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Intramolecular inverse electron-demand [4+2] cycloadditions of ynamidyl-tethered pyrimidines: Comparative studies in trifluorotoluene and sulfolane

*Cycloaddition [4+2] intramoléculaire à demande électronique inverse d'ynamidyl pyrimidine : études comparatives dans le trifluorotoluène et le sulfolane*Morgan Donnard ^{a, b}, Guillaume Duret ^c, Philippe Bisseret ^c,
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ABSTRACT

Three representative 6,7-dihydro-5*H*-cyclopenta[*b*]pyridin-4-amines were synthesized using an intramolecular inverse electron demand hetero-Diels-Alder/retro-Diels-Alder sequence between pyrimidines (acting as azadienes) and ynamides (acting as dienophiles). Two solvents of this reaction, sulfolane and trifluorotoluene, were compared at 210 °C and the former consistently led to higher yields. In addition, these studies confirmed the importance of the steric bulk of the C5-position of the pyrimidinyl cycloaddition precursor.

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R É S U M É

Trois 6,7-dihydro-5*H*-cyclopenta[*b*]pyridin-4-amines représentatives ont été synthétisées par une réaction d'hétérocycloaddition [4+2] intramoléculaire à demande électronique inverse (*ihDA*)/rétro-Diels-Alder (*rDA*) entre des pyrimidines (jouant le rôle d'azadiènes) et des ynamides (jouant le rôle de diénophiles). Deux solvants de cette transformation, le sulfolane et le trifluorotoluène, ont été comparés à 210 °C; le premier des deux a conduit systématiquement à de meilleurs rendements. De plus, ces études confirment l'importance de l'encombrement stérique de la position C5 du précurseur de cycloaddition de type pyrimidinyl.

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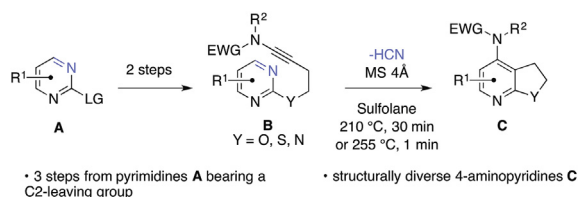
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1. Introduction

The rapid access to polysubstituted 4-amino pyridines is a central endeavor in chemical sciences, owing to the importance of these nitrogenated heterocycles as building blocks or lead compounds in medicinal and agrochemical chemistries [1], as ligands in organometallic complexes [2] or as efficient catalysts [3]. Among the strategies leading to pyridines, cycloaddition reactions proceed under neutral conditions and have been used as key steps in numerous syntheses of biologically relevant organic compounds [4]. In line with our interest in alkyne [5] and heterosubstituted alkyne chemistry, we have recently reported that polysubstituted 4-aminopyridines **C** could be synthesized in three simple steps from **A** (Scheme 1) via an inverse electron demand hetero-Diels-Alder (*ihDA*)/retro-Diels-Alder (*rDA*) cycloaddition between a pyrimidine and a ynamide, the latter acting as the electron-rich 2π partner [6].

This intramolecular cycloaddition/cycloreversion of **B** is general and tolerates various electron-withdrawing groups on the nitrogen atom (such as oxazolidinone, azetidinone,



Scheme 1. A three-step synthesis of pyridines **C** via the first *ihDA/rDA* of ynamides and pyrimidines [6].

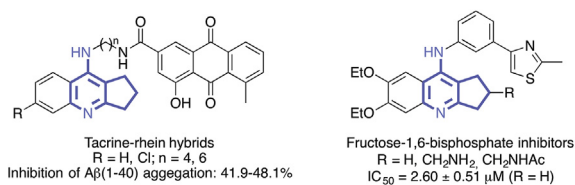


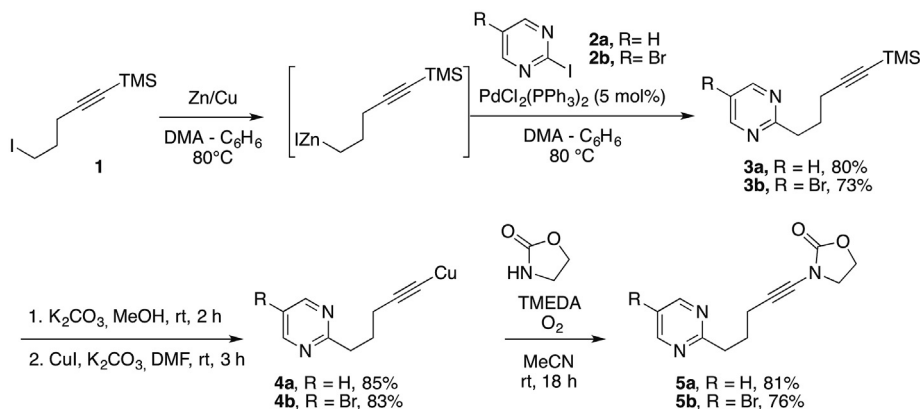
Fig. 1. Selected biologically relevant compounds possessing the 4-aminopyridine motif (in light blue) [8,9].

sultame, sulfonamide, and indole). We also demonstrated that various types of tethers between the pyrimidine and the ynamide could be successfully used in this *ihDA/rDA* sequence, such as ethoxy, ethylamino, and ethylthio linkers. The corresponding cycloadducts **C** were pyridines fused to oxygen-, sulfur-, and nitrogen-containing five-membered heterocycles.

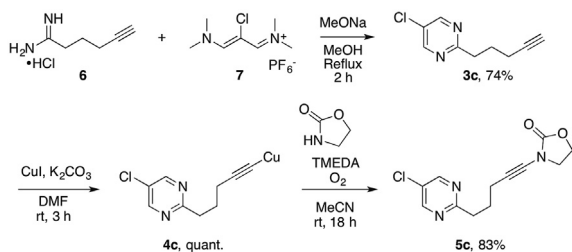
In the late 1980s, the pioneering work of van der Plas [7] has demonstrated that a fully carbon-substituted tether between an alkyne and a pyrimidine was tolerated in the *ihDA/rDA* sequence, leading to 6,7-dihydro-5*H*-cyclopenta[*b*]pyridine in moderate yields. In continuation of our investigations of this *ihDA/rDA* sequence between ynamides and pyrimidines, we were keen to study if a carbon tether, such as a propyl unit, was also tolerated in this reaction. This would constitute a novel approach to biologically important 6,7-dihydro-5*H*-cyclopenta[*b*]pyridin-4-amines that are found, for example, in some tacrine-rhein hybrids [8] and some fructose-1,6-bisphosphate inhibitors [9] (Fig. 1). We report therein that such fused pyridines are indeed attainable using the intramolecular *ihDA/rDA* sequence between pyrimidines and ynamides, and that sulfolane performs better as a solvent compared to trifluorotoluene.

2. Results and discussion

To investigate the relevance of a carbon-tether between the pyrimidine (4π component) and the ynamide (2π component), we synthesized a small subset of representative cycloaddition precursors **5** that differ only by the nature of the C5-substituent of the pyrimidine (**5a**, C5-H; **5b**, C5-Br; and **5c**, C5-Cl), according to two different strategies (Schemes 2 and 3). In a first approach, the bis-homopropargyl derivative **1** [10] was converted into the corresponding organozinc iodide using the zinc/copper amalgam [11] in a dimethylacetamide (DMA)-benzene (1:15) mixture at 80 °C. 2-Iodo pyrimidines **2a** and **2b** were added, followed by PdCl₂(PPh₃)₂ (5 mol %). This Negishi cross-coupling reaction delivered the expected C2-alkylated pyrimidines **3a** and **3b** in 80% and 73% yields, respectively [12]. The latter were then treated with potassium carbonate in methanol, and the intermediate terminal



Scheme 2. Synthesis of *ihDA/rDA* precursors **5a** and **5b**.



Scheme 3. Synthesis of *ihDA/rDA* precursor **5c**.

alkynes were submitted to a cupration reaction using copper(I) iodide and potassium carbonate in dimethylformamide (DMF) [13]. In the last step, the copper acetylides **4a** and **4b** were transformed into the corresponding ynamides **5a** and **5b** using Evano's method [13] (*N,N,N',N'*-tetramethylethylenediamine (TMEDA), oxygen atmosphere in acetonitrile at room temperature) in good yields (81% and 76%, respectively).

The third cycloaddition precursor **5c** was prepared from alkyne-aminidinium salt **6** and the iminium salt **7** in three steps (Scheme 3). The initial condensation of **6** and **7** forged the pyrimidine ring substituted in C5 by a chlorine atom and in C2 by the desired pent-1-ynyl chain [14]. The ynamide motif was then introduced using Evano's method [13], delivering the cycloaddition precursor **5c** in 83% over two steps.

Having in hand the three cycloaddition precursors **5a–c**, their reactivity in the *ihDA/rDA* sequence was evaluated (Scheme 4). On the basis of our preliminary screening of reaction conditions [6], we selected two solvents having different dipolar moments, trifluorotoluene (relative permittivity, 9.18; dipolar moment, 2.86 D) and sulfolane (relative permittivity, 43.4; dipolar moment, 4.69 D) [15]. Systematic studies demonstrated that the optimal conditions were 210 °C for 2 h in trifluorotoluene (conditions A) and for 30 min in sulfolane (conditions B). The best results were obtained with the cycloaddition precursor **5a**, because the fused pyridine **8a** was obtained in 43% in trifluorotoluene and 59% in sulfolane. On the other hand, pyrimidines **5b** and **5c** lead to a more sterically demanding [4+2]-transition state and the impact of the C5 substituents (a bromine atom in **5b** and a chlorine atom in **5c**) is obvious from the isolated yields of the fused pyridines **8b** and **8c** (12–29%). These results are in agreement with our previous

investigations [6]. It should be noted that sulfolane performed systematically better in terms of yields in these *ihDA/rDA* sequences, which could be attributed to its increased relative permittivity and dipolar moment compared with trifluorotoluene. These observations are in agreement with the known solvent effect on this class of pericyclic reactions [4c,6,7]. Combined with its ease of removal (by simple aqueous washings of the reaction mixture with hot water followed by extraction with *tert*-butylmethylether), this makes sulfolane a practical solvent for this transformation.

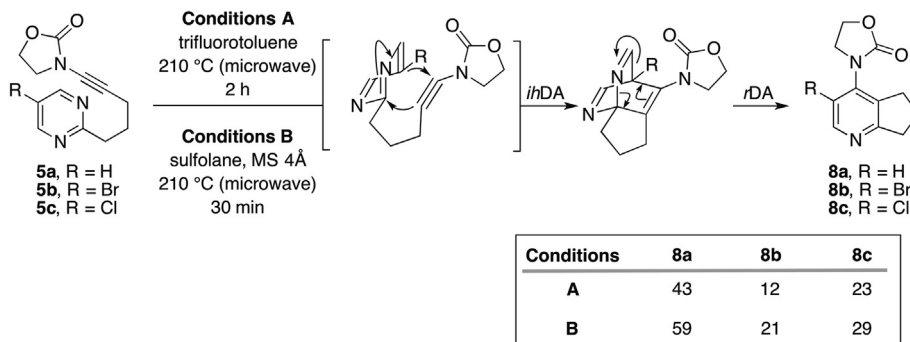
3. Conclusions

Following our previous studies on the *ihDA/rDA* sequence of pyrimidines tethered with ynamides, we have reported in this letter that 6,7-dihydro-5*H*-cyclopenta[*b*]pyridin-4-amines were easily accessible in three steps from simple starting materials. In addition, comparative studies between two solvents, trifluorotoluene and sulfolane, demonstrated that the latter leads to higher-yielding reactions, while being practical to discard from the reaction mixture by simple aqueous washings. Further studies aiming at exploring further the nature of the tether between the pyrimidine and the ynamide are in progress and will be reported in due course.

4. Materials and methods

4.1. General consideration

All reagents, chemicals, and dry solvents were purchased from commercial sources and used without purification. Reactions were monitored by thin-layer silica gel chromatography using Merck silica gel 60 F254 on aluminum sheets. Thin-layer silica gel chromatography plates were visualized under ultraviolet light and revealed with acidic *p*-anisaldehyde stain or KMnO₄ stain. Crude products were purified by flash column chromatography on Merck silica gel Si 60 (40–63 μm). All NMR spectra were recorded in CDCl₃ on Bruker spectrometers at 300 or 400 MHz for ¹H analyses and 75 or 100 MHz for ¹³C analyses. Proton chemical shifts are reported in ppm (δ), relatively to residual CHCl₃ (δ 7.27 ppm). Multiplicities are reported as follows: singlet



Scheme 4. *ihDA/rDA* sequence of ynamidyl-pyrimidines **5a–c**.

(s), doublet (d), triplet (t), quartet (q), broad singlet (br s), combinations of those, or multiplet (m). Coupling constants values J are given in Hz. Carbon chemical shifts are reported in ppm (δ), relatively to the internal standard (CDCl_3 , δ 77.23 ppm). High-resolution mass spectral analysis (HRMS) was performed using an Agilent 1200 RRLC high pressure liquid chromatography (HPLC) chain coupled with an Agilent 6520 Accurate mass quadrupole time of flight (QToF).

4.1.1. Negishi coupling reaction leading to 2-alkylated pyrimidines **3a** and **3b**

A mixture of Zn–Cu couple (230 mg) and 5-iodo-1-trimethylsilylpent-1-yne **1** (500 mg, 1.9 mmol) in benzene/DMA (15:1, 4 mL) was stirred at 80 °C for 4 h. Subsequently, to this solution, $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (74 mg, 0.01 mmol) and 2-iodopyrimidine **2a** or **2b** (0.75 mmol) were added, and the reaction was let to stir at the same temperature for 48 h. The reaction mixture was cooled down to room temperature, washed with water (5 mL), and dried over MgSO_4 . The organic layers were filtered, concentrated, and purified by silica gel flash chromatography (DCM/EtOAc 9:1) to give the targeted product **3**.

4.1.1.1. 2-(5-(Trimethylsilyl)pent-4-yn-1-yl)pyrimidine (3a). Yield 80% (131 mg, 0.6 mmol). ^1H NMR (300 MHz, CDCl_3): 8.69 (d, $J = 4.9$ Hz, 2H), 7.15 (t, $J = 4.9$ Hz, 1H), 3.09 (t, $J = 7.6$ Hz, 2H), 2.37 (t, $J = 7.6$ Hz, 2H), 2.08 (tt, $J = J' = 7.6$ Hz, 2H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): 171.0, 157.3 (2C), 118.8, 106.9, 85.2, 38.6, 27.4, 19.9, 0.4 (3C).

4.1.1.2. 5-Bromo-2-(5-(trimethylsilyl)pent-4-yn-1-yl)pyrimidine (3b). Yield 73% (163 mg, 0.55 mmol). ^1H NMR (300 MHz, CDCl_3): 8.43 (s, 2H), 2.76 (t, $J = 7.2$ Hz, 2H), 2.09 (t, $J = 6.9$ Hz, 2H), 1.77 (tt, $J = 7.2$ Hz, 6.9 Hz, 2H), -0.136 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): 169.0, 157.8 (2C), 118.0, 106.6, 85.3, 37.8, 27.2, 19.7, 0.3 (3C).

4.1.2. Deprotection of silylalkynes **2a** and **2b**

To a solution of the pyrimidine **2a** or **2b** (0.6 mmol) in methanol (2 mL) was added potassium carbonate (5 mg, 0.04 mmol) in one portion and the mixture was then let to stir for 2 h at room temperature. The reaction mixture was then concentrated under vacuum, and the residue was dissolved in ethyl acetate (5 mL), washed with brine (5 mL), and dried over MgSO_4 . After filtration and concentration, the corresponding terminal alkyne was directly used in the next step without further purification.

4.1.2.1. Alkyne from 3a. ^1H NMR (400 MHz, CDCl_3): 8.67 (d, $J = 4.8$ Hz, 2H), 7.10 (t, $J = 4.8$ Hz, 1H), 3.06 (t, $J = 7.7$ Hz, 2H), 2.37 (td, $J = 7.7$ Hz, 3.5 Hz, 2H), 2.10 (m, 2H), 1.97 (t, $J = 3.5$ Hz, 1H).

4.1.2.2. Alkyne from 3b. ^1H NMR (300 MHz, CDCl_3): 8.66 (s, 2H), 3.01 (t, $J = 7.8$ Hz, 2H), 2.25 (td, $J = 6.9$ Hz, 2.7 Hz, 2H), 2.01 (m, 2H), 1.95 (t, $J = 2.7$ Hz, 1H).

4.1.3. 5-Chloro-2-pent-4-ynyl-pyrimidine (**3c**)

To a mixture of hex-5-ynamidine hydrochloride **6** (1 g, 5.3 mmol) and (*Z*)-*N*-(2-chloro-3-(dimethylamino)allylidene)-*N*-methylmethanaminium hexafluorophosphate **7** (1.1 g, 3.6 mmol) in methanol (30 mL) was added sodium methoxide (0.49 g, 9 mmol) and the solution was subsequently refluxed for 2 h. Then, it was cooled down to room temperature and the reaction mixture was concentrated under vacuum. The residue was then dissolved in DCM (20 mL) and washed with brine (10 mL). The organic layer was dried over MgSO_4 , filtrated, concentrated, and finally purified by silica gel flash chromatography (cyclohexane/EtOAc 8:2) to give the desired alkyne **3c** in 74% yield (482 mg, 2.7 mmol). ^1H NMR (300 MHz, CDCl_3): 8.62 (s, 2H), 3.08 (t, $J = 8.1$ Hz, 2H), 2.37 (td, $J = 8.1$ Hz, 3.5 Hz, 2H), 2.05 (m, 2H), 1.98 (t, $J = 3.5$ Hz, 1H). These data are in accordance with the values reported in the literature.

4.1.4. Synthesis of alkynyl copper **4a–c**

Under Argon, to a suspension of CuI (518 mg, 2.7 mmol) in DMF (68 mL) was added a solution of alkyne **3** (2.7 mmol) in DMF (5 mL) followed by potassium carbonate (166 mg, 1.2 mmol). The reaction was let to stir at room temperature for 3 h and the yellow precipitate formed during the reaction was collected by filtration and successively washed with ammonium hydroxide (10% NH_4OH solution, 2×8 mL), water (2×8 mL), absolute ethanol (2×8 mL), and finally diethyl ether (2×8 mL). The yellow solid was then dried under vacuum overnight to afford the desired alkynyl copper **4**.

4.1.4.1. (5-(Pyrimidin-2-yl)pent-1-yn-1-yl)copper (4a). 479 mg, 2.3 mmol, 85%.

4.1.4.2. (5-(5-Bromopyrimidin-2-yl)pent-1-yn-1-yl)copper (4b). 645 mg, 2.2 mmol, 83%.

4.1.4.3. (5-(5-Chloropyrimidin-2-yl)pent-1-yn-1-yl)copper (4c). 657 mg, 2.7 mmol, quantitative.

4.1.5. General procedure for the synthesis of ynamides **5a–c**

To a solution of oxazolidinone (176 mg, 2 mmol) and the alkynyl copper reagent **4** (0.5 mmol) in acetonitrile (1 mL) was added *N,N,N',N'*-tetramethylethylenediamine (76 μL , 0.5 mmol) and the resulting reaction mixture was vigorously stirred at room temperature and under an atmosphere of oxygen for 18 h. After complete disappearance of the yellow suspension (to become a homogenous deep blue solution), the crude reaction mixture was concentrated under vacuum and purified by flash chromatography over silica gel (cyclohexane/EtOAc 6:4) to afford the targeted ynamide **5**.

4.1.5.1. 3-(5-(Pyrimidin-2-yl)pent-1-yn-1-yl)oxazolidin-2-one (5a). Yield 81% (95 mg, 0.41 mmol). ^1H NMR (300 MHz, CDCl_3): 8.66 (d, $J = 5.1$ Hz, 2H), 7.13 (t, $J = 5.1$ Hz, 1H), 4.40 (t, $J = 8.1$ Hz, 2H), 3.87 (t, $J = 8.1$ Hz, 2H), 3.07 (t, $J = 7.4$ Hz, 2H), 2.43 (t, $J = 7.4$ Hz, 2H), 2.07 (tt, $J = J' = 7.4$ Hz, 2H); ^{13}C NMR

(75 MHz, CDCl₃): 170.8, 157.2 (3C), 118.8, 70.7 (2C), 63.0, 47.2, 38.5, 27.6, 18.3.

4.1.5.2. 3-(5-(5-Bromopyrimidin-2-yl)pent-1-yn-1-yl)oxazolidin-2-one (**5b**). Yield 76% (120 mg, 0.38 mmol). ¹H NMR (300 MHz, CDCl₃): 8.69 (s, 2H), 4.39 (t, *J* = 8.1 Hz, 2H), 3.85 (t, *J* = 8.1 Hz, 2H), 3.02 (t, *J* = 7.5 Hz, 2H), 2.41 (t, *J* = 7.3 Hz, 2H), 2.07 (tt, *J* = 7.5 Hz, 7.3 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃): 168.9, 157.8 (3C), 118.0, 70.9, 70.5, 63.0, 47.2, 37.8, 27.4, 18.3.

4.1.5.3. 3-(5-(5-Chloropyrimidin-2-yl)pent-1-yn-1-yl)oxazolidin-2-one (**5c**). Yield 83% (113 mg, 0.42 mmol). ¹H NMR (300 MHz, CDCl₃): 8.50 (s, 2H), 4.31 (t, *J* = 8.3 Hz, 2H), 3.77 (t, *J* = 8.3 Hz, 2H), 2.93 (t, *J* = 7.7 Hz, 2H), 2.30 (t, *J* = 8.3 Hz, 2H), 1.93 (tt, *J* = *J'* = 7.9 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃): 168.3, 156.5, 155.2 (2C), 128.8, 70.7, 70.04, 62.9, 46.9, 37.4, 27.1, 17.9.

4.1.6. General procedure for the *ihDA/DA* reaction to form bicyclic pyridines **8a–c**

A solution of ynamide **5** (0.4 mmol) in trifluorotoluene (1 mL) was transferred in a microwaveable tube and irradiated under microwaves (300 W) at 210 °C for 2 h. The reaction mixture was then cooled down to room temperature and directly purified by flash chromatography on silica gel (cyclohexane/EtOAc 1:0 to remove the PhCF₃ then 6:4) to give the targeted bicyclic pyridine derivative **8**.

4.1.6.1. 3-(6,7-Dihydro-5H-cyclopenta[*b*]pyridin-4-yl)oxazolidin-2-one (**8a**). Yield 43% (37 mg, 0.18 mmol). ¹H NMR (300 MHz, CDCl₃): 8.33 (d, *J* = 5.7 Hz, 1H), 7.10 (d, *J* = 5.7 Hz, 1H), 4.52 (t, *J* = 7.4 Hz, 2H), 4.12 (t, *J* = 7.4 Hz, 2H), 3.10–2.99 (m, 4H), 2.14 (tt, *J* = *J'* = 7.5 Hz, 2H).

4.1.6.2. 3-(3-Bromo-6,7-dihydro-5H-cyclopenta[*b*]pyridin-4-yl)oxazolidin-2-one (**8b**). ¹H NMR (300 MHz, CDCl₃) (complex multiplicities and broad signals because of rotamers): 8.53 (br s, 1H), 4.59 (m, 2H), 4.28 (m, 2H), 3.15–3.01 (m, 2H), 2.87–2.79 (m, 2H), 2.26–2.11 (m, 2H).

4.1.6.3. 3-(3-Chloro-6,7-dihydro-5H-cyclopenta[*b*]pyridin-4-yl)oxazolidin-2-one (**8c**). Yield 23% (21 mg, 0.09 mmol). ¹H NMR (300 MHz, CDCl₃): 8.35 (d, *J* = 6.1 Hz, 1H), 4.56 (t, *J* = 7.6 Hz, 2H), 4.19 (t, *J* = 7.6 Hz, 2H), 3.21 (t, *J* = 7.5 Hz, 2H), 3.09 (t, *J* = 7.5 Hz, 2H), 2.20 (tt, *J* = *J'* = 7.5 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃): 162.9, 154.7, 144.9, 131.0, 129.21262, 62.7, 46.5, 33.7, 31.5, 23.5. HRMS (ESI) calculated for C₁₁H₁₂ClN₂O₂ [M+H]⁺: 239.0587; found: 239.0587.

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References

- [1] (a) A. Andreani, A. Leoni, A. Locatelli, R. Morigi, M. Rambaldi, C. Pietra, G. Villetti, *Eur. J. Med. Chem.* 35 (2000) 77–82; (b) L. Scipione, D. De Vita, A. Musella, L. Flammini, S. Bertoni, E. Barocelli, *Bioorg. Med. Chem. Lett.* 18 (2008) 309–312.
- [2] N. Lah, J. Koller, G. Giester, P. Segedin, I. Leban, *New J. Chem.* 26 (2002) 933–938.
- [3] R.P. Wurz, E.C. Lee, J.C. Ruble, G.C. Fu, *Adv. Synth. Catal.* 349 (2007) 2345–2352.
- [4] (a) D.L. Boger, *Tetrahedron* 39 (1983) 2869–2939; (b) D.L. Boger, *Chem. Rev.* 86 (1986) 781–793; (c) H. van der Plas, *Chem. Heterocycl. Compd.* 30 (1994) 1427–1443; (d) R.A.A. Foster, M.C. Willis, *Chem. Soc. Rev.* 42 (2013) 63–76; (e) J.M. Neely, T. Rovis, *Org. Chem. Front.* 1 (2014) 1010–1015.
- [5] (a) G. Evano, K. Jouvin, C. Theunissen, C. Guissart, A. Laouiti, C. Tresse, J. Heimburger, Y. Bouhoute, R. Veillard, M. Lecomte, A. Nitelet, S. Schweizer, N. Blanchard, C. Alayrac, A.C. Gaumont, *Chem. Commun.* 50 (2014) 10008–10018; (b) C. Tresse, C. Guissart, S. Schweizer, Y. Bouhoute, A.-C. Chany, M.-L. Goddard, N. Blanchard, G. Evano, *Adv. Synth. Catal.* 356 (2014) 2051–2060; (c) S. Schweizer, C. Tresse, P. Bissere, J. Lalevée, G. Evano, N. Blanchard, *Org. Lett.* 17 (2015) 1794–1797; (d) C. Tresse, S. Schweizer, P. Bissere, J. Lalevée, G. Evano, N. Blanchard, *Synthesis* 19 (2016) 3317–3330; (e) C. Guissart, A. Dolbois, C. Tresse, S. Saint-Auret, G. Evano, N. Blanchard, *Synlett* 27 (2016) 2575–2580.
- [6] (a) G. Duret, R. Quinlan, R.E. Martin, P. Bissere, M. Neuburger, V. Gandon, N. Blanchard, *Org. Lett.* 18 (2016) 1610–1613; (b) G. Duret, R. Quinlan, B. Yin, R.E. Martin, P. Bissere, M. Neuburger, V. Gandon, N. Blanchard, *J. Org. Chem.* 82 (2017) 1726–1742.
- [7] (a) A.E. Frissen, A.T.M. Marcelis, G. Geurtsen, D.A. de Bie, H.C. van der Plas, *Tetrahedron* 16 (1989) 5151–5162; (b) A.E. Frissen, A.T.M. Marcelis, W.C. Melger, H.C. van der Plas, *Tetrahedron* 45 (1989) 6891–6900.
- [8] S.-Y. Li, N. Jiang, S.-S. Xie, K.D.G. Wang, X.-B. Wang, L.-Y. Kong, *Org. Biomol. Chem.* 12 (2014) 801–814.
- [9] M. Rosini, F. Mancini, A. Tarozzi, F. Colizzi, V. Andrisano, M.L. Bolognesi, P. Hrelia, C. Melchiorre, *Bioorg. Med. Chem.* 14 (2006) 7846–7853.
- [10] S. Bräse, H. Wertal, D. Frank, D. Vidović, A. de Meijere, *Eur. J. Org. Chem.* (2005) 4167–4178.
- [11] J.P. Després, A.E. Greene, *Org. Synth.* 68 (1990) 41.
- [12] H. Yamanaka, T. Sakamoto, S. Nishimura, Y. Kondo, *Heterocycles* 27 (1988) 475–478.
- [13] K. Jouvin, J. Heimburger, G. Evano, *Chem. Sci.* 3 (2012) 756–760.
- [14] R.E. Martin, F. Morawitz, C. Kuratli, A.M. Alker, A.I. Alanine, *Eur. J. Org. Chem.* (2012) 47–52.
- [15] U. Tilstam, *Org. Process Res. Dev.* 16 (2012) 1273–1278.