

CHEMISTRY

A European Journal

A Journal of



Accepted Article

Title: Decarboxylative Aminomethylation of Arylsulfonates

Authors: Magnus Rueping

This manuscript has been accepted after peer review and the authors have elected to post their Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Chem. Eur. J. 10.1002/chem.201604452

Link to VoR: <http://dx.doi.org/10.1002/chem.201604452>

Supported by
ACES

WILEY-VCH

Decarboxylative Aminomethylation of Aryl- and Vinylsulfonates through Combined Nickel and Photoredox Catalyzed Cross Coupling

Lulu Fan, Jiaqi Jia, Hong Hou, Quentin Lefebvre and Magnus Rueping*

Abstract: A mild approach for the decarboxylative aminomethylation of aryl sulfonates by the combination of photoredox and nickel catalysis via C-O bond cleavage is described for the first time. A wide range of aryl triflates as well as aryl mesylates, tosylates and alkenyl triflates afford the corresponding products in good to excellent yields.

Over the past decades, transition-metal catalyzed cross-coupling reactions were established as a powerful strategy to form a variety of C-C and C-heteroatom bonds.^[1] The well-known coupling reactions (Suzuki-Miyaura, Negishi, Kumada, Hiyama and Stille coupling) typically involve the reaction of organic electrophiles such as aryl or vinyl halides with organometallic nucleophiles including aryl or vinyl boronic acids/esters, zinc halides, Grignard reagents, organosilanes or stannanes. So far, numerous efforts have been made in this flourishing area to provide various synthetic building blocks with high functional group tolerance in an efficient manner.^[2] Whereas, extensive studies were concentrated on the construction of C(sp²)-C(sp²) bonds, the formation of C(sp²)-C(sp³) bonds, which is more demanding, is less explored. Recently, visible-light photoredox catalysis has emerged as a powerful tool to perform valuable transformations in synthetic organic chemistry.^[3] Moreover, the newly introduced dual catalysis concept by combining photoredox with organo- and transition-metal catalysis has shown even greater advantages in addressing various challenges in organic synthesis.^[4] In particular, the use of photoredox/nickel dual catalysis approach has received recently great attention for accomplishing challenging targets.^[5,6] Regarding the construction of C(sp²)-C(sp³) bonds by means of photoredox/nickel dual catalysis strategy, the electrophilic cross-coupling partners are so far restricted to aryl and vinyl halides.^[5-7] In recent years, the use of phenol derivatives as electrophiles in nickel-catalyzed cross-coupling reactions via C(sp²)-O bond cleavage has attracted the attention of many organic chemists including our group.^[8-10a-c] During our continuous studies on nickel catalysis, we questioned whether phenol derivatives could

be used as electrophilic cross-coupling partners in photoredox/nickel dual catalysis. We considered this strategy appealing because, if successful, it has important advantages including the greater availability and easier accessibility of phenyl derivatives compared to most aryl diazonium salts or aryl halides.

With these considerations in mind, we initially examined the photoredox catalyzed decarboxylative^[11] aminomethylation of 2-naphthylpivalate with *N*-phenylglycine using various nickel/phosphine complexes.^[12] Unfortunately, no desired product was detected. This may be due to the oxidative addition step which we hoped to be possible with more activated phenol derivatives. To our delight, when we carried out the dual catalysis approach with the corresponding triflate **1a** and *N*-phenylglycine (**2a**) the desired cross-coupling product *N*-(naphthalen-2-ylmethyl)aniline (**3a**) could be obtained. Importantly the yield is highly depended on the ligands used and phosphine ligands provided the best results (see supporting information for details). In fact this is the first example in which metal-phosphine complexes have been successfully applied in a dual photoredox and metal catalyzed cross coupling reaction. Given that many chiral phosphines are available the development of further asymmetric reactions should be feasible.

Table 1. Optimization of reaction conditions.^[a]

Entry	Variation from the standard conditions	Yield (%) ^[b]
1	None	98(84)
2	NiCl ₂ ·glyme as Ni catalyst	87
3	Ni(cod) ₂ as Ni catalyst	77
4	Ni(cod) ₂ as Ni catalyst, DMF as solvent	35
5	Ni(cod) ₂ as Ni catalyst, dtbbpy as ligand, DMF as solvent	5
6	No photocatalyst	0
7	No Ni catalyst	0
8	No P(4-MeO-Ph) ₃	0
9	In the dark	0

[a] Standard conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), MeCN (0.1 M), Ir(dFCF₃(ppy))₂(dtbbpy)PF₆ (1 mol %), Ni(OTf)₂ (10 mol %), P(4-MeO-Ph)₃ (25

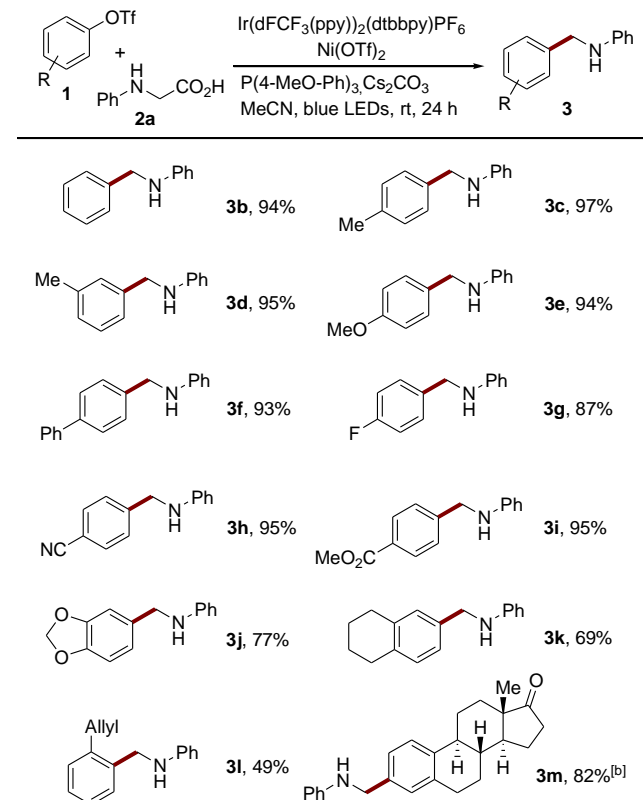
[*] Dr. L. Fan, M.Sc. J. Qi, Dr. H. Hou, Dr. Q. Lefebvre, Prof. Dr. M. Rueping
Institute of Organic Chemistry, RWTH Aachen University
Landoltweg 1, 52074 Aachen (Germany)
E-mail: magnus.rueping@rwth-aachen.de
Prof. Dr. M. Rueping
King Abdullah University of Science and Technology (KAUST),
KAUST Catalysis Center (KCC), Thuwal, 23955-6900 (Saudi Arabia); E-mail: magnus.rueping@Kaust.edu.sa

mol %), Cs₂CO₃ (2 equiv.), blue LEDs, rt, 21 h. [b] Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as internal standard, isolated yield in parentheses. bpy = 2,2'-bipyridine, dtbbpy = 4,4'-di-*tert*-butyl-2,2'-bipyridyl, cod = 1,5-cyclooctadiene.

After optimizing various reaction parameters, the desired product **3a** was obtained in 98% yield if 1 mol % of the Ir-photocatalyst in combination with the Ni(OTf)₂ complex was employed at room temperature under irradiation with blue LEDs (Table 1). All other reaction parameters tested including the use of other nickel complexes, photocatalysts or solvents resulted in a decreased yield of **3a**. Control experiments demonstrated that in the absence of photocatalyst, Ni-catalyst, phosphine ligand, base or light, no reaction occurred, indicating that each component is crucial for this transformation.

With the optimized reaction conditions in hand, we next explored the substrate scope of this new aminomethylation reaction with respect to aryl triflates (Table 2). The photoredox/nickel dual catalytic transformation showed very good tolerance towards a variety of phenol derived triflates. For example, phenyl triflate (**1b**) reacted with *N*-phenylglycine (**2a**) to give the desired product *N*-benzylaniline (**3b**) in 94% yield. The substituted phenyl triflates **1c-e**, which possess electron-donating groups in the *para*- or *meta*-position of the phenyl ring gave the corresponding aniline products **3c-e** in excellent yields of 94% to 97%.

Table 2. Substrate scope of aryl triflates in photoredox/Ni-catalyzed cross-coupling reactions.^[a]

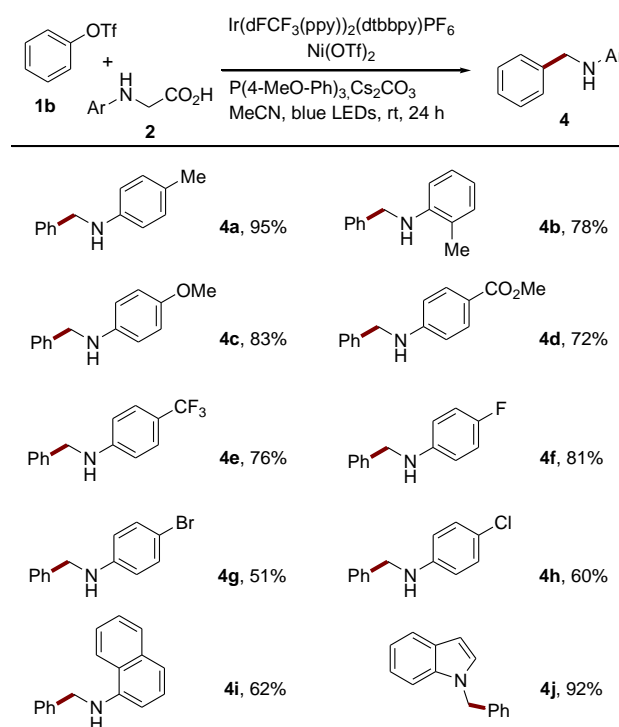


[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), MeCN (0.1 M), Ir(dFCF₃(ppy))₂(dtbbpy)PF₆ (1.5 mol %), Ni(OTf)₂ (10 mol %), P(4-MeO-Ph)₃ (22 mol %), Cs₂CO₃ (2 equiv.), blue LEDs, rt, 24 h, isolated yields. [b] 48 h.

Similarly, the *para*-fluorophenyl triflate (**1g**) with an electron-withdrawing substituent reacted as well and afforded the product **3g** in 87% yield. Moreover, other functionalized triflates like **1h** and **1i** with nitrile and methyl ester substituents were tolerated well in the reaction, providing the products **3h** and **3i** in excellent yields. In addition, the sesamol derived triflate **1j** reacted smoothly with **2a** to afford the desired product **3j** in 77% yield. The 5,6,7,8-tetrahydro-2-naphthol derived triflate **1k** provided the product **3k** in a good yield of 69%. However, *ortho*-allylphenyl triflate **1l** proved to be less favoured substrate, giving the desired product **3l** in 49% yield only, probably due to steric hindrance. To our delight, the estrone derived triflate **1m** reacted well to deliver the desired product **3m** in 82% yield.

The scope of the reaction with respect to α -amino moiety is summarized in Table 3. The *para*- and *ortho*-substituted *N*-phenylglycines reacted with phenyl triflate (**1b**) to afford the corresponding aniline products **4a-c** in good to high yields. Similarly, substrates with electron-withdrawing groups, such as methylester and trifluoromethyl underwent the reaction well to give the desired products **4d** and **4e** in 72% and 76% yield, respectively. In addition, halogenated *N*-phenylglycines were tolerated as well under the described reaction conditions, providing the benzyl protected aniline products **4f-h** in good yields. Notably, the additional bromide and chloride rests could be used in further cross-coupling reaction to construct another carbon-carbon or carbon-heteroatom bond.

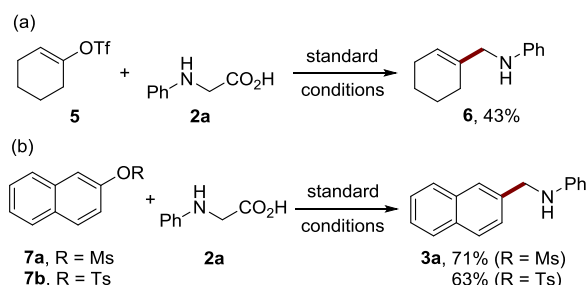
Table 3. Substrate scope of aminomethylation cross coupling reaction.^[a]



[a] Reaction conditions: **1b** (0.1 mmol), **2** (0.2 mmol), MeCN (0.1 M), Ir(dFCF₃(ppy))₂(dtbbpy)PF₆ (1.5 mol %), Ni(OTf)₂ (10 mol %), P(4-MeO-Ph)₃ (22 mol %), Cs₂CO₃ (2 equiv.), blue LEDs, rt, 24 h isolated yields.

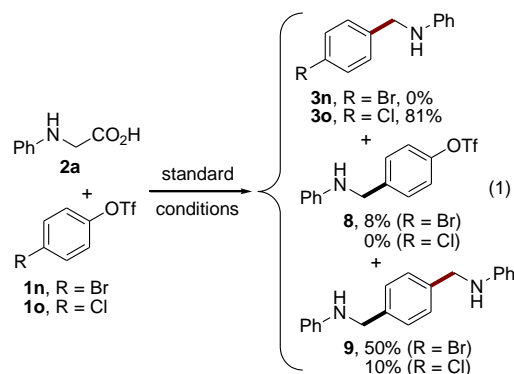
The 1-naphthylglycine was also a compatible substrate and the desired product **4i** was obtained with a slightly lower yield of 62%. However, the indole derived acid could afford the product *N*-benzylindole **4j** in an excellent yield of 92%.

In addition to the substrates mentioned above, we were interested in whether our catalytic system could be applied to the alkenyl triflates which are readily accessible from ketones (Scheme 1a). To our delight, when the alkenyl triflate **5** was applied under the standard reaction conditions, the desired product **6** was isolated in 43% yield. Additionally, when the relatively unreactive electrophilic 2-naphthyl mesylate (**7a**) and tosylate (**7b**) were subjected to the conditions using 1 mol% photocatalyst, the corresponding cross-coupling product **3a** was obtained in 71% and 63% yield, respectively (Scheme 1b).



Scheme 1. Extension of the Nickel/photoredox catalyzed cross coupling; (a) Aminomethylation of alkenyltriflates; (b) use of mesylates and tosylates.

(Hetero)Aryl bromides and chlorides have been reported to be good electrophiles previously.^[5] Hence, we were interested in the relative reactivity of aryl halides and triflates in our cross-coupling reaction using a photoredox catalyst and the Ni/P(4-MeO-Ph)₃ complex. For this purpose, we subjected the *para*-bromo- and *para*-chloro phenyltriflates (**1n** and **1o**) to the standard reaction conditions (eq. 1, scheme 2)). The reaction of **1n** with **2a** occurred mainly at both triflate and bromide sites providing the bis-alkylated product **9** in 50% yield along with the triflate product **8** in 8% yield. In the case of *para*-chloro phenyltriflate (**1o**), the reaction occurred mainly for the triflate, providing **3o** in 81% yield. In this case, product **8** was not detected, however, product **9** was obtained in 10% yield. These results suggest that: 1) the reactivity of phenylbromide might be relatively higher than phenyltriflate under our reaction conditions; 2) aryl triflates could be alternative cross-coupling partners when aryl bromides are difficult to prepare; 3) the reactivity of chloride in **1o** indicates that our photoredox/Ni-P(4-MeO-Ph)₃ system can also be applied to aryl chlorides, which was not described to date.



Scheme 2. Nickel/photoredox catalyzed cross coupling of aryl chlorides, bromides and triflates.

A plausible mechanism for the photoredox/Ni-catalyzed cross-coupling of α -amino acids with aryl sulfonates is proposed in Figure 1 and is in agreement with a previously conducted study by Molander and Kozlowski.⁶⁰ One electron oxidation of α -amino acid **2a** by the excited state Ir^{III}* generates the radical cation, followed by deprotonation and decarboxylation to give radical **2a'**, which subsequently undergoes radical addition to Ni⁰ **D** to deliver the Ni^I intermediate **E**. The oxidative addition of aryl triflate **1** to **E** produces the Ni^{III} intermediate **F**. Subsequently, reductive elimination of **F** delivers the cross-coupling product **3** and Ni^I species **G**, which undergoes one electron reduction by Ir^{II} to regenerate Ni⁰ along with the ground state photocatalyst Ir^{III}, restarting then the catalytic cycles.

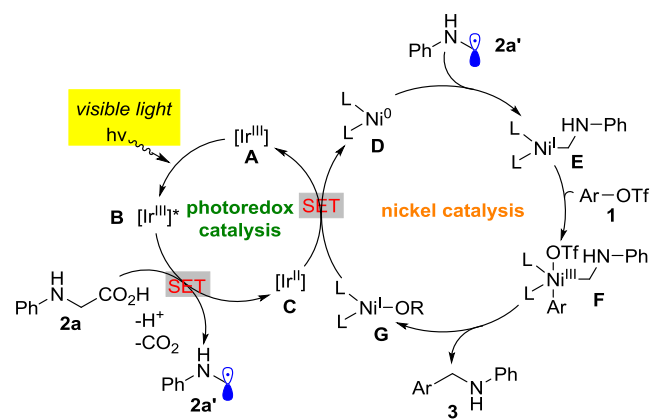


Figure 1. Proposed mechanism for the aminomethylation of arylsulfonates.

In conclusion, we have developed a mild decarboxylative aminomethylation of aryl- and vinyl sulfonates using a combination of visible light photoredox and nickel catalysis via a C-O bond cleavage procedure for the first time. The reaction has broad substrate scope and aryl- triflates, mesylates, tosylates and alkenyl triflates can be applied to give the desired aminoalkylated products and benzyl protected anilines in good to excellent yields. The reaction conditions, allowing the cross-

coupling to occur under visible light at room temperature in the presence of various functional groups, are rather mild and can be selectively performed or even be extended to chlorinated arenes if needed. Furthermore, we demonstrate that phosphine complexes can be used in the dual catalytic procedure calling for the development of combined metal and photoredox catalyzed asymmetric reactions, a research goal which we are currently pursuing.

Acknowledgments

The research leading to these results has received funding from the European Research Council under the European Union's Seventh Framework Programme (FP/2007-2013) / ERC Grant Agreement no. 617044 (SunCatChem).

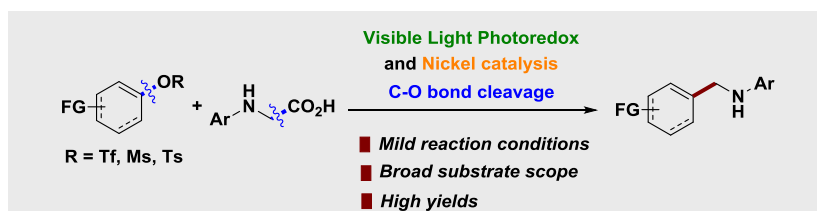
Keywords: photoredox catalysis • nickel catalysis • cross-coupling • amino acid • decarboxylation

- [1] a) *Metal-Catalyzed Cross-Coupling Reactions and More* (Eds.: A. de Meijere, S. Bräse, M. Oestreich), Wiley-VCH, Weinheim, **2014**; b) *New Trends in Cross-Coupling Theory and Applications* (Ed.: T. J. Colacot), RSC Catalysis Series, London, **2015**.
- [2] *Applied Cross-Coupling Reactions (Lecture Notes in Chemistry)*, Vol. 80, Y. Nishihara, Ed, Springer, **2013**.
- [3] For selected general reviews on photoredox catalysis, see: a) K. Zeitler, *Angew. Chem. Int. Ed.* **2009**, *48*, 9785-9789; b) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, *2*, 527-532; c) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102-113; d) F. Teply, *Collect. Czech. Chem. Commun.* **2011**, *76*, 859-917; e) J. Xuan, W. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828-6838; f) L. Shi, W.-J. Xia, *Chem. Soc. Rev.* **2012**, *41*, 7687-7697; g) D. Ravelli, M. Fagnoni, *ChemCatChem* **2012**, *4*, 169-171; h) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322-5363; i) N. Hoffmann, *ChemCatChem*, **2015**, *7*, 393-394; j) J. Xuan, Z.-G. Zhang, W.-J. Xia, *Angew. Chem. Int. Ed.* **2015**, *54*, 15632-15641.
- [4] N. Hoffmann, *ChemSusChem* **2012**, *5*, 352-371; b) M. N. Hopkinson, B. Sahoo, J.-L. Li, F. Glorius, *Chem. - Eur. J.* **2014**, *20*, 3874-3886; c) E. Meggers, *Chem. Commun.* **2015**, *51*, 3290-3301; d) L. N. Cavalcanti, G. A. Molander, *Top. Curr. Chem.* **2016**, *374*, 39.
- [5] For initial work in the field of photoredox/nickel dual catalysis, see: a) J. C. Tellis, D. N. Primer, G. A. Molander, *Science* **2014**, *345*, 433-436; b) Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science* **2014**, *345*, 437-440.
- [6] For selected recent reports on photoredox/nickel dual catalysis, see: a) M. H. Shaw, V. W. Shurtleff, J. A. Terrett, J. D. Cuthbertson, D. W. C. MacMillan, *Science* **2016**, *352*, 1304-1308; b) Z. Zuo, H. Cong, W. Li, J. Choi, G. C. Fu, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2016**, *138*, 1832-1835; c) P. Zhang, C. C. Le, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2016**, *138*, 8084-8087; d) J. A. Terrett, J. D. Cuthbertson, V. W. Shurtleff, D. W. C. MacMillan, *Nature* **2015**, *524*, 330-334; e) A. Noble, S. J. McCarver, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2015**, *137*, 624-627; f) C. C. Le, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2015**, *137*, 11938-11941; g) L. Chu, J. M. Lipshultz, D. W. C. MacMillan, *Angew. Chem. Int. Ed.* **2015**, *54*, 7929-7933; h) J. C. Tellis, J. Amani, G. A. Molander, *Org. Lett.* **2016**, *18*, 2994-2997; i) R. Karimi-Nami, J. C. Tellis, G. A. Molander, *Org. Lett.* **2016**, *18*, 2572-2575; j) M. Jouffroy, G. H. M. Davies, G. A. Molander, *Org. Lett.* **2016**, *18*, 1606-1609; k) M. El Khatib, R. A. M. Serafim, G. A. Molander, *Angew. Chem. Int. Ed.* **2016**, *55*, 254-258; l) J. Amani, E. Sodagar, G. A. Molander, *Org. Lett.* **2016**, *18*, 732-735; m) D. N. Primer, I. Karakaya, J. C. Tellis, G. A. Molander, *J. Am. Chem. Soc.* **2015**, *137*, 2195-2198; n) I. Karakaya, D. N. Primer, G. A. Molander, *Org. Lett.* **2015**, *17*, 3294-3297; o) O. Gutierrez, J. C. Tellis, D. N. Primer, G. A. Molander, M. C. Kozlowski, *J. Am. Chem. Soc.* **2015**, *137*, 4896-4899; p) S. Z. Tasker, T. F. Jamison, *J. Am. Chem. Soc.* **2015**, *137*, 9531-9534; q) V. Corce, L.-M. Chamoiseau, E. Derat, J.-P. Goddard, C. Ollivier, L. Fensterbank, *Angew. Chem., Int. Ed.* **2015**, *54*, 11414-11418; r) M. S. Oderinde, M. Frenette, D. W. Robbins, B. Aquila, J. W. Johannes, *J. Am. Chem. Soc.* **2016**, *138*, 1760-1763; s) C. L. Joe, A. G. Doyle, *Angew. Chem. Int. Ed.* **2016**, *55*, 4040-4043.
- [7] For selected reports using aryl and vinyl halides, see: a) N. R. Patel, C. B. Kelly, M. Jouffroy, G. A. Molander, *Org. Lett.* **2016**, *18*, 764-767; b) M. Jouffroy, D. N. Primer, G. A. Molander, *J. Am. Chem. Soc.* **2016**, *138*, 475-478; c) D. Ryu, D. N. Primer, J. C. Tellis, G. A. Molander, *Chem. - Eur. J.* **2016**, *22*, 120-123.
- [8] For reviews on the use of C-O electrophiles, see: a) D. G. Yu, B. J. Li, Z. J. Shi, *Acc. Chem. Res.* **2010**, *43*, 1486-1495; b) B. J. Li, D. G. Yu, C. L. Sun, Z. J. Shi, *Chem. Eur. J.* **2011**, *17*, 1728-1759; c) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A. M. Resmerita, N. K. Garg, V. Percec, *Chem. Rev.* **2011**, *111*, 1346-1416; d) T. Mesganaw, N. K. Garg, *Org. Process Res. Dev.* **2013**, *17*, 29-39; e) M. Tobisu, N. Chatani, *Top. Organomet. Chem.* **2013**, *44*, 35-54; f) S. I. Kozhushkov, H. K. Potukuchi, L. Ackermann, *Catal. Sci. Technol.* **2013**, *3*, 562-571; g) J. Cornella, C. Zarate, R. Martin, *Chem. Soc. Rev.* **2014**, *43*, 8081-8097; h) M. Tobisu, N. Chatani, *Acc. Chem. Res.* **2015**, *48*, 1717-1726.
- [9] For selected recent reviews on Ni-catalyzed reactions, see: a) Y. Tamaru, *Modern Organonickel Chemistry*, Wiley-VCH, Weinheim, Germany, **2005**; b) V. B. Phapale, D. J. Cárdenas, *Chem. Soc. Rev.* **2009**, *38*, 1598-1607; c) J. Yamaguchi, K. Muto, K. Itami, *Eur. J. Org. Chem.* **2013**, 19-30; d) F.-S. Han, *Chem. Soc. Rev.* **2013**, *42*, 5270-5298; e) S. Z. Tasker, E. A. Standley, T. F. Jamison, *Nature* **2014**, *509*, 299-309.
- [10] a) M. Leiendecker, C.-C. Hsiao, L. Guo, N. Alandini, M. Rueping, *Angew. Chem. Int. Ed.* **2014**, *53*, 12912-12915; b) M. Leiendecker, A. Chatupheeraphat, M. Rueping, *Org. Chem. Front.*, **2015**, *2*, 350-353; c) L. Guo, M. Leiendecker, C.-C. Hsiao, C. Baumann, M. Rueping, *Chem. Commun.*, **2015**, 51, 1937-1940; d) X. Liu, C.-C. Hsiao, I. Kalvet, M. Leiendecker, L. Guo, F. Schoenebeck, M. Rueping, *Angew. Chem. Int. Ed.* **2016**, *55*, 6093-6098; e) L. Guo, C.-C. Hsiao, H. Yue, X. Liu, M. Rueping, *ACS Catal.* **2016**, *6*, 4438-4442; f) L. Guo, A. Chatupheeraphat, M. Rueping, *Angew. Chem. Int. Ed.* **2016**, *55*, 11810-11813.
- [11] For an early example of a photoredox catalyzed decarboxylation, see: L. Chen, C. S. Chao, Y. Pan, S. Dong, Y. C. Teo, J. Wang, C.-H. Tan, *Org. Biomol. Chem.*, **2013**, *11*, 5922-5925, and references cited therein; recent example from our group: b) A. Millet, Q. Lefebvre, M. Rueping, *Chem. Eur. J.* **2016**, *22*, 13464-13468.
- [12] During the publication process the use of aryltriflates with alkylsilicates has been published: N.R. Patel, G. A. Molander *J. Org. Chem.* **2016**, *81*, 7271-7275.

Entry for the Table of Contents (Please choose one layout)

Layout 2:

COMMUNICATION



A mild approach for the decarboxylative aminomethylation of aryl sulfonates by the combination of photoredox and nickel catalysis via C-O bond cleavage is described. A variety of aryl triflates, mesylates, tosylates and alkenyl triflates react with α-amino acids to afford the corresponding aminomethylated products in good to excellent yields.

L. Fan, J. Jia, H. Hou, Q. Lefebvre, M. Rueping*

Page No. – Page No.

Decarboxylative Aminomethylation of Aryl- and Vinylsulfonates through Combined Nickel and Photoredox Catalyzed Cross Coupling

Accepted Manuscript