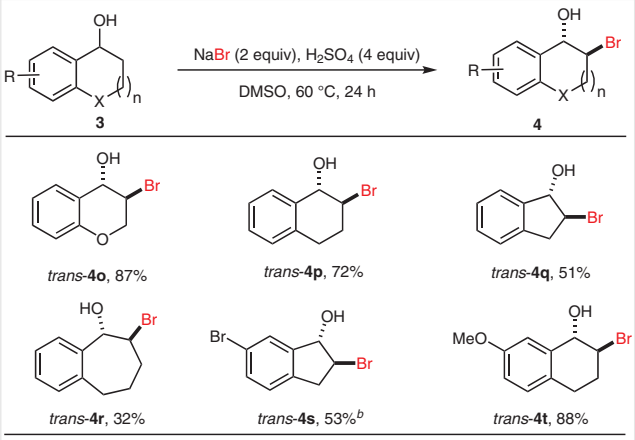
[a] Reaction conditions: The solution of **3a** (0.5 mmol), bromide source, and additive in solvent (1 mL) was stirred under air for 24 h.
[b] Isolated yields.

We then investigated the substrate scope of this novel bromination (Scheme 3). Various benzylic alcohols worked well under the standard conditions. It was noteworthy that when an electron-donating group such as methoxy, *tert*-butyl, or methyl was contained at the aryl ring, the corresponding bromohydrins **4d**,**e** and **4g** were highly selectively obtained in good yields, respectively. The reported bromination on the electron-rich arenes was not detected in this protocol. In addition, heteroarenes such as benzothiophenyl- and benzofuranyl-substituted alcohols were well tolerated in this transformation and converted into bromohydrins **4m**,**n** in moderate yields. Furthermore, the gram-scale reaction of **3a** with 69% yield shows the potential application of this low-cost protocol. However, no bromohydrin was detected when alcohols without benzylic substituent was exposed under the standard conditions.

It is very challenging to control the diastereoselectivity of β-functionalization of alcohols. To our delight, the six-membered cyclic alcohols **3o**,**p** produced *trans*-bromohydrins **4o**,**p** as the sole product in high efficiency (Scheme 4). Although the five-membered and seven-membered cyclic alcohols **3q**,**r** afforded the target bromohydrins **4q**,**r** in moderate yields, the diastereoselectivities of these brominations were also very high (>25:1).[18] The substituents on the phenyl ring had little influence on the efficiency and diastereoselectivity.

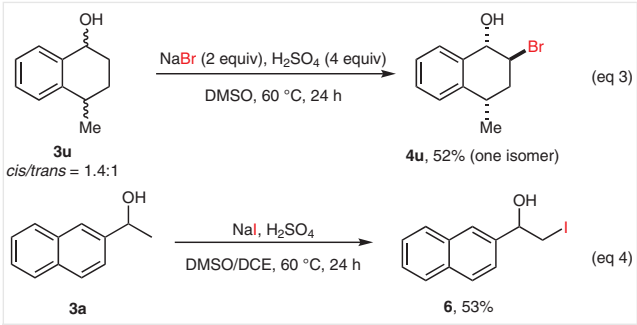


Scheme 3 Substrate scope of benzylic alcohols.[a] [a]Reaction conditions: The solution of **3a** (0.5 mmol), NaBr (1 mmol), and H_2SO_4(2 mmol) in DMSO (1 mL) was stirred under air at 60 °C for 24 h. Isolated yields. [b]H_2SO_4(4 mmol) was used. [c]H_2SO_4(1.2 mmol) was used.



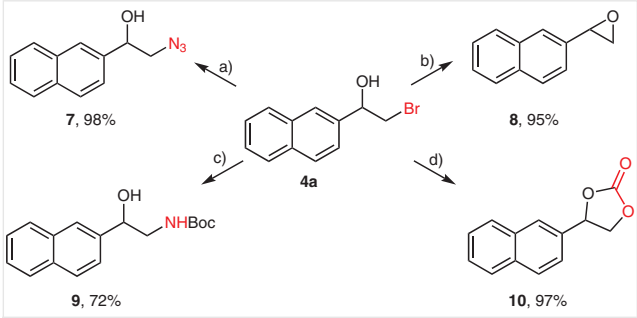
Scheme 4 Diastereoselective bromination of alcohols.[a] [a] Reaction conditions: The solution of **3** (0.5 mmol), NaBr (1 mmol), and H_2SO_4 (2 mmol) in DMSO (1 mL) was stirred under air at 60 °C for 24 h. Isolated yields. [b] H_2SO_4(4 mmol) was used.

When mixture of *cis*/*trans* (1.4:1) alcohol **3u** was subjected to the standard conditions, bromohydrin **4u** was produced with only one diastereoselective isomer in 52% yield (Scheme 5, eq 3). This experiment demonstrates the excellent diastereoselectivity of present bromination reaction. Compared to C–Br bond, the C–I bonds are more reactive but hard to construct. To our delight, the β-iodination of alcohol **3a** also underwent smoothly and produced the desired iodohydrin **6** in 53% yield using NaI and H_2SO_4 as the simple reagents (Scheme 5, eq 4).



Scheme 5

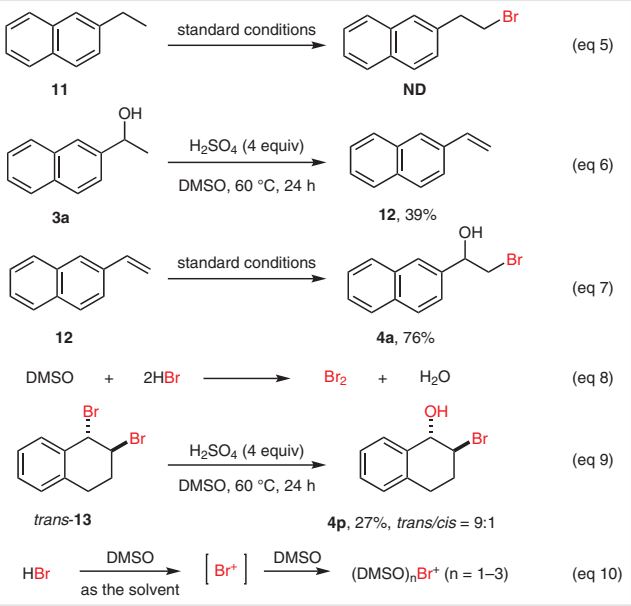
The bromohydrin **4a** was conveniently converted into other valuable products (Scheme 6). Azido alcohol **7**, the key intermediate of β-blocker pronethalol[19a] and other bioactive molecules,[19b] was synthesized in 98% yield by stirring **4a** with NaN_3 at 60 °C in DMSO. Exposure of **4a** with aqueous NaOH solvent in THF afforded epoxide **8** in 95% yield, which could easily react with amines to produce amino alcohol drugs.[19c] Amino alcohol **9** also could be synthesized by treating **4a** with ammonium hydroxide in MeOH. The reaction of **4a** and CO_2 in the presence of NMe_4HCO_3 provided carbonic ester **10** in 97% yield.



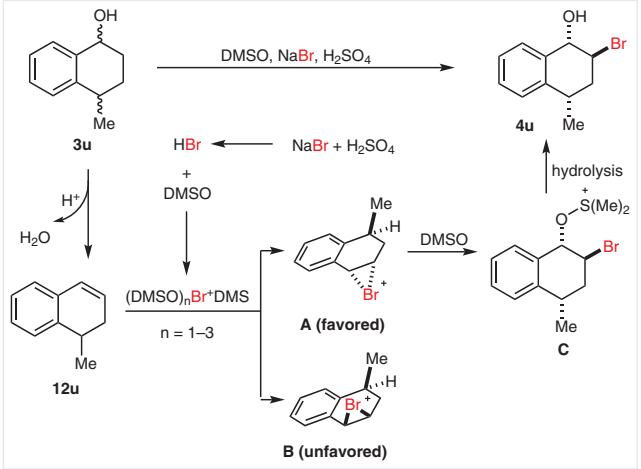
Scheme 6 Transformation of bromohydrin **4a**. Reaction conditions: a) NaN_3 (2 equiv), DMSO, 60 °C, 12 h. b) Aqueous NaOH (4 equiv), THF, 0 °C, 1 h. c) $NH_3{\cdot}H_2O$ (28%), MeOH, 25 °C, 4 h, then Boc_2O (2 equiv), NEt_3 (2 equiv), DCM, 25 °C, 4 h. d) NH_4HCO_3 (2 equiv), CO_2 (1 atm), MeCN, 25 °C, 0.5 h.

To investigate the mechanism of this bromination, control experiments were performed. Ethyl naphthalene **11** could not be brominated under the standard conditions, indicating the hydroxyl was indispensable for present bromination (Scheme 7, eq 5). Treatment of alcohol **3a** under standard conditions in the absence of NaBr afforded alkene **12** in 39% yield (Scheme 7, eq 6). Subjecting the obtained alkene **12** back to the standard conditions led to **4a** in 76% yield, which indicated that alkene **12** might be the key intermediate of this transformation (Scheme 7, eq 7).

Previous studies reported that the hydrobromic acids could be oxidized by DMSO to molecular bromine (Scheme 7, eq 8).[17] If Br_2 was generated, it would readily react with



Scheme 7



Scheme 8 Proposed mechanism

the *in situ* generated alkene **12** to afford a *trans*-dibrominated product **13**.[13d] However, exposure of *trans*-**13** under the conditions for 24 h provided the product **4p** only in 27% yield and showed much lower diastereoselectivity (*trans*/*cis* = 9:1, Scheme 7, eq 9). This experiment demonstrated that the corresponding dibromination was not involved in this process. We therefore suspected that the HBr was oxidized to bromo cation (Br^+) which was stabilized by DMSO through coordination (Scheme 7, eq 10).[10j]

On the basis of the above experimental results and previous reports,[18,20] we proposed the mechanism of this halogenation of alcohols in Scheme 8. Under acidic conditions, alkene **12u** is generated by the hydroxyl elimination process. Meanwhile, Br^+ is generated and immediately coordinated by DMSO to give $(DMSO)_nBr^+DMS$ (n = 1–3).[10j] The electrophilic addition of Br^+ to alkene **12u** preferentially affords bromonium **A** rather than **B** because of the steric hindrance of the methyl group. Further nucleophilic attack of DMSO to **A** delivers the alkoxysulfonium **C** which quickly decomposes to produce *trans*-bromohydrin **4u**.[10j,16a,i]

In conclusion, we have developed a novel β-halogenation of benzylic alcohols for the efficient synthesis of high-value halohydrins. The simple reaction conditions, easily available reagents, and high diastereoselectivity control make this protocol very attractive and practical. Mechanistic studies reveal that halo cation (X^+) rather than molecular halogen is involved in the transformation. This reaction demonstrates a new application of DMSO and HX in organic synthesis and would promote the application of the alkene *in situ* generation strategy.

Funding Information

Financial support from the National Basic Research Program of China (973 Program) (grant No. 2015CB856600), the National Natural Science Foundation of China (Nos. 21602005, 21632001, 21772002), and the State Key Laboratory of Drug Research are greatly appreciated.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610385.

References

(1) Gribble, G. W. *J. Chem. Educ.* **2004**, *81*, 1441.
(2) Dagani, M. J.; Barda, H. J.; Benya, T. J.; Sanders, D. C. *Bromine Compounds in Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, **2002**.
(3) *Organic Bromine and Iodine Compounds in The Handbook of Environmental Chemistry*; Neilson, A. H., Ed.; Springer: Berlin, Heidelberg, **2003**.
(4) Buckles, R. E.; Maurer, J. E. *J. Org. Chem.* **1953**, *18*, 1585.
(5) Naimi-Jamal, M. R.; Mokhtari, J.; Dekamin, M. G.; Kaupp, G. *Eur. J. Org. Chem.* **2009**, 3567.
(6) (a) Ren, W. M.; Liu, Y.; Lu, X. B. *J. Org. Chem.* **2014**, *79*, 9771. (b) Naeimi, H. *J. Chin. Chem. Soc.* **2008**, *55*, 1156.
(7) Bhosale, S. S.; Joshi, P. L.; Rao, A. S. *Org. Prep. Proced. Int.* **1992**, *24*, 695.
(8) For selected reviews on enzyme-catalyzed oxidative halogenations, see: (a) Vaillancourt, F. H.; Yeh, E.; Vosburg, D. A.; Garneau-Tsodikova, S.; Walsh, C. T. *Chem. Rev.* **2006**, *106*, 3364. (b) Lewis, J. C.; Coelho, P. S.; Arnold, F. H. *Chem. Soc. Rev.* **2011**, *40*, 2003.
(9) (a) Podgoršek, A.; Zupan, M.; Iskra, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 8424. (b) Yonehara, K.; Kamata, K.; Yamaguchi, K.; Mizuno, N. *Chem. Commun.* **2011**, *47*, 1692. (c) Yang, L.; Lu, Z.; Stahl, S. S. *Chem. Commun.* **2009**, *45*, 6460. (d) Podgorsek, A.; Eissen, M.; Fleckenstein, J.; Stavber, S.; Zupan, M.; Iskra, J. *Green Chem.* **2009**, *11*, 120. (e) Zhang, G. F.; Liu, R. H.; Xu, Q.; Ma, L. X.; Liang,

X. M. *Adv. Synth. Catal.* **2006**, *348*, 862. (f) Yu, T.-Y.; Wang, Y.; Hu, X.-Q.; Xu, P.-F. *Chem. Commun.* **2014**, *50*, 7817. (g) Wang, G.-W.; Gao, J. *Green Chem.* **2012**, *14*, 1125. (h) Adimurthy, S.; Ghosh, S.; Patoliya, P. U.; Ramachandraiah, G.; Agrawal, M.; Gandhi, M. R.; Upadhyay, S. C.; Ghosh, P. K.; Ranu, B. C. *Green Chem.* **2008**, *10*, 232. (i) Rana, S.; Bag, S.; Patra, T.; Maiti, D. *Adv. Synth. Catal.* **2014**, *356*, 2453. (j) Bedrač, L.; Iskra, J. *Adv. Synth. Catal.* **2013**, *355*, 1243.

(10) (a) Sels, B. F.; De Vos, D. E.; Jacobs, P. A. *J. Am. Chem. Soc.* **2001**, *123*, 8350. (b) Pandit, P.; Gayen, K. S.; Khamarui, S.; Chatterjee, N.; Maiti, D. K. *Chem. Commun.* **2011**, *47*, 6933. (c) Dewkar, G. K.; Narina, S. V.; Sudalai, A. *Org. Lett.* **2003**, *5*, 4501. (d) Yang, X.; Wu, J.; Mao, X.; Jamison, T. F.; Hatton, T. A. *Chem. Commun.* **2014**, *50*, 3245. (e) Darensbourg, D. J.; Wilson, S. J. *J. Am. Chem. Soc.* **2011**, *133*, 18610. (f) Kozhushkov, S. I.; Yufit, D. S.; de Meijere, A. *Adv. Synth. Catal.* **2005**, *347*, 255. (g) Sels, B.; De Vos, D.; Buntinx, M.; Pierard, F.; Kirsch-De Mesmaeker, A.; Jacobs, P. *Nature* **1999**, *400*, 855. (h) Barluenga, J.; Gonzalez, J. M.; Campos, P. J.; Asensio, G. *Angew. Chem.* **1985**, *97*, 341. (i) Rao, D. S.; Reddy, T. R.; Babachary, K.; Kashyap, S. *Org. Biomol. Chem.* **2016**, *14*, 7529. (j) Ashikari, Y.; Shimizu, A.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2013**, *135*, 16070.

(11) For α-functionalization of alcohols, see: (a) Jeffrey, J. L.; Terrett, J. A.; MacMillan, D. W. *Science* **2015**, *349*, 1532. (b) Shi, L.; Tu, Y.-Q.; Wang, M.; Zhang, F.-M.; Fan, C.-A.; Zhao, Y.-M.; Xia, W.-J. *J. Am. Chem. Soc.* **2005**, *127*, 10836. (c) Zhang, S.-Y.; Tu, Y.-Q.; Fan, C.-A.; Zhang, F.-M.; Shi, L. *Angew. Chem. Int. Ed.* **2009**, *48*, 8761. For β-functionalization of alcohols, see: (d) Espino, C. G.; Du Bois, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 598. (e) Ren, Z.; Mo, F.; Dong, G. *J. Am. Chem. Soc.* **2012**, *134*, 16991. (f) Wappes, E. A.; Nakafuku, K. M.; Nagib, D. A. *J. Am. Chem. Soc.* **2017**, *139*, 10204. (g) Bunescu, A.; Butcher, T. W.; Hartwig, J. F. *J. Am. Chem. Soc.* **2018**, *140*, 1502. For γ-functionalization of alcohols, see: (h) Simmons, E. M.; Hartwig, J. F. *Nature* **2012**, *483*, 70. (i) Alderson, J. M.; Phelps, A. M.; Scamp, R. J.; Dolan, N. S.; Schomaker, J. M. *J. Am. Chem. Soc.* **2014**, *136*, 16720. (j) Espino, C. G.; Wehn, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935. (k) Chen, K.; Richter, J. M.; Baran, P. S. *J. Am. Chem. Soc.* **2008**, *130*, 7247. (l) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2008**, *130*, 9220. For δ-functionalization of alcohols, see: (m) Hu, A.; Guo, J.-J.; Pan, H.; Tang, H.; Gao, Z.; Zuo, Z. *J. Am. Chem. Soc.* **2018**, *140*, 1612. (n) Wu, X.; Wang, M.; Huan, L.; Wang, D.; Wang, J.; Zhu, C. *Angew. Chem. Int. Ed.* **2018**, *57*, 1640. (o) Zhang, J.; Li, Y.; Zhang, F.; Hu, C.; Chen, Y. *Angew. Chem. Int. Ed.* **2016**, *55*, 1872. (p) Wang, C. Y.; Harms, K.; Meggers, E. *Angew. Chem. Int. Ed.* **2016**, *55*, 13495.

(12) (a) Cami-Kobeci, G.; Williams, J. M. J. *Synlett* **2003**, 124. (b) Ajvazi, N.; Stavber, S. *Molecules* **2016**, *21*, 1325. (c) Klimczyk, S.; Huang, X.; Farès, C.; Maulide, N. *Org. Biomol. Chem.* **2012**, *10*, 4327.

(13) (a) Song, S.; Sun, X.; Li, X.; Yuan, Y.; Jiao, N. *Org. Lett.* **2015**, *17*, 2886. (b) Liang, Y.-F.; Li, X.; Wang, X.; Zou, M.; Tang, C.; Liang, Y.; Song, S.; Jiao, N. *J. Am. Chem. Soc.* **2016**, *138*, 12271. (c) Liang, Y.-F.; Wu, K.; Song, S.; Li, X.; Huang, X.; Jiao, N. *Org. Lett.* **2015**, *17*, 876. (d) Song, S.; Li, X.; Sun, X.; Yuan, Y.; Jiao, N. *Green Chem.* **2015**, *17*, 3285. (e) Song, S.; Zhang, Y.; Yeerlan, A.; Zhu, B.; Liu, J.; Jiao, N. *Angew. Chem. Int. Ed.* **2017**, *56*, 2487.

(14) For reviews on DMSO as the reagent in organic synthesis, see: (a) Wu, X.-F.; Natte, K. *Adv. Synth. Catal.* **2016**, *358*, 336. (b) Jones-Mensah, E.; Karki, M.; Magolan, J. *Synthesis* **2016**, *48*, 1421.

(15) (a) Huang, H.; Tang, L.; Liu, Q.; Xi, Y.; He, G.; Zhu, H. *Chem. Commun.* **2016**, *52*, 5605. (b) Kawaguchi, T.; Miyata, H.; Ataka, K.; Mae, K.; Yoshida, J. *Angew. Chem. Int. Ed.* **2005**, *44*, 2413. (c) Ge, W.; Wei, Y. *Green Chem.* **2012**, *14*, 2066. (d) Chen, J.; Li, G.; Xie, Y.; Liao, Y.; Xiao, F.; Deng, G.-J. *Org. Lett.* **2015**, *17*, 5870. (e) Mal, K.; Kaur, A.; Haque, F.; Das, I. *J. Org. Chem.* **2015**, *80*, 6400. (f) Sun, J.-G.; Weng, W.-Z.; Li, P.; Zhang, B. *Green Chem.* **2017**, *19*, 1128. (g) Liang, Y.-F.; Yuan, Y.; Shen, T.; Song, S.; Jiao, N. *Chin. J. Chem.* **2018**, *36*, 233. (h) Mupparapu, N.; Khan, S.; Battula, S.; Kushwaha, M.; Gupta, A. P.; Ahmed, Q. N.; Vishwakarma, R. A. *Org. Lett.* **2014**, *16*, 1152. (i) Kohmoto, S.; Kobayashi, T.; Minami, J.; Ying, X.; Yamaguchi, K.; Karatsu, T.; Kitamura, A.; Kishikawa, K.; Yamamoto, A. *J. Org. Chem.* **2001**, *66*, 66. (j) Khenkin, A. M.; Neumann, R. *J. Org. Chem.* **2002**, *67*, 7075. (k) Saba, S.; Rafique, J.; Braga, A. L. *Adv. Synth. Catal.* **2015**, *357*, 1446.

(16) (a) Tomita, R.; Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 7144. (b) Ashikari, Y.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2011**, *133*, 11840. (c) Ashikari, Y.; Nokami, T.; Yoshida, J. *Org. Lett.* **2012**, *14*, 938. (d) Xu, R.; Wan, J.-P.; Mao, H.; Pan, Y. *J. Am. Chem. Soc.* **2010**, *132*, 15531. (e) Wu, X.; Gao, Q.; Geng, X.; Zhang, J.; Wu, Y. D.; Wu, A. *Org. Lett.* **2016**, *18*, 2507. (f) Xiang, J. C.; Cheng, Y.; Wang, M.; Wu, Y.; Wu, A. *Org. Lett.* **2016**, *18*, 4360. (g) Deshidi, R.; Kumar, M.; Devari, S.; Shah, B. A. *Chem. Commun.* **2014**, *50*, 9533. (h) Li, X.; Song, S.; Jiao, N. *Acta Chim. Sin.* **2017**, *75*, 1202. (i) Reddi, R. N.; Prasad, P. K.; Sudalai, A. *Angew. Chem. Int. Ed.* **2015**, *54*, 14150. (j) Wu, X.; Gao, Q.; Liu, S. *Wu A.* **2014**, *16*, 2888. (k) Song, S.; Huang, X.; Liang, Y.-. F.; Tang, C.; Li, X.; Jiao, N. *Green Chem.* **2015**, *17*, 2727. (l) Gao, Q.; Wu, X.; Liu, S.; Wu, A. *Org. Lett.* **2014**, *16*, 1732. (m) Gao, Q.; Zhang, J.; Wu, X.; Liu, S.; Wu, A. *Org. Lett.* **2015**, *17*, 134.

(17) Majetich, G.; Hicks, R.; Reister, S. *J. Org. Chem.* 13.

(18) Karki, M.; Magolan, J. *J. Org. Chem.* **2015**, *80*, 3701.

(19) (a) Sayer, J. R.; Wallden, K.; Pesnot, T.; Campbell, F.; Gane, P. J.; Simone, M.; Koss, H.; Buelens, F.; Boyle, T. P.; Selwood, D. L.; Waksman, G.; Tabor, A. B. *Bioorg. Med. Chem.* **2014**, *22*, 6459. (b) Neyyappadath, R. M.; Chisholm, R.; Greenhalgh, M. D.; Rodríguez-Escrich, C.; Pericàs, M. A.; Hähner, G.; Smith, A. D. *ACS Catal.* **2018**, *8*, 1067. (c) Wei, S.; Messerer, R.; Tsogoeva, S. B. *Chem. Eur. J.* **2011**, *17*, 14380.

(20) (a) Mislow, K.; Simmons, T.; Melillo, J.; Ternay, A. *J. Am. Chem. Soc.* **1964**, *86*, 1452. (b) Floyd, M.; Du, M. T.; Fabio, P. F.; Jacob, L. A.; Johnson, B. D. *J. Org. Chem.* **1984**, *50*, 5022.