ChemComm

COMMUNICATION

View Article Online
View Journal

Cite this: DOI: 10.1039/c7cc07926e

Received 13th October 2017,
Accepted 14th November 2017

DOI: 10.1039/c7cc07926e

rsc.li/chemcomm

Catalytic substitution/cyclization sequences of *O*-substituted Isocyanates: synthesis of 1-alkoxybenzimidazolones and 1-alkoxy-3,4-dihydroquinazolin-2(1*H*)-ones†

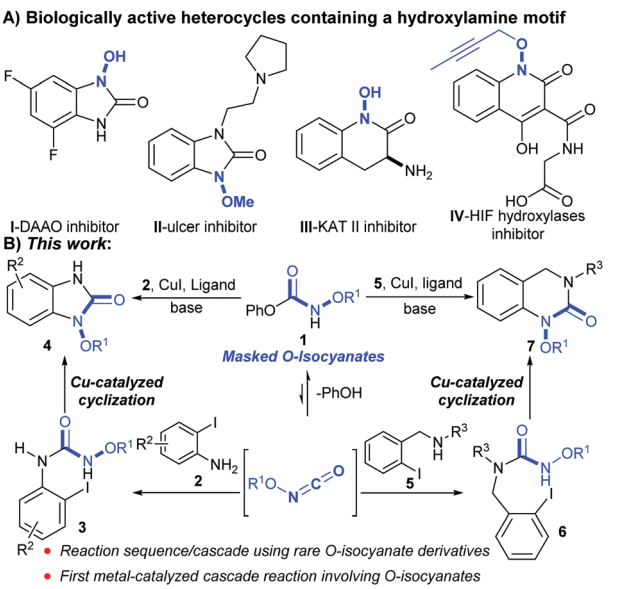
Qiang Wang,[ab] Jing An,[b] Howard Alper,[ab] Wen-Jing Xiao [a] and André M. Beauchemin *[ab]

***O*-Substituted isocyanates (*O*-isocyanates) have rarely been used in organic synthesis, given their tendency to undergo side reactions (*e.g.*, trimerization). Herein, we show that masked (blocked) *O*-isocyanate precursors allow one-pot or cascade reaction sequences featuring base-catalyzed substitution with 2-iodoanilines and 2-iodobenzylamines followed by copper-catalyzed cyclization, to form benzimidazolones and 3,4-dihydroquinazolin-2(1*H*)-ones. This work shows that *O*-isocyanates can serve as efficient building blocks for the synthesis of hydroxylamine-containing heterocycles.**

Hydroxylamines and their derivatives are an important family of compounds in organic chemistry, which have many applications[1] and are often found in bioactive natural products and pharmaceuticals.[2] The weak N–O σ bond has an average energy of ∼57 kcal mol^{-1}, which is significantly lower than the energies of σ_{C-X} bonds (X = C, N, O; 69–91 kcal mol^{-1}).[1b] For this reason, hydroxylamine derivatives can be difficult to form as the weakness of the N–O bond can lead to rearrangements and other side reactions.[3] Over the past decade, our group has developed Cope-type hydroaminations of hydroxylamines, forming various types of N–O bond containing molecules through intra- or intermolecular reactions.[4] This work made us aware of the limitations of many hydroxylamine syntheses. In addition, recent synthetic developments exploiting complex hydroxylamine derivatives in amination[5,6] and photoredox catalysis[7] and also the frequent use of such derivatives in medicinal chemistry efforts (*e.g.*, Scheme 1A)[8–11] suggest that the development of new methods for their synthesis is needed. Given this and as part of our efforts on amphoteric *N*-isocyanate intermediates,[12] we were drawn to *O*-isocyanates, a rare class of isocyanates[13] with excellent potential to assemble N–O bond containing motifs.[14]

In contrast to the ubiquitous *C*-isocyanates, the chemistry of highly reactive *O*-isocyanates remains largely unexplored due to side reactions (*e.g.* trimerization).[15] Our recent results showed that controlled formation and reactivity is possible from blocked *O*-isocyanate precursors,[14,16] allowing them to be suitable components of cascade reactions. Herein, we expand this approach to reaction sequences involving the substitution of 2-iodoanilines and 2-iodobenzylamines onto *in situ* generated *O*-isocyanates, followed by a copper-catalyzed cyclization that is compatible with the weak N–O bond,[17] to form complex hydroxylamine-containing heterocycles: 1-alkoxy-benzimidazolones[18] and -3,4-dihydroquinazolin-2(1*H*)-ones[19] (Scheme 1B).

To our knowledge *O*-isocyanates have not been used in combination with metal-catalyzed reactions, a strategy that would enable access to various complex hydroxylamine derivatives.



Scheme 1 (A) Biologically active heterocycles containing a hydroxylamine motif. (B) This work: catalytic heterocyclic synthesis using rare *O*-isocyanates as key intermediates.

[a] *CCNU-uOttawa Joint Research Centre, Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, 152 Luoyu Road, Wuhan, Hubei 430079, China*

[b] *Centre for Catalysis Research and Innovation, Department of Chemistry and Biomolecular Sciences, University of Ottawa, 10 Marie-Curie, Ottawa, ON, K1N 6N5, Canada. E-mail: andre.beauchemin@uottawa.ca*

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c7cc07926e

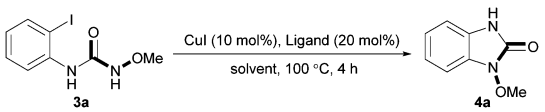
To address this void and expand the synthetic reach of *O*-isocyanates, it was necessary to synthesize suitable cyclization precursors. From a blocked isocyanate perspective, phenol is a common blocking group that typically provides stable isocyanate precursors, which can be deblocked upon heating or in the presence of a base as a catalyst.[12b,c,e,f] We thus selected the readily accessible phenyl methoxycarbamate **1a** (R^1 = Me) and 2-iodoaniline **2a** as model substrates to optimize the *O*-isocyanate substitution reaction (see ESI† for details and discussion). Gratifyingly, substitution proceeded in the presence of several bases to afford the desired mixed *N*-methoxyurea **3a** upon heating at 100 °C (Table S1 (ESI†), entries 1–5). Further optimization led to the cyclization precursor **3a** being isolated in 92% yield. With a robust procedure available to form the cyclization precursors, the identification of suitable conditions to convert mixed urea **3a** into *N*-methoxybenzimidazolone **4a** began (Table 1).

To our delight, the copper-catalyzed cyclization proceeded smoothly in the presence of CuI (10 mol%), 1,10-phenanthroline (**L1**, 20 mol%), DABCO as a base and DMSO as a solvent, providing the desired product **4a** in 96% yield (entry 1). These conditions were adapted from our recent study of related cascade reactions using *N*-isocyanate derivatives.[12f] However, investigation of ligand effects revealed that *N,N′*-dimethyl-1,2-ethanediamine (**L2**) was the best ligand for the cyclization (entries 1–4), as a quantitative yield of product **4a** was detected by NMR. The effect of the base on the coupling reaction was further explored (entries 5–9). Interestingly, inorganic bases commonly used in copper-catalyzed C–N coupling reactions, K_2CO_3 and K_3PO_4, only led to the decomposition of the starting material (entries 5 and 6). This was not surprising, given our recent observation that mixed ureas from anilines can act as *N*-isocyanate blocking (masking) groups.[12d,e] In contrast, the organic base Et_3N gave a comparable result to DABCO (99% yield, entry 7) but other organic bases such as i-Pr_2NEt and DMAP gave inferior results (entries 8 and 9). Further exploration of solvent effects using DMF, MeCN and 1,4-dioxane only led to low reaction efficiency and moderate yields (entries 10–12). Control experiments revealed that both CuI and ligand were necessary for this reaction (entries 13–15). Given the efficiency observed for each individual step, a one-pot approach was attempted by: (1) performing the substitution step in *p*-xylene in the presence of DABCO, (2) concentrating *in vacuo*, (3) adding CuI, ligand **L2** and DMSO: this gave the desired product **4a** in 87% isolated yield (entry 2). When 2-bromoaniline was used, product **4a′** was formed in 43% yield (Table 2). With the optimal reaction conditions in hand, we then examined the scope of 2-iodoanilines for this one-pot reaction (Table 2).

The conditions identified for the one-pot sequence proved versatile for the synthesis of various 1-alkoxy-imidazolones (Table 2). For example, a variety of *para*-substituted 2-iodo-anilines showed good reactivity and the corresponding products **4b–4g** were obtained in 70–92% yields over two steps. This included substrates with an electron-withdrawing group (CO_2Me, **4g**, 70% yield) and with fluoro, chloro, bromo and trifluoromethyl groups. 2-Iodoanilines bearing methyl group(s) at different positions were explored, and as expected sterically hindered anilines afforded the desired product in lower yields (**4i–j**, 45–49% yields). Then different substitutions with different *O*-isocyanate precursors were investigated. Precursors bearing benzyl, allyl, and cyclohexyl functional groups exhibited good compatibility under the present conditions, forming products **4k–m** efficiently (75–82% yields). A synthetically useful alkyne moiety was also well-tolerated under the one-pot conditions, affording product **4n** in 84% yield.

Then we sought to extend the approach to form 6-membered heterocycles bearing a hydroxylamine functionality.[19,20] This implied

Table 1 Optimization of reaction conditions for cyclization[a]



Entry	Ligand	Base	Solvent	Yield[b] (%)
1	**L1**	DABCO	DMSO	96
2	**L2**	DABCO	DMSO	>98 (87)[c]
3	**L3**	DABCO	DMSO	76
4	**L4**	DABCO	DMSO	70
5	**L2**	K_2CO_3	DMSO	0
6	**L2**	K_3PO_4	DMSO	0
7	**L2**	Et_3N	DMSO	99
8	**L2**	i-Pr_2NEt	DMSO	90
9	**L2**	DMAP	DMSO	51
10[d]	**L2**	DABCO	DMF	52
11[e]	**L2**	DABCO	MeCN	32
12[e]	**L2**	DABCO	1,4-Dioxane	66
13[f]	**L2**	DABCO	DMSO	19
14[g]	—	DABCO	DMSO	63
15[h]	—	DABCO	DMSO	<5

[a] Conditions: **3a** (0.10 mmol), base (0.20 mmol), solvent (1.0 mL). [b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] Isolated yield of one-pot reaction in parentheses. [d] Reaction time: 12 h. [e] Reaction time: 36 h. [f] Without CuI. [g] Without **L2**. [h] Without CuI and **L2**.

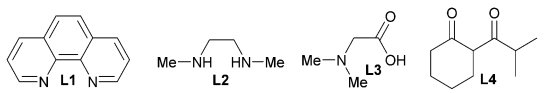
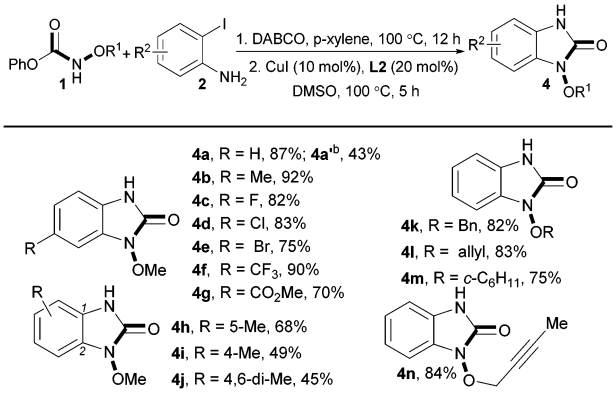


Table 2 Substrate scope of 1-alkoxybenzimidazolones[a]

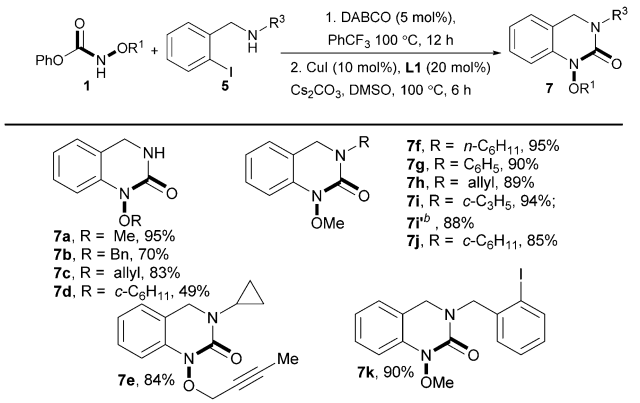


[a] Conditions: **1** (0.20 mmol), **2** (0.30 mmol), DABCO (0.40 mmol), *p*-xylene (2.0 mL), 100 °C, 12 h, and then concentrated; adding CuI (0.02 mmol), **L2** (0.04 mmol), and DMSO (2.0 mL), then stirred at 100 °C for 5 h. [b] 2-Bromoaniline and **L1** were used, 12 h for cyclization.

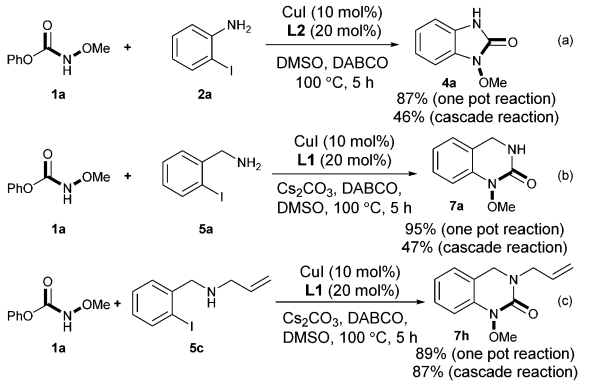
using the substitution of 2-iodobenzylamines on the *O*-isocyanate derivative, which we felt would benefit from the higher nucleophilicity of such amines. In contrast, the copper-catalyzed cyclization would likely require some reoptimization. Indeed, the substitution reaction of *O*-isocyanate precursor **1a** and 2-iodobenzylamine **5a** did occur under the standard conditions. In contrast, the copper-catalyzed cyclization failed under the standard conditions for benzimidazolone synthesis (see ESI† Scheme S1). Fortunately, after a brief screen of the effect of the ligand, base and solvent on this reaction, optimal reaction conditions were identified and the desired 6-membered heterocycle **6a** was formed in 95% yield following a two-step, one-pot sequence (see footnote, Table 3). The substrate scope of this one-pot reaction sequence was examined, and the results are summarized in Table 3.

Generally, *O*-isocyanate precursors bearing different functional groups and various *N*-substituted-2-iodo-benzylamines engaged in productive reaction sequences (Table 3). For example, *O*-isocyanate precursors with benzyl and allyl functional groups gave the corresponding products **7b** and **7c** in good yields (70% and 83%, respectively). A precursor with an *O*-cyclohexyl group gave the desired product **7d** in moderate yield (**7d**, 49% yield). The formation of product **7e** illustrates the possibility of rapidly assembling molecular complexity with this sequence: a product with *N*-cyclopropyl and *O*-propargyl substituents was isolated in 84% yield under standard conditions. The impact of the nitrogen substituent on the 2-iodobenzylamine **5** was examined. Substrates with hexyl, phenyl and allyl groups reacted smoothly under the standard conditions and were converted to products **7f–h** in excellent yields (**7f–7h**, 89–95% yields). When the *ortho*-bromo substrate was used, product **7i′** was isolated in comparable yield (**7i**, 94% *vs.* **7i′**, 88%). Even a sterically hindered substrate such as the *N*-cyclohexyl benzylic amine also showed high reaction efficiency, with product **7j** being isolated in 85% yield. Moreover, the substrate bearing an iodo substituent was untouched during the reaction and produced the desired product **7k** in 90% yield. The iodo substituent in product **7k** provides a convenient handle for further incorporation of complexity, for example using a cross-coupling reaction.

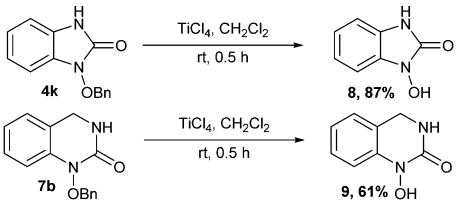
Table 3 Substrate scope of 1-alkoxy-3,4-dihydroquinazolin-2(1*H*)-ones[a]



[a] Conditions: **1** (0.20 mmol), **5** (0.30 mmol), DABCO (0.01 mmol), $PhCF_3$ (2.0 mL), 100 °C, 12 h, and then concentrated; adding CuI (0.02 mmol), **L1** (0.04 mmol), Cs_2CO_3 (0.4 mmol) and DMSO (2.0 mL), then stirred at 100 °C for 6 h. [b] Corresponding *o*-bromo substrate was used, 12 h for cyclization.



Scheme 2 A comparison of cascade *vs.* one-pot reaction for three substrate types.



Scheme 3 Removal of the benzyl group to form the free hydroxyamic acid heterocycles.

In order to further simplify the process, we investigated cascade reactions of *O*-isocyanate precursors with 2-iodoaniline or 2-iodobenzylamines (Scheme 2). In the presence of a copper catalyst and DMSO as the solvent, the cascade reaction of phenyl methoxycarbamate **1a** and 2-iodoanilines **2a** did indeed occur albeit in relatively moderate yield compared with the one-pot reaction sequence (Scheme 2a). When the cascade reaction of **1a** and 2-iodobenzylamine **5a** was examined, the corresponding product **7a** was isolated in lower yield (47% *vs.* 95%) (Scheme 2b). In contrast, the cascade reaction of **1a** and *N*-(2-iodobenzyl)prop-2-en-1-amine **5c** produced the desired product **7h** in comparable efficiency to the one-pot sequence (Scheme 2c). We believe the differences above are consistent with the ability of anilines to act as blocked isocyanate precursors, leading to the degradation of intermediate **3a** (Scheme 2a).[12d,e] The cyclization of ureas derived from secondary 2-iodobenzylic amines (Scheme 2c) is significantly more favourable than the cyclization of the parent primary amine adducts (Scheme 2b), due to the strong conformational preferences of s-*cis* urea present that disfavour the latter cyclization.

To expand the synthetic utility of this strategy, we removed the benzyl group from products **4k** and **7b** using $TiCl_4$ under mild conditions. This afforded the free hydroxamic acid products **8** and **9** in moderate to good yields (Scheme 3, **8**: 87%; **9**: 61%).

In summary, we have developed a new reaction sequence for the rapid synthesis of complex 5- and 6-membered hydroxylamine-derived heterocycles: benzimidazolones and 3,4-dihydroquinazolin-

2(1*H*)-ones. This sequence builds on the rarely utilized reactivity of *O*-isocyanates, using masked *O*-isocyanate precursors in a base-catalyzed substitution reaction, followed by a copper-catalyzed cyclization. The cyclization is not inhibited by the phenol released in the substitution step, which allowed the development of a high yielding one-pot, two-step reaction sequence. While the cascade reactions can also afford the desired heterocycles, their efficiency is often lower. To our knowledge, this is the first example of work combining a metal-catalyzed reaction with the use of masked *O*-isocyanate precursors. The development of other metal-catalyzed reaction sequences involving *O*-isocyanates as building blocks is underway, and will be reported in due course.

We are grateful to the University of Ottawa, NSERC, CFI, and the Ontario MRI, Q. W. thanks the China Scholarship Council and excellent doctoral dissertation cultivation grant from Central China Normal University for generous financial support.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 For selected reviews: (*a*) Z. Rappoport and J. F. Liebman, *The chemistry of hydroxylamines, oximes and hydroxamic acids*, John Wiley and Sons, Chichester, 2009; (*b*) A. A. Tabolin and S. L. Ioffe, *Chem. Rev.*, 2014, **114**, 5426; (*c*) H. Huang, X. Ji, W. Wu and H. Jiang, *Chem. Soc. Rev.*, 2015, **44**, 1155.

2 (*a*) R. C. Hider and X. Kong, *Nat. Prod. Rep.*, 2010, **27**, 637; (*b*) S. P. Gupta, *Hydroxamic Acids: A unique family of chemicals with multiple biological activities*, Springer, Berlin, 2013; (*c*) R. Rani and C. Granchi, *Eur. J. Med. Chem.*, 2015, **97**, 505.

3 (*a*) L. Bauer and O. Exner, *Angew. Chem., Int. Ed.*, 1974, **13**, 376; (*b*) H. L. Yale, *Chem. Rev.*, 1943, **33**, 209.

4 Selected examples: (*a*) J. Moran, S. I. Gorelsky, E. Dimitrijevic, M. E. Lebrun, A. C. Bedard, C. Seguin and A. M. Beauchemin, *J. Am. Chem. Soc.*, 2008, **130**, 17893; (*b*) M. J. MacDonald, D. J. Schipper, P. J. Ng, J. Moran and A. M. Beauchemin, *J. Am. Chem. Soc.*, 2011, **133**, 20100; For an overview: (*c*) A. M. Beauchemin, *Org. Biomol. Chem.*, 2013, **11**, 7039. See also: (*d*) J. Y. Pfeiffer and A. M. Beauchemin, *J. Org. Chem.*, 2009, **74**, 8381.

5 Selected reviews on amination: (*a*) M. T. Pirnot, Y. M. Wang and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2016, **55**, 48; (*b*) B. Morandi, L. Legnani and B. Bhawal, *Synthesis*, 2016, 776; (*c*) S. L. McDonald, *Copper-Catalyzed Electrophilic Amination of sp^2 and sp^3 C–H Bonds*, Springer, 2016; (*d*) C. E. Hendrick and Q. Wang, *J. Org. Chem.*, 2017, **82**, 839.

6 Selected examples for amination: (*a*) A. M. Berman and J. S. Johnson, *J. Am. Chem. Soc.*, 2004, **126**, 5680; (*b*) N. Matsuda, K. Hirano, T. Satoh and M. Miura, *Angew. Chem., Int. Ed.*, 2012, **51**, 3642; (*c*) R. P. Rucker, A. M. Whittaker, H. Dang and G. Lalic, *J. Am. Chem. Soc.*, 2012, **134**, 6571; (*d*) G. S. Liu, Y. Q. Zhang, Y. A. Yuan and H. Xu, *J. Am. Chem. Soc.*, 2013, **135**, 3343; (*e*) J. L. Jat, M. P. Paudyal, H. Gao, Q. L. Xu, M. Yousufuddin, D. Devarajan, D. H. Ess, L. Kurti and J. R. Falck, *Science*, 2014, **343**, 61; (*f*) S. Zhu and S. L. Buchwald, *J. Am. Chem. Soc.*, 2014, **136**, 15913; (*g*) N. Niljianskul, S. Zhu and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2015, **54**, 1638; (*h*) M. P. Paudyal, A. M. Adebesin, S. R. Burt, D. H. Ess, Z. Ma, L. Kürti and J. R. Falck, *Science*, 2016, **353**, 1144; (*i*) S. A. Shuler, G. Yin, S. B. Krause, C. M. Vesper and D. A. Watson, *J. Am. Chem. Soc.*, 2016, **138**, 13830; (*j*) S. L. Shi, Z. L. Wong and S. L. Buchwald, *Nature*, 2016, **532**, 353.

7 Selected examples: (*a*) G. Cecere, C. M. Konig, J. L. Alleva and D. W. MacMillan, *J. Am. Chem. Soc.*, 2013, **135**, 11521; (*b*) L. J. Allen, P. J. Cabrera, M. Lee and M. S. Sanford, *J. Am. Chem. Soc.*, 2014, **136**, 5607; (*c*) Q. X. Qin and S. Y. Yu, *Org. Lett.*, 2014, **16**, 3504; (*d*) J. Davies, T. D. Svejstrup, D. Fernandez Reina, N. S. Sheikh and D. Leonori, *J. Am. Chem. Soc.*, 2016, **138**, 8092; (*e*) S.-H. Cai, J.-H. Xie, S. Song, L. Ye, C. Feng and T.-P. Loh, *ACS Catal.*, 2016, **6**, 5571; (*f*) W. Shu and C. Nevado, *Angew. Chem., Int. Ed.*, 2017, **56**, 1881.

8 Compound **I**: J. F. Berry, D. V. Ferraris, B. Duvall, N. Hin, R. Rais, J. Alt, A. G. Thomas, C. Rojas, K. Hashimoto, B. S. Slusher and T. Tsukamoto, *ACS Med. Chem. Lett.*, 2012, **3**, 839.

9 Compound **II**: M. Kobayashi, M. Kitazawa, T. Saito, M. Akaha and T. Tsukamoto, *Jpn. Kokai Tokkyo Koho*, 16218126, 1987.

10 Compound **III**: A. B. Dounay, *et al.*, *ACS Med. Chem. Lett.*, 2012, **3**, 187.

11 Compound **IV**: R. C. Desal, V. Pandya and P. R. Patel, *PCT Pat. Appl.*, 102818, 2014.

12 For selected examples: (*a*) J.-G. Roveda, C. Clavette, A. D. Hunt, C. J. Whipp, S. I. Gorelsky and A. M. Beauchemin, *J. Am. Chem. Soc.*, 2009, **131**, 8740; (*b*) C. Clavette, W. Gan, A. Bongers, T. Markiewicz, A. B. Toderian, S. I. Gorelsky and A. M. Beauchemin, *J. Am. Chem. Soc.*, 2012, **134**, 16111; (*c*) J.-F. Vincent-Rocan, R. A. Ivanovich, C. Clavette, K. Leckett, J. Bejjani and A. M. Beauchemin, *Chem. Sci.*, 2016, **7**, 315; (*d*) R. A. Ivanovich, C. Clavette, J. F. Vincent-Rocan, J. G. Roveda, S. I. Gorelsky and A. M. Beauchemin, *Chem. – Eur. J.*, 2016, **22**, 7906; (*e*) A. Bongers, C. Clavette, W. Gan, S. I. Gorelsky, L. Betit, K. Lavergne, T. Markiewicz, P. J. Moon, N. Das Neves, N. K. Obhi, A. B. Toderian and A. M. Beauchemin, *J. Org. Chem.*, 2017, **82**, 1175; (*f*) J. An, H. Alper and A. M. Beauchemin, *Org. Lett.*, 2016, **18**, 3482. For a review: (*g*) J.-F. Vincent-Rocan and A. M. Beauchemin, *Synthesis*, 2016, 3625.

13 (*a*) J. U. Nef, *Liebigs Ann. Chem.*, 1894, **280**, 263–291; (*b*) L. W. Jones, *J. Am. Chem. Soc.*, 1898, **20**, 1; (*c*) L. W. Jones and L. Neuffer, *J. Am. Chem. Soc.*, 1917, **39**, 652; (*d*) W. Mormann and G. Leukel, *Synthesis*, 1988, 990; (*e*) V. D. Sheludyakov, A. B. Dmitrieva, A. D. Kirilin and E. A. Chernyshev, *Russ. J. Gen. Chem.*, 1983, **53**, 2051; (*f*) J. H. Teles and G. Maier, *Chem. Ber.*, 1989, **122**, 745; (*g*) J. L. Romine, S. W. Martin, N. A. Meanwell and J. R. Epperson, *Synthesis*, 1994, 846; (*h*) C. Wentrup, J. J. Finnerty and R. Koch, *Curr. Org. Chem.*, 2011, **15**, 1745; (*i*) Z. W. Wicks Jr., F. N. Jones, S. P. Pappas and D. A. Wicks, *Organic Coatings: Science and Technology, Wiley-VCH*, 2007.

14 R. Ivanovich, D. Polat and A. M. Beauchemin, *Adv. Synth. Catal.*, 2017, DOI: 10.1002/adsc.201701046.

15 A. F. McKay, D. L. Garmaise, G. Y. Paris and S. Gelblum, *Can. J. Chem.*, 1960, **38**, 343–358, See ref. 13*g* for a discussion.

16 For selected reviews: (*a*) D. A. Wicks and Z. W. Wicks Jr., *Prog. Org. Coat.*, 1999, **36**, 148; (*b*) D. A. Wicks and Z. W. Wicks Jr., *Prog. Org. Coat.*, 2001, **41**, 1; (*c*) E. Delebecq, J.-P. Pascault, B. Boutevin and F. Ganachaud, *Chem. Rev.*, 2013, **113**, 80.

17 (*a*) K. L. Jones, A. Porzelle, A. Hall, M. D. Woodrow and N. C. Tomkinson, *Org. Lett.*, 2008, **10**, 797; (*b*) M. Katkevics, T. Kukosha and N. Trufilkina, *Synlett*, 2011, 2525; (*c*) M. Katkevics, T. Kukosha, N. Trufilkina and S. Belyakov, *Synthesis*, 2012, 2413; (*d*) Z. M. Khoder, C. E. Wong and S. R. Chemler, *ACS Catal.*, 2017, **7**, 4775.

18 For selected examples, see: (*a*) J. H. Cooley and P. T. Jacobs, *J. Org. Chem.*, 1975, **40**, 552; (*b*) A. G. Romero, W. H. Darlington, E. J. Jacobsen and J. W. Mickelson, *Tetrahedron Lett.*, 1996, **37**, 2361; (*c*) V. G. Shtamburg, O. V. Shishkin, V. V. Shtamburg, R. I. Zubatyuk, A. V. Mazepa and R. G. Kostyanovsky, *Chem. Heterocycl. Compd.*, 2013, **49**, 1195, and ref. 8.

19 For a rare example, see: R. T. Coutts, D. Noble and D. G. Wibberley, *J. Pharm. Pharmacol.*, 1964, **16**, 773.

20 For selected examples using isocyanates, see: (*a*) R. Ferraccioli and D. Carenzi, *Synthesis*, 2003, 1383; (*b*) N. A. Magnus, P. N. Confalone and L. Storace, *Tetrahedron Lett.*, 2000, **41**, 3015; (*c*) Z. Xin, Z. Pei, T. von Geldem and M. Jirousek, *Tetrahedron Lett.*, 2000, **41**, 1147; (*d*) Y. Jing, R. Liu, Y. Lin and X. Zhou, *Sci. China: Chem.*, 2014, **57**, 1117.

