Copper-catalyzed direct coupling of benzoxazin-2-ones with indoles for the synthesis of diverse 3-indolylbenzoxazin-2-ones: access to natural cephalandole A†

Rameshwar Prasad Pandit, a Jae-Jin Shim, a Sung Hong Kimb and Yong Rok Lee a,*

A novel and facile copper-catalyzed direct coupling for the synthesis of diverse and functionalized 3-indolyl benzoxazin-2-ones from benzoxazin-2-ones and indoles has been developed. This new methodology offers an easy and rapid approach to a variety of 3-indolylbenzo[b][1,4]oxazin-2-ones in high yield. As an application of this protocol, a gram-scale synthesis of naturally occurring cephalandole A has also been accomplished.

Introduction

Benzoxazines and benzoxazin-2-ones are important heterocyclic compounds found in natural products and biologically active molecules (Fig. 1).1,2 These compounds possess a wide range of pharmaceutical properties such as antihypertensive,3 anti-fungal,4 antimycobacterial,5 anti-inflammatory,6 bacterial histidine protein kinase inhibitory,7 and D2 receptor antagonist activities.8 In addition, compound 1 exhibits a potent effect of pyruvate kinase activators for the treatment of hereditary non-spherocytic hemolytic anemia and sickle cell anemia9 and compound 2 is useful for the treatment of lung cancer.10 Naturally occurring alkaloid, cephalandole A was originally isolated from Taiwanese orchid Cephalanceopsis gracilis11 and its structure was later revised into 3 by organic structure determination using atomic resolution scanning probe microscopy.12 Moreover, molecules bearing these skeletons have been also used as valuable building blocks for the synthesis of pharmaceuticals and photoactive materials.13,14 Owing to the importance of benzoxazin-2-ones, several methods for their synthesis have been reported.15,16 The general methods for benzoxazin-2-ones include the domino reaction of o-aminophenol with b-nitroacrylates,17 cleavage of resin-bound pseudooxazolones with 2-aminophenols,18 and TFA-catalyzed tandem reaction of benzoxazoles with 2-oxo-2-arylacetic acids.19 In addition, enantioselective hydrogenation of benzoxazinones and enantioselective addition of indoles to ketimines to give chiral dihydrobenzoxazinones have been accomplished.20,21 Although several methodologies for the synthesis of benzoxazin-2-ones and dihydrobenzoxazinones have been developed, there are no reports on the direct coupling of benzoxazin-2-ones with indoles for the construction of 3-indolylbenzoxazin-2-ones so far. Recently, an iron-catalyzed oxidative sp3 carbon–hydrogen bond functionalization of dihydrobenzoxazin-2-ones with indoles for the synthesis of 3-indolyl dihydrobenzoxazin-2-ones has been described (Scheme 1a).22 As a part of continuing efforts to develop new synthetic protocols for nitrogen heterocycles,23 we herein report the copper-catalyzed direct coupling of benzoxazin-2-ones with indoles for the formation of diverse 3-indolyl benzoxazin-2-ones in air (Scheme 1b).

Results and discussion

Our initial study commenced with the model reaction between benzoxazin-2-one 4a and N-methylindole 5a for the optimization of reaction condition (Table 1). Various metals were
examined as catalysts under several solvents in air. When using 10 mol% of CoCl₂, ZnCl₂ and NiCl₂ at 80 °C for 24 h in dichloroethane, product 6a was isolated in 32, 40, and 41% yields, respectively (entries 1–3, Table 1). Encouraged by these results, we screened other catalysts for the reaction. With 10 mol% of FeCl₃ and CuCl₂, the yield of 6a increased to 80 and 89% respectively (entries 4–5). However, additional attempt using other copper catalysts such as CuF₂, Cu(OAc)₂, and Cu(OTf)₂, failed to further increase the yield (entries 6–8).

Results of solvent screening showed that tetrahydrofuran (THF) was the best solvent (94%) among the solvents such as dioxane (87%), ethanol (66%), and water (60%) (entries 9–12). Changes in the loading of CuCl₂ to 5 mol%, 2 mol%, and 13 mol% did not improve the yield of 6a (entries 13–15). In addition, the effect of temperature was next studied. It was found out that decreasing or increasing temperature decreased the yield of 6a (entries 16 and 17). The structure of 6a was determined by spectroscopic analysis. The ¹H NMR spectrum of 6a showed a characteristic singlet singlet for indolyl C2 proton at δ 8.60 ppm and N-methyl peak on indolyl moiety at δ 3.85 ppm.

With the optimized reaction condition in hand, we further investigated the substrates scope employing different indoles 5b–5m (Table 2). Reaction of 4a with indoles 5b–5d bearing N-ethyl, N-benzyl, and N-phenyl moieties provided the desired products 6b–6d in 91, 67, and 72% yield, respectively. Treatment of 4a with N-arylated indoles 5e–5g having electron-donating or electron-withdrawing groups on the N-aryl ring, such as 4-Me, 4-OMe, and 4-Cl afforded the corresponding products 6e–6g in 76%, 70%, and 77% yield, respectively. Indoles 5h–5l bearing electron-donating or electron-withdrawing groups on the benzene ring were successful to afford the desired products. For example, reaction with N-methylindoles 5h–5i bearing electron-donating groups like methyl at 5- and 6-position on the aryl ring provided 6h (72%) and 6i (70%), respectively. The reaction of N-methylindoles 5j–5l bearing electron-withdrawing groups (5-F, 6-Cl, and 5-CHO) afforded products 6j–6l in 66, 61, and 78% yield, respectively.

To demonstrate the versatility of this coupling reaction, further reactions between various substituted benzoxazin-2-ones 4b–4g and several N-substituted indoles 5a, 5b, 5d, and 5g were examined (Table 3). The reactions of 4b–4e bearing electron-donating groups such as 6-methyl, 7-methyl, 6-tert-butyl, and 6-phenyl with N-substituted indoles 5a, 5b, 5d, or 5g provided products 7a–7g in the range of 60–88% yield. The

Table 1  Optimization of reaction condition for the synthesis of 6a

| Entry | Catalyst | Solvent | Temp (°C) | Time [h] | Yield [%] |
|-------|----------|---------|-----------|----------|-----------|
| 1     | CoCl₂ (10 mol%) | CICH₂CH₂Cl | 60 | 24 | 32 |
| 2     | ZnCl₂ (10 mol%)  | CICH₂CH₂Cl | 60 | 24 | 40 |
| 3     | NiCl₂ (10 mol%)  | CICH₂CH₂Cl | 60 | 24 | 41 |
| 4     | FeCl₃ (10 mol%)  | CICH₂CH₂Cl | 60 | 24 | 80 |
| 5     | CuCl₂ (10 mol%)  | CICH₂CH₂Cl | 60 | 24 | 89 |
| 6     | CuF₂ (10 mol%)   | CICH₂CH₂Cl | 60 | 24 | 80 |
| 7     | Cu(OAc)₂ (10 mol%) | CICH₂CH₂Cl | 60 | 24 | 78 |
| 8     | Cu(OTf)₂ (10 mol%) | CICH₂CH₂Cl | 60 | 12 | 85 |
| 9     | CuCl₂ (10 mol%)  | THF | 60 | 12 | 94 |
| 10    | CuCl₂ (10 mol%)  | Dioxane | 60 | 12 | 87 |
| 11    | CuCl₂ (10 mol%)  | EtOH | 60 | 12 | 87 |
| 12    | CuCl₂ (10 mol%)  | H₂O | 60 | 12 | 60 |
| 13    | CuCl₂ (5 mol%)   | THF | 60 | 12 | 91 |
| 14    | CuCl₂ (2 mol%)   | THF | 60 | 12 | 78 |
| 15    | CuCl₂ (13 mol%)  | THF | 60 | 6 | 82 |
| 16    | CuCl₂ (10 mol%)  | THF | 50 | 12 | 90 |
| 17    | CuCl₂ (10 mol%)  | THF | 70 | 10 | 85 |

* Reaction conditions: 4a (0.5 mmol), 5a (0.5 mmol), and catalyst (10 or 5 mol%) in solvent (3.0 mL) under air. ¹ Yield of the isolated product 6a after column chromatography.
The reactions of 4f and 4g bearing electron-withdrawing groups of 6-F and 6-Cl with 5a afforded the products 7h and 7i in 82% and 93% yield, respectively.

The utility of this new methodology for the gram-scale synthesis of naturally occurring cephalandole A (3) was next demonstrated (Scheme 2). Upon treatment of 4a with indole 5m at 60 °C for 12 h in THF, 3 was obtained in 75% yield. This one-pot protocol has several advantages such as higher yield, fewer steps, and lower cost. The synthesized compound was confirmed to be natural product 3 by comparison of its spectroscopic data with those previously reported.22

To elucidate the mechanism of this coupling reaction, we performed a control experiment (Scheme 3). The reaction between 4a with 5a in the absence of CuCl₂ in THF at room temperature for 30 h provided compound 8 in 93% yield. Further reaction of 8 in the presence of 10 mol% of CuCl₂ in THF at 60 °C for 1 h furnished 6a in 96% yield. These results suggest that compound 8 might be the intermediate in the coupling reaction.

Based on the above experiment, the mechanism for the formation of 6a is proposed as shown in Scheme 4. First, CuCl₂...
catalyst binds to 4a gives complex 4a', which subsequently undergoes nucleophilic attack by 5a to give 9. Deprotonation and protonation of 9 would afford intermediate 8, which undergoes air oxidation to give 6a**

Conclusions

In summary, a novel and efficient copper-catalyzed direct coupling of benzoxazin-2-ones with indoles for the synthesis of diverse and functionalized 3-indolylbenzoxazin-2-ones has been developed. This methodology provides a rapid synthetic route to natural cephalandole A and its derivatives. The proposed protocol has a wide substrate scope for both benzoxazin-2-ones and indoles.

Experimental

Imino cyclic esters were synthesized in the laboratory according to known procedure.** All indoles were prepared by either N-alkylation or N-arylation according to known method.** Solvents were used without further purification. Merck precoated silica gel plates (Art. 5554) with fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). Melting points are uncorrected and were determined on Fisher-Johns Melting Point Apparatus. 1H NMR and 13C NMR spectra were recorded on a Varian VNS (600 and 150 MHz, respectively) spectrometer in CDCl3 using δ = 7.24 and 77.0 ppm as solvent chemical shift. Chemical shifts (δ) are expressed in units of ppm and coupling constants (J) values are given in Hz. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet and td = triplet of doublet. FT-IR (neat) spectra were recorded on ATR (PerkinElmer Spectrum 2) and HRMS was obtained on JEOL JMS-700 spectrometer at Korean Basic Science Institute.

General procedure for synthesis of 3-indolylbenzoxazin-2-ones

To the solution of imino cyclic esters (0.5 mmol) and indoles (0.5 mmol) in THF (3.0 mL), CuCl2 (7 mg, 10 mol%) was added at room temperature and heated at 60 °C for 3–24 h. Upon completion of reaction as indicated by thin layer chromatography, the reaction mixture was concentrated under reduced pressure, and the crude material was purified by column chromatography (hexane/ethyl acetate = 20:1) to afford the desired compounds.

3-(1-Methyl-1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (6a).

Prepared from 4a (74 mg, 0.5 mmol) and N-methylindole 5a (65 mg, 0.5 mmol) according to general procedure in 3 h as a yellow solid (130 mg, 94%); mp 195–197 °C; 1H NMR (600 MHz, CDCl3) δ 8.87–8.83 (m, 1H), 8.60 (s, 1H), 7.85–7.82 (m, 1H), 7.38–7.32 (m, 5H), 7.27 (dd, J = 7.2, 1.6 Hz, 1H), 3.85 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 152.70, 147.32, 145.01, 137.40, 137.12, 132.38, 128.52, 28.20, 127.02, 125.29, 123.53, 123.40, 122.19, 115.94, 110.48, 109.61, 33.47; ATR-IR (neat) 2927, 1728, 1531, 1077, 773 cm⁻¹; HRMS (EI) m/z (M⁺) calcd for C18H14N2O2: 290.1055; found: 290.1053.

3-(1-Benzyloxy-1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (6b).

Prepared from 4a (74 mg, 0.5 mmol) and N-ethylindole 5b (72 mg, 0.5 mmol) according to general procedure in 6 h as a yellow solid (132 mg, 91%); mp 180–182 °C; 1H NMR (600 MHz, CDCl3) δ 8.90–8.86 (m, 1H), 8.69 (s, 1H), 7.85 (dd, J = 7.8, 1.8 Hz, 1H), 7.41–7.33 (m, 5H), 7.29–7.27 (m, 1H), 4.25 (q, J = 7.2 Hz, 2H), 1.55 (t, J = 7.2 Hz, 3H); 13C NMR (150 MHz, CDCl3) δ 152.76, 147.39, 145.03, 136.50, 135.60, 132.45, 128.51, 128.22, 127.26, 125.31, 123.68, 123.32, 122.15, 115.95, 110.62, 109.74, 41.78, 15.25; ATR-IR (neat) 2973, 1725, 1528, 1386, 737 cm⁻¹; HRMS (EI) m/z (M⁺) calcd for C18H14N2O2: 290.1055; found: 290.1053.
145.13, 137.35, 136.22, 132.36, 131.46, 128.88, 128.39, 127.20, 126.40, 125.47, 123.73, 123.85, 123.62, 122.61, 116.02, 114.86, 111.95, 110.87, 55.63; ATR-IR (neat) 2921, 1726, 1518, 1251, 739 cm⁻¹; HRMS (EI) m/z (M⁺) calcd for C₃₂H₂₄N₄O₈: 368.1611; found: 368.1614.

3-(1-(4-Chlorophenyl)-1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (6g). Prepared from 4a (74 mg, 0.5 mmol) and 1-(4-chlorophenyl)-1H-indole 5g (114 mg, 0.5 mmol) according to general procedure in 12 h as a yellow solid (143 mg, 77%); mp 209–211 °C;¹H NMR (600 MHz, CDCl₃) δ 8.94 (d, J = 7.8 Hz, 1H), 8.82 (s, 1H), 7.90 (dd, J = 7.8, 1.8 Hz, 1H), 7.55–7.48 (m, 4H), 7.44–7.37 (m, 3H), 7.35–7.33 (m, 1H), 7.31 (dd, J = 8.4, 1.8 Hz, 1H);¹C NMR (150 MHz, CDCl₃) δ 152.55, 147.27, 145.17, 137.12, 137.63, 135.48, 133.48, 132.24, 129.99, 122.22, 128.51, 127.46, 126.13, 125.46, 124.21, 123.84, 122.95, 116.09, 112.72, 110.66; ATR-IR (neat) 2921, 1729, 1535, 1087, 740 cm⁻¹; HRMS (EI) m/z (M⁺) calcd for C₂₂H₁₂ClIN₂O₃: 372.0666; found: 372.0664.

3-(1,5-Dimethyl-1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (6h). Prepared from 4a (74 mg, 0.5 mmol) and 1,5-dimethyl-1H-indole 5h (72 mg, 0.5 mmol) according to general procedure in 12 h as a yellow solid (104 mg, 72%); mp 220–222 °C;¹H NMR (600 MHz, CDCl₃) δ 8.64 (s, 1H), 8.57 (s, 1H), 7.87–7.86 (m, 1H), 7.37–7.35 (m, 2H), 7.28–7.24 (m, 2H), 7.16 (dd, J = 8.4, 1.2 Hz, 1H), 3.83 (s, 3H), 2.55 (s, 3H);¹C NMR (150 MHz, CDCl₃) δ 152.74, 147.36, 144.96, 139.67, 135.79, 132.42, 131.80, 128.35, 128.14, 127.22, 125.23, 124.86, 123.22, 115.91, 110.03, 109.29, 33.50, 21.80; ATR-IR (neat) 2916, 1729, 1525, 1366, 744 cm⁻¹; HRMS (EI) m/z (M⁺) calcd for C₁₉H₁₄N₂O₄: 344.0954; found: 343.0958.

6-Methyl-3-(1-ethyl-1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (7a). Prepared from 6-methyl-2H-benzo[b][1,4]oxazin-2-one 4b (81 mg, 0.5 mmol) and N-methylindole 5a (65 mg, 0.5 mmol) according to general procedure in 12 h as a yellow solid (88 mg, 61%); mp 218–220 °C;¹H NMR (600 MHz, CDCl₃) δ 8.88–8.85 (m, 1H), 8.61 (s, 1H), 7.65 (s, 1H), 7.38–7.32 (m, 3H), 7.19–7.15 (m, 2H), 3.87 (s, 3H), 2.44 (s, 3H);¹C NMR (150 MHz, CDCl₃) δ 152.95, 147.29, 143.00, 137.42, 137.01, 135.11, 132.10, 129.54, 128.16, 127.07, 123.56, 123.36, 122.13, 115.52, 110.58, 109.60, 33.48, 20.89; ATR-IR (neat) 2908, 1735, 1498, 739 cm⁻¹; HRMS (EI) m/z (M⁺) calcd for C₁₈H₁₄N₂O₄: 328.1055; found: 329.0952.

7-Methyl-3-(1-ethyl-1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (7c). Prepared from 7-methyl-2H-benzo[b][1,4]oxazin-2-one 4c (81 mg, 0.5 mmol) and N-methylindole 5a (65 mg, 0.5 mmol) according to general procedure in 12 h as a yellow solid (122 mg, 84%); mp 216–218 °C;¹H NMR (600 MHz, CDCl₃) δ 8.85–8.82 (m, 1H), 8.55 (s, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.36–7.31 (m, 3H), 7.16–7.13 (m, 1H), 7.05 (s, 1H), 3.83 (s, 3H), 2.43 (s, 3H);¹C NMR (150 MHz, CDCl₃) δ 152.85, 146.36, 144.86, 139.53, 137.34, 136.64, 130.29, 127.80, 126.98, 123.67, 123.47, 123.25, 121.99, 116.03, 110.48, 109.51, 33.39, 21.54; ATR-IR
9.0 Hz, 1H), 3.85 (s, 3H), 1.41 (s, 9H). 13C NMR (150 MHz, CDCl3) δ 7.42 (dd, 145.00, 140.08, 138.64, 136.77, 135.38, 130.22, 129.72, 129.02, 127.62, 127.43, 126.47, 128.86, 132.84, 134.77, 122.59, 116.12, 112.40, 110.82, 21.60; ATR-IR (neat) 3051, 1738, 1514, 1228, 736 cm⁻¹; HRMS (EI) m/z (M⁺) calecd for C23H16N2O2: 352.1212; found: 352.1214.

6-(tert-Butyl)-3-(1-methyl-1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (7e). Prepared from 6-(tert-butyl)-2H-benzo[b][1,4]oxazin-2-one 4d (101 mg, 0.5 mmol) and 1H-Indole (114 mg, 0.5 mmol) according to general procedure in 12 h as a yellow solid (86% yield); mp 177-178 °C; 1H NMR (600 MHz, CDCl3) δ 8.10 (d, J = 7.8 Hz, 1H), 8.48 (d, J = 2.4 Hz, 1H), 7.60 (d, J = 1.8 Hz, 1H), 7.30 (d, J = 6.8 Hz, 1H), 7.39-7.33 (m, 5H), 6.90-6.60 ppm; HRMS (EI) m/z (M⁺) calecd for C21H18N2O2: 310.1527; found: 310.1527.

3-(1-Methyl-1H-indol-3-yl)-6-phenyl-2H-benzo[b][1,4]oxazin-2-one (7g). Prepared from 6-phenyl-2H-benzo[b][1,4]oxazin-2-one 4e (116 mg, 0.5 mmol) and N-methylindole 5a (65 mg, 0.5 mmol) according to general procedure in 12 h as a yellow solid (86% yield); mp 177-178 °C; 1H NMR (600 MHz, CDCl3) δ 8.01-8.10 (m, 1H), 7.56-7.60 (m, 1H), 7.30 (d, J = 6.8 Hz, 1H), 6.80-6.60 ppm; HRMS (EI) m/z (M⁺) calecd for C26H19N2O2: 328.1289; found: 328.1289.
7.8, 1.2 Hz, 1H), 7.00 (td, J = 7.8, 1.2 Hz, 1H), 6.98 (s, 1H), 6.87 (td, J = 7.8, 1.2 Hz, 1H), 6.76 (dd, J = 7.8, 1.2 Hz, 1H), 5.33 (s, 1H), 3.70 (s, 4H). 13C NMR (150 MHz, CDCl3) δ 165.15, 141.31, 137.10, 132.83, 127.74, 125.99, 124.99, 122.42, 120.36, 119.99, 119.24, 116.89, 115.04, 109.69, 109.63, 52.56, 32.89; ATR-IR (neat) 3346, 1735, 1529, 1129, 737 cm⁻¹; HRMS (El) m/z (M⁺) calcd for C17H14N2O2: 278.1055; found: 278.1058.

To the solution of 8 (139 mg, 0.5 mmol) in THF (3.0 mL), CuCl₂ (7 mg, 10 mol%) was added at room temperature and concentrated under reduced pressure, and the crude material was purified by column chromatography (hexane/ethyl acetate = 20:1) to afford 6a as a solid (132 mg, 96%).

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This research was supported by the Nano Material Technology Development Program of the Korean National Research Foundation (NRF) funded by the Korean Ministry of Education, Science, and Technology (2012M3A7B4049675) and Priority Research Centers Program (2014R1A6A1031189).

Notes and references

1 (a) Antibiotics and Antiviral Compounds, ed. K. Krohn, H. A. KIRST and H. Maag, VCH, Weinheim, 1993; (b) Pharmaceutical Substances, ed. A. Kleemann, J. Engel, B. Kutscher and D. Reichert, Thieme, Stuttgart, New York, 4th edn, 2001; (c) Houben-Weyl Methods of Organic Chemistry, Heterenes IV, Six-Membered and Large Hetero-Rings with Maximum Unsaturation, ed. J. Teller and E. Schaumann, Georg Thieme, Stuttgart, 1997, vol. E9a, pp. 141-177; (d) J. Ilaš, P. S. Anderluh, M. S. Dolenc and D. Kikelj, Tetrahedron, 2005, 61, 7325; (e) B. Achari, S. B. Mandal, P. K. Dutta and C. Chowdhury, Synlett, 2004, 2449.

2 (a) T. Hasui, N. Matsunaga, T. Ora, N. Ohyabu, N. Nishigaki, J. Ilaš, P. S. Anderluh, M. S. Dolenc and D. Kikelj, J. Med. Chem., 2011, 54, 8616; (b) H. Matsuoka, K. Maruyama, T. Katsuyama, T. Masuda, M. Shimizu, T. Iida, T. Kasai, Y. Kato, T. Akimoto, K. Takeda, K. Yano and T. Kuroki, J. Med. Chem., 1997, 40, 105; (c) S. M. Bromidge, B. Bertani, M. Borriello, S. Faedo, L. J. Gordon, E. Granci, M. Hill, L. P. Stasi, V. Zuchelli, G. Merlo, A. Vesentini, J. M. Watson and L. Zonzini, Bioorg. Med. Chem. Lett., 2008, 18, 5653; (d) S. M. Bromidge, B. Bertani, M. Borriello, A. Bozzoli, S. Faedo, M. Gianotti, L. J. Gordon, M. Hill, V. Zuchelli, J. M. Watson and L. Zonzini, Bioorg. Med. Chem. Lett., 2009, 19, 2338; (e) T. Hasui, T. Ohra, N. Ohyabu, K. Asano, H. Matsu, A. Mizukami, N. Habuka, S. Sogabe, S. Endo, C. S. Siedem, T. P. Tang, C. Gauthier, L. A. De Meese, S. A. Boyd and S. Fukumoto, Bioorg. Med. Chem., 2013, 21, 5983.

3 F. Touzeau, A. Arrault, G. Guillaumet, E. Scalbert, B. Pfeiffer, M.-C. Rettori, P. Renard and J.-Y. Mérour, J. Med. Chem., 2003, 46, 1962.

4 K. Waisser, L. Kubcová, V. Buchta, P. Kubanova, K. Bajerová, L. Jirásková, O. Bednářík, O. Bureš and P. Holý, Folia Microbiol., 2002, 47, 488.

5 K. Waisser, M. Peřina, J. Kuneš, V. Klimešová and J. Kaustová, Il Farmaco, 2003, 58, 1137; (b) S. Konda, S. Raptarthi, K. Bhaskar, R. K. Munagati, V. Guguloth, L. Nagarapu and D. M. Akkerwar, Bioorg. Med. Chem. Lett., 2015, 25, 1643.

6 (a) A. Khalaj, M. Abdollahi, A. Kebriaeezadeh, N. Adibpour, Z. Pandi and S. Rasoulamini, Indian J. Pharmacol., 2002, 34, 184; (b) I. V. Mashevakayka, L. V. Anikina, Y. B. Vikharev, V. A. Safin, S. V. Koltsova and A. N. Maslivets, Pharm. Chem. J., 2001, 35, 414.

7 R. Frechette and M. A. Weidner-Wells, WO Patent Appl. 9717333, 1997.

8 L. D. Wise, D. J. Wustrow and T. Belliotti, WO Patent Appl. 9745419, 1997.

9 S. U. S.-S. Michael, WO Patent 2012151440, 2012.

10 C. Li and G. Xiaoxia, Patent CN 103664919 A, 2014.

11 (a) P.-L. Wu, Y.-L. Hsu and C.-W. Jao, Nat. Prod., 2006, 69, 1467; (b) Y.-T. Wu, Y.-L. Hsu and P.-L. Wu, Heterocycles, 2008, 75, 1191.

12 (a) J. J. Mason, J. Bergman and T. Janosik, J. Nat. Prod., 2008, 71, 1447; (b) L. Gross, F. Mohn, N. Moll, G. Meyer, W. M. Abdel-Megeed and M. Japsars, Nat. Chem., 2010, 2, 821.

13 (a) Q. Chen, M. Chen, C. Yu, L. Shi, D. Wang, Y. Yang and Y. Zhou, J. Am. Chem. Soc., 2011, 133, 16432; (b) M. Rueping, A. P. Antonchick and T. Theissmann, Angew. Chem., Int. Ed., 2006, 45, 6751; (c) C. Saiz, H. Rodríguez, A. Márquez, A. Cánete, C. Jullian and A. Zanocco, Synth. Commun., 2001, 31, 135; (d) H. Miyabe, Y. Yamaoka and Y. Takemoto, J. Org. Chem., 2006, 71, 2099.

14 (a) R. A. Duval, G. Lewin, E. Peris, N. Chahboune, A. Garofano, S. Drçe, D. Cortes, U. Brandt and R. Hocquemiller, Biochemistry, 2006, 45, 2721; (b) V. L. Gein, N. A. Rassudikhina, N. V. Shepelina, M. I. Vakhirin, E. B. Babushkina and E. V. Voronina, Pharm. Chem. J., 2008, 42, 519; (c) X. Li, N. Liu, H. Zhang, S. E. Knudson, R. A. Sladiten and P. J. Tongsue, Bioorg. Med. Chem. Lett., 2010, 20, 6306; (d) M. Hu, J. Fan, H. Li, K. Song, S. Wang, G. Cheng and X. Peng, Org. Biomol. Chem., 2011, 9, 980; (e) S. Bondock, S. Adel, H. A. Etman and F. A. Badria, Eur. J. Med. Chem., 2012, 48, 192; (f) K. Azuma, S. Suzuki, S. Uchiyama, T. Kajiro, T. Santa and K. Imai, Photochem. Photobiol. Sci., 2003, 2, 443; (g) T. Nishio, J. Chem. Soc., Perkin Trans. 1, 1990, 565; (h) S. Nonell, L. R. Feiriras, A. Caete, E. Lemp, G. Günther, N. Pizarro and A. L. Zanocco, J. Org. Chem., 2008, 73, 5371.

15 (a) Y. M. Lee and Y. S. Park, Heterocycles, 2009, 78, 2233; (b) S. Luo and J. K. De Brabander, Tetrahedron Lett., 2015, 56, 3179; (c) R. I. Storer, D. E. Carrera, Y. K. Ni and...
D. W. C. MacMillan, J. Am. Chem. Soc., 2006, 128, 84; (d) M. Rueping, A. P. Antonchick and T. Theissmann, Angew. Chem. Int. Ed., 2006, 45, 6751; (e) F. Shi, W. Tan, H.-H. Zhang, M. Li, Q. Ye, G.-H. Ma, S.-J. Tu and G.-G. Li, Adv. Synth. Catal., 2013, 355, 3715; (f) A. V. Maikov, K. Vrankova, S. Stoncius and P. Kocovsky, J. Org. Chem., 2009, 74, 5839; (g) X.-Z. Peng, W.-C. Yuan and X.-M. Zhang, Adv. Synth. Catal., 2010, 352, 2132; (h) Q.-A. Chen, M.-W. Chen, C.-B. Yu, L. Shi, D.-S. Wang, Y. Yang and Y.-G. Zhou, J. Am. Chem. Soc., 2011, 133, 16432; (i) Q.-A. Chen, K. Gao, Y. Duan, Z.-S. Ye, Y. Yang and Y.-G. Zhou, J. Am. Chem. Soc., 2012, 134, 2442; (j) L.-Q. Lu, Y.-H. Li, K. Junge and M. Beller, J. Am. Chem. Soc., 2015, 137, 2763; (k) J. L. Núñez-Rico and A. Vidal-Ferran, Org. Lett., 2013, 15, 2066.

16 (a) C. Trebaul, J. Roncali, F. Garnier and R. Guglielmetti, Bull. Chem. Soc. Jpn., 1987, 60, 2657; (b) R. B. Moffet, J. Med. Chem., 1966, 9, 475; (c) A. Chilin, A. Confente, G. Pastorini and A. Guiotto, Eur. J. Org. Chem., 2002, 1987; (d) D. N. Nicolaides, D. R. Gautam, K. E. Litinas, D. J. Hadjipavlou-Litina and C. A. Kontogiorgis, J. Heterocycl. Chem., 2004, 41, 605; (e) D. N. Nicolaides, R. W. Awad and E. A. Varella, J. Heterocycl. Chem., 1996, 33, 633; (f) I. Yavari, S. Souri, M. Sirouspour and H. Djahanian, Synthesis, 2006, 3243; (g) N. Zidar and D. Kikelj, Tetrahedron, 2008, 64, 5756; (h) R. Ballini, A. Palmieri, M. A. Talaq and S. Gabrielli, Adv. Synth. Catal., 2009, 351, 2611.

17 R. Ballini, A. Palmieri, M. A. Talaq and S. Gabrielli, Adv. Synth. Catal., 2009, 351, 2611.

18 S. Gräfsle, S. Vanderheiden, P. Hodapp, B. Bulat, M. Niegier, N. Jung and S. Bräse, Org. Lett., 2016, 18, 3598.

19 S. Yan, L. Ye, M. Liu, J. Chen, J. Ding, W. Gao, X. Huang and H. Wu, RSC Adv., 2014, 4, 16705.

20 (a) L.-Q. Lu, Y. Li, K. Junge and M. Beller, J. Am. Chem. Soc., 2015, 137, 2763; (b) Q.-A. Chen, K. Gao, Y. Duan, Z.-S. Ye, L. Shi, Y. Yang and Y.-G. Zhou, J. Am. Chem. Soc., 2012, 134, 2442; (c) Q.-A. Chen, M.-W. Chen, C.-B. Yu, L. Shi, D.-S. Wang, Y. Yang and Y.-G. Zhou, J. Am. Chem. Soc., 2011, 133, 16432; (d) M. Rueping, A. P. Antonchick and T. Theissmann, Angew. Chem. Int. Ed., 2006, 45, 6751.

21 T. Kano, R. Takechi, R. Kobayashi and K. Maruoka, Org. Biomol. Chem., 2014, 12, 724.

22 C. Huo, J. Dong, Y. Su, J. Tang and F. Chen, Chem. Commun., 2016, 52, 13341.

23 (a) R. P. Pandit, S. H. Kim and Y. R. Lee, Adv. Synth. Catal., 2016, 358, 3586; (b) R. P. Pandit, S. H. Kim and Y. R. Lee, Org. Biomol. Chem., 2016, 14, 6996; (c) R. P. Pandit and Y. R. Lee, Adv. Synth. Catal., 2015, 357, 2657; (d) R. P. Pandit, K. Sharma and Y. R. Lee, Synthesis, 2015, 47, 3881; (e) R. P. Pandit and Y. R. Lee, RSC Adv., 2013, 3, 22039.

24 (a) S. E. Allen, R. R. Walvoord, R. Padilla-Salinas and M. C. Kozlowski, Chem. Rev., 2013, 113, 6234; (b) S. D. McCann and S. S. Stahl, Acc. Chem. Res., 2015, 48, 1756.

25 P.-L. Shao, J.-Y. Liao, Y. A. Ho and Y. Zhao, Angew. Chem. Int. Ed., 2014, 53, 5435.

26 (a) Y. Wu, X. Peng, B. Luo, F. Wu, B. Liu, F. Song, P. Huang and S. Wen, Org. Biomol. Chem., 2014, 12, 9777; (b) R. R. Singh and R.-S. Liu, Chem. Commun., 2017, 53, 4593; (c) F. Damkaci, A. Alawaed and E. Vik, Tetrahedron Lett., 2016, 57, 2197.