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Synthesis and Reactivity of *o*-Enoyl Arylisocyanides: Access to Phenanthridine-8-Carboxylate Derivatives

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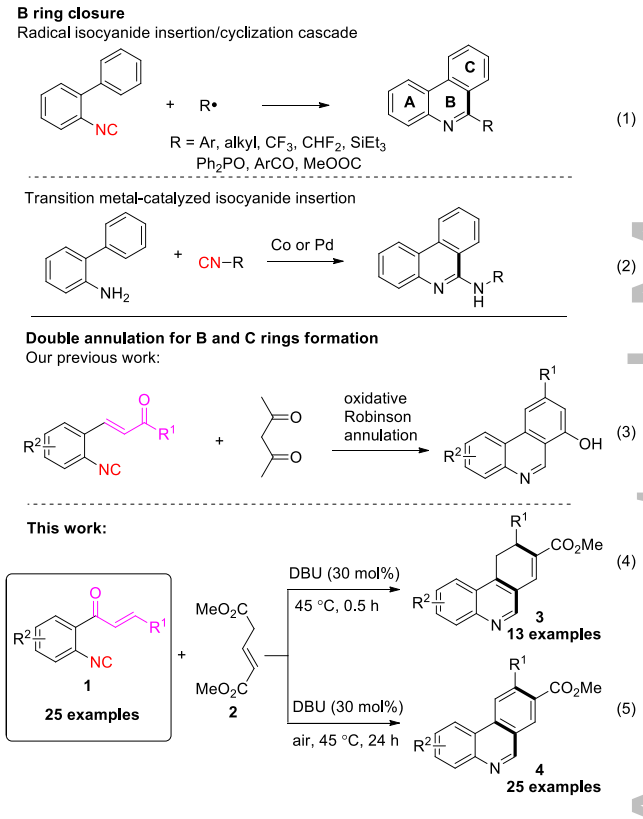
Abstract. Various *o*-enoyl arylisocyanides were prepared from readily available reactants and found to undergo a double annulation with glutaconate to provide straightforward access to phenanthridine-8-carboxylates and hydrophenanthridine-8-carboxylates under mild aerobic conditions. In this domino transformation, two rings and three bonds were successively created. A mechanism involving tandem [3+3]-annulation/intramolecular cyclization/ demethoxycarbonylation/aerobic oxidative aromatization sequence was proposed.

Keywords: *o*-enoyl arylisocyanides; double annulation; phenanthridines; aerobic oxidation; glutaconate

Phenanthridine framework exists in a large number of natural products, pharmacological agents, and functional molecules.[1] Given their significance, great effort has been devoted to developing new methods for the synthesis of these tricyclic heterocycles during the past several decades.[2,3] Among these methods, the construction of phenanthridines from the domino reactions of readily accessible functionalized isocyanides has lately attracted enormous attention.[3-6] Recently, the tandem insertion/cyclization of *ortho*-isocyanobiphenyls with various radicals has become a popular method for the synthesis of a wide range of 6-functionalized phenanthridines (Scheme 1, eq 1).[3,4] In 2014, Ji, Wang[5a] and Jiang[5b] groups independently reported elegant syntheses of 6-amino phenanthridine derivatives via Co- or Pd-catalyzed oxidative isocyanide insertion with 2-aryl anilines (Scheme 1, eq 2). These isocyanide-based synthetic strategies rely on the closure of the central pyridine ring and provide the phenanthridines bearing a variety of substituents on the 6-position. Very recently, we reported a DBU-catalyzed aerobic oxidative Robinson-type double annulation of



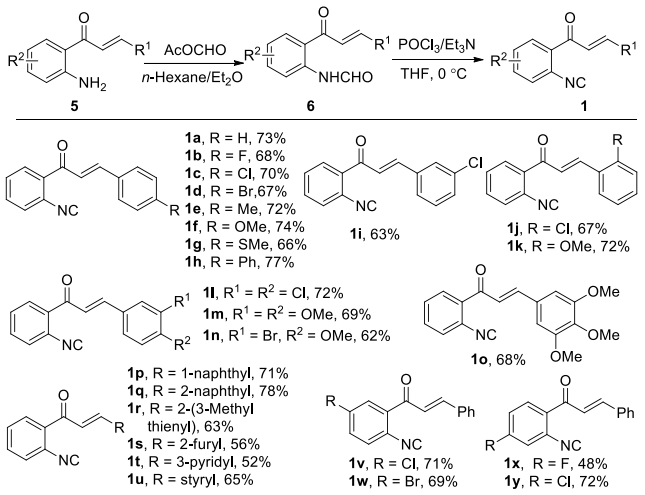
Scheme 1. Synthesis of phenanthridines from isocyanides

2-isocyanochalcones with active methylene ketones for the expedient synthesis of 6-*H*-phenanthridines (Scheme 1, eq 3).[6] In this domino transformation, the tricyclic phenanthridine scaffolds were efficiently created by the successive formation of the central pyridine and one of the benzene rings.

Isocyanides are useful synthons in the synthesis of heterocycles.[7] Great progress has been made in this

area in the past several decades.[8] Along with our continuous interest in isocyanide chemistry[9] and the importance of phenanthridine carboxylic acid derivatives,[10] we initiated a project towards the preparation of functionalized arylisocyanides and their application in the synthesis of phenanthridine carboxylates. Although several *o*-functionalized arylisocyanides, such as *o*-alkenyl,[11] alkynyl,[12] acyl,[13] aryl,[3,14] cyano,[15] halo,[16] methoxycarbonyl[17] and aminocarbonyl arylisocyanides,[18] have been employed for the synthesis of diverse class of benzo-fused heterocycles, to our knowledge, the synthetic utility of *o*-enoyl arylisocyanides have barely been exploited.[19] We recently reported the only transformation of *o*-enoyl arylisocyanides, i.e., *o*-cinnamoyl phenylisocyanide, as functionalized arylisocyanides in the chemoselective [4+2] annulation of two different isocyanides.[9a] However, in this reaction, the cinnamoyl group was intacted. We envisioned that the reactive enoyl functional group could bestow new reactivities to theses substrates, especially in domino reactions. Herein, we report the preparation of a variety of *o*-enoyl arylisocyanides and their double annulation with glutaconate for the efficient construction of both phenanthridine-8-carboxylate and dihydro phenanthridine-8-carboxylate derivatives in a single operation under mild aerobic conditions (Scheme 1, eqs 4 and 5). Two rings and three bonds were successively created and one C–C bond was cleavaged in this domino transformation.

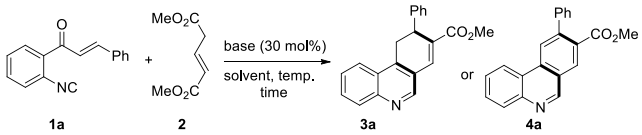
A series of *o*-enoyl arylisocyanides **1** were easily prepared from 1-(2-aminophenyl)prop-2-en-1-one derivatives **5**[20] by a routine procedure involving amine formylation and dehydration[21] (Scheme 2).



Scheme 2. Synthesis of *o*-enoyl arylisocyanides **1**. Yields of isolated products in two steps.

Employing *o*-cinnamoyl arylisocyanide **1a** and methyl glutaconate **2** as model substrates, we surveyed the reaction conditions (Table 1). When a mixture of isocyanide **1a** (0.3 mmol), **2** (1.2 equiv), and DBU[22] (0.3 equiv) in acetonitrile (2 mL) was stirred at room temperature in air for 0.5 h, dihydro phenanthridine-8-carboxylate **3a**[23] was obtained in 81% yield (Table 1, entry 1). The reaction at 45 °C gave a higher yield of **3a** (93%) than those at room temperature or 60 °C (Table 1, entries 2 and 3). Decreasing the amount of DBU to 10 mol% and 20 mol% led to lower yields of product **3a** (Table 1, entries 4 and 5). Different solvents such as 1,4-dioxane, THF, DMF, and CH_2Cl_2 were also screened. However, these solvents gave slightly lower yields of **3a** compared to acetonitrile (Table 1, entries 6−9 vs 2). Bases such as NaOH, K_2CO_3, and *t*-BuOK were then tested. **3a** was also obtained in slightly lower yield (Table 1, entries 10−12 vs 2). To our delight, when the reaction time was prolonged to 24 h, the aromatized phenanthridine-8-carboxylate **4a** was obtained in 90% yield (Table 1, entry 13). However, the reaction under oxygen atmosphere gave a slightly lower yield of **4a** (Table 1, entry 14).

Table 1. Screening of Reaction Conditions[a]



entry	base	solvent	T (°C)	T. (h)	Yield (%)[b] 3a	4a
1	DBU	CH_3CN	RT	0.5	81	
2	DBU	CH_3CN	45	0.5	93	
3	DBU	CH_3CN	60	0.5	89	
4	DBU	CH_3CN	45	0.5	76[c]	
5	DBU	CH_3CN	45	0.5	88[d]	
6	DBU	dioxane	45	1.5	80	
7	DBU	THF	45	1	79	
8	DBU	DMF	45	0.5	89	
9	DBU	DCM	45	1	87	
10	NaOH	CH_3CN	45	1	71	
11	K_2CO_3	CH_3CN	45	1	74	
12	*t*-BuOK	CH_3CN	45	1	68	
13	DBU	CH_3CN	45	24		90
14	DBU	CH_3CN	45	24		82[e]

[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.36 mmol), base (30 mol%), solvent (2 mL), air atmosphere.
[b] Yield of isolated products.
[c] 10 mol% DBU was used.
[d] 20 mol% DBU was used.
[e] Under O_2 atmosphere.

With the optimal conditions at hand, we first examined the substrate scope for the aromatic phenanthridine-8-carboxylate **4** (Table 1, entry 11). As shown in Scheme 3, this domino double annulation/aerobic oxidation reaction tolerates a wide range of *o*-enoyl arylisocyanides **1** bearing various electronically and sterically different R^1 groups, such as *para*- (Scheme 3, **1b−h**), *meta*- (Scheme 3, **1i**), or

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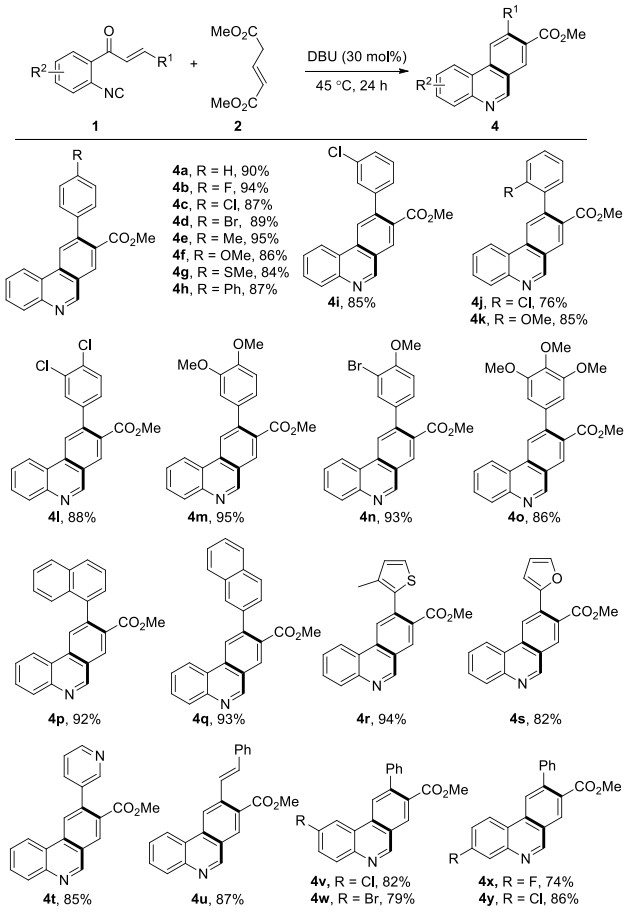
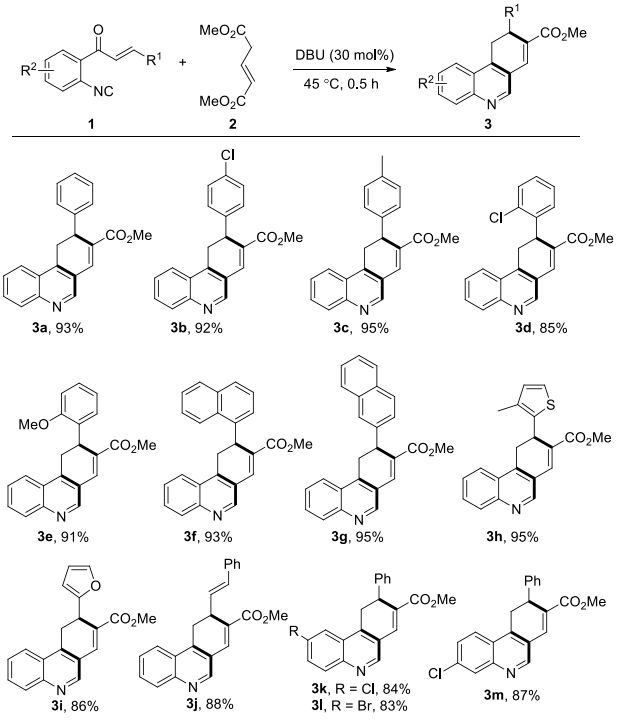
ortho-substituted aryl (Scheme 3, **1j** and **1k**), di- and (Scheme 3, **1l**–**n**), trisubstituted aryl (Scheme 3, **1o**), 1- and 2-naphthyl (Scheme 3, **1p** and **1q**), heteroaryl (Scheme 3, **1r**–**t**) and vinyl groups (Scheme 3, **1u**). The steric and electronic effects of substituents on the phenyl ring seem to have no obvious effect on the transformation (Scheme 3, **1a**–**k**). In addition, 5-chloro and -bromo, as well as 4-fluoro and -chloro, substituted isocyanides **1v**–**1y** also gave the corresponding phenanthridines **4v**–**y** in good yields. Notably, this reaction is high yielding and gave products **4** in high to excellent yields (74–95%).



Scheme 3. Synthesis of phenanthridines **4**.
Reaction conditions: **1** (0.3 mmol), **2** (0.36 mmol) and DBU (30 mol%) in CH_3CN (2 mL) at 45 ºC for 24 h; yields of isolated products.

Hydrophenanthridine derivatives are valuable molecules because they exhibited promising biological activities[24] and have been used as a key intermediate for the synthesis of the natural product[25] as well as pharmaceutical agents.[26] Thus, the scope of preparation of dihydrophenanthridine-8-carboxylates **3** was also explored under the optimal conditions (Table 1, entry 2). As depicted in Scheme 4, a wide range of *o*-enoyl arylisocyanides **1** with different R^1 groups such as electron-neutral (Scheme 4, **3a**), electron-poor (Scheme 4, **3b** and **3d**) and electron-rich aryl (Scheme 4, **3c** and **3e**), naphthyl (Scheme 4, **3f** and **3g**), heteroaryl (Scheme 4, **3h** and **3i**) and vinyl groups (Scheme 4, **3j**) were tolerated in this domino reaction, and the dihydrophenanthridine **3a-j** were obtained in high to excellent yields. Furthermore, 5-chloro and -bromo as well as 4-chloro substituted isocyanide **1v**, **1w** and **1y** also gave the corresponding dihydrophenanthridines **3k**–**m** in good yields.

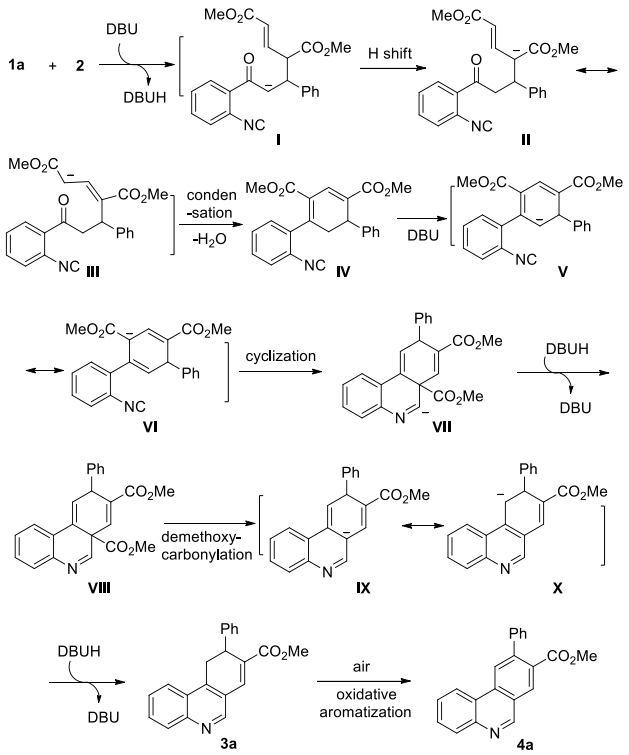


Scheme 4. Synthesis of dihydrophenanthridines **3**.
Reaction conditions: **1** (0.3 mmol), **2** (0.36 mmol) and DBU (30 mol%) in CH_3CN (2 mL) at 45 ºC for 0.5 h; yields of isolated products.

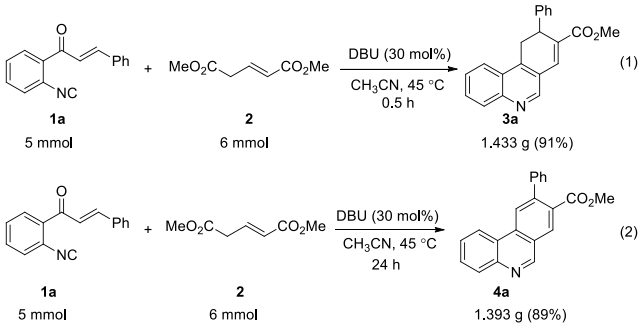
On the basis of previous[6] and present observations as well as literature precedent,[20a,27] a plausible pathway for this domino reaction is proposed in Scheme 5 (exemplified by the generation of **3a** and **4a**). First, in the presence of DBU, Michael addition of glutaconate **2** to the enone moiety of isocyanide **1a** occurs to produce intermediate **I**,[20a,27] which was detected by high-resolution mass spectra ($[M+Na]^+$ = 414.1323, Figure S1). Intermediate **I** undergoes 1,3-proton shift and isomerization to generate the anion **III**. Then intramolecular condensation of **III** takes place to give the cyclohexa-1,3-diene **IV**, which undergoes deprotonation and isomerization to generate anion **VI**, following by intramolecular cyclization and protonation to form the tricyclic intermediate **VIII**.[6] Subsequent demethoxycarbonylation,[6] isomerization and protonation afforded the hydrophenanthridine **3a**. Finally, aerobic oxidative aromatization of **3a** by air afforded phenanthridine **4a**.

To test the practicability of the present double annulation, 5 mmol scale synthesis was performed. As shown in Scheme 6, 1.433 g of hydrophenanthridine **3a** and 1.393 g of

phenanthridine **4a** were obtained, when isocyanide **1a** (5 mmol) and glutaconate **2** (6 mmol) were treated under the optimized reaction conditions, respectively.



Scheme 5. Proposed mechanism.



Scheme 6. 5 mmol scale synthesis.

In summary, a series of *o*-enoyl arylisocyanides were prepared from readily accessible starting materials and their double annulation with glutaconate was discolsed. The domino transformation of these functionalized isocyanides provided a convenient and efficient protocol for the synthesis of a wide range of phenanthridine-8-carboxylates and hydrophenanthridine-8-carboxylates. In this multi-step domino transformation, two rings and three bonds were created and one C–C bond was cleaved, which involves a tandem [3+3]-annulation/ intramolecular cyclization/demethoxycarbonylation/ aerobic oxidative aromatization sequence. This protocol features advantages such as readily available substrates, mild reaction conditions, high efficiency and high to excellent product yields. Further studies on the domino reaction of functionalized isocyanides are ongoing.

Experimental Section

Typical Procedure for the Synthesis of Imidazole 4a

To a solution of (*E*)-1-(2-isocyanophenyl)-3-phenylprop-2-en-1-one (**1a**) (0.3 mmol, 70 mg) and dimethyl glutaconate **2** (0.36 mmol, 0.046 mL) in CH_3CN (2 mL) at 45 ºC, DBU (0.09 mmol, 0.014 mL) was added. After stirred the resulting mixture for 24 h in the open air, the substrate **1a** was consumed as indicated by TLC. Then the mixture was cooled to room temperature, poured into water (50 mL) and the resulting mixture was extracted with dichloromethane (3×20 mL). The organic layer was washed with brine (20 mL), dried over $MgSO_4$ and concentrated. Purification of the crude product by flash column chromatography (silica gel; petroleum ether: ethyl acetate = 10:1) gave **4a** (84.5 mg, 90% yield) as a white solid. m. p. 190-192 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H), 7.41–7.54 (m, 5H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 8.58 (d, *J* = 11.2 Hz, 3H), 9.37 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 52.2, 122.6, 123.2, 124.2, 124.6, 127.4, 127.7, 128.1, 128.4, 129.6, 130.1, 130.3,131.2,133.9,140.9, 144.3, 145.2, 153.1, 167.9. HRMS (ESI-TOF) calculated for $C_{21}H_{15}NNaO_2^+$ ([M+Na]$^+$): 336.0995, Found: 336.0999.

Acknowledgments

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References

[1] a) L. -M. Tumir, M. R. Stojković, I. Piantanida, *Beilstein J. Org. Chem.* **2014**, *10*, 2930; b) Z. Luo, F. Wang, J. Zhang, X. Li, M. Zhang, X. Hao, Y. Xue, Y. Li, F. D. Horgen, G. Yao, Y. Zhang, *J. Nat. Prod.* **2012**, *75*, 2113; c) S. D. Phillips, R. N. Castle, *J. Heterocycl. Chem.* **1981**, *18*, 223.

[2] a) J. C. Walton, *Molecules*, **2016**, *21*, 660; (b) P. A. Keller, in *Science of Synthesis*, ed. D. StC. Black, Thieme, Stuttgart, 2004, vol. 15, p. 1065.

[3] a) B. Zhang, A. Studer, *Chem. Soc. Rev.* **2015**, *44*, 3505; b) B. Song, B. Xu, *Chem. Soc. Rev.* **2017**, *46*, 1103.

[4] For some selected recent examples, see: a) T. Xiao, L. Li, G. Lin, Q. Wang, P. Zhang, Z.-W. Mao, L. Zhou, *Green Chem.* **2014**, *16*, 2418; c) B. Zhang, C. G. Daniliuc, A. Studer, *Org. Lett.* **2014**, *16*, 250; d) H. Jiang, Y. Cheng, R. Wang, M. Zheng, Y. Zhang, S. Yu, *Angew. Chem. Int. Ed.* **2013**, *52*, 13289; e) L. Wang, H. Zhu, S. Gao, J. Cheng, J.-T. Yu, *Chem. Commun.* **2014**, *50*, 10864; f) J. -J. Cao, X. Wang, S.-Y. Wang, S.-J. Ji, *Chem. Commun.* **2014**, *50*, 12892; g) J. Rong, L. Deng, P. Tan, C. Ni, Y. Gu, J. Hu, *Angew. Chem. Int. Ed.* **2016**, *55*, 2743.

[5] a) T. -H. Zhu, S.-Y. Wang, Y.-Q. Tao, T.-Q. Wei, S.-J. Ji, *Org. Lett.* **2014**, *16*, 1260; b) H. Jiang, H. Gao, B. Liu, W. Wu, *RSC Adv.* **2014**, *4*, 17222.

[6] Z. Hu, J. Dong, Y. Men, Y. Li, X. Xu, *Chem. Commun*. **2017**, *53*, 1739.

[7] For recent reviews, see: a) V. P. Boyarskiy, N. A. Bokach, K. V. Luzyanin, V. Yu. Kukushkin, *Chem. Rev.* **2015**, *115*, 2698; b) T. Vlaar, E. Ruijter, B. U. W. Maes, R. V. A. Orru, *Angew. Chem. Int. Ed.* **2013**, *52*, 7084; c) S. Lang, *Chem. Soc. Rev.* **2013**, *42*, 4867; d) G. Qiu, Q. Ding, J. Wu, *Chem. Soc. Rev.* **2013**, *42*, 5257.

[8] For recent articles, see: a) P. Mampuys, H. Neumann, S. Sergeyev, R. V. A. Orru, H. Jiao, A. Spannenberg, B.U. W. Maes, M. Beller, *ACS Catal.* **2017**, *7*, 5549; b) G. Qiu, Q. Wang, J. Zhu, *Org. Lett.* **2017**, *19*, 270; c) W. Kong, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2016**, *55*, 9714; d) X. Jiang, T. Tang, J.- M. Wang, Z. Chen, Y.-M. Zhu, S.-J. Ji, *J. Org. Chem.* **2014**, *79*, 5082; e) G. Pandey, S. Bhowmika, S. Batra, *RSC Adv.* **2014**, *4*, 41433; f) T. Vlaar, P. Mampuys, M. Helliwell, B. U. W. Maes, R. V. A. Orru, E. Ruijter, *J. Org. Chem.* **2013**, *78*, 6735; g) S. Luo, Z. Xiong, Y. Lu, Q. Zhu, *Org. Lett.* **2018**, *20*, 1837; h) X. Wang, W. Xiong, Y. Huang, J. Zhu, Q. Hu, W. Wu, H. Jiang, *Org. Lett.* **2017**, *19*, 5818; C.-G. Liu, Z.-Y. Gu, H.-W. Bai, Sh.-Y. Wang, S.-J. Ji, *Org. Chem. Front*. **2016**, *3*, 1299.

[9] a) Z. Hu, J. Dong, Y. Men, Z. Lin, J. Cai, X. Xu, *Angew. Chem.* **2017**, *129*, 1831; *Angew. Chem. Int. Ed.* **2017**, *56*, 1805; b) J. Dong, L. Bao, Z. Hu, S. Ma, X. Zhou, M. Hao, N. Li, X. Xu, *Org. Lett.* **2018**, *20*, 1244; c) Z. Hu, J. Dong, X. Xu, *Adv. Synth. Cat.* **2017**, *359*, 3585; d) X. Zhang, X. Wang, Y. Gao, X. Xu, *Chem. Commun.* **2017**, *53*, 2427; e) X. Xu, L. Zhang, X. Liu, L. Pan, Q. Liu, *Angew. Chem.* **2013**, *125*, 9441; *Angew. Chem. Int. Ed.* **2013**, *52*, 9271.

[10] a) G. J. Atwell, B. C. Baguley, W. A. Denny, *J. Med. Chem.* **1988**, *31*, 774; b) S. Zhu, A. L. Ruchelman, N. Zhou, A. A. Liu, L. F. Liu, E. J. LaVoie, *Bioorg. Med. Chem.* **2005**, *13*, 6782; c) X. Li, M. Fang, P. Hu, G. Hong, Y. Tang, X. Xu, *Adv. Synth. Catal.* **2014**, *356*, 2103; d) C. Pan, J. Han, H. Zhang, C. Zhu, *J. Org. Chem.* **2014**, *79*, 5374; e) Y. Zhou, C. Wu, X. Dong, J. Qu, *J. Org. Chem.* **2016**, *81*, 5202.

[11] a) T. Fukuyama, X. Chen, G. Peng, *J. Am. Chem. Soc.* **1994**, *116*, 3127; b) M. Tobisu, H. Fujihara, K. Koh, N. Chatani, *J. Org. Chem.* **2010**, *75*, 4814; (c) B. Zhang, A. Studer, *Org. Lett.* **2014**, *16*, 1216; d) Z. Hu, H. Yuan, Y. Men, Q. Liu, J. Zhang, X. Xu, *Angew. Chem.* **2016**, *128*, 7193; *Angew. Chem. Int. Ed.* **2016**, *55*, 7077; e) L. Bao, J. Liu, L. Xu, Z. Hu, X. Xu, *Adv. Synth. Catal.* **2018**, *360*, 1870.

[12] a) J. D. Rainier, A. R. Kennedy, E. Chase, *Tetrahedron Lett.* **1999**, *40*, 6325; b) J. Zhao, C. Peng, L. Liu, Y. Wang, Q. Zhu, *J. Org. Chem*. **2010**, *75*, 7502; c) T. Mitamura, A. Ogawa, *J. Org. Chem.* **2011**, *76*, 1163; d) T. Nanjo, C. Tsukano, Y. Takemoto, *Org. Lett.* **2012**, *14*, 4270; e) T. Nanjo, S. Yamamoto, C. Tsukano, Y. Takemoto, *Org. Lett.* **2013**, *15*, 3754; f) S. Kamijo, Y. Yamamoto, *J. Am. Chem. Soc.* **2002**, *124*, 11940.

[13] a) K. Kobayashi, Y. Okamura, S. Fukamachi, H. Konishi, *Tetrahedron* **2010**, *66*, 7961; b) B. Neue, R. Reiermann, R. Fröhlich, B. Wibbeling, K. Bergander, E. U. Würthwein, *Eur. J. Org. Chem.* **2013**, 4944; c) L. Zhang, J. Li, Z. Hu, J. Dong, X.-M. Zhang, X. Xu, *Adv. Synth. Catal.* **2018**, *360*, 1938; d) Y. Gao, Z. Hu, J. Dong, J. Liu, X. Xu, *Org. Lett.* **2017**, *19*, 5292.

[14] a) D. Nanni, P. Pareschi, C. Rizzoli, P. Sgarabotto, A. Tundo, *Tetrahedron* **1995**, *51*, 9045; b) D. Leifert, C. G. Daniliuc, A. Studer, *Org. Lett.* **2013**, *15*, 6286.

[15] M. Suginome, T. Fukuda, Y. Ito, *Org. Lett.* **1999**, *1*, 1977.

[16] a) C. Kalinski, M. Umkehrer, S. Gonnard, N. Jaeger, G. Ross, W. Hiller, *Tetrahedron Lett.* **2006**, *47*, 2041; b) J. H. Spatza, T. Bach, M. Umkehrera, J. Bardina, G. Rossa, C. Burdacka, J. Kolba, *Tetrahedron Lett.* **2007**, *48*, 9030; c) A. V. Lygin, A. de Meijere, *Eur. J. Org. Chem.* **2009**, 5138; d) A. V. Lygin, A. de Meijere, *Org. Lett.* **2009**, 11, 389; e) A. V. Lygin, A. de Meijere, *J. Org. Chem.* **2009**, *74*, 4554.

[17] a) V. Atlan, C. Buron, L. El Kaïm, *Synlett 2000*, 489; b) R. S. Borisov, A. I. Polyakov, L. A. Medvedeva, V. N. Khrustalev, N. I. Guranova, L. G. Voskressensky, *Org. Lett.* **2010**, *12*, 3894; c) S. G. Yerande, K. M. Newase, B. Singh, A. Boltjes, A. Dömling, *Tetrahedron Lett*. **2014**, *55*, 3263; d) S. Takiguchi, T. Iizuka, Y. Kumakura, K. Murasaki, N. Ban, K. Higuchi, T. Kawasaki, *J. Org. Chem.* **2010**, *75*, 1126; e) A. Clemenceau, Q. Wang, J. Zhu, *Org. Lett.* **2017**, *19*, 4872.

[18] a) D. Bonne, M. Dekhane, J. Zhu, *Org. Lett*. **2005**, *7*, 5285; b) S. Sharma, R. A. Maurya, K. I. Min, G. Y. Jeong, D. P. Kim, *Angew. Chem. Int. Ed.* **2013**, *52*, 7564.

[19] M. Giustiniano, A. Basso, V. Mercalli, A. Massarotti, E. Novellino, G. C. Tron, J. Zhu, *Chem. Soc. Rev*. **2017**, *46*, 1295.

[20] a) L. Li, J.-J. Chen, X.-L. Kan, L. Zhang, Y.-L. Zhao, Q. Liu, *Eur. J. Org. Chem.* **2015**, 4892; b) J.-F. Wang, Y.-X. Liao, P.-Y. Kuo, Y.-H. Gau, D.-Y. Yang, *Synlett* **2006**, 2791.

[21] D. Seebach, G. Adam, T. Gees, M. Schiess, W. Weigand, *Chem. Ber.* **1988**, *121*, 507.

[22] For selected DBU-mediated tandem reactions, see: a) X. Yu, G. Zhou, J. Zhang, *Chem. Commun.* **2012**, *48*, 4002; b) Y. Xiao, J. Zhang, *Chem. Commun.* **2009**, *45*, 3594; c) F. Wang, S. Cai, Z. Wang, C. Xi, *Org. Lett.* **2011**, *13*, 3202; d) A. J. Alford, Q. Lin, *J. Org. Chem.* **2017**, *82*, 9873; e) Y. Li, X. Xu, J. Tan, C. Xia, D. Zhang, Q. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 1775; f) J. Tan, X. Xu, L. Zhang, Y. Li, Q. Liu, *Angew. Chem.* **2009**, *121*, 2912; *Angew. Chem. Int. Ed.* **2009**, *48*, 2868; g) Y. Men, J. Dong, S. Wang, X. Xu, *Org. Lett.* **2017**, *19*, 6712.

[23] CCDC: 1842130 (**3a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[24] a) F. Castan, D. C. H. Bigg, *J. Heterocycl. Chem.* **1993**, *30*, 1125; b) J. A. Valderrama, A. Ibacache, J. A. Rodriguez, C. Theoduloz, J. Benites, *Eur. J. Med. Chem.* **2011**, *46*, 3398.

[25] a) A. E. Bunnell, L. A. Flippin, Y. Liu, *J. Org. Chem.* **1997**, *62*, 9305; b) T. Kumemura, T. Choshi, J. Yukawa, *Heterocycles* **2005**, *66*, 87.

[26] M. P. Hay, W. A. Denny, *Synth. Commun*. **1998**, *28*, 463.

10.1002/adsc.201800606

[27] A. Diallo, Y.-L. Zhao, H. Wang, S.-S. Li, C.-Q. Ren, Q. Liu, *Org. Lett.* **2012**, *14*, 5776.

10.1002/adsc.201800606

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