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Cu-Catalyzed Aminoacyloxylation of Unactivated Alkenes of Unsaturated Hydrazones with Manifold Carboxylic Acids toward Ester-Functionalized Pyrazolines

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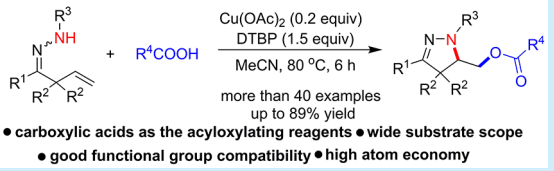
Supporting Information

ABSTRACT: A copper-catalyzed aminoacyloxylation of unactivated alkenes of unsaturated hydrazones is achieved by using various commercially available carboxylic acids as the acyloxylating reagents and di-*tert*-butyl peroxide (DTBP) as the oxidant. By using this method, a sequence of structurally diversiform acyloxyl-substituted pyrazolines are efficiently synthesized. Significantly, many carboxyl-containing drugs and bioactive molecules with unprotected functional groups are compatible in this reaction.

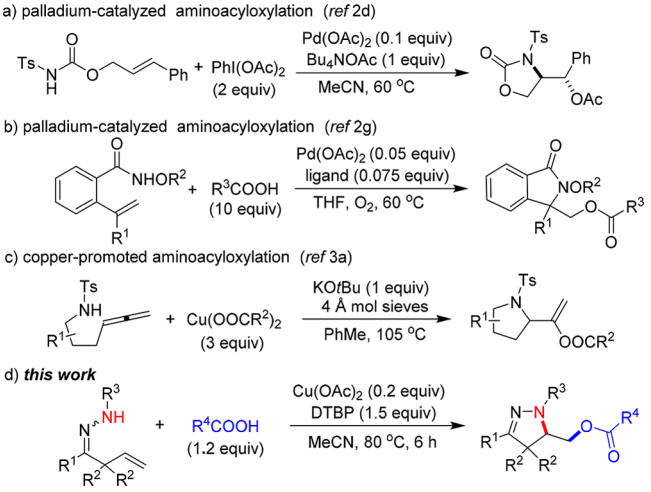


The vicinal aminoacyloxylation of unactivated alkenes is of great significance for the preparation of β-acyloxyl amines which not only consist of pharmaceuticals but also serve as useful synthetic intermediates in organic transformations.[1] Therefore, chemists have made great efforts to develop various efficient synthetic tactics for enriching aminoacyloxylation of alkenes.[2,3] For example, Sorensen developed an elegant palladium-catalyzed aminoacyloxylation of alkenes by using a stoichiometric amount of $PhI(OAc)_2$ as the acetoxylating reagent as well as the oxidant[2d] (Scheme 1a). Zhang reported a novel palladium-catalyzed aerobic aminoacyloxylation strategy by employing large excess carboxylic acids as the acyloxylating reagents[2g] (Scheme 1b). Chemler described a fascinating copper-promoted aminoacyloxylation of allenes utilizing a stoichiometric amount of preprepared cupric carboxylates as the acyloxylating reagents and oxidants[3a] (Scheme 1c). Although great achievements have been made in this field, these reactions usually require prefunctionalized carboxylates or a massive surplus of carboxylic acids as the acyloxylating reagents.[2,3] Thus, it is highly desirable to expand the more efficient aminoacyloxylation of alkenes by using manifold carboxylic acids, especially the valuable carboxyl-containing natural products, drugs, and bioactive molecules, as the acyloxylating reagents.

Carboxylic acids are cheap, easily available substances and are widely applied in synthetic chemistry.[4] A great many carboxyl-containing drugs and bioactive molecules are essential for human health and the development of pharmaceutical science.[5] The esterification of carboxyl-containing drugs is a very important tool to ameliorate pharmaceutical absorption, improve pharmaceutical effect, and enhance pharmaceutical stability for a longer half-life.[6] For example, pivampicillin,[6d−f] as a prodrug, is derived from the esterification of the high-efficiency antibiotic ampicillin,[6g,h] which greatly increases the bioavailability and prolongs its effects.[6d−f] In this context, the use of various readily accessible carboxylic acids and carboxyl-containing drugs as the acyloxylating reagents would be of great significance for organic synthesis and pharmaceutical chemistry.[5c,6a]

Pyrazoline derivatives are essential heterocyclic compounds and have been extensively applied in pharmaceutical chemistry and bioorganic chemistry.[7] Therefore, the efficient construction of pyrazoline scaffolds has always drawn attention from chemists and pharmacists. In recent years, we and other groups have developed a hydrazonyl radical-participating cyclization tactic for the preparation of pyrazoline derivatives.[8] However, the aminoacyloxylation of unsaturated hydrazones with carboxylic

Scheme 1. Strategies for Aminoacyloxylation of Alkenes



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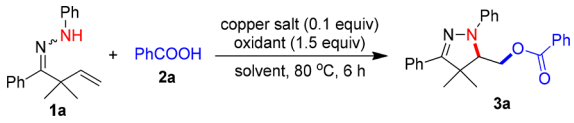
acids toward acyloxyl-substituted pyrazolines has not been realized yet. Herein, we present a practical and efficient approach for the synthesis of structurally useful acyloxyl-featured pyrazolines through Cu-catalyzed aminoacyloxylation of unsaturated hydrazones with carboxylic acids under the oxidation conditions of di-*tert*-butyl peroxide (DTBP). Notably, besides simple aliphatic and aromatic acids, many carboxyl-containing drugs and bioactive molecules with unprotected functional groups are all good candidates in this protocol. Consequently, this reaction not only supplies an effective strategy for the preparation of structurally diversiform acyloxyl-featured pyrazolines but also provides a feasible way to realize the esterification of valuable carboxyl-containing drugs and bioactive molecules by incorporating useful nitrogen-containing heterocycles.[5c,6a]

We initiated the aminoacyloxylation of alkenes by using unsaturated ketohydrazone **1a** and benzoic acid **2a** as the model substrates under the conditions of DTBP and CuI in acetontrile at 80 °C for 6 h. The anticipated aminoacyloxylation product (**3a**) was isolated in 15% yield (Table 1, entry 1). After the screening of a variety of copper salts (Table 1, entries 2−5), $Cu(OAc)_2$ was found to be the most efficient catalyst for this transformation, and the yield of **3a** was improved to 71% (Table 1, entry 4). No better yield was afforded when the reaction was carried out under the conditions of other solvents and oxidants (Table 1, entries 6−11). In addition, the addition of ligands, such as phenanthroline and bipyridine, was destructive for the aminoacyloxylation process (Table 1, entries 12 and 13). Moreover, the amount of $Cu(OAc)_2$ was also evaluated to enhance the yield of **3a** (Table 1, entries 14 and 15), and the result indicated that the yield can be increased to 82% when 0.2 equiv of $Cu(OAc)_2$ was used.

Table 1. Optimization of the Reaction Conditions[a]

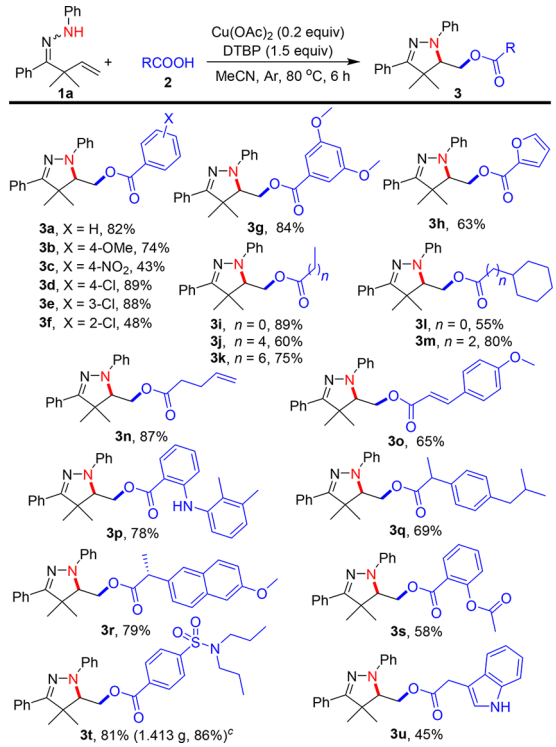


entry	copper salt	solvent	oxidant	ligand	yield (%)[b]
1	CuI	MeCN	DTBP		15
2	CuCl	MeCN	DTBP		25
3	$CuCl_2$	MeCN	DTBP		5
4	$Cu(OAc)_2$	MeCN	DTBP		71
5	$CuSO_4$	MeCN	DTBP		8
6	$Cu(OAc)_2$	PhMe	DTBP		62
7	$Cu(OAc)_2$	EA	DTBP		65
8	$Cu(OAc)_2$	DMF	DTBP		34
9	$Cu(OAc)_2$	EtOH	DTBP		65
10	$Cu(OAc)_2$	MeCN	TBHP		45
11	$Cu(OAc)_2$	MeCN	DCP		69
12	$Cu(OAc)_2$	MeCN	DTBP	phen	20
13	$Cu(OAc)_2$	MeCN	DTBP	bpy	25
14[c]	$Cu(OAc)_2$	MeCN	DTBP		78
15[d]	**$Cu(OAc)_2$**	**MeCN**	**DTBP**		**82**

[a]Conditions: **1a** (0.30 mmol), **2a** (0.36 mmol), copper (0.03 mmol), oxidant (0.45 mmol), ligand (0.03 mmol, 0.1 equiv), solvent (2 mL), Ar, 80 °C, 6 h. [b]Isolated yield based on **1a**. [c]$Cu(OAc)_2$ (0.045 mmol) was used. [d]$Cu(OAc)_2$ (0.06 mmol) was used. TBHP = *tert*-butyl hydroperoxide, DCP = dicumyl peroxide, EA = ethyl acetate, DMF = dimethylformamide, bpy = bipyridine, phen = phenanthroline.

With the optimized conditions in hand (Table 1, entry 15), various carboxylic acids were first tested in the reaction. As depicted in Scheme 2, both aromatic and aliphatic carboxylic acids were compatible with this protocol, giving the desired aminoacyloxylation products in moderate to excellent yields. Substituted benzoic acids with a series of electronic properties participated very well in the reaction, as demonstrated in cases **3a−g**. Satisfyingly, heterocyclic carboxylic acid such as furoic acid was also suitable for this conversion, affording the corresponding product **3h** in 63% yield. It is worth noting that both linear and cyclic aliphatic carboxylic acids were all amenable in this transformation, providing the aminoacyloxylation products **3i−m** in good yields. In addition, carboxylic acids with additional olefin groups were also good partners in the reaction, as proven by the formation of **3n** and **3o** in good yields. To manifest the breadth and scope of this agreement, some important carboxyl-containing drugs and bioactive molecules were also employed as the acyloxylating reagents. For instance, mefenamic acid,[9a] ibuprofen,[9b,c] and naproxen,[9d] which have been widely applied to treat pain, fever, and inflammation as nonsteroidal anti-inflammatory drugs,[9] were transformed smoothly in the reaction, delivering the aminoacyloxylation products **3p−r** in good yields. When acetylsalicylic acid, a well-known drug to treat inflammation, ischemic strokes, blood clots, and colorectal cancer,[10] participated in the reaction, the corresponding product **3s** was also obtained in 58% yield. When indole-3-acetic acid,[11] which served as plant hormone of the auxin class, was applied to this reaction, the anticipated product **3u** was formed in moderate yield, indicating that an unprotected indole skeleton was well tolerated in the protocol.

Scheme 2. Scope of Carboxylic Acids[a,b]



[a]Conditions: **1a** (0.30 mmol), carboxylic acids **2** (0.36 mmol), $Cu(OAc)_2$ (0.06 mmol) and DTBP (0.45 mmol), MeCN, Ar, 80 °C, 6 h. [b]Isolated yields. [c]**1a** (3.0 mmol) was used, and the corresponding aminoacyloxylation product **3t** was isolated in 1.413 g (86%).

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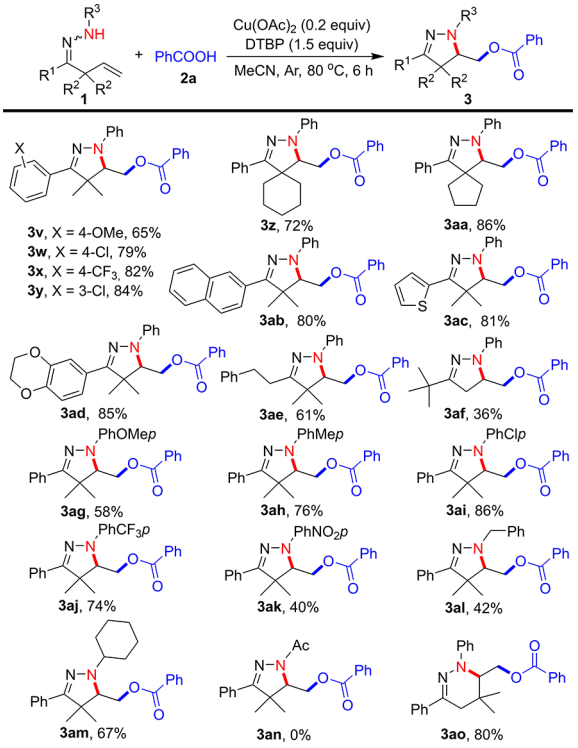
Notably, there was no difficulty when the reaction was carried out on a gram-scale, as demonstrated in the case of **3t**, in which gout suppressant probenecid[12] was involved, indicating the practicability of this tactic.

To further explore the applicability of this approach, multifarious unsaturated ketohydrazones were then examined (Scheme 3). Both aryl and heterocycle substituted unsaturated

Scheme 3. Scope of Unsaturated Ketohydrazones[a,b]

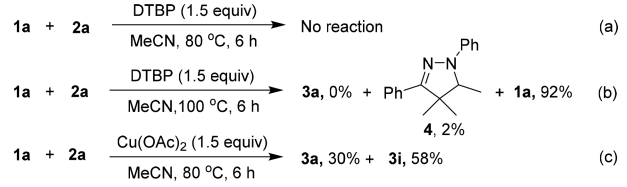


[a]Conditions: hydrazones **1** (0.30 mmol), **2a** (0.36 mmol), $Cu(OAc)_2$ (0.06 mmol), and DTBP (0.45 mmol), MeCN, Ar, 80 °C, 6 h. [b]Isolated yields.

hydrazones were feasible in this transformation, affording the anticipated aminoacyloxylation products **3v**–**ad** in good to excellent yields. Alkyl-substituted unsaturated hydrazones were also compatible in this protocol to yield **3ae** and **3af** in moderate yields. *N*-Phenyl hydrazones bearing substituents such as *p*-MeO, *p*-Me, *p*-Cl, *p*-CF_3, and *p*-NO_2 were all smoothly converted to the desired products **3ag**–**ak**. When *N*-benzyl and *N*-cyclohexyl substituted ketohydrazones were subjected to react with **2a**, the reaction produced **3al** and **3am** in 42% and 67% yields, respectively. However, *N*-acetyl substituted ketohydrazone was inert in the reaction, and the desired product **3an** was not observed. Notably, *γ*,*δ*-unsaturated hydrazone was also a good partner in this approach, yielding the acyloxyl-fabricated tetrahydropyridazine **3ao** in 80% yield.

To probe the mechanism of this reaction, control experiments have been conducted as depicted in Scheme 4. When the reaction was carried out under the copper-free conditions, no reaction took place (Scheme 4a). To ensure the effective formation of the tertiary butoxy radical from the decomposition of DTBP under the copper-free conditions, the reaction temperature was improved to 100 °C (Scheme 4b).[8c] However, no aminoacyloxylation product was obtained, but the hydroamination product **4** was formed in 2% yield, along with 92% of **1a** recovered. These results indicated that $Cu(OAc)_2$ was

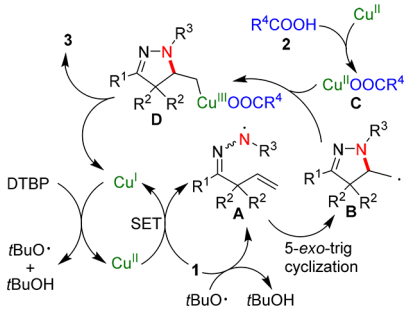
Scheme 4. Control Experiments



essential for this reaction. When a stoichiometric amount of $Cu(OAc)_2$ was used as the oxidant, the reaction produced the aminoacyloxylation products **3a** and **3i** in 30% and 58% yields, respectively (Scheme 4c). This result disclosed that a ligand exchange process occurred between carboxylic acids and $Cu(OAc)_2$.

Based on our previous work on the radical cyclization reactions of unsaturated hydrazones[8] and oximes[13] and the results of control experiments in this work, a copper-catalyzed hydrazonyl radical-promoted aminoacyloxylation process is proposed in Scheme 5. First, Cu^{II} grabs an electron from

Scheme 5. Proposed Mechanism



hydrazone **1** via a single-electron transfer (SET) process to produce the hydrazonyl radical **A** and Cu^{I} species,[8,13d,e] and the latter is oxidized by DTBP to regenerate Cu^{II} species. A possible alternative process for the generation of the hydrazonyl radical **A** is that a hydrogen-atom transfer process occurs between hydrazones **1** and tertiary butoxy radical which is derived from the decomposition of DTBP under the catalysis of copper salt.[8c] The hydrazonyl radical **A** subsequently experiences the N atom 5-*exo*-trig cyclization to form the intermediate **B**. The reaction of the intermediate **B** with the copper species **C**, which is derived from ligand exchange between Cu^{II} species and carboxylic acids, produces the intermediate **D**. Finally, the intermediate **D** undergoes reductive elimination to yield the aminoacyloxylation product **3** and Cu^{I} species.[13d,14]

In conclusion, we have developed a facile and practical method for the aminoacyloxylation of unactivated alkenes by applying unsaturated ketohydrazones and carboxylic acids as the easily available substrates and DTBP as the oxidant under copper catalysis. By utilizing the approach, a variety of structurally useful acyloxyl-featured pyrazolines are efficiently synthesized. This reaction not only presents a new strategy for the introduction of carboxylic acids into important heterocycles but also features a broad scope of substrates and a good functional group compatibility. Further studies on the application of carboxylic acids as the acyloxylating reagents are underway in our laboratory.

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■ ASSOCIATED CONTENT

Supporting Information

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Detailed experimental procedures and spectral data for all products (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Huizing, A. P.; Mondal, M.; Hirsch, A. K. *J. Med. Chem.* **2015**, *58*, 5151−5163. (b) Schroeder, J. C.; Dinatale, B. C.; Murray, I. A.; Flaveny, C. A.; Liu, Q.; Laurenzana, E. M.; Lin, J. M.; Strom, S. C.; Omiecinski, C. J.; Amin, S.; Perdew, G. H. *Biochem.* **2010**, *49*, 393−400.

(2) (a) Farid, U.; Wirth, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 3462−3465. (b) Rao, W. H.; Yin, X. S.; Shi, B. F. *Org. Lett.* **2015**, *17*, 3758−3761. (c) Desai, L. V.; Sanford, M. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5737−5740. (d) Alexanian, E. J.; Lee, C.; Sorensen, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 7690−7691. (e) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179−7181. (f) Zhu, H.; Chen, P.; Liu, G. *Org. Lett.* **2015**, *17*, 1485−1488. (g) Kou, X.; Li, Y.; Wu, L.; Zhang, X.; Yang, G.; Zhang, W. *Org. Lett.* **2015**, *17*, 5566−5569. (h) Liu, G. S.; Zhang, Y. Q.; Yuan, Y. A.; Xu, H. *J. Am. Chem. Soc.* **2013**, *135*, 3343−3346. (i) Lu, D. F.; Liu, G. S.; Zhu, C. L.; Yuan, B.; Xu, H. *Org. Lett.* **2014**, *16*, 2912−2915. (j) Lu, D. F.; Zhu, C. L.; Jia, Z. X.; Xu, H. *J. Am. Chem. Soc.* **2014**, *136*, 13186−13189. (k) Zhang, Y.-Q.; Yuan, Y.-A.; Liu, G.-S.; Xu, H. *Org. Lett.* **2013**, *15*, 3910−3913. (l) Li, G. G.; Chang, H. T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 451−454. (m) Wang, T.; Jiao, N. *J. Am. Chem. Soc.* **2013**, *135*, 11692−11695. (n) Sun, X.; Li, X.; Song, S.; Zhu, Y.; Liang, Y.-F.; Jiao, N. *J. Am. Chem. Soc.* **2015**, *137*, 6059−6066. (o) Wang, S.; Guo, Y.-Q.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. *Org. Lett.* **2017**, *19*, 1574−1577.

(3) (a) Casavant, B. J.; Khoder, Z. M.; Berhane, I. A.; Chemler, S. R. *Org. Lett.* **2015**, *17*, 5958−5961. (b) Hemric, B. N.; Shen, K.; Wang, Q. *J. Am. Chem. Soc.* **2016**, *138*, 5813−5816. (c) Ortiz, G. X.; Kang, J. B.; Wang, Q. *J. Org. Chem.* **2014**, *79*, 571−581. (d) Wu, F.; Stewart, S.; Ariyarathna, J. P.; Li, W. *ACS Catal.* **2018**, *8*, 1921−1925. (e) Ren, S.; Song, S.; Ye, L.; Feng, C.; Loh, T. P. *Chem. Commun.* **2016**, *52*, 10373−10376. (f) Sherman, E. S.; Chemler, S. R. *Adv. Synth. Catal.* **2009**, *351*, 467−471. (g) Schmidt, V. A.; Alexanian, E. J. *J. Am. Chem. Soc.* **2011**, *133*, 11402−11405. (h) Liu, L.; Wang, Z. *Green Chem.* **2017**, *19*, 2076−2079. (i) Cochran, B. M.; Michael, F. E. *Org. Lett.* **2008**, *10*, 5039−5042.

(4) (a) Weaver, J. D.; Recio, A., III; Grenning, A. J.; Tunge, J. A. *Chem. Rev.* **2011**, *111*, 1846−1913. (b) Xuan, J.; Zhang, Z.-G.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2015**, *54*, 15632−15641. (c) Qin, T.; Cornella, J.; Li, C.; Malins, L. R.; Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. *Science* **2016**, *352*, 801−805. (d) Liu, X.; Wang, Z.; Cheng, X.; Li, C. *J. Am. Chem. Soc.* **2012**, *134*, 14330−14333. (e) Li, Z.; Wang, Z.; Zhu, L.; Tan, X.; Li, C. *J. Am. Chem. Soc.* **2014**, *136*, 16439−16443.

(5) (a) Warden, S. J. *Physician and Sports Medicine* **2010**, *38*, 132−138. (b) Buer, J. K. *Inflammopharmacology* **2014**, *22*, 263−267. (c) Blakemore, D. C.; Castro, L.; Churcher, I.; Rees, D. C.; Thomas, A. W.; Wilson, D. M.; Wood, A. *Nat. Chem.* **2018**, *10*, 383−394.

(6) (a) Foley, D. J.; Nelson, A.; Marsden, S. P. *Angew. Chem., Int. Ed.* **2016**, *55*, 13650−13657. (b) Malhotra, B.; Gandelman, K.; Sachse, R.; Wood, N.; Michel, M. C. *Curr. Med. Chem.* **2009**, *16*, 4481−4489. (c) Stella, V. J.; Charman, W. N. A.; Naringrekar, V. H. *Drugs* **1985**, *29*, 455−473. (d) Holme, E.; Jacobson, C.-E.; Nordin, I.; Greter, J.; Lindstedt, S.; Kristiansson, B.; Jodal, U. *Lancet* **1989**, *334*, 469−473. (e) Brass, E. P. *Pharmacol Rev.* **2002**, *54*, 589−598. (f) Holme, E.; Hospital, S.; Jodal, U.; Linstedt, S.; Nordin, I. *Scand. J. Clin. Lab. Invest.* **1991**, *52*, 361−372. (g) Delcour, A. H. *Biochim. Biophys. Acta, Proteins Proteomics* **2009**, *1794*, 808−816. (h) Akova, M. *Clin. Microbiol. Infect.* **2008**, *14*, 185−188.

(7) (a) Lee, M.; Brockway, O.; Dandavati, A.; Tzou, S.; Sjoholm, S.; Satam, V.; Westbrook, C.; Mooberry, S. L.; Zeller, M.; Babu, B.; Lee, M. *Eur. J. Med. Chem.* **2011**, *46*, 3099−3104. (b) Padmavathi, V.; Thriveni, P. G.; Reddy, S.; Deepti, D. *Eur. J. Med. Chem.* **2008**, *43*, 917−924.

(8) (a) Duan, X.-Y.; Zhou, N.-N.; Fang, R.; Yang, X.-L.; Yu, W.; Han, B. *Angew. Chem., Int. Ed.* **2014**, *53*, 3158−3162. (b) Duan, X.-Y.; Yang, X.-L.; Fang, R.; Peng, X.-X.; Yu, W.; Han, B. *J. Org. Chem.* **2013**, *78*, 10692−10704. (c) Duan, X.-Y.; Yang, X.-L.; Jia, P.-P.; Zhang, M.; Han, B. *Org. Lett.* **2015**, *17*, 6022−6025. (d) Hu, X.-Q.; Chen, J.-R.; Wei, Q.; Liu, F.-L.; Deng, Q.-H.; Beauchemin, A. M.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2014**, *53*, 12163−12167. (e) Hu, X.-Q.; Qi, X.; Chen, J.-R.; Zhao, Q.-Q.; Wei, Q.; Lan, Y.; Xiao, W.-J. *Nat. Commun.* **2016**, *7*, 11188−11200. (f) Zhu, M.-Z.; Chen, Y.-C.; Loh, T.-P. *Chem. - Eur. J.* **2013**, *19*, 5250−5254. (g) Zhu, X.; Wang, Y.-F.; Ren, W.; Zhang, F.-L.; Chiba, S. *Org. Lett.* **2013**, *15*, 3214−3217.

(9) (a) Pringsheim, T.; Davenport, W. J.; Dodick, D. *Neurology* **2008**, *70*, 1555−1563. (b) Davies, N. M. *Clin. Pharmacokinet.* **1998**, *34*, 101−154. (c) Davanzo, R.; Bua, J.; Paloni, G.; Facchina, G. *Eur. J. Clin. Pharmacol.* **2014**, *70*, 1313−1324. (d) Angiolillo, D. J.; Weisman, S. M. *Am. J. Cardiovasc. Drugs* **2017**, *17*, 97−107.

(10) (a) Algra, A. M.; Rothwell, P. M. *Lancet Oncol.* **2012**, *13*, 518−527. (b) Guirguis-Blake, J. M.; Evans, C. V.; Senger, C. A.; O'Connor, E. A.; Whitlock, E. P. *Ann. Intern. Med.* **2016**, *164*, 804−813. (c) Morris, T.; Stables, M.; Hobbs, A.; de Souza; Colville-Nash, P. P.; Warner, T.; Newson, J.; Bellingan, G.; Gilroy, D. W. *J. Immunol.* **2009**, *183*, 2089−2096. (d) Patrignani, P.; Patrono, C. *J. Am. Coll. Cardiol.* **2016**, *68*, 967−976.

(11) (a) Simon, S.; Petrasek, J. *Plant Sci.* **2011**, *180*, 454−460. (b) Zhao, Y. *Annu. Rev. Plant Biol.* **2010**, *61*, 49−64.

(12) Mason, R. M. *Ann. Rheum. Dis.* **1954**, *13*, 120−130.

(13) (a) Han, B.; Yang, X.-L.; Fang, R.; Yu, W.; Wang, C.; Duan, X.-Y.; Liu, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 8816−8820. (b) Peng, X.-X.; Deng, Y.-J.; Yang, X.-L.; Zhang, L.; Yu, W.; Han, B. *Org. Lett.* **2014**, *16*, 4650−4653. (c) Yang, X.-L.; Chen, F.; Zhou, N.-N.; Yu, W.; Han, B. *Org. Lett.* **2014**, *16*, 6476−6479. (d) Liu, R.-H.; Wei, D.; Han, B.; Yu, W. *ACS Catal.* **2016**, *6*, 6525−6530. (e) Peng, X.-X.; Wei, D.; Han, W.-J.; Chen, F.; Yu, W.; Han, B. *ACS Catal.* **2017**, *7*, 7830−7834.

(14) (a) Chemler, S. R. *Science* **2013**, *341*, 624−626. (b) Sequeira, F. C.; Turnpenny, B. W.; Chemler, S. R. *Angew. Chem., Int. Ed.* **2010**, *49*, 6365−6368. (c) Zhang, W.; Wang, F.; McCann, S. D.; Wang, D.; Chen, P.; Stahl, S. S.; Liu, G. *Science* **2016**, *353*, 1014−1018. (d) Fuller, P. H.; Kim, J.-W.; Chemler, S. R. *J. Am. Chem. Soc.* **2008**, *130*, 17638−17639. (e) Wdowik, T.; Chemler, S. R. *J. Am. Chem. Soc.* **2017**, *139*, 9515−9518. (f) Shen, K.; Wang, Q. *Chem. Sci.* **2015**, *6*, 4279−4283. (g) Shen, K.; Wang, Q. *J. Am. Chem. Soc.* **2017**, *139*, 13110−13116. (h) Lin, J.-S.; Dong, X.-Y.; Li, T.-T.; Jiang, N.-C.; Tan, B.; Liu, X.-Y. *J. Am. Chem. Soc.* **2016**, *138*, 9357−9360.

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