Organic LETTERS

Letter

pubs.acs.org/OrgLett

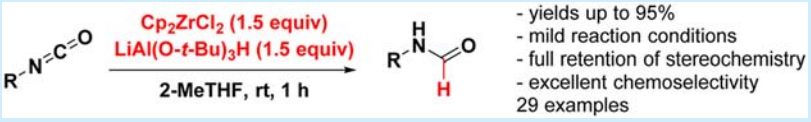
Chemoselective Schwartz Reagent Mediated Reduction of Isocyanates to Formamides

Vittorio Pace,*[,†] Karen de la Vega-Hernández,[†,‡] Ernst Urban,[†] and Thierry Langer[†]

[†]Department of Pharmaceutical Chemistry, University of Vienna, Althanstrasse, 14, A-1090 Vienna, Austria

[‡]Institute of Pharmacy and Food Sciences, University of Havana, 23rd Street, 21425-13600 Havana, Cuba

Supporting Information

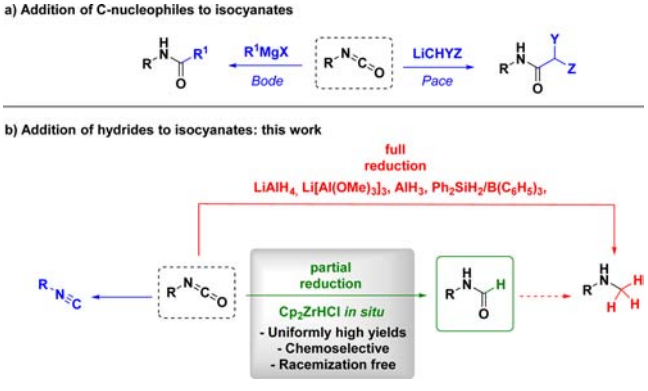


ABSTRACT: Addition of the in situ generated Schwartz reagent to widely available isocyanates constitutes a chemoselective, high-yielding, and versatile approach to the synthesis of variously functionalized formamides. Steric and electronic factors or the presence of sensitive functionalities (esters, nitro groups, nitriles, alkenes) do not compromise the potential of the method. Full preservation of the stereochemical information contained in the starting materials is observed. The use of formamides in the nucleophilic addition of organometallic reagents (Chida−Sato allylation, Charette−Huang addition to imidoyl triflate activated amides, Matteson homologation of boronic esters) is briefly investigated.

Isocyanates represent a versatile class of organic molecules[1] which, due to the excellent electrophilicity of the heterocumulene carbon, enables the smooth addition of a plethora of nucleophiles including alcohols (synthesis of carbamates),[2] amines (synthesis of ureas),[3] and carbanions (synthesis of amides, vide infra). The reaction of Grignard reagents and isocyanates—a long known reaction since the seminal work by Gilman,[4] although nonfrequently applied to synthetic processes[5]—constitutes an excellent method to access hindered amides, as elegantly showcased by Bode in 2012.[6] Subsequently, our group documented the addition of lithium halocarbenoids ($LiCH_2Z$ and LiCHYZ) to isocyanates to reach halomethyl- and dihalomethylamides (Scheme 1a).[7] Both Bode's and our own methods were general in scope, high yielding (in many circumstances, no chromatography was required), and adaptable to the synthesis of optically active amide derivatives starting from chiral isocyanates. Compared to conceptually distinct tactics for the synthesis of amides (e.g., the reaction of amines with carboxylic acid derivatives),[8] the key factor accounting for the success of the reactions is the easy attack of the organometallic nucleophile to the isocyanate carbon, whose reactivity is practically uninfluenced by the steric and electronic properties of the substituent on nitrogen. If the procedure could be extended to the addition of a hydride nucleophile, a straightforward and direct route to inaccessible formamides[9] could be envisaged. The reduction of isocyanates with $LiAlH_4$ has been known since the 1950s when Wessely and Swoboda[10] reported their first full reduction to *N*-methylamines, confirmed shortly after by Finholt.[11] The same outcome was also observed with other powerful reducing agents such as Ph_2SiH_2/$B(C_6F_5)_3$[12] or $NaBH_4$/TFA.[13]

As depicted in Scheme 1b, the ideal reducing agent for the desired transformation should present two main features: (1) it should chemoselectively halt the reduction at the formamide level (i.e., partial reduction), and (2) it should not react with additional functionalities under the reductive conditions employed. In this context, such a likelihood has been considered in the literature: Lorenz and Becker reported two examples of *N*-arylformamides obtained via the reduction of isocyanates with Ph_3SnH with poor yields (40−50%),[14] while Noltes observed that trialkyltin hydrides reacted better with arylisocyanates than alkyl counterparts.[15a] Moreover, scattered examples of this chemistry come from work by Ojima (Pd-catalyzed hydrosilylation)[15b] and Howell (amine-catalyzed hydrogenation).[16] As noticed by Baldwin, the reduction of isocyanates can be further complicated by their reduction to isocyanides in the presence of $Ph_2(t\text{-Bu})SiLi$ or Cl_3SiH/amine.[17] Taking into account these

Scheme 1. General Context of Presented Work



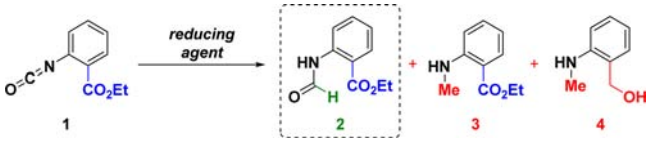
Received: April 26, 2016
Published: May 24, 2016

DOI: 10.1021/acs.orglett.6b01226
Org. Lett. 2016, 18, 2750−2753

examples and considering the lack of studies on the subject in the last >30 years, we looked at redesigning the transformation, considering that crucial for its success was identifying a reliable reducing agent possessing the chemoselective features defined above.

We began our investigations with model isocyanate **1**, which presents an ester as an additional electrophilic moiety susceptible to reduction. As summarized in Table 1, treatment with various

Table 1. Model Reaction: Optimization



entry	reducing agent (equiv)	solvent	temp (°C)/ time (h)	2/3/4 ratio	yield of 2 (%)[a]
1	DIBAL-H (1.0)	THF	0/0.5	2:1:1	12
2	$LiAlH_4$ (0.3)	THF	0/0.5	0:0:1	*b*
3	$NaBH_4$ (0.3)	THF	0/0.5	1:0:0	30
4	$NaBH_4$ (1.0)	THF	0/0.5	1:0:0	34
5	$NaBH_4$ (1.0)	THF	40/2	1:0:0	37
6	Et_3SiH (1.5)	THF	0/1	1:1:1	6[c]
7	Hantzsch ester (1.2)	THF	0/1	1.5:1.5:1	36
8	Cp_2ZrHCl[d] (1.2)	THF	rt/1	1:0:0	78
9	Cp_2ZrHCl[e] (1.2)	THF	rt/1	1:0.2:0	65
10	Cp_2ZrHCl[e,f] (1.2)	THF	rt/1	1:0:0	87
11	Cp_2ZrHCl[e,f] (1.2)	MTHF	rt/1	1:0:0	92

[a]Isolated yield. [b]Compound **4** was obtained in 46% isolated yield. [c]An overall conversion of 22% was observed by ^1H NMR. [d]Cp_2ZrHCl was supplied from a commercial source. [e]Cp_2ZrHCl was prepared according Snieckus.[22b] [f]$LiAl(O\text{-}t\text{-}Bu)_3H$ (1 M in THF) was added to Cp_2ZrCl_2 at 0 °C.

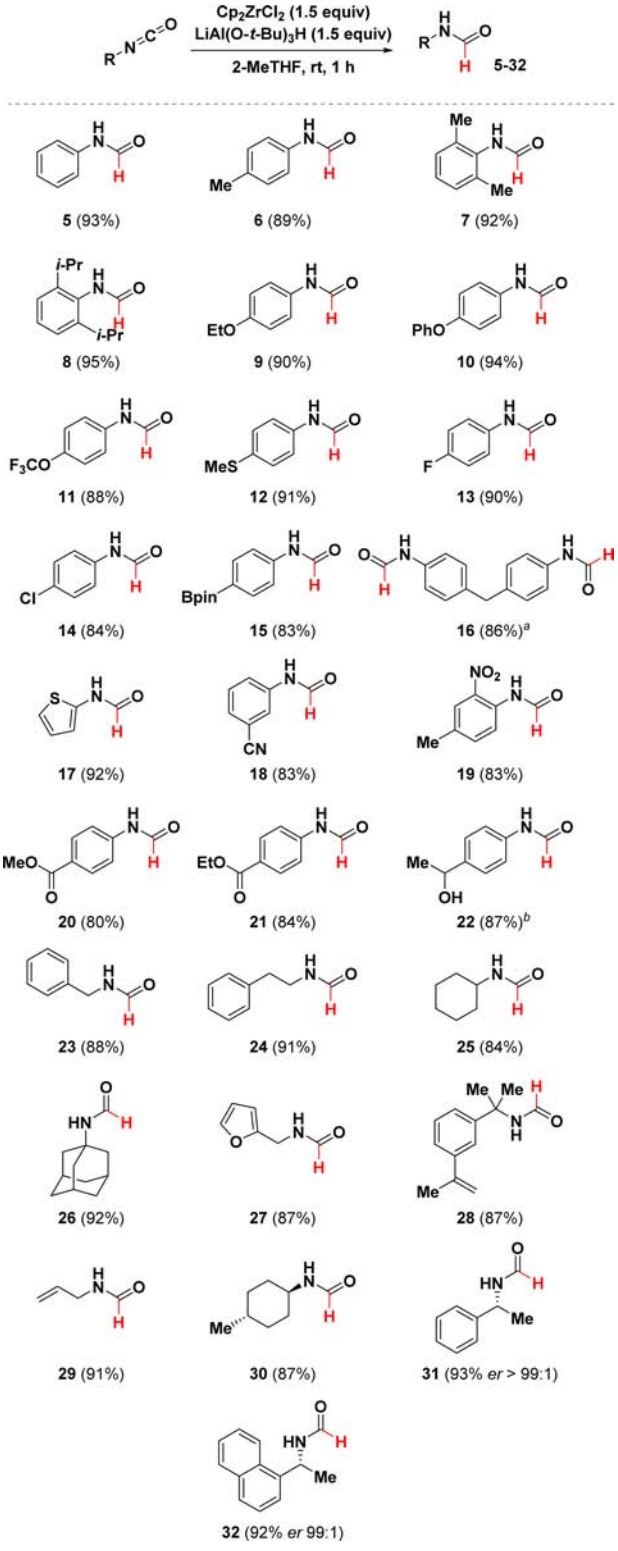
reducing agents could, in principle, provide a mixture of three different products, namely, the targeted 2-ethoxycarbonyl formamide **2**, 2-methylaminobenzoate **3** (in which the starting isocyanate was fully reduced at the corresponding amine), and the completely reduced 2-methylaminobenzylic alcohol **4**. The use of DIBAL-H afforded a mixture of the three possible products with a limited conversion (entry 1). When the reducing power of the reagent ($LiAlH_4$) was increased, fully reduced compound **4** was formed as the unique product (entry 2), in agreement with the seminal studies discussed above. A milder reagent such as $NaBH_4$ improved the selectivity dramatically. However, the yield was far from optimal (entry 3), even in the presence of increased loading or after higher temperatures/longer reaction times (entries 4 and 5). Other common reagents such as triethylsilane (entry 6) or the Hantzsch ester[18] (entry 7) provided mixtures of the three possible products in limited yields. A satisfactory 78% yield of desired compound **2**, under full chemocontrol, was achieved by employing the commercially available Schwartz reagent[19] (Cp_2ZrClH, entry 8). Indeed, this reagent features excellent chemoselectivities, as showcased in works by Georg,[20] Ganem,[21] Snieckus,[22] and Furman[23] among others,[24] during independent investigations on amide-type reduction chemistry. Because of the well-known issues associated with the use of commercially available reagents (e.g., moisture, air, light sensitivity, limited solubility in common organic solvents),[25] we found it highly beneficial to generate it according to the recently described Snieckus protocol from Cp_2ZrCl_2 and $LiAl(O\text{-}t\text{-}Bu)_3H$.[22b] Interestingly, when the latter reagent was added at rt, chemoselectivity was affected as a consequence of the reducing capability of the same $LiAl(O\text{-}t\text{-}Bu)_3H$ (entry 9). However, performing such an addition at 0 °C and removing the cooling bath enabled us to access **2** in 87% isolated yield with full chemocontrol (entry 10). Further improvement could be observed by running the reaction in 2-methyltetrahydrofuran (MTHF, entry 11), nowadays considered a versatile alternative to THF in terms of eco-compatibility for organometallic reactions.[26]

With these optimized conditions in hand, we explored the scope of the reaction (Scheme 2). Both aromatic and aliphatic isocyanates react smoothly, providing the corresponding formamides **5**−**22** and **23**−**32**, respectively, in high yields. Substitution on the aromatic ring does not adversely influence the reaction outcome: both electron-releasing (alkyl, alkoxy, e.g., **6**−**12**) and electron-withdrawing [halogens (**13** and **14**), nitrile (**18**), nitro (**19**), esters (**20**,**21**)] functionalities are tolerated. Interestingly, sterically hindered isocyanates provide the expected products in high yield not only in the case of aromatic substituents (**7** and **8**) but also for aliphatic analogues (**26** and **28**), thus overcoming the well-known issues concerning the low reactivity of the corresponding amines toward acylating agents.[8b] The following additional points on the chemoselectivity of the protocol are worthy of mention: (*a*) Hydride delivery takes place exclusively on the isocyanate without affecting sensitive functionalities such as nitrile **18** or nitro **19**. (*b*) Additionally, the presence of esters decorating aromatic nuclei at different positions does not alter the chemoselectivity (**20** and **21**); the concomitant reduction of this functional group was not observed at all. (*c*) Olefinic fragments (known to be susceptible to the Schwartz reagent under different conditions)[19c,e,22b,27] were not affected under the reaction conditions (**28** and **29**). (*d*) Use of optically active isocyanates allowed us to prepare the corresponding formamides in excellent enantiopurity without minimal erosion of the stereochemical information (**30**−**32**). (*e*) Heteroaromatic rings in the cases of both aromatic and aliphatic isocyanates (**17** and **27**) or a boronic acid pinacol ester (**15**) susceptible of further derivatization[28] did not compromise the efficiency of the methodology. (*f*) Multiple reduction of a bis-isocyanate was possible as indicated in the case of diformamide **16**. In line with previous studies by Georg,[20a] a highly reactive aromatic ketone was concomitantly reduced to the secondary alcohol under the reaction conditions (**22**). Of particular significance is the one-step, straightforward access to formamide **10** known to manifest mutagenic properties.[29]

Because of our interest toward the addition of organometallic reagents to amide type substrates,[30] and being cognisant of the fact that formamides have not been studied recently in reactions with analogous species, we tested their behavior in such nucleophilic additions (Scheme 3). In particular, the activation of the inert amide bond could be realized through two conceptually distinct approaches, namely, (*a*) formation of an iminium ion with the same Schwartz reagent according to the protocol of Chida−Sato[31] and (b) formation of an imidoyl triflate species reported by the groups of Charette[32] and Huang.[33] Thus, the former strategy[31] enabled the smooth addition of an allylic fragment via the reaction of formamide **5** with $allylSn(n\text{-}Bu)_3$, providing homoallylic aniline **33** in high yield. When the formamide link of **5** was preactivated with an electrophilic reagent (Tf_2O), subsequent addition of a Grignard reagent afforded, upon acidic hydrolysis, aldehyde **34** (Charette conditions).[32a] By employing Huang's chemoselective $NaBH_4$-mediated reduction of a preactivated amide,[34] the complete

DOI: 10.1021/acs.orglett.6b01226
Org. Lett. 2016, 18, 2750−2753

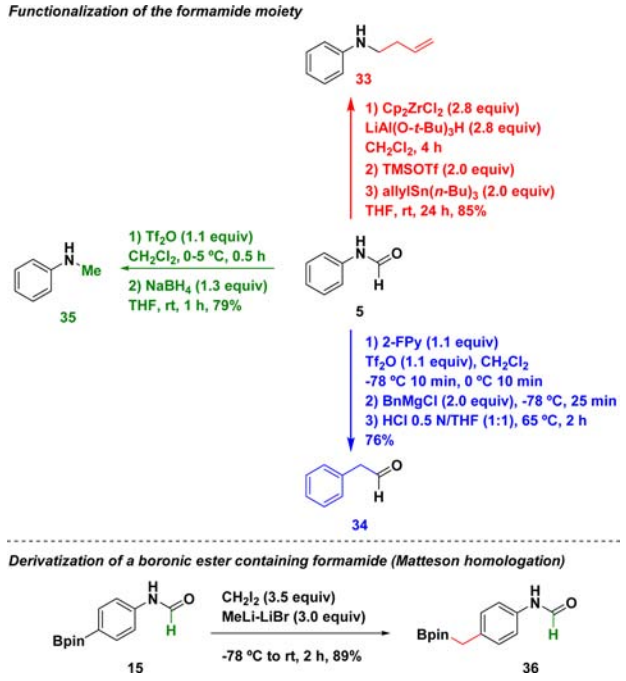
Scheme 2. Scope of the Reaction



[a]With 3.0 equiv of Schwartz reagent. [b]With 2.0 equiv of Schwartz reagent.

reduction of formamide **5** was observed, thus yielding *N*-methylaniline **35**. Finally, with the aim of gaining further insights into the portfolio of lithium carbenoid mediated homologations currently underway in our group,[35] we evaluated the chemoselectivity of the Matteson boronic ester homologation[28,36] in the presence of a *N*-formylamide derivative **15**. The attack of the carbenoidic iodomethyllithium took place exclusively at the boronic moiety (no modification occurred at the formamide moiety), affording compound **36** in very high yield.

Scheme 3. Reactivity of Formamides toward Organometallic Reagents



In conclusion, we have developed an expeditious route to *N*-formamides through the highly chemoselective nucleophilic addition of the in situ generated Schwartz reagent to widely available isocyanates. Key characteristics of the transformation are (1) uniformly high yields and full retention of the steric information contained in the starting materials and (2) excellent chemoselectivity in the presence of functionalities sensitive to the Schwartz reagent such as nitro, cyano, ester, and alkene groups. The synthetic potential of the formamide moiety in reactions with organometallic reagents such as stannane, hydride, Grignard, and carbenoid reagents has been documented.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01226.

Experimental procedure, NMR spectra, HPLC traces, and analytical data for all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: vittorio.pace@univie.ac.at.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the University of Vienna for financial support. K.d.V.H. acknowledges the OEAD for a postgraduate Mach grant.

DOI: 10.1021/acs.orglett.6b01226
Org. Lett. 2016, 18, 2750−2753

REFERENCES

(1) For reviews, see: (a) Ozaki, S. *Chem. Rev.* **1972**, *72*, 457−496. (b) Ulrich, H. *Chemistry and Technology of Isocyanates*; Wiley: New York, 1996.

(2) Spino, C.; Joly, M.-A.; Godbout, C.; Arbour, M. *J. Org. Chem.* **2005**, *70*, 6118−6121.

(3) (a) Spyropoulos, C.; Kokotos, C. G. *J. Org. Chem.* **2014**, *79*, 4477−4483. (b) Dubé, P.; Nathel, N. F. F.; Vetelino, M.; Couturier, M.; Aboussafy, C. L.; Pichette, S.; Jorgensen, M. L.; Hardink, M. *Org. Lett.* **2009**, *11*, 5622−5625. (c) Le, H. V.; Ganem, B. *Org. Lett.* **2011**, *13*, 2584−2585.

(4) (a) Gilman, H.; Furry, M. *J. Am. Chem. Soc.* **1928**, *50*, 1214−1216. (b) Gilman, H.; Kinney, C. R. *J. Am. Chem. Soc.* **1924**, *46*, 493−497.

(5) For selected examples, see: (a) Padwa, A.; Crawford, K. R.; Rashatasakhon, P.; Rose, M. *J. Org. Chem.* **2003**, *68*, 2609−2617. (b) Antczak, M. I.; Ready, J. M. *Chem. Sci.* **2012**, *3*, 1450−1454. (c) Zhang, Y.; Jiang, J.; Chen, Y. *Tetrahedron Lett.* **1987**, *28*, 3815−3816. (d) Stefanuti, I.; Smith, S. A.; Taylor, R. J. K. *Tetrahedron Lett.* **2000**, *41*, 3735−3738.

(6) (a) Schäfer, G.; Matthey, C.; Bode, J. W. *Angew. Chem., Int. Ed.* **2012**, *51*, 9173−9175. (b) Schäfer, G.; Bode, J. W. *Chimia* **2014**, *68*, 252−255.

(7) (a) Pace, V.; Castoldi, L.; Holzer, W. *Chem. Commun.* **2013**, *49*, 8383−8385. (b) Pace, V.; Castoldi, L.; Mamuye, A. D.; Holzer, W. *Synthesis* **2014**, *46*, 2897−2909. For analogous nucleophilic additions to isothiocyanates, see: (c) Pace, V.; Castoldi, L.; Monticelli, S.; Safranek, S.; Roller, A.; Langer, T.; Holzer, W. *Chem. - Eur. J.* **2015**, *21*, 18966−18970.

(8) (a) Pattabiraman, V. R.; Bode, J. W. *Nature* **2011**, *480*, 471−479. (b) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *38*, 606−631.

(9) For recent examples on the use (and synthesis) of formamides, see: (a) Li, W.; Wu, X.-F. *Chem. - Eur. J.* **2015**, *21*, 14943−14948. (b) Zhang, C.; Xu, Z.; Shen, T.; Wu, G.; Zhang, L.; Jiao, N. *Org. Lett.* **2012**, *14*, 2362−2365. (c) Yang, Y.; Huang, H.; Wu, L.; liang, Y. *Org. Biomol. Chem.* **2014**, *12*, 5351−5355. (d) Armanino, N.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 6814−6817. (e) Nakao, Y.; Morita, E.; Idei, H.; Hiyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 3264−3267. (f) Fujihara, T.; Katafuchi, Y.; Iwai, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2010**, *132*, 2094−2098. (g) Dine, T. M. E.; Evans, D.; Rouden, J.; Blanchet, J. *Chem. - Eur. J.* **2016**, *22*, 5894−5898.

(10) Wessely, F.; Swoboda, W. *Monatsh. Chem.* **1951**, *82*, 621−627.

(11) Finholt, A. E.; Anderson, C. D.; Agre, C. L. *J. Org. Chem.* **1953**, *18*, 1338−1340.

(12) Tan, M.; Zhang, Y. *Tetrahedron Lett.* **2009**, *50*, 4912−4915.

(13) Turnbull, K.; Krein, D. M. *Synthesis* **1999**, *1999*, 391−392.

(14) Lorenz, D. H.; Becker, E. I. *J. Org. Chem.* **1963**, *28*, 1707−1708.

(15) (a) Noltes, J. G.; Janssen, M. J. *J. Organomet. Chem.* **1964**, *1*, 346−355. See also: (b) Ojima, I.; Inaba, S.; Nagai, Y. *Tetrahedron Lett.* **1973**, *14*, 4363−4366.

(16) Howell, H. G. *Synth. Commun.* **1983**, *13*, 635−637.

(17) Baldwin, J. E.; Bottaro, J. C.; Riordan, P. D.; Derome, A. E. *J. Chem. Soc., Chem. Commun.* **1982**, 942−943.

(18) (a) Hantzsch, A. *Ber. Dtsch. Chem. Ges.* **1881**, *14*, 1637−1638. (b) Zheng, C.; You, S.-L. *Chem. Soc. Rev.* **2012**, *41*, 2498−2518.

(19) For seminal studies, see: (a) Wailes, P. C.; Weigold, H. *J. Organomet. Chem.* **1970**, *24*, 405−411. (b) Wailes, P. C.; Weigold, H.; Bell, A. P. *J. Organomet. Chem.* **1971**, *27*, 373−378. (c) Hart, D. W.; Schwartz, J. *J. Am. Chem. Soc.* **1974**, *96*, 8115−8116. (d) Hart, D. W.; Blackburn, T. F.; Schwartz, J. *J. Am. Chem. Soc.* **1975**, *97*, 679−680. For reviews, see: (e) Marek, I.; Chinkov, N.; Levin, A. *Synlett* **2006**, 0501−0514. (f) Negishi, E.-i.; Takahashi, T. *Synthesis* **1988**, *1988*, 1−19.

(20) (a) Spletstoser, J. T.; White, J. M.; Tunoori, A. R.; Georg, G. I. *J. Am. Chem. Soc.* **2007**, *129*, 3408−3419. (b) White, J. M.; Tunoori, A. R.; Georg, G. I. *J. Am. Chem. Soc.* **2000**, *122*, 11995−11996. (c) Spletstoser, J. T.; White, J. M.; Georg, G. I. *Tetrahedron Lett.* **2004**, *45*, 2787−2789.

(21) (a) Schedler, D. J. A.; Godfrey, A. G.; Ganem, B. *Tetrahedron Lett.* **1993**, *34*, 5035−5038. (b) Schedler, D. J. A.; Li, J.; Ganem, B. *J. Org. Chem.* **1996**, *61*, 4115−4119. (c) Ganem, B.; Franke, R. R. *J. Org. Chem.* **2007**, *72*, 3981−3987.

(22) (a) Morin, J.; Zhao, Y.; Snieckus, V. *Org. Lett.* **2013**, *15*, 4102−4105. (b) Zhao, Y.; Snieckus, V. *Org. Lett.* **2014**, *16*, 390−393.

(23) Ulikowski, A.; Furman, B. *Org. Lett.* **2016**, *18*, 149−151.

(24) (a) McGilvra, J. D.; Unni, A. K.; Modi, K.; Rawal, V. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 6130−6133. (b) Gondi, V. B.; Hagihara, K.; Rawal, V. H. *Chem. Commun.* **2010**, *46*, 904−906. (c) Piperno, A.; Carnovale, C.; Giofrè, S. V.; Iannazzo, D. *Tetrahedron Lett.* **2011**, *52*, 6880−6882.

(25) (a) Wipf, P.; Kendall, C. *Top. Organomet. Chem.* **2004**, *8*, 1−25. (b) Wipf, P.; Jahn, H. *Tetrahedron* **1996**, *52*, 12853−12910. (c) Huang, Z.; Negishi, E.-i. *Org. Lett.* **2006**, *8*, 3675−3678.

(26) Pace, V.; Hoyos, P.; Castoldi, L.; Domínguez de María, P.; Alcántara, A. R. *ChemSusChem* **2012**, *5*, 1369−1379.

(27) Marek, I. *Titanium and Zirconium in Organic Synthesis*; Wiley-VCH: Weinheim, 2002.

(28) Matteson, D. S. *J. Org. Chem.* **2013**, *78*, 10009−10023.

(29) Miyauchi, M.; Endoh, Y.; Uematsu, T. *Bull. Environ. Contam. Toxicol.* **1995**, *55*, 446−452.

(30) For reviews, see: (a) Pace, V.; Holzer, W.; Olofsson, B. *Adv. Synth. Catal.* **2014**, *356*, 3697−3736. (b) Pace, V.; Holzer, W. *Aust. J. Chem.* **2013**, *66*, 507−510. (c) Seebach, D. *Angew. Chem., Int. Ed.* **2011**, *50*, 96−101. (d) Sato, T.; Chida, N. *Org. Biomol. Chem.* **2014**, *12*, 3147−3150. (e) Murai, T.; Mutoh, Y. *Chem. Lett.* **2012**, *41*, 2−8.

(31) (a) Oda, Y.; Sato, T.; Chida, N. *Org. Lett.* **2012**, *14*, 950−953. (b) Nakajima, M.; Oda, Y.; Wada, T.; Minamikawa, R.; Shirokane, K.; Sato, T.; Chida, N. *Chem. - Eur. J.* **2014**, *20*, 17565−17571.

(32) (a) Bechara, W. S.; Pelletier, G.; Charette, A. B. *Nat. Chem.* **2012**, *4*, 228−234. (b) Pelletier, G.; Bechara, W. S.; Charette, A. B. *J. Am. Chem. Soc.* **2010**, *132*, 12817−12819. (c) Barbe, G.; Charette, A. B. *J. Am. Chem. Soc.* **2008**, *130*, 18−19. (d) Magnus, P.; Gazzard, L.; Hobson, L.; Payne, A. H.; Rainey, T. J.; Westlund, N.; Lynch, V. *Tetrahedron* **2002**, *58*, 3423−3443. (e) Bélanger, G.; O'Brien, G.; Larouche-Gauthier, R. *Org. Lett.* **2011**, *13*, 4268−4271.

(33) (a) Xiao, K.-J.; Luo, J.-M.; Ye, K.-Y.; Wang, Y.; Huang, P.-Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 3037−3040. (b) Xiao, K.-J.; Wang, Y.; Ye, K.-Y.; Huang, P.-Q. *Chem. - Eur. J.* **2010**, *16*, 12792−12796. (c) Xiao, K.-J.; Wang, A.-E.; Huang, P.-Q. *Angew. Chem., Int. Ed.* **2012**, *51*, 8314−8317. (d) Xiao, K.-J.; Wang, A.-E.; Huang, Y.-H.; Huang, P.-Q. *Asian J. Org. Chem.* **2012**, *1*, 130−132. (e) Huang, P.-Q.; Geng, H. *Org. Chem. Front.* **2015**, *2*, 150−158.

(34) Xiang, S.-H.; Xu, J.; Yuan, H.-Q.; Huang, P.-Q. *Synlett* **2010**, *2010*, 1829−1832.

(35) (a) Pace, V.; Pelosi, A.; Antermite, D.; Rosati, O.; Curini, M.; Holzer, W. *Chem. Commun.* **2016**, *52*, 2639−2642. (b) Pace, V.; Castoldi, L.; Mamuye, A. D.; Langer, T.; Holzer, W. *Adv. Synth. Catal.* **2016**, *358*, 172−177. (c) Pace, V.; Castoldi, L.; Holzer, W. *Adv. Synth. Catal.* **2014**, *356*, 1761−1766. (d) Pace, V.; Holzer, W.; Verniest, G.; Alcántara, A. R.; De Kimpe, N. *Adv. Synth. Catal.* **2013**, *355*, 919−926. (e) Pace, V.; Castoldi, L.; Holzer, W. *J. Org. Chem.* **2013**, *78*, 7764−7770. (f) Pace, V.; Murgia, I.; Westermayer, S.; Langer, T.; Holzer, W. *Chem. Commun.* **2016**, DOI: 10.1039/C6CC03532A. See also: (g) Pace, V. *Aust. J. Chem.* **2014**, *67*, 311−313 and references cited therein.

(36) (a) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588−7590. (b) Sonawane, R. P.; Jheengut, V.; Rabalakos, C.; Larouche-Gauthier, R.; Scott, H. K.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2011**, *50*, 3760−3763. (c) Burns, M.; Essafi, S.; Bame, J. R.; Bull, S. P.; Webster, M. P.; Balieu, S.; Dale, J. W.; Butts, C. P.; Harvey, J. N.; Aggarwal, V. K. *Nature* **2014**, *513*, 183−188.

DOI: 10.1021/acs.orglett.6b01226
Org. Lett. 2016, 18, 2750−2753