Novel, One-Pot, Three-Component Route to Indol-3-yl Substituted Spirooxindole Derivatives

Tao Chen, Xiao-Ping Xu, and Shun-Jun Ji*

Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, China

Received April 15, 2010

A simple and efficient approach to the synthesis of a novel series of polysubstituted 6′-(1*H*-indol-3-yl)-1′,7′-dihydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-2-one derivatives in high yields was developed from a one-pot, three-component reaction of 3-cyanoacetyl indoles, isatins, and 1*H*-pyrazol-5-amines in H_2O/HOAc.

Introduction

A wide range of advantages offered by multicomponent reactions (MCRs), such as high degree of atom economy, convergence, ease of execution, and access to complex molecules has been recognized in the past decade. The utility of MCRs in preparing libraries to screen for biologically active compounds and potent drug candidates is well-appreciated.[1] Thus, the search and discovery of new MCRs is still of considerable current interest.

The indole ring system is probably the most ubiquitous heterocycle in nature. Because of the great structural diversity of biologically active indoles, it is not surprising that the indole ring system has become an important structural component in many pharmaceutical agents.[2] Furthermore, indoles substituted with heterocyclic rings at the 3-position have been found in a fascinating array of bioactive natural products and pharmaceutical compounds (Figure 1). New indole alkaloids with a broad spectrum of biological properties are being discovered rapidly as marine invertebrate metabolites.[3−6] For example, nortopsentins A−C exhibit in vitro cytotoxicity against P388 cells;[7] hamacanthin B reveals cytotoxic activities against a wide range of human tumor cell lines with GI50 values at micromolar concentration;[8] meridianins A−E show cytotoxicity toward murine tumor cell lines and have potent inhibition against several protein kinases.[9] Moreover, many other analogous indole derivatives[10−13] demonstrate strong inhibitory effects against a variety of tumor cell lines, including leukemia, non-small-cell lung cancer, ovarian cancer, colon cancer, renal cancer, and breast cancer.

On the other hand, spirooxindole derivatives occupy a special place in organic and medicinal chemistry because these compounds are well-known as microtubule assembly inhibitors (spirotryprostatin A and B),[14] muscarinic M1, and serotonin receptor modulators (pteropodine and isopteropodine)[15] and nonpeptidyl growth-hormone secretagogues (MK-0677).[16] Similarly, considerable attention has been focused on the development of new methodologies to synthesize many kinds of pyrazolopyridine ring systems because of their interesting biological and pharmacological properties, such as vasodilatory, hypoglycemic, anti-inflammatory, analgesic, and antipyretic activities.[17,18] Furthermore, spiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridines] seem to be promising candidates for biological responses because it has been reported that sharing of the indole 3-carbon atom in the formation of spirooxindole derivatives highly enhances biological activity.[19−21]

Despite the potent and diverse biological activities of indoles and spiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridines], no report is yet available on the synthesis of substituted indoles containing spiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine] structures at the 3-position. Out of our interest in the multicomponent synthesis and in continuation of our work on the synthesis of indole and spirooxindole derivatives,[22] guided by the observation that the presence of two or more different heterocyclic moieties in a single molecule often enhances the biocidal profile remarkably and that water is a nontoxic, cheap, abundantly available and environmentally benign solvent,[23] herein, we report the synthesis of various polysubstituted 6′-(1*H*-indol-3-yl)-1′,7′-dihydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-2-one derivatives via a facile, atom-economical, one-pot, three-component condensation reaction in H_2O/HOAc.

Results and Discussion

The reaction of 3-(1*H*-indol-3-yl)-3-oxopropanenitrile **1a** (0.5 mmol) with an equimolar amount of 5-bromoindoline-2,3-dione **2a** and 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **3a** as a simple model system was examined to establish the feasibility of the strategy and optimize the reaction conditions. It is well-known that the choice of an appropriate reaction medium is of crucial importance for successful synthesis. The growing demand for clean and efficient eco-friendly chemical synthesis has been increasing our interest in synthesizing indole derivatives. So, to begin with, the model reaction was employed in water without any catalyst at 100 °C (Table 1, entry 1). To our delight, the saffron

* To whom correspondence should be addressed. E-mail: chemjsj@suda.edu.cn.

10.1021/cc100064c
Published on Web 07/01/2010

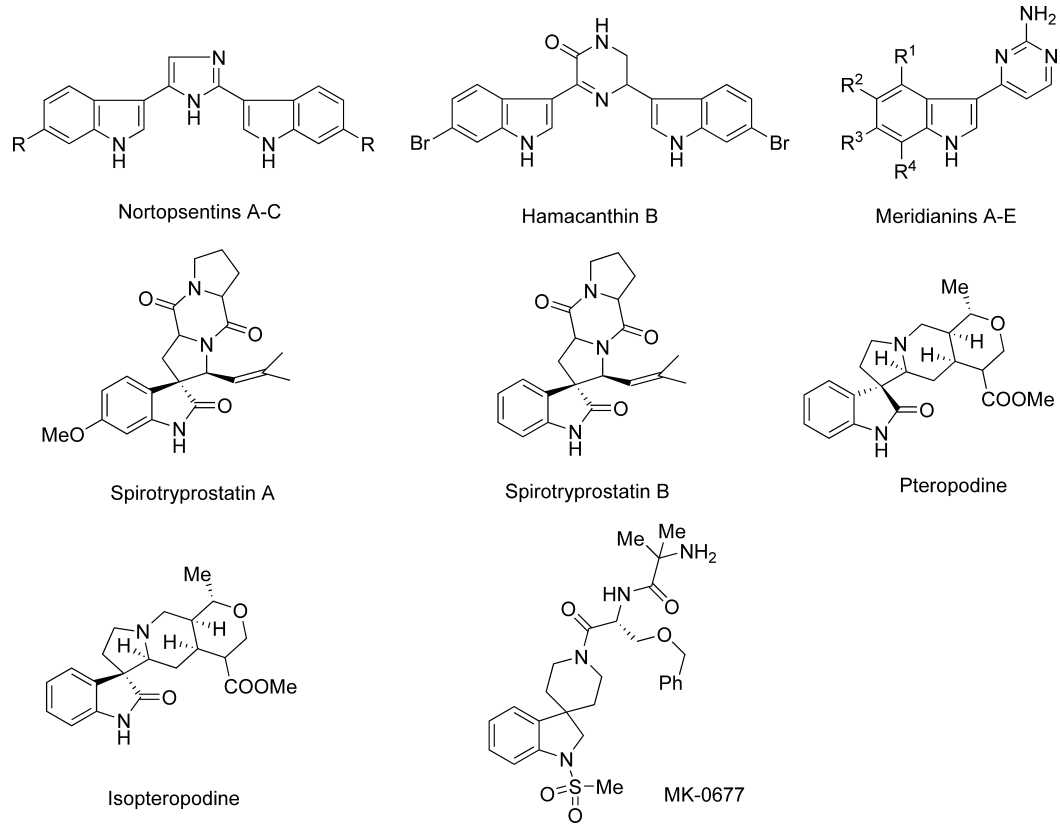
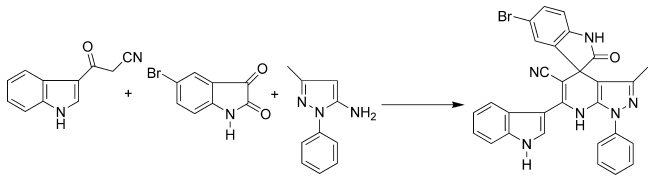


Figure 1. Representatives of important indol-3-yl substituted heterocycles and spirooxindoles.

Table 1. Model Reaction, Conditions, and Yields[a]

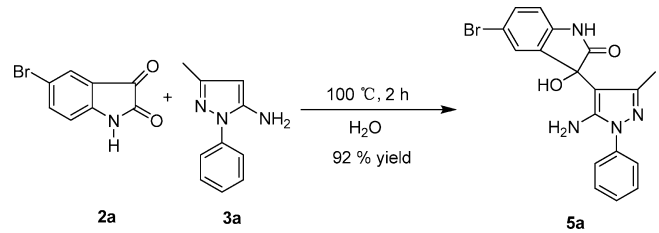


entry	solvent (H_2O/HOAc) (v/v)	temperature (°C)	time (h)	yield (%)
1	1:0	100	24	0
2[b]	1:0	100	12	trace
3[b]	1:0	100	12	trace
4[b]	1:0	100	12	trace
5[b]	1:0	100	12	trace
6[b]	1:0	100	12	trace
7[b]	1:0	100	12	trace
8	2:1	100	12	38
9	1:1	100	12	48
10	1:2	100	12	50
11	1:1	120	12	66
12	**1:1**	**140**	**12**	**80**
13	1:1	140	6	52
14	0:1	120	12	61
15[c]		140	12	30
16[d]		140	12	37

[a] Isolated yield. [b] The reaction was catalyzed by 10 mol % $CeCl_3 \cdot 7H_2O$, $Yb(OTf)_3$, $InCl_3$, HOAc, *p*-toluenesulfonic acid or HCl respectively. [c] The reaction was carried out in $H_2O/(CH_2OH)_2$ (1:1 v/v). [d] The reaction was catalyzed by 10 mol % HOAc in $H_2O/(CH_2OH)_2$ (1:1 v/v).

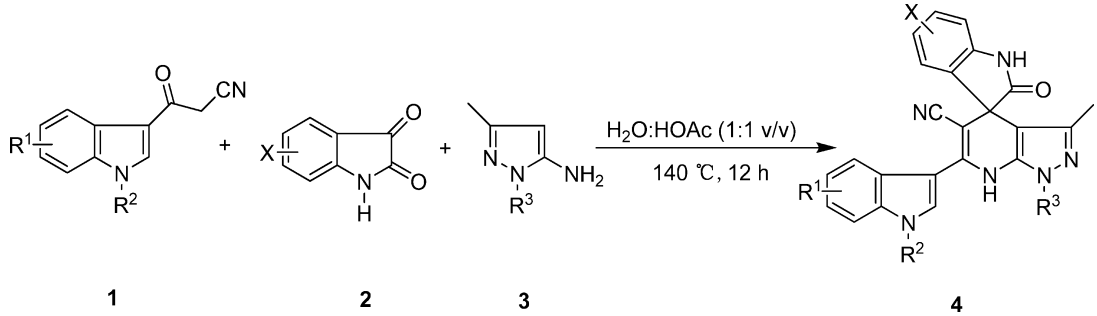
yellow color of **2a** faded out during the reaction. After heating for 2 h, **2a** and **3a** almost disappeared according to thin layer chromatography analysis. Unfortunately, product

Scheme 1. Synthesis of the Intermediate **5a**



4a was not obtained. Instead, compound **5a**, which is a Baylis−Hillman type adduct of **2a** and **3a** was isolated even when the reaction time was prolonged to 24 h (Scheme 1).[24] The intermediate **5a** was characterized by spectroscopic methods. Considering the above observation, a variety of Lewis and Brønsted acid catalysts, such as $CeCl_3 \cdot 7H_2O$, $Yb(OTf)_3$, $InCl_3$, HOAc, *p*-toluenesulfonic acid, and HCl were tested (Table 1, entries 2−7), but the results was also disappointing because the desired product **4a** was only obtained in trace amount. Although the yield was very low, we were encouraged to examine other reaction conditions to increase the yield. Thus, H_2O/HOAc was employed as solvent in this reaction considering that intermediate **5a** was obtained in excellent yield when the solvent was water and that HOAc can be used as both catalyst and solvent because of the very low solubility of **1a** and **5a**. The volume ratio 1:1 (H_2O/HOAc) gave the better result at 100 °C, as shown in Table 1, entry 9. Then, the synthesis of **4a** was performed at temperatures ranging from 120 to 140 °C and reaction times ranging from 6 to 12 h in H_2O/HOAc (1:1 v/v) (Table 1, entries 11−13). The yield of **4a** was highest (80%) when the reaction was carried out at 140 °C for 12 h in the mixed

Scheme 2. Synthesis of 6′-(1*H*-Indol-3-yl)-1′,7′-dihydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-2-one Derivatives **4**



1 **2** **3** **4**

Table 2. 6′-(1*H*-Indol-3-yl)-1′,7′-dihydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-2-one Derivatives **4**

entry	R^1	R^2	R^3	X	product	yield[a] (%)
1	H	H	Ph	5-Br	**4a**	80
2	H	H	Ph	5-Cl	**4b**	82
3	H	H	Ph	6-Br	**4c**	81
4	H	H	Ph	H	**4d**	87
5	6-CH_3	H	Ph	5-Br	**4e**	83
6	6-CH_3	H	Ph	5-Cl	**4f**	86
7	6-CH_3	H	Ph	6-Br	**4g**	81
8	H	CH_3	Ph	5-Br	**4h**	78
9	H	CH_3	Ph	5-Cl	**4i**	80
10	H	CH_3	Ph	6-Br	**4j**	81
11	H	CH_3	Ph	H	**4k**	86
12	7-CH_3	H	Ph	5-Br	**4l**	88
13	7-CH_3	H	Ph	6-Br	**4m**	85
14	7-CH_3	H	Ph	H	**4n**	82
15	5-Br	H	Ph	5-Br	**4o**	90
16	5-Br	H	Ph	5-Cl	**4p**	86
17	5-Br	H	Ph	6-Br	**4q**	81
18	5-Br	H	Ph	H	**4r**	92
19	H	H	CH_3	5-Br	**4s**	80
20	H	H	CH_3	6-Br	**4t**	88
21	H	H	CH_3	H	**4u**	87
22	6-CH_3	H	CH_3	5-Br	**4v**	84
23	6-CH_3	H	CH_3	6-Br	**4w**	82
24	6-CH_3	H	CH_3	H	**4x**	88
25	5-Br	H	CH_3	5-Br	**4y**	90
26	5-Br	H	CH_3	6-Br	**4z**	83

[a] Isolated yield.

solvent (Table 1, entry 12), in contrast with HOAc as sole solvent (Table 1, entry 14) or $H_2O/(CH_2OH)_2$ as mixed solvent (Table 1, entries 15 and 16).

Encouraged by this success, we extended this reaction to commercially available isatins, 1*H*-pyrazol-5-amines and a range of 3-(1*H*-indol-3-yl)-3-oxopropanenitriles with both electron withdrawing and electron releasing substituents in indole heterocycles under the same conditions, resulting in high yields of the corresponding 6′-(1*H*-indol-3-yl)-1′,7′-dihydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-2-one derivatives (Scheme 2). We have shown that the use of a range of substituents in 3-(1*H*-indol-3-yl)-3-oxopropanenitriles **1**, isatins **2** and 1*H*-pyrazol-5-amines **3** in this three-component reaction makes possible the synthesis of libraries under the same circumstances. The results are summarized in Table 2. In this work, the products were characterized by melting point, IR, NMR, HRMS (or LC-MS) and combustion analysis. Furthermore, the structure of **4d** was established by X-ray crystallographic analysis (see Supporting Information).

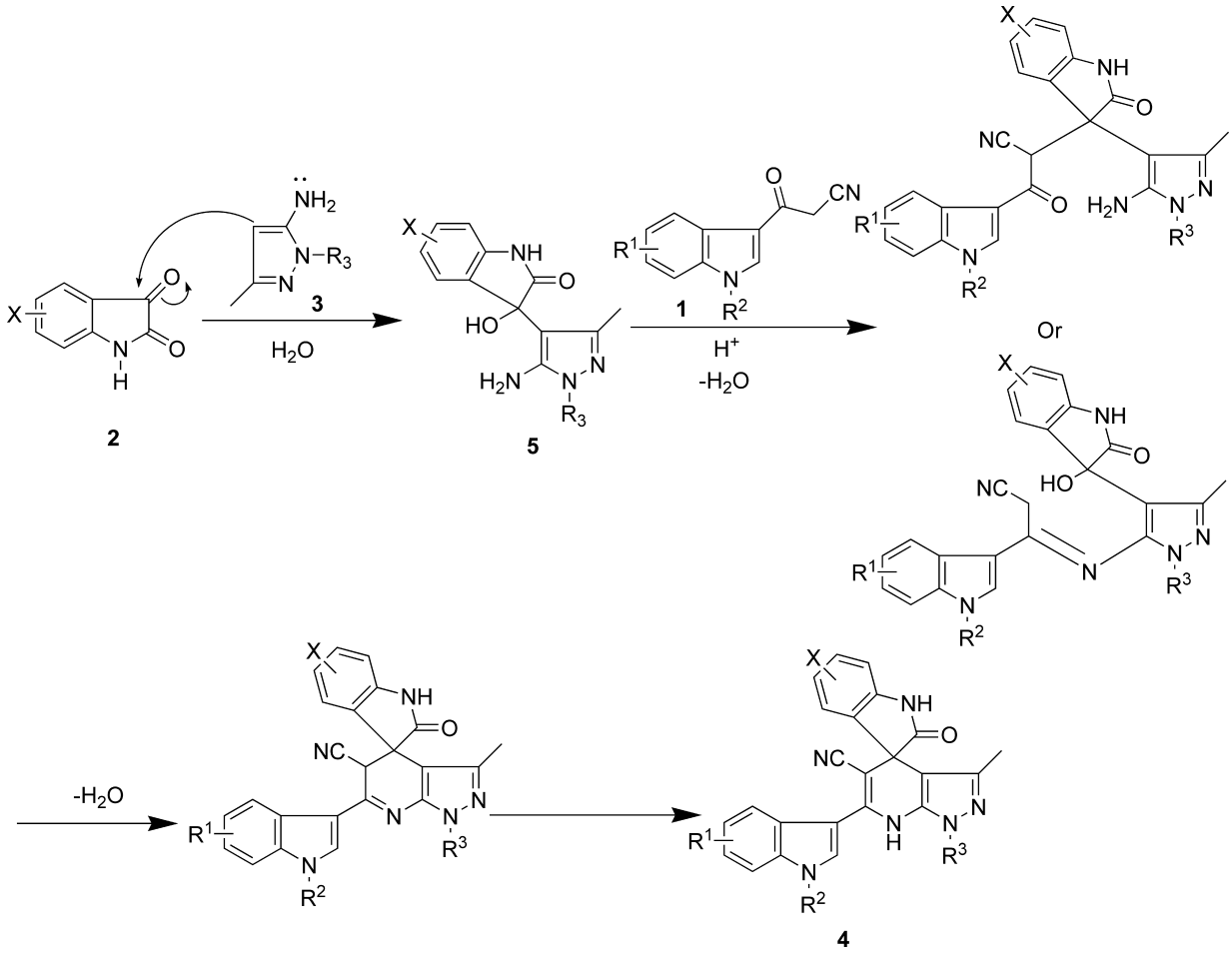
Although the detailed mechanism of the above reaction remains to be fully clarified, according to the experimental observation, compound **4** could be formed from the intermediate **5** via nucleophilic substitution and condensation with 3-cyanoacetyl indole **1,** followed by tautomerization (Scheme 3). Evidence supporting this proposed mechanism came from the observation that when the intermediate **5a** was prepared as a separate exercise and subsequently reacted with **1a** under the same conditions, the expected product **4a** was obtained in a yield similar to that obtained in the one-pot reaction (Scheme 4).

In summary, we have demonstrated a simple, atom-economical, and efficient approach for synthesis of highly functionalized indole-containing spirooxindole derivatives via one-pot, three-component reactions using readily available starting materials. This method incorporates both indole and spiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine] moieties into a single molecule. In view of those molecules having either functionality, these novel compounds may potentially have enhanced biological activities. Prominent among the advantages of this new method are novelty, operational simplicity, high yields, and easy workup procedures employed. Further reactivity studies and synthetic applications of this methodology are in progress in our laboratory.

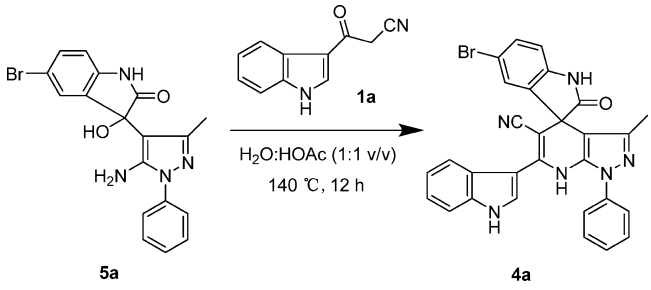
Experimental Section

Typical Procedure for the Synthesis of 5-Bromo-6′-(1*H*-indol-3-yl)-3′-methyl-2-oxo-1′-phenyl-1′,7′-dihydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-5′-carbonitrile 4a. A mixture of 3-(1*H*-indol-3-yl)-3-oxopropanenitrile **1a** (0.5 mmol) with an equimolar amount of 5-bromoindoline-2,3-dione **2a** and 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **3a** in 4 mL of H_2O/HOAc (1:1 v/v) at 140 °C was stirred for 12 h (the progress was monitored by TLC). After completion, the reaction mixture was neutralized by the freshly prepared saturated solution of $NaHCO_3$; then, it was filtered. The precipitate was washed with water (10 mL) and ethanol (5 mL) to afford the pure **4a** as a white solid (yield 80%). mp: 243−245 °C. IR (KBr): ν 3425, 3356, 3090, 2195, 1730, 1629, 1529, 1472, 1394, 1217, 752 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 11.70 (s, 1H, NH), 10.81 (s, 1H, NH), 10.06 (s, 1H, NH), 7.86 (d, J = 1.6 Hz, 1H, ArH), 7.71 (d, 1H, J = 7.2 Hz, ArH), 7.65 (d, J = 8.0 Hz, 2H, ArH), 7.47−7.55 (m, 4H, ArH), 7.36−7.41 (m, 2H, ArH), 7.16−7.22 (m, 2H, ArH), 6.94 (d, J = 8.4 Hz, 1H, ArH), 1.61 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 177.8, 147.2, 144.3, 140.4, 138.3, 138.2, 136.9, 136.0, 132.0, 129.2, 128.4, 127.9, 127.1, 125.4, 123.4, 122.0, 120.1, 120.0,

Scheme 3. Possible Mechanism for the Synthesis of Product **4**



Scheme 4. Synthesis of **4a** According to the Reaction of **1a** and **5a**



119.6, 114.4, 112.2, 111.8, 107.9, 98.5, 78.8, 51.3, 11.4. HRMS: calculated for $C_{29}H_{19}BrN_6O$ [MH^+]: 547.0876; found 547.0867.

Acknowledgment. The work was partially supported by the National Natural Science Foundation of China (No. 20672079, 20910102041), Natural Science Foundation of Jiangsu Province (No. BK 2006048), Nature Science Key Basic Research of Jiangsu Province for Higher Education (No. 06KJ A15007), the Specialized Research Fund for the Doctoral Program of Higher Education (No. 20060285001), and Key Project in Science and Technology Innovation Cultivation Program of Soochow University.

Supporting Information Available. Experimental details and characterization data including IR, MS, ^{1}H, and ^{13}C NMR spectra for compounds **4a**−**z** and **5a**, as well as X-ray crystallography for compounds **4d**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Wender, P. A.; Handy, S. T.; Wright, D. L. *Chem. Ind.* **1997**, 765. (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259. (c) Weber, L.; Illgen, K.; Almstetter, M. *Synlett* **1999**, 366. (d) Bienaymé, H.; Hulme, C.; Oddon, G.; Schmitt, P. *Chem.—Eur. J.* **2000**, *6*, 3321. (e) Terrett, N. K. *Combinatorial Chemistry*; Oxford University Press: New York, 1998.

(2) (a) Sundberg, R. J. *The Chemistry of Indoles*; Academic Press: New York, 1970. (b) Sundberg, R. J. Pyrroles and Their Benzoderivatives: Synthesis and Applications. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, U.K., 1984; Vol. 4, pp 313−376. (c) Sundberg, R. J. In *Best Synthetic Methods, Indoles*; Academic Press: New York, 1996; pp 7−11. (d) Joule, J. A. Indole and its Derivatives. In *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*; Thomas, E. J., Ed.; George Thieme Verlag: Stuttgart, Germany, 2000; Category 2, Vol. 10, Chapter 10.13. (e) Brown, R. K. In *Indoles*; Houlihan, W. J., Ed.; Wiley-Interscience: New York, 1972. (f) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Ress, C. W., Scriven, E. F. V., Bird, C. W., Eds.; Pergamon Press: Oxford, 1996; Vol. 2, p 119. (g) Gribble, G. W. *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Ress, C. W., Scriven, E. F. V., Bird, C. W., Eds.; Pergamon Press: Oxford, 1996; Vol. 2, p 207. (h) *Indoles*; Sundberg, R. J., Ed.; Academic Press: London, 1996.

(3) Sundberg, R. J. *The Chemistry of Indoles*; Academic Press: New York, 1996.

(4) (a) Casapullo, A.; Bifulco, G.; Bruno, I.; Riccio, R. *J. Nat. Prod.* **2000**, *63*, 447. (b) Bao, B.; Sun, Q.; Yao, X.; Hong, J.; Lee, C. O.; Sim, C. J.; Im, K. S.; Jung, J. H. *J. Nat. Prod.* **2005**, *68*, 711.

(5) Skibo, E. B.; Xing, C.; Dorr, R. T. *J. Med. Chem.* **2001**, *44*, 3545.

(6) (a) Gupta, L.; Talwar, A.; Palne, N. S.; Gupta, S.; Chauhan, P. M. S. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4075. (b) Kaniwa, K.; Arai, M. A.; Li, X.; Ishibashi, M. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4254.

(7) (a) Sakemi, S.; Sun, H. H. *J. Org. Chem.* **1991**, *56*, 4304. (b) Kawasaki, I.; Yamashita, M.; Ohta, S. *Chem. Pharm. Bull.* **1996**, *44*, 1831.

(8) (a) Kouko, T.; Matsumura, K.; Kawasaki, T. *Tetrahedron* **2005**, *61*, 2309. (b) Higuchi, K.; Takei, R.; Kouko, T.; Kawasaki, T. *Synthesis* **2007**, 669.

(9) (a) Jiang, B.; Yang, C.-G.; Xiong, W.-N.; Wang, J. *Bioorg. Med. Chem.* **2001**, *9*, 1149. (b) Gompel, M.; Leost, M.; Joffé, E. B. K.; Puricelli, L.; Franco, L. H.; Palermo, J.; Meijer, L. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1703.

(10) (a) Jiang, B.; Xiong, X.; Yang, C. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 475. (b) Jiang, B.; Gu, X. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 363. (c) Gu, X.; Wan, X.; Jiang, B. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 569. (d) Jiang, B.; Xiong, X.; Yang, C. *Bioorg. Med. Chem.* **2001**, *9*, 1149. (e) Xiong, W.; Yang, C.; Jiang, B. *Bioorg. Med. Chem.* **2001**, *9*, 1773. (f) Diana, P.; Carbone, A.; Barraja, P.; Montalbano, L.; Martorana, A.; Dattolo, G.; Gia, O.; Via, D. L.; Cirrincione, G. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2342. (g) Kawasaki, Y.; Yamashita, M.; Otha, S. *J. Chem. Soc., Chem. Commun.* **1994**, 2085. (h) Kawasaki, Y.; Yamashita, M.; Otha, S. *Chem. Pharm. Bull.* **1996**, *44*, 1831. (i) Kawasaki, Y.; Katsuma, H.; Nakayama, Y.; Yamashita, M.; Otha, S. *Heterocycles* **1998**, *48*, 1887.

(11) (a) Sun, H. H.; Sakemi, J. *J. Org. Chem.* **1991**, *56*, 4307. (b) Vervoort, H. C.; Richards-Gross, S. E.; Fenical, W.; Lee, A. Y.; Clardy, J. *J. Org. Chem.* **1997**, *62*, 1486. (c) Takahashi, S.; Matsunaga, T.; Hasegawa, C.; Saito, H.; Fujita, D.; Kiuchi, F.; Tsuda, Y. *Chem. Pharm. Bull.* **1998**, *46*, 1527.

(12) (a) N'Diaye, Y.; Guella, G.; Chiasera, G.; Mancini, Y.; Pietra, F. *Tetrahedron Lett.* **1994**, *50*, 4147. (b) Guella, G.; Mancini, Y.; N'Diaye, Y.; Pietra, F. *Helv. Chim. Acta* **1999**, *77*, 1994.

(13) (a) Bergmann, T.; Schories, D.; Steffan, B. *Tetrahedron* **1997**, *53*, 2055. (b) Kohmoto, S.; Kashman, Y.; McConnell, O. J.; Rinehart, K. L.; Wright, A., Jr.; Koehn, F. *J. Org. Chem.* **1988**, *53*, 3116.

(14) (a) Khafagy, M. M.; El-Wahas, A. H. F. A.; Eid, F. A.; El-Agrody, A. M. *Farmaco* **2002**, *57*, 715. (b) Sebahar, P. R.; Williams, R. M. *J. Am. Chem. Soc.* **2000**, *122*, 5666.

(15) Kang, T. H.; Matsumoto, K.; Murakami, Y.; Takayama, H.; Kitajima, M.; Aimi, N.; Watanabe, H. *Eur. J. Pharmacol.* **2002**, *444*, 39.

(16) (a) Maligres, P. E.; Houpis, I.; Rossen, K.; Molina, A.; Sager, J.; Upadhyay, V.; Wells, K. M.; Reamer, R. A.; Lynch, J. E.; Askin, D.; Volante, R. P.; Reider, P. J. *Tetrahedron* **1997**, *53*, 10983. (b) Palucki, B. L.; Feighner, S. D.; Pong, S. S.; McKee, K. K.; Hrenuik, D. L.; Tan, C.; Howard, A. D.; Van der Ploeg, L. H. Y.; Patchett, A. A.; Nargund, R. P. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1955.

(17) (a) Gein Stein, R.; Biel, J. H.; Singh, T. *J. Med. Chem.* **1979**, *13*, 153. (b) Farghaly, A. M.; Habib, N. S.; Khalil, M. A.; El-Sayed, O. A. *Alexandria J. Pharm. Sci.* **1989**, *3*, 90. (c) Gatta, F.; Pomponi, M.; Marta, M. *J. Heterocycl. Chem.* **1991**, *28*, 1301. (d) Kohara, T.; Fukunaga, K.; Fujimura, M.; Hanano, T.; Okabe, H. U. S. Patent 0052822, 2004.

(18) (a) Elnagdi, M. H.; Al-awadi, N.; Erian, A. N.; In *Compensative Heterocyclic Chemistry II*, 1st ed.; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press, Oxford, U.K., 1996; Vol. 7, p 431. (b) Ghahremanzadeh, R.; Sayyafi, M.; Ahadi, S.; Bazgir, A. *J. Comb. Chem.* **2009**, *11*, 393. (c) Ahadi, S.; Ghahremanzadeh, R.; Mirzaei, P.; Bazgir, A. *Tetrahedron* **2009**, *65*, 9316.

(19) Da-Silva, J. F. M.; Garden, S. J.; Pinto, A. C. *J. Braz. Chem. Soc.* **2001**, *12*, 273.

(20) (a) Joshi, K. C.; Chand, P. *Pharmazie* **1982**, *37*, 1. (b) Joshi, K. C.; Jain, R.; Sharma, K. *J. Indian Chem. Soc.* **1988**, *115*, 202.

(21) Abdel-Rahman, A. H.; Keshk, E. M.; Hanna, M. A.; El-Bady, Sh. M. *Bioorg. Med. Chem.* **2004**, *12*, 2483.

(22) (a) Ji, S.-J.; Wang, S.-Y. *Synlett* **2003**, 2074. (b) Ji, S.-J.; Wang, S.-Y.; Zhang, Y.; Loh, T.-P. *Tetrahedron* **2004**, *60*, 2051. (c) Gu, D.-G.; Ji, S.-J.; Jiang, Z.-Q.; Zhou, M.-F.; Loh, T.-P. *Synlett* **2005**, 959. (d) Wang, S.-Y.; Ji, S.-J. *Tetrahedron* **2006**, *62*, 1527. (e) Sun, C.; Ji, S.-J. *Tetrahedron Lett.* **2007**, *48*, 8987. (f) Wang, S.-Y.; Ji, S.-J. *Synlett* **2007**, 2222. (g) Zhu, S.-L.; Ji, S.-J.; Zhang, Y. *Tetrahedron* **2007**, *63*, 9365. (h) Zhu, S.-L.; Ji, S.-J.; Su, X.-M.; Sun, C.; Liu, Y. *Tetrahedron Lett.* **2008**, *49*, 1777. (i) Zhu, S.-L.; Ji, S.-J.; Zhao, K.; Liu, Y. *Tetrahedron Lett.* **2008**, *49*, 2578. (j) Zhao, K.; Xu, X.-P.; Zhu, S.-L.; Shi, D.-Q.; Zhang, Y.; Ji, S.-J. *Synthesis* **2009**, 2697. (k) Zhao, K.; Zhu, S.-L.; Shi, D.-Q.; Zhang, Y.; Xu, X.-P.; Ji, S.-J. *Synthesis* **2010**, 1793.

(23) (a) LindstrÖm, U. M. *Chem. Rev.* **2002**, *102*, 2751. (b) Kobayashi, S.; Manabe, K. *Acc. Chem. Res.* **2002**, *35*, 209.

(24) Pushechnikov, A; Volochnyuk, D.; Tolmachev, A. *Synlett* **2002**, 1140.

CC100064C