# Total Synthesis of Rutaecarpine and Analogues by Tandem Azido Reductive Cyclization Assisted by Microwave Irradiation

Ahmed Kamal,*[a] M. Kashi Reddy,[a] T. Srinivasa Reddy,[b] Leonardo Silva Santos,[c] Nagula Shankaraiah*[b]

[a] Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 607, India
Fax +91(40)27193189; E-mail: ahmedkamal@iict.res.in

[b] National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad 500 037, India

[c] Laboratory of Asymmetric Synthesis, Chemistry Institute of Natural Resources, University of Talca, P.O. Box 747, Talca, Chile
Fax +56(71)200448; E-mail: lssantos@utalca.cl

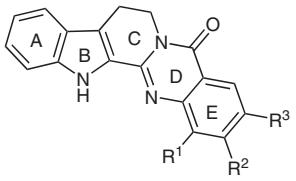
*Received 13 August 2010*

**Abstract:** The total synthesis of rutaecarpine and several analogues has been developed by using an azido reductive cyclization process starting from substituted azido benzoic acids. The intramolecular azido reductive cyclization step was performed with triphenylphosphine or $Ni_2B$ in HCl–MeOH (1 M) using microwave irradiation. This synthetic route is amenable for the generation of a library of quinazolinone compounds.

**Key words:** quinazolinones, β-carbolines, azido-reductive cyclization, $Ni_2B$, microwave irradiation

The quinazolinone skeleton is an important building block for a large number of naturally occurring alkaloids[1] and their synthetic analogues. Such compounds possess a variety of biological properties, such as antimalarial,[2] anticonvulsant,[3] antibacterial,[4] antidiabetic,[5] and anticancer activity.[6] Thus, due to the diverse range of the pharmacological activities of quinazolinones and their derivatives, numerous methods have been developed for their synthesis.[7] Rutaecarpine is the major alkaloid component of Wu-Chu-Yu, a Chinese herbal drug, and the rutaecarpine scaffold has been found to act by suppressing platelet plug formation in mesenteric venules and increasing intracellular $Ca^{2+}$ in endothelial cells.[8] Recently, Don and co-workers[9] reported that rutaecarpine derivatives selectively inhibited human CYP1A1, CYP1A2, and CYP2B1, and exhibit cytotoxicity[10] as well as inhibitory effects on COX-2.[11]

Rutaecarpine (**1a**; Figure 1)[12] was originally isolated from the dried fruits of *Evodia rutaecarpa* and callus tissue cultured from the stem of *Phellodendron amurense*.[13–16] It has been extensively used as a remedy for headache, dysentery, cholera, worm infections, and postpartum.[17] Moreover, the analogues, euxylophoricine A (**1b**) and euxylophoricine C (**1c**), have also been found to possess anti-stomachic, antiemetic, anti-nociceptive, anti-inflammatory, anti-pyretic, analgesic, astringent, anti-hypertensive, uterotonic, and TCDD-receptor agonist activities.[18] Robinson and co-workers[19] reported the first total synthesis of rutaecarpine and, since then, several routes to **1a** and its derivatives have been developed.[20–23] In addition, numerous methods have been reported for the construction of the D ring and/or for building the connection between the D and B rings starting from tryptamine derivatives.[24] Recently, Lee and co-workers developed a versatile synthetic strategy to rutaecarpine by nitro reductive cyclization with $SnCl_2{\cdot}2H_2O$.[25] In spite of the advantages of tin reduction, there are instances in the literature wherein substantial quantities of tin by-products are formed. Furthermore, most of the cell lines that have been biologically screened have proven to be intolerant of tin even at very low levels. We have been involved in the synthesis of bioactive fused quinazolinone natural products, such as (–)-vasicinone and its deoxy derivatives, by employing azido reductive cyclization approaches[26] using lactams and substituted azido benzoic acids as precursors. In this context, we became interested in the total synthesis of rutaecarpine (**1a**) and its analogues **1b–h** by employing azido reductive cyclization assisted by microwave irradiation.




$R^1 = R^2 = R^3 = H$, rutaecarpine (**1a**)
$R^1 = H$, $R^2 = R^3 = OMe$ (**1b**)
$R^1 = H$, $R^2$–$R^3 = -OCH_2O-$ (**1c**)
$R^1 = H$, $R^2 = OMe$, $R^3 = H$ (**1d**)
$R^1 = H$, $R^2 = OBn$, $R^3 = OMe$ (**1e**)
$R^1 = H$, $R^2 = Cl$, $R^3 = H$ (**1f**)
$R^1 = H = R^2 = H$, $R^3 = Br$ (**1g**)
$R^1 = OBn$, $R^2 = R^3 = H$ (**1h**)

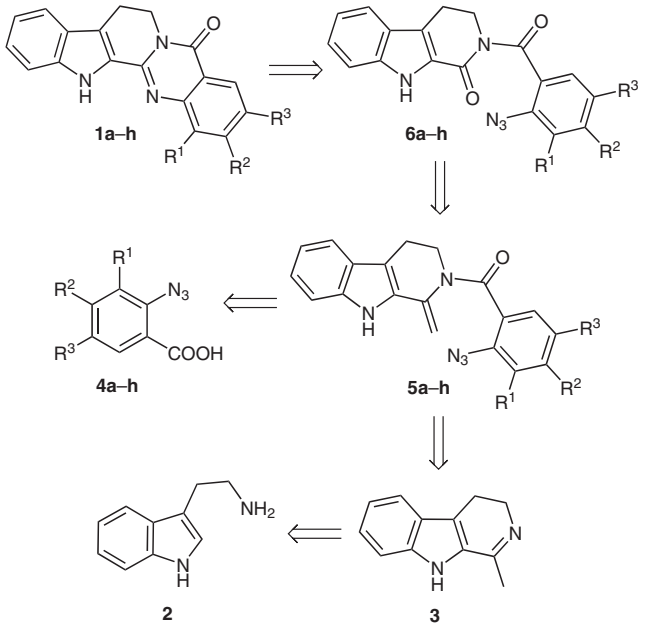
**Figure 1** Representative chemical structure of rutaecarpine (**1a**) and its analogues **1b–h**

Microwave-assisted (MWA) organic synthesis has played a pivotal role in the preparation of N-heterocyclic compounds.[27] In contrast to conventional heating, application of microwave energy has the major advantage of shorter reaction times because of the rapid core heating associated with microwaves. Therefore, reactions frequently exhibit cleaner product profiles and use minimal amounts of solvent. This prompted us to synthesize these quinazolinones using a CEM Discovery microwave reactor with nickel boride ($Ni_2B$) as a reducing reagent.[26b] As expected, the

*SYNLETT* 2011, No. 1, pp 0061–0064
Advanced online publication: 10.12.2010
DOI: 10.1055/s-0030-1259095; Art ID: D22210ST

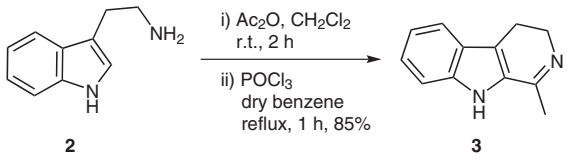
reaction time was reduced dramatically. The mild reaction conditions, as well as the high yield of this reaction, encouraged us to apply this methodology to its derivatives. During the course of this synthesis, we noted that $Ni_2B$ was the reagent of choice to obtain such heterocyclic compounds.

The retrosynthetic analysis of the central framework of rutaecarpine (**1a**) and analogues is depicted in Scheme 1. The synthetic features include isomerization of the endocyclic imine double bond into an exocyclic olefin by benzoylation, oxidation of the terminal double bond to form a cyclic amide, and azido reductive cyclization, as key steps. Imine **3** was obtained from tryptamine (**2**) by treatment with $Ac_2O$ followed by Bischler–Napieralsky cyclization.[28] Having prepared imine **3**, the stage was set for an important coupling reaction with suitably substituted azido benzoyl chlorides, which were prepared from a variety of azido benzoic acids by treatment with $COCl_2$. Next, the key intermediates **5a**–**h** were oxidized with $KMnO_4$ to convert the exocyclic double bond into cyclic amides **6a**–**h**. We also attempted an intramolecular aza-Wittig reductive cyclization approach to the synthesis of **5a** using TPP followed by treatment with aqueous ammonia under heating; however, this approach afforded the quinazolinone natural product **1a** in lower yield (62%). These results prompted us to explore MWA reactions to improve the yields in the final step of the azido-reductive cyclization of the key intermediates **6a**–**h** by using $Ni_2B$ as a reducing reagent.




**Scheme 1** Retrosynthetic analysis of rutaecarpine (**1a**) and its analogues **1b**–**h**

Our synthetic work began with substituted azido benzoic acids **4a**–**h**, which were prepared by reported methods.[26a] The acids **4a**–**h** were converted into their acid chlorides by employing $COCl_2$ in anhydrous $CH_2Cl_2$ at 0 °C to room temperature for six hours. 1-Methyl-4,9-dihydro-3*H*-β-carboline (**3**) was prepared from the commercially available tryptamine (**2**) by treatment with acetic anhydride in anhydrous $CH_2Cl_2$ at room temperature for two hours to give the N-acetylated amide; subsequent Bischler–Napieralsky cyclization with $POCl_3$ in anhydrous benzene at reflux for one hour gave imine **3** in good yield (85%) as shown in Scheme 2.




**Scheme 2** Synthesis of β-carboline **3** by employing Bischler–Napieralsky cyclization

The key intermediates **5a**–**h** (77–84%)[30] were obtained by mixing tricyclic β-carboline **3** and a variety of substituted 2-azidobenzoyl chlorides in $CH_2Cl_2$ at room temperature for two hours (Scheme 3). After isomerization of the endocyclic double bond to the exocyclic double bond, an oxidative cleavage step was carried out by using $KMnO_4$ to give the requisite 2,3,4,9-tetrahydro-β-carbolin-1-one derivatives **6a**–**h**[25,30] in moderate yields (58–67%). Then, we explored an intramolecular aza-Wittig reductive-cyclization with **5a** using TPP in THF for 12 hours to give phosphine intermediate **7a**, although a considerable amount of the azido starting material remained (indicated by TLC). To this reaction mixture was added 1–2 mL of ammonia solution, and the mixture was heated at 60–70 °C for two hours to afford the quinazolinone natural product **1a** in moderate yield (62%).

Based on the results of this study we decided to explore the reduction of azido functionality with $Ni_2B$/HCl–MeOH (1 M) using microwave irradiation (70 W)[26b] to afford the final products (**1a**–**h**)[31] in excellent yields (80–90%) as shown in Scheme 3.

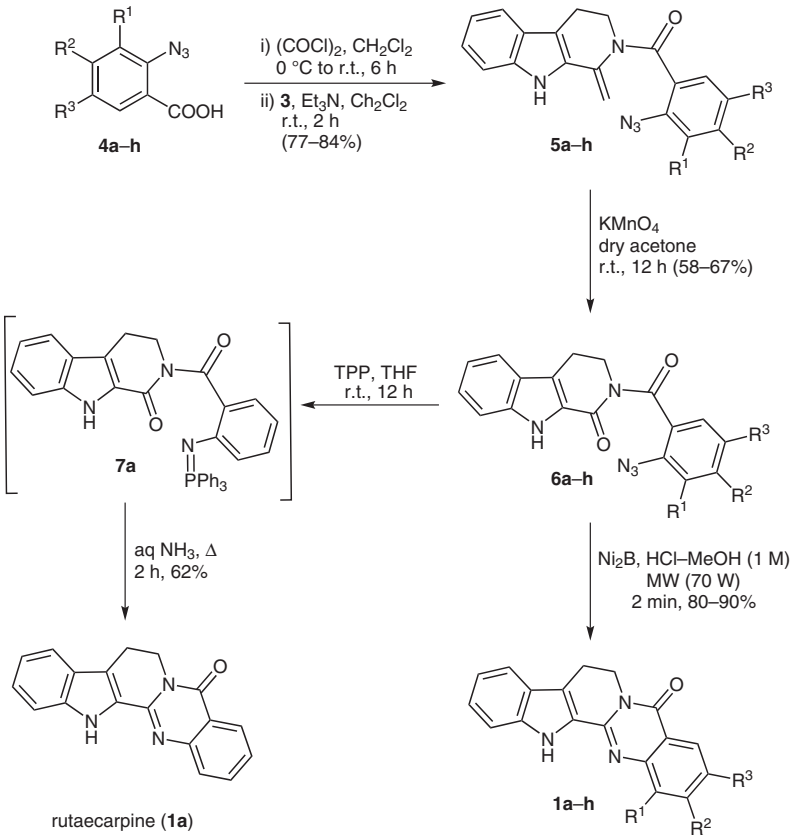
In conclusion, we have developed a simple and efficient synthetic strategy to rutaecarpine and its derivatives by employing an azido reductive tandem-cyclization approach.[29–31] A successful microwave-assisted reaction with nickel boride as a reducing reagent has been used in the final cyclization step of the synthesis. The reaction conditions are particularly attractive and mild, and the synthetic route allows easy access to the quinazolinone alkaloids.

## Acknowledgment

M.K.R. thanks CSIR New Delhi for the award of a research fellowship. L.S.S. thanks Fondecyt (1085308) for support.

## References and Notes

(1) Mhaske, S. B.; Argade, P. *Tetrahedron* **2005**, *62*, 9787.
(2) Takaya, Y.; Tasaka, H.; Chiba, T.; Uwai, K.; Tanitsu, M.-A.; Kim, H.-S.; Wataya, Y.; Miura, M.; Takeshita, M.; Oshima, Y. *J. Med. Chem.* **1999**, *42*, 3163.




**Scheme 3** An intramolecular tandem azido reduction cyclization approach to rutaecarpine (**1a**) and analogues **1b–h**


(3) (a) Gupta, C. M.; Bhaduri, A. P.; Khanna, N. M. *J. Med. Chem.* **1968**, *11*, 392. (b) Welch, W. M.; Ewing, F. E.; Huang, J.; Menniti, F. S.; Pagnozzi, M. J.; Kelly, K.; Seymoyr, P. A.; Guanowsky, V.; Guhan, S.; Guinn, M. R.; Critchett, D.; Lazzaro, J.; Ganong, A. H.; DeVries, K. M.; Staigers, T. L.; Chenard, B. L. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 177.

(4) Kung, P.-P.; Casper, M. D.; Cook, K. L.; Wilson-Lingard, L.; Risen, L. M.; Vickers, T. A.; Ranken, R.; Blyn, L. B.; Wyatt, R.; Cook, P. D.; Ecker, D. J. *J. Med. Chem.* **1999**, *42*, 4705.

(5) Malamas, M. S.; Millen, J. *J. Med. Chem.* **1991**, *34*, 1492.

(6) Fetter, J.; Czuppo, T.; Hornyak, G.; Feller, A. *Tetrahedron* **1991**, *47*, 9393.

(7) (a) Padala, S. R.; Padi, P. R.; Thipireddy, V. *Heterocycles* **2003**, *60*, 183. (b) Larksarp, C.; Alper, H. *J. Org. Chem.* **2000**, *65*, 2773. (c) Wang, L.; Xia, J.; Qin, F.; Qian, C.; Sun, J. *Synthesis* **2003**, 1241. (d) Dabiri, M.; Salehi, P.; Khajavi, M. S.; Mohammadi, A. A. *Heterocycles* **2004**, *63*, 1417. (e) Bhat, B. A.; Sahu, D. P. *Synth. Commun.* **2004**, *34*, 2169. (f) Connoly, D. J.; Cusack, D.; O'Sullivan, T. P.; Guiry, P. J. *Tetrahedron* **2005**, *61*, 10153. (g) Potewar, T. M.; Nadaf, R. N.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V. *Synth. Commun.* **2005**, *35*, 231. (h) Liu, J.-F.; Lee, J.; Dalton, A. M.; Bi, G.; Yu, L.; Baldino, C. M.; McElory, E.; Brown, M. *Tetrahedron Lett.* **2005**, *46*, 1241.

(8) (a) Wu, S. N.; Lo, Y. K.; Chen, H.; Li, H. F.; Chiang, H. T. *Neuropharmacology* **2001**, *41*, 834. (b) Sheu, J. R.; Hung, W. C.; Wu, C. H.; Lee, Y. M.; Yen, M. H. *Br. J. Haematol.* **2000**, *110*, 110. (c) Wang, G. J.; Shan, J.; Pang, P. K. T.; Yang, M. C. M.; Chou, C. J.; Chen, C. F. *J. Pharmacol. Exp. Ther.* **1996**, *270*, 1016.

(9) Don, M. J.; Lewis, D. F. V.; Wang, S. Y.; Tsai, M. W.; Ueng, Y. F. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2535.

(10) Baruah, B.; Dasu, K.; Valtilingam, B.; Mamnoor, P.; Venkata, P. P.; Rajagopal, S.; Yeleswarapu, K. R. *Bioorg. Med. Chem.* **2004**, *12*, 1991.

(11) Chang, H. W.; Kim, S. I.; Jung, H.; Jahng, Y. *Heterocycles* **2003**, *60*, 1359.

(12) Asahina, Y. *Acta Phytochim.* **1922**, *1*, 67.

(13) Kamikado, T.; Murakoshi, S.; Tamura, S. *Agric. Biol. Chem.* **1978**, *42*, 1515.

(14) Bergman, J. *The Alkaloids,* In *The Quinazolinocarboline alkaloids*, Vol. 21; Brossi, A. R., Ed.; Academic Press: New York, **1983**, 29–54.

(15) (a) Ikuta, A.; Urabe, H.; Nakamura, T. *J. Nat. Prod.* **1998**, *61*, 1012. (b) Ikuta, A.; Nakamura, T.; Urabe, H. *Phytochemistry* **1998**, *48*, 285.

(16) Michael, J. P. *Nat. Prod. Rep.* **1999**, *16*, 697.

(17) Chen, A. L.; Chen, K. K. *J. Am. Pharm. Assoc.* **1933**, *22*, 716.

(18) (a) King, C. L.; Kong, Y. C.; Wong, N. S.; Yeung, H. W.; Fong, H. H. S.; Sankawa, U. *J. Nat. Prod.* **1980**, *43*, 577. (b) Gillner, M.; Bergman, J.; Cambillau, C.; Gustafsson, J.-A. *Carcinogenesis* **1989**, *10*, 651. (c) Rannug, U.; Sjógren, M.; Rannug, A.; Gillner, M.; Toftgard, R.; Gustafsson, J. A.; Rosenkranz, H.; Klopman, G. *Carcinogenesis* **1991**, *12*, 2007. (d) Matsuda, H.; Yoshikawa, M.; Ko, S.; Iinuma, M.; Kubo, M. *Nat. Med.* **1998**, *52*, 203. (e) Hibino, S.; Choshi, T. *Nat. Prod. Rep.* **2001**, *18*, 66.

(19) Asahina, Y.; Manske, R. H. F.; Robinson, R. *J. Chem. Soc.* **1927**, 1708.

(20) Mhaske, S. B.; Argade, N. P. *Tetrahedron* **2004**, *60*, 3417; and references cited therein.

(21) (a) Kökösi, J.; Hermecz, I.; Szász, G.; Mészáros, Z. *Tetrahedron Lett.* **1981**, *22*, 4861. (b) Kökösi, J.; Szász, G.; Hermecz, I. *Tetrahedron Lett.* **1992**, *33*, 2995. (c) Lee, S.

H.; Kim, S. I.; Park, J. G.; Lee, E. S.; Jahng, Y. *Heterocycles* **2001**, *55*, 1555. (d) Chang, H. W.; Kim, S. I.; Jung, H.; Jahng, Y. *Heterocycles* **2003**, *60*, 1359. (e) Chavan, S. P.; Sivappa, R. *Tetrahedron Lett.* **2004**, *45*, 997.

(22) Lee, E. S.; Park, J.-G.; Jahng, Y. *Tetrahedron Lett.* **2003**, *44*, 1883.

(23) Pereira, M.-F.; Picot, L.; Guillon, J.; Léger, J.-M.; Jarry, C. R.; Thiéry, V.; Besson, T. *Tetrahedron Lett.* **2005**, *46*, 3445.

(24) (a) Kametani, T.; Higa, T.; Von Loc, C.; Ihara, M.; Koizumi, M.; Fukumoto, K. *J. Am. Chem. Soc.* **1976**, *98*, 6186. (b) Kametani, T.; Von Loc, C.; Higa, T.; Koizumi, M.; Ihara, M.; Fukumoto, K. *J. Am. Chem. Soc.* **1977**, *99*, 2306. (c) Bergman, J.; Bergman, S. *J. Org. Chem.* **1985**, *50*, 1246. (d) Mohanta, P. K.; Kim, K. *Tetrahedron Lett.* **2002**, *43*, 3993. (e) Harayama, T.; Hori, A.; Serban, G.; Morikami, Y.; Matsumoto, T.; Abe, H.; Takeuchi, Y. *Tetrahedron* **2004**, *60*, 10645.

(25) Lee, C. S.; Liu, C. K.; Chiang, Y. L.; Cheng, Y. Y. *Tetrahedron Lett.* **2008**, *49*, 481.

(26) (a) Kamal, A.; Markandeya, N.; Shankaraiah, N.; Reddy, Ch. R.; Prabhakar, S.; Reddy, Ch. S.; Eberlin, M. N.; Santos, L. S. *Chem. Eur. J.* **2009**, *15*, 7214. (b) Shankaraiah, N.; Markandeya, N.; Moraga, M. E.; Arancibia, C.; Kamal, A.; Santos, L. S. *Synthesis* **2009**, 2163. (c) Kamal, A.; Shankaraiah, N.; Markandeya, N.; Reddy, Ch. S. *Synlett* **2008**, 1297. (d) Kamal, A.; Devaiah, V.; Reddy, K. L.; Shankaraiah, N. *Adv. Synth. Catal.* **2006**, *348*, 249. (e) Kamal, A.; Shankaraiah, N.; Reddy, K. L.; Devaiah, V. *Tetrahedron Lett.* **2006**, *47*, 4253. (f) Kamal, A.; Devaiah, V.; Shankaraiah, N.; Reddy, K. L. *Synlett* **2006**, 2609. (g) Kamal, A.; Shankaraiah, N.; Devaiah, V.; Reddy, K. L. *Tetrahedron Lett.* **2006**, *47*, 9025. (h) Kamal, A.; Ramana, K. V.; Rao, M. V. *J. Org. Chem.* **2001**, *66*, 997. (i) Kamal, A.; Damayanthi, Y.; Reddy, B. S. N.; Lakshminarayana, B.; Reddy, B. S. P. *Chem. Commun.* **1997**, 1015.

(27) (a) Kappe, C. O. *Angew. Chem. Int. Ed.* **2004**, *43*, 6250. (b) Lew, A.; Krutzik, P. O.; Hart, M. E.; Chamberlin, A. R. *J. Comb. Chem.* **2002**, *4*, 95. (c) Kaddar, H.; Hamelin, J.; Benhaoua, H. *J. Chem. Res.* **1999**, 718.

(28) (a) Silva, W. A.; Rodrigues, M. T.; Shankaraiah, N.; Ferreira, R. B.; Andrade, C. K. Z.; Pilli, R. A.; Santos, L. S. *Org. Lett.* **2009**, *11*, 3238. (b) Shankaraiah, N.; Santos, L. S. *Tetrahedron Lett.* **2009**, *50*, 520. (c) Shankaraiah, N.; Silva, W. A.; Andrade, C. K. Z.; Santos, L. S. *Tetrahedron Lett.* **2008**, *49*, 4289.

(29) Coupling reaction procedure for {2-azidophenyl)-(1-methylene-3,4-dihydro-1*H*-pyrido[3,4-*b*]indol-2 (9*H*)-yl}methanone (**5a**): To a stirred solution of **3** (0.250 g, 1.53 mmol) in $CH_2Cl_2$ (10 mL) was added $Et_3N$ (0.22 mL, 1.63 mmol) dropwise at 0 °C over 10 min, then 2-azidobenzoyl chloride (0.295 g, 1.62 mmol) dissolved in $CH_2Cl_2$ (5 mL) was added at the same temperature. The reaction was brought to r.t. and stirred for another 2 h. After completion of the reaction, the solvent was evaporated and extracted with $CH_2Cl_2$ (3 × 20 mL), washed with aqueous $NaHCO_3$ followed by brine, separated, and dried over anhydrous $Na_2SO_4$. The combined organic extracts were evaporated under reduced pressure and further purified by column chromatography with EtOAc–hexane (1:1) as eluent to afford **5a** in 84% yield as a white solid; mp 86–88 °C. IR (KBr): 3381, 2105, 1638, 1415 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 8.12 (br s, 1 H), 7.53 (d, *J* = 7.55 Hz, 1 H), 7.36–7.43 (m, 2 H), 7.32 (d, *J* = 7.55 Hz, 1 H), 7.20–7.25 (m, 1 H), 7.11–7.16 (m, 3 H), 4.93 (s, 1 H), 4.07 (s, 1 H), 4.00 (t, *J* = 8.58, 9.09 Hz, 2 H), 3.24 (t, *J* = 8.08 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 167.6, 136.9, 132.3, 132.1, 130.3, 129.1, 128.2, 126.7, 125.1, 124.7, 123.5, 119.9, 119.0, 118.4, 112.0, 111.1, 101.8, 41.1, 29.6; HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{19}H_{15}N_5O$: 352.1174; found: 352.1182.

(30) Oxidation reaction procedure for 2-(2-azidobenzoyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (**6a**): To a stirred solution of **5a** (0.400 g, 1.13 mmol) in anhydrous acetone (20 mL) was added $KMnO_4$ (0.264 g, 1. 70 mmol) at r.t. and the mixture was stirred for 12 h. The solvent was evaporated under reduced pressure and the reaction mixture was diluted with EtOAc (40 mL) and filtered through Celite. The organic layer was washed with aqueous $NaHCO_3$ followed by brine and dried over anhydrous $Na_2SO_4$. After filtration and evaporation, the crude product was purified by column chromatography, eluting with EtOAc–hexane (7:3) to afford **6a** in 67% yield as a white solid; mp 87–90 °C. IR (KBr): 3421, 2111, 1697, 1634 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.18 (br s, 1 H), 7.84 (d, *J* = 7.84 Hz, 1 H), 7.63–7.59 (m, 2 H), 7.38–7.32 (m, 1 H), 7.23–7.20 (m, 2 H), 7.18 (d, *J* = 7.55 Hz, 1 H), 7.16–7.19 (m, 1 H), 4.43 (br, 2 H), 3.24 (t, *J* = 8.10 Hz, 2 H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 167.9, 161.2, 142.6, 137.8, 132.6, 130.1, 129.5, 128.1, 126.5, 124.8, 124.6, 123.4, 119.8, 118.9, 118.0, 101.9, 41.9, 21.7; HRMS (ESI): *m/z* $[M]^+$ calcd for $C_{18}H_{13}N_5O_2Na$: 354.3186; found: 354.3207.

(31) Typical procedure for preparation of rutaecarpine (**1a**): A mixture of **6a** (0.100 g, 0.302 mmol) in MeOH (2.0 mL) and $Ni_2B$ (0.114 g, 0.906 mmol) and 1.0 M HCl (1.0 mL) in a glass tube was placed in a microwave reactor (CEM Discovery LabMate) and irradiated at 70 W for 2 min, during which time the temperature was kept at 52 °C with cooling. The reaction mixture was brought to ambient temperature and the solvent was evaporated, the residue was neutralized with saturated aqueous 5% $NaHCO_3$ solution, and then extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with brine, dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The crude product thus obtained was purified by column chromatography on silica (60–120 mesh) to afford the final compound **1a** (0.072 g, 90%); mp 254–255 °C. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.25 (br s, 1 H), 8.33 (dd, *J* = 1.23, 7.85 Hz, 1 H), 7.62–7.74 (m, 3 H), 7.43–7.69 (m, 2 H), 7.35 (dt, *J* = 1.22, 6.85 Hz, 1 H), 7.20 (t, *J* = 8.44 Hz, 1 H), 4.57 (t, *J* = 6.96 Hz, 2 H), 3.25 (t, *J* = 6.95 Hz, 2 H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 161.6, 147.5, 144.9, 138.2, 134.3, 127.2, 126.6, 126.1, 125.6, 125.5, 121.3, 120.6, 120.1, 118.3, 112.1, 19.6, 41.1, 20.2; HRMS (ESI): *m/z* $[M + H]^{+\cdot}$ calcd for $C_{18}H_{13}N_3O$: 287.1054; found: 287.1057.

Euxylophoricine A (**1b**): Yield: 0.043 g (82%); mp 293–295 °C; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 9.25 (br s, 1 H), 7.65 (s, 1 H), 7.63 (d, *J* = 8.1 Hz, 1 H), 7.44 (d, *J* = 8.1 Hz, 1 H), 7.35 (dd, *J* = 7.8, 8.1 Hz, 1 H), 7.20 (t, *J* = 7.8 Hz, 1 H), 7.06 (s, 1 H), 4.60 (t, *J* = 7.0 Hz, 2 H), 4.01 (s, 3 H), 3.99 (s, 3 H), 3.24 (t, *J* = 7.0 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 161.1, 155.1, 148.7, 143.9, 143.6, 138.2, 127.3, 125.7, 125.3, 120.6, 119.9, 117.6, 114.5, 111.9, 107.1, 106.4, 56.3, 56.2, 41.1, 19.6; HRMS: *m/z* $[M + H]^{+\cdot}$ calcd for $C_{20}H_{17}N_3O_3$: 347.1263; found: 347.1266.

Euxylophoricine C (**1c**): Yield: 0.041 g (80%); mp 307–309 °C; $^1H$ NMR (300 MHz, $CDCl_3$): δ = 9.10 (br s, 1 H), 7.65 (s, 1 H), 7.64 (d, *J* = 6.95 Hz, 1 H), 7.44 (d, *J* = 6.92 Hz, 1 H), 7.36 (t, *J* = 6.95 Hz, 1 H), 7.20 (t, *J* = 6.9 Hz, 1 H), 7.06 (s, 1 H), 6.10 (s, 2 H), 4.57 (t, *J* = 6.9 Hz, 2 H), 3.27 (t, *J* = 6.9 Hz, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 160.9, 153.5, 147.1, 143.9, 143.8, 138.1, 127.2, 125.7, 125.4, 120.6, 120.0, 117.6, 116.1, 111.9, 105.9, 104.2, 102.5, 41.8, 19.8; HRMS: *m/z* $[M + H]^{+\cdot}$ calcd for $C_{19}H_{13}N_3O_3$: 331.0955; found: 331.0961.