UvA-DARE (Digital Academic Repository)

Ligand-Enabled γ -C(sp³)-H Acetoxylation of Triflyl-Protected Amines

Jia, W.-L.; Fernández-Ibáñez, M.Á.

DOI

[10.1002/ejoc.201800891](https://doi.org/10.1002/ejoc.201800891)

Publication date

2018

Document Version

Final published version

Published in

European Journal of Organic Chemistry

License

Article 25fa Dutch Copyright Act

[Link to publication](#)

Citation for published version (APA):

Jia, W.-L., & Fernández-Ibáñez, M. Á. (2018). Ligand-Enabled γ -C(sp³)-H Acetoxylation of Triflyl-Protected Amines. *European Journal of Organic Chemistry*, 2018(44), 6088-6091. <https://doi.org/10.1002/ejoc.201800891>

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

SPECIAL
ISSUE

C–H Activation

Ligand-Enabled γ -C(sp³)-H Acetoxylation of Triflyl-Protected AminesWen-Liang Jia^[a] and M. Ángeles Fernández-Ibáñez^{*[a]}

Abstract: A palladium-catalyzed γ -C(sp³)-H acetoxylation of triflyl-protected amines has been achieved. The use of pyridine or 2-alkoxyquinoline-type ligands is key to the success of this transformation. The reaction is highly diastereoselective and

easily scalable, and constitutes a direct approach for the synthesis of γ -hydroxy- α -amino acids and β,γ -dihydroxy amines, which are not readily accessible by other routes.

Introduction

In the past decades, palladium-catalyzed C–H functionalization reactions have attracted substantial attention from organic chemists.^[1] The ability to install functionalities into molecules directly from inert C–H bonds can streamline and shorten substantially the synthesis of target compounds. A common practice to increase both the reactivity and selectivity of these processes is the use of directing groups.^[2] In the case of less reactive C(sp³)-H bonds, generally, a bidentate directing group is needed in order to achieve good reactivity.^[3] Recently, the direct and selective functionalization of C(sp³)-H bonds has been achieved combining monodentate directing groups and ligands.^[4–6] In these transformations, the selectivity is controlled by the directing group and the ligand plays a pivotal role in increasing the reactivity of the inert C(sp³)-H bond. For example, triflyl- or nosyl-protected amines can be efficiently γ -arylated or -alkylated in the presence of mono-protected-amino acid or -aminomethyl oxazoline ligands.^[4] Since amines are ubiquitous subunits in organic molecules, the development of new methodologies that permit their direct functionalization are of great interest.^[7] For instance, γ -hydroxy- α -amino acids widely exist in many peptide-based drugs and can be used for native chemical ligation (NCL).^[8] Although several examples of direct γ -C(sp³)-H acetoxylation of α -amino acids have been reported, they all rely on the use of a bidentate directing group to achieve good reactivity.^[9] In our group, we are interested in the development of new ligands capable of promoting C–H functionalization reactions.^[10] Herein, we report the first example of Pd-catalyzed γ -C(sp³)-H acetoxylation of triflyl-protected amines assisted by pyridine-based ligands.^[11]

Results and Discussion

We started our investigations using methyl *N*-triflyl-L-valinate (**1a**) as the model substrate, Pd(OAc)₂ (10 mol-%) as the palla-

dium catalyst and PhI(OAc)₂ as the oxidant, in 1,2-dichloroethane (0.1 M) at 110 °C. Under these conditions, only trace amount of acetoxyated product **2a** were detected after 20 h (Table 1).

Table 1. Screening of ligands for the γ -C(sp³)-H acetoxylation of *N*-triflyl-L-valinate.^[a,b]

without ligand
traces 2a	L1 (29% + traces)	L2 (30% + traces)	L3 (21% + traces)

L4 (0%)	L5 (11% + traces)	L6 (24% + traces)	L7 (40% + traces)

L8 (20% + traces)	L9 (traces 2a)	L10 (41% + traces)	L11 (0%)

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), Pd(OAc)₂ (0.01 mmol, 10 mol-%), ligand (0.02 mmol, 20 mol-%), PhI(OAc)₂ (0.25 mmol, 2.5 equiv.), DCE (1.0 mL), 110 °C, 20 h. [b] Yields were determined by ¹H NMR analysis of the crude mixture using CH₂Br₂ as internal standard.

In order to increase the reactivity of the C(sp³)-H bond, we decided to evaluate different ligands in this transformation. Thus, under the standard reaction conditions, the addition of 1-methylpyrazole (**L1**, 20 mol-%) provided the desired acetoxyated product **2a** in 29 % yield, together with trace amount of diacetoxyated product **2a'**. Encouraged by this result, other protected 1-methylpyrazole-type ligands were tested. The 5-methyl-substituted ligand **L2**, exhibited similar behaviour (30 % yield) than **L1**. When the 5-position of the pyrazole ligand

[a] Van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Science Park 904, 1098 XH, Amsterdam, The Netherlands
E-mail: m.a.fernandezibanez@uva.nl
<http://www.fernandezibanezgroup.com/>

Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under <https://doi.org/10.1002/ejoc.201800891>.

bore a methoxy group, only 21 % yield of the desired product was detected, while the unprotected 5-hydroxy-1-methylpyrazole (**L4**) completely inhibited the reaction. Pyridine-type ligands are known to be effective ligands in C–H functionalization reactions.^[12] Therefore, we evaluated their effect in the C(sp³)–H acetoxylation reaction. The model reaction in the presence of pyridine (**L5**) furnished **2a** in 11 % yield. The electron-deficient 3-nitropyridine ligand (**L6**) provided improved results compared with pyridine, giving **2a** in 24 % yield. We also tested different 2-substituted pyridine ligands. The use of 2-picoline (**L7**) improved the yield of **2a** up to 40 %. The introduction of a methoxy group in the pyridine ring (**L8**) showed once more negative effects in the reaction (20 % yield). Very low conversion was also observed when 2-(trifluoromethyl)pyridine (**L9**) was employed as ligand, but the reaction in the presence of 2,6-lutidine (**L10**) gave **2a** in 41 % yield. It is worth mentioning that the reaction proceeds cleanly and mainly the acetoxyated product and starting material were detected in the crude mixture. Finally, we also tried the reaction using a mono-protected amino acid ligand, Boc-L-isoleucine (**L11**), which was an efficient ligand in the C(sp³)–H γ -arylation and -alkylation of triflyl- or nosyl-protected amines.^[4a,4b] However, under our reaction conditions, no acetoxyated product was detected.

With a suitable ligand in hand, other reaction conditions were evaluated (Table 2). A systematic screening of solvents revealed that dichloromethane (DCM) gave similar yield (42 %) than 1,2-dichloroethane (entries 1–2). Other solvents such as toluene or acetonitrile provided the monoacetoxyated product **2a** in lower yields (26 % and 21 % yield, respectively; entries 3–4). When using AcOH as solvent, almost no conversion was obtained (entry 5). When the reaction was performed at higher concentration (0.5 M DCM) similar yield for **2a** was obtained (entry 6). Having identified the best solvent, we tested other co-oxidants in the reaction. Although the use of PhCO₃tBu completely inhibited the reaction (entry 7), the conversion was improved to 63 % and 59 % when AgOAc and K₂S₂O₈ were employed, respectively (entries 8–9). We further screened other pyridine and 2-alkoxyquinoline-type ligands using DCM as solvent and AgOAc as co-oxidant (see Supporting Information, Table S4). We found out that some 2-alkoxyquinoline ligands (**L21**–**L23**) provided comparable yields of acetoxyated products **2a** and **2a'** than 2,6-lutidine. Given that 2,6-lutidine is easily accessible, we used it as the optimal ligand for further screening of reaction conditions. Different palladium sources were evaluated (entries 10–13), and only Pd(OPiv)₂ furnished slightly better yield than Pd(OAc)₂. The reaction using Pd(OPiv)₂ and 1 equiv. of AgOAc furnished the acetoxyated products in 63 % total isolated yield (56 % monoacetoxyated product **2a** and 7 % diacetoxyated product **2a'**, entry 14). We performed a control experiment in the absence of palladium-catalyst and, as expected, no conversion to the desired product was observed (entry 15). Finally, we executed the reaction in the absence of 2,6-lutidine (**L10**) under the optimal reaction conditions and only 17 % yield was detected, which highlights the crucial role of the ligand in this transformation (entry 16). Important features of the 2,6-lutidine enabled C(sp³)–H γ -acetoxylation of methyl *N*-triflyl-L-valinate (**1a**) are that the monoacetoxyated

product was obtained with very high diastereoselectivity (*dr* = 13:1; determined by ¹H-NMR) and that no-gemdiacetoxyated product was observed. The synthetic utility of our methodology was highlighted in a scale-up of the reaction to a 1.0 mmol of **1a**, providing the acetoxyated products in comparable yields than to the original value (Table 3).

Table 2. Optimization of reaction conditions.

Entry	Variations from standard reaction conditions	Yield ^[a] (2a + 2a')
1	None	41 % + traces
2	DCM as solvent	42 % + traces
3	Toluene as solvent	26 % + traces
4	CH ₃ CN as solvent	21 % + traces
5	AcOH/Ac ₂ O (9:1, v/v) as solvent	< 10 %
6	DCM (0.5 M)	42 % + 3 %
7	PhCO ₃ tBu (2.0 equiv.), DCM (0.5 M)	traces
8	AgOAc (2.0 equiv.), DCM (0.5 M)	58 % + 5 %
9	K ₂ S ₂ O ₈ (2.0 equiv.), DCM (0.5 M)	53 % + 6 %
10	PdCl ₂ , AgOAc (2.0 equiv.), DCM (0.5 M)	32 % + 2 %
11	Na ₂ PdCl ₄ , AgOAc (2.0 equiv.), DCM (0.5 M)	25 % + traces
12	Pd(TFA) ₂ , AgOAc (2.0 equiv.), DCM (0.5 M)	41 % + 2 %
13	Pd(OPiv) ₂ , AgOAc (2.0 equiv.), DCM (0.5 M)	62 % + 7 %
14	Pd(OPiv) ₂ , AgOAc (1.0 equiv.), DCM (0.5 M)	60 % + 7 %, (56 % + 7 %) ^[b]
15	No Pd-catalyst, AgOAc (1.0 equiv.), DCM (0.5 M)	0 %
16	No ligand, AgOAc (1.0 equiv.), DCM (0.5 M)	17 % + traces

[a] The yield was determined by ¹H NMR analysis of the crude mixture using CH₂Br₂ as internal standard. [b] Isolated yield.

With the optimized reaction conditions in hand, we sought to explore the substrate scope and limitations of this transformation (Table 3). First, we tested different alkyl *N*-triflyl amino esters. The reaction with ethyl (**1b**) or benzyl (**1c**) *N*-triflyl-L-valinate provided the desired monoacetoxyated product in 56 % and 49 % yield, respectively, with very high diastereoselectivity. However, only trace amount of product was detected when *tert*-butyl *N*-triflyl-L-valinate (**1d**) was used. The reaction with the more conformationally flexible methyl *N*-triflyl-L-homalaninate (**1e**) provided the corresponding γ -acetoxyated product in moderate yield (36 %). The reaction with *N*-triflyl isoleucine and alloisoleucine derivatives showed a very different reactivity profile in agreement with the high stereoselectivity observed in the reaction with *N*-triflyl-L-valinates. While the reaction with the isoleucine derivative **1f** provided the acetoxyated product **2f** in 39 % isolated yield, the diastereoisomeric alloisoleucine derivative **1g** furnished the acetoxyated product **2g** in 87 % isolated yield. The difference in reactivity between the two diastereoisomers can be attributed to the greater accessibility of the C(sp³)–H bond in the palladation step. Indeed, this behaviour has been previously observed in other C(sp³)–H functionalization reactions of amino acid derivatives.^[3e,3h] Taking into consideration the outcome of the reaction of *N*-triflyl isoleucine **1f** and alloisoleucine **1g**, we propose that the γ -acetoxylation of valine derivatives **1a**–**c** occurs mainly at the pro-*R* methyl group.

Table 3. Substrate scope.^[a,b]

[a] See supporting information for detailed reaction conditions. [b] Isolated yields. [c] The reaction was performed on a 1.0 mmol scale. [d] From ¹H NMR analysis of the crude mixture, the conversion to diacetoxyated product was ca 5 %. The diacetoxyated product could not be isolated pure by column chromatography. [e] 20 mol-% of Pd(OPiv)₂ and 40 mol-% of ligand were used. [f] **L22** was used instead of 2,6-lutidine.

The reaction with the *O*-tBu threonine derivative **1h**, under optimized reaction conditions, provided the γ -acetoxyated product **2h** in 45 % isolated yield. When the reaction was performed with the *O*-TBS protected threonine derivative **1i** the product **2i** was obtained in lower yield (23 %). Nevertheless, when the reaction was carried out with *O*-TBS allothreonine derivative **1j**, the acetoxyated product was formed in higher yield (49 %). Finally, we evaluated if amino alcohols were suitable substrates for this transformation. When we performed the reaction of *O*-acetyl-*N*-triflyl-*L*-tert-leucinol (**1k**) under the optimized reaction conditions, only 20 % ¹H-NMR yield was obtained. Fortunately, the use of the 2-alkoxyquinoline ligand **L22**, which had proved equally efficient than 2,6-lutidine in the C–H acetoxylation of amino acid derivatives (see supporting information, Table S10), provided the acetoxyated products in 47 % isolated yield. Similarly, the reaction of *O*-acetyl-*N*-triflyl-L-valinol (**1l**), using **L22** as external ligand, provided 38 % total yield of acetoxyated products, being the monoacetoxyated product **2l** obtained with high diastereoselectivity (*dr* = 17:1; determined by ¹H-NMR).^[13]

On the basis of previous reports, a plausible mechanism for this transformation is presented in Figure 1.^[4c,14] First, we postu-

late that the palladium(II) coordinates to the nitrogen followed by the γ -C(sp³)–H activation and oxidative addition of PhI(OAc)₂ to form organopalladium(IV) complex. This palladium(IV) complex can then undergo a C–O bond reductive elimination to form the acetoxyated product and the palladium(II) catalyst.

Figure 1. Proposed catalytic cycle.

Conclusions

In summary, we have developed a palladium-catalyzed γ -C(sp³)–H acetoxylation of *N*-triflyl protected amines. The key to the success of this transformation is the use of pyridine or 2-alkoxyquinoline-type ligands. The reaction is highly diastereoselective and takes place with a variety of amino acid and amino alcohol derivatives in moderate to good yields. This protocol is easily scalable and constitutes a direct approach for the synthesis of γ -hydroxy- α -amino acids and β,γ -dihydroxy amines, which are not readily accessible by other routes. Future efforts will focus on improving the efficiency of these transformations by ligand design.

Acknowledgments

We acknowledge financial support from NWO through a VIDI grant (723.013.006). Wen-Liang Jia gratefully acknowledges the financial support from China Scholarship Council (CSC).

Keywords: C–H activation · Amines · Ligand design · Palladium · Acetoxylation

- [1] For general reviews on palladium-catalyzed C–H functionalization, see: a) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174; b) O. Daugulis, H.-Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074; c) J.-Q. Yu, Z. Shi, *C–H activation*; Springer, **2010**, Vol. 292; For a special issue dedicated to this topic, see: d) *Acc. Chem. Res.* **2012**, *45*, 777; e) J. F. Hartwig, *J. Am. Chem. Soc.* **2016**, *138*, 2; f) H. M. L. Davies, D. Morthon, *J. Org. Chem.* **2016**, *81*, 343; g) T. Gensch, M. J. James, T. Dalton, F. Glorius, *Angew. Chem. Int. Ed.* **2018**, *57*, 2296; *Angew. Chem.* **2018**, *130*, 2318. [2] a) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; b) Z. Chen, B. Wang, J. Zhang, W. Yu, Z. Liu, Y. Zhang, *Org. Chem. Front.* **2015**, *2*, 1107;

- c) W. Ma, P. Gandeepan, J. Li, L. Ackermann, *Org. Chem. Front.* **2017**, 4, 1435. For a review about non-directed C–H activation of aromatic compounds, see: d) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, 51, 10236; *Angew. Chem.* **2012**, 124, 10382.
- [3] For a general review on C–H functionalization by using bidentate directing groups, see: a) G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, 52, 11726; *Angew. Chem.* **2013**, 125, 11942; For a general review on C(sp³)–H functionalization, see: b) J. He, M. Wasa, K. S. L. Chan, Q. Shao, J.-Q. Yu, *Chem. Rev.* **2017**, 117, 8754; For a general review on C(sp³)–H functionalization by using bidentate directing groups, see: c) O. Daugulis, J. Roane, L. D. Tran, *Acc. Chem. Res.* **2015**, 48, 1053; For selective examples on C(sp³)–H functionalization by using bidentate directing groups, see: d) V. G. Zaitsev, D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2005**, 127, 13154; e) B. V. S. Reddy, L. R. Reddy, E. J. Corey, *Org. Lett.* **2006**, 8, 3391; f) D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2010**, 132, 3965; g) L. D. Tran, O. Daugulis, *Angew. Chem. Int. Ed.* **2012**, 51, 5188; *Angew. Chem.* **2012**, 124, 5278; h) N. Rodríguez, J. A. Romero-Revilla, M. Á. Fernández-Ibáñez, J. C. Carretero, *Chem. Sci.* **2013**, 4, 175; i) F.-J. Chen, S. Zhao, F. Hu, K. Chen, Q. Zhang, S.-Q. Zhang, B.-F. Shi, *Chem. Sci.* **2013**, 4, 4187; j) Q. Zhang, K. Chen, W.-H. Rao, Y. Zhang, F.-J. Chen, B.-F. Shi, *Angew. Chem. Int. Ed.* **2013**, 52, 13588; *Angew. Chem.* **2013**, 125, 13833; k) J.-W. Xu, Z.-Z. Zhang, W.-H. Rao, B.-F. Shi, *J. Am. Chem. Soc.* **2016**, 138, 10750; l) G. He, G. Chen, *Angew. Chem. Int. Ed.* **2011**, 50, 5192; *Angew. Chem.* **2011**, 123, 5298; m) G. He, G. Lu, Z.-W. Guo, P. Liu, G. Chen, *Nat. Chem.* **2016**, 8, 1131; n) S. Guin, A. Deb, P. Dolui, S. Chakraborty, V. K. Singh, D. Maiti, *ACS Catal.* **2018**, 8, 2664.
- [4] For references of C(sp³)–H functionalization by using sulfonyl-protected amines as directing group, see: a) K. S. L. Chan, M. Wasa, L. Chu, B. N. Laforteza, M. Miura, J.-Q. Yu, *Nat. Chem.* **2014**, 6, 146; b) K. S. L. Chan, H.-Y. Fu, J.-Q. Yu, *J. Am. Chem. Soc.* **2015**, 137, 2042; c) H. Jiang, J. He, T. Liu, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, 138, 2055; d) Q. Shao, J. He, Q.-F. Wu, J.-Q. Yu, *ACS Catal.* **2017**, 7, 7777; e) Q. Shao, Q.-F. Wu, J. He, J.-Q. Yu, *J. Am. Chem. Soc.* **2018**, 140, 5322.
- [5] For references on C(sp³)–H functionalization by using carboxylic acids as directing group, see: a) R. Giri, N. L. Mangel, J.-J. Li, D.-H. Wang, S. P. Breazzano, L. B. Saunders, J.-Q. Yu, *J. Am. Chem. Soc.* **2007**, 129, 3510; b) G. Chen, Z. Zhuang, G.-C. Li, T. G. Saint-Denis, Y. Xiao, C. L. Joe, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2017**, 56, 1506; *Angew. Chem.* **2017**, 129, 1528; c) P.-X. Shen, L. Hu, Q. Shao, K. Hong, J.-Q. Yu, *J. Am. Chem. Soc.* **2018**, 140, 6545.
- [6] For selected examples on C(sp³)–H activation by using monodentate carboxylic derivatives as directing group, see: a) M. Wasa, K. M. Engle, J.-Q. Yu, *J. Am. Chem. Soc.* **2009**, 131, 9886; b) M. Wasa, K. M. Engle, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, 132, 3680; c) M. Wasa, K. M. Engle, D. W. Lin, E. J. Yoo, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, 133, 19598; d) M. Wasa, K. S. L. Chan, X.-G. Zhang, J. He, M. Miura, J.-Q. Yu, *J. Am. Chem. Soc.* **2012**, 134, 18570; e) J. He, M. Wasa, K. S. L. Chan, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, 135, 3387; f) J. He, S.-H. Li, Y.-Q. Deng, H.-Y. Fu, B. N. Laforteza, J. E. Spangler, A. Homs, J.-Q. Yu, *Science* **2014**, 343, 1216; g) J. He, R. Takise, H.-Y. Fu, J.-Q. Yu, *J. Am. Chem. Soc.* **2015**, 137, 4618; h) S.-H. Li, R.-Y. Zhu, K.-J. Xiao, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2016**, 55, 4317; *Angew. Chem.* **2016**, 128, 4389; i) R.-Y. Zhu, T. G. Saint-Denis, Y. Shao, J. He, J. D. Sieber, C. H. Senanayake, J.-Q. Yu, *J. Am. Chem. Soc.* **2017**, 139, 5724; j) Q.-F. Wu, P.-X. Shen, J. He, X.-B. Wang, F. Zhang, Q. Shao, R.-Y. Zhu, C. Mapelli, J. X. Qiao, M. A. Poss, J.-Q. Yu, *Science* **2017**, 355, 499.
- [7] a) A. Ricci, *Amino Group Chemistry: From Synthesis to the Life Sciences*, Wiley-VCH, Weinheim, **2008**; b) C. Sánchez, C. Méndez, J. A. Salas, *Nat. Prod. Rep.* **2006**, 23, 1007; c) R. Hili, A. K. Yudin, *Nat. Chem. Biol.* **2006**, 2, 284.
- [8] D. J. Craik, D. P. Fairlie, S. Liras, D. Price, *Chem. Biol. Drug Des.* **2013**, 81, 136.
- [9] For a review on C–H functionalization of amino acids and peptides, see: a) A. F. M. Noisier, M. A. Brimble, *Chem. Rev.* **2014**, 114, 8775. For references on γ -C(sp³)–H acetoxylation of α -amino acids, see reference^[3e] and: b) Q. Li, S.-Y. Zhang, G. He, W. A. Nack, G. Chen, *Adv. Synth. Catal.* **2014**, 356, 1544; c) X.-H. Ye, Z.-R. He, T. Ahmed, K. Weise, N. G. Akhmedov, J. L. Petersena, X.-D. Shi, *Chem. Sci.* **2013**, 4, 3712; d) K. K. Pasunooti, R.-L. Yang, B. Banerjee, T. Yap, C.-F. Liu, *Org. Lett.* **2016**, 18, 2696; e) Y. Zheng, W.-B. Song, Y.-F. Zhu, B.-L. Wei, L.-J. Xuan, *J. Org. Chem.* **2018**, 83, 2448.
- [10] a) C. Valderas, K. Naksomboon, M. Á. Fernández-Ibáñez, *ChemCatChem* **2016**, 8, 3213; b) K. Naksomboon, C. Valderas, M. Gómez-Martínez, Y. Álvarez-Casao, M. Á. Fernández-Ibáñez, *ACS Catal.* **2017**, 7, 6342; c) K. Naksomboon, Y. Álvarez-Casao, M. Uiterweerd, N. Westerveld, B. Maciá, M. Á. Fernández-Ibáñez, *Tetrahedron Lett.* **2018**, 59, 379; d) Y. Álvarez-Casao, C. A. M. R. van Slagmaat, G. K. M. Verzijl, L. Lefort, P. L. Alsters, M. Á. Fernández-Ibáñez, *ChemCatChem* **2018**, 10, 2620.
- [11] For an example of C(sp²)–H acetoxylation of amino acids directed by triflyl-protected amine, see, C. Vickers, T.-S. Mei, J.-Q. Yu, *Org. Lett.* **2010**, 12, 2511.
- [12] For selective examples, see: a) Y.-H. Zhang, B.-F. Shi, J.-Q. Yu, *J. Am. Chem. Soc.* **2009**, 131, 5072; b) Y. Izawa, S. S. Stahl, *Adv. Synth. Catal.* **2010**, 352, 3223; c) C. Wang, S. Rakshit, F. Glorius, *J. Am. Chem. Soc.* **2010**, 132, 14006; d) M. H. Emmert, A. K. Cook, Y. J. Xie, M. S. Sanford, *Angew. Chem. Int. Ed.* **2011**, 50, 9409; *Angew. Chem.* **2011**, 123, 9581; e) A. K. Cook, M. H. Emmert, M. S. Sanford, *Org. Lett.* **2013**, 15, 5428; f) J. B. Gary, A. K. Cook, M. S. Sanford, *ACS Catal.* **2013**, 3, 700.
- [13] For the removal of the triflamide group, several procedures described in the following references were tested. Unfortunately, all attempts were unsuccessful; a) W.-Z. Zhang, Q.-Y. Wang, A.-P. Zhang, Z.-B. Tong, Z.-C. Yin, W. Huang, Z.-X. Cai, S. Gao, *Faming Zhuanli Shenqing* **2011**, 102070480; b) L. Chu, X.-C. Wang, C. E. Moore, A. L. Rheingold, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, 135, 16344; c) See ref.^[4b]; d) See ref.^[4e].
- [14] a) J. B. Gary, M. S. Sanford, *Organometallics* **2011**, 30, 6143; b) M. C. Nielsen, E. Lyngvi, F. Schoenebeck, *J. Am. Chem. Soc.* **2013**, 135, 1978; c) A. K. Cook, M. S. Sanford, *J. Am. Chem. Soc.* **2015**, 137, 3109.

Received: June 7, 2018