A Flexible Synthesis of Indoles from *ortho*-Substituted Anilines: A Direct Synthesis of Isocryptolepine

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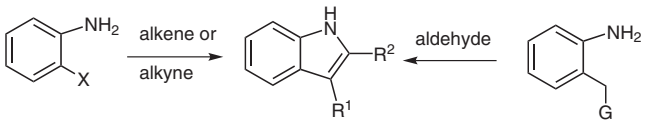
Abstract: The reaction of anilines bearing a benzylic activating group in the ortho position with aromatic aldehydes or α,β-unsaturated aldehydes results in an efficient synthetic route to substituted indoles.

Key words: alkaloids, carbanions, electrocyclic reactions, indoles

Introduction

The indole subunit is found in a wide variety of biologically active natural products.[1] As a consequence, a number of useful synthetic methods for the preparation of indoles have been devised. Sundberg collated these methods.[2] Hydrazones and anilines are among the most common precursors to indoles. Hydrazones are intermediates in both the Fischer indole synthesis[3] and the Japp–Klingemann indole synthesis.[4] *ortho*-Haloanilines react with either alkenes or alkynes and a palladium catalyst to provide substituted indoles[5] (Scheme 1). Several research groups have utilized this strategy for the construction of indole alkaloids.[6]



Scheme 1

ortho-Alkylindoles have been less frequently employed. One example is the Madelung synthesis, in which the dianion of an anilide undergoes cyclization at high temperatures.[7] A second example is the Bischler indole synthesis, involving the coupling of anilines and bromoacetophenones. The reported microwave-assisted synthesis[8] of 2-arylindoles is based on this mode of indole synthesis.

Recently, we communicated a flexible synthesis of indoles by way of an electrocyclic closure of the anion of an imine derived from the reaction of a commercially available phosphonium salt **1** with an aromatic aldehyde (Scheme 2).[9] Our method proceeds under mild conditions in high yields (81–95%) using readily available reagents.

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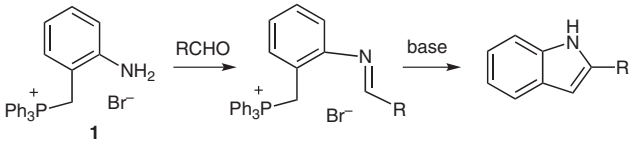
We describe herein not only an expansion of the scope of this practical and convenient synthetic method to include additional activating groups but also the application of this methodology to the efficient synthesis of heterocyclic indole-containing natural products.



Scheme 2

The method outlined in Scheme 2 permits the synthesis of a wide range of substitution patterns. The method is compatible with both electron-withdrawing groups and electron-donating groups. Figure 1 shows the indoles that we have prepared.

Results and Discussion

We prepared a series of anilines shown in Figure 2 to understand the range of activating groups G that would permit cyclization. All five compounds were considerably more soluble than phosphonium salt **1** and therefore could allow a wider range of reaction conditions for both the imine formation step and the base-mediated cyclization step.

The synthesis of imines under microwave conditions involves combining the aniline and the aldehyde with a catalytic amount of acetic acid in methanol and heating in a sealable tube to 80 °C. The formation of the imine required only a few minutes to go to completion. After imine formation was complete, the imine was dissolved in THF and treated with one equivalent of potassium *tert*-butoxide at 0 °C to produce the indole.

Sulfone **2** was generated from the corresponding benzylic alcohol by reaction with benzenesulfinic acid.[10] This appears to be a reasonably general method for aminobenzyl sulfone synthesis. The reaction of sulfone **2** with representative aldehydes is depicted below in Table 1.

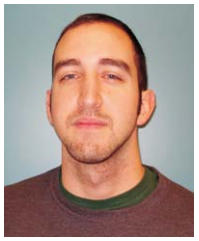
Commercially available 2-cyanomethylaniline was next studied. Surprisingly, this compound reacted with aldehydes under the standard conditions to generate 3-cy-

Biographical Sketches

Dr. George A. Kraus received a B.S. degree in chemistry from the University of Rochester in 1972 and a Ph.D. in chemistry from Columbia University in 1976. He is now a University Professor of Chemistry at Iowa State University. His research interests include the development of new synthetic methods and their application to the synthesis of natural products. Dr. Kraus has over 280 publications in refereed journals.

Dr. Haitao Guo received his B.S. in 1999 and Masters in 2002 in Chemistry from Dalian University of Technology. He obtained his Ph.D. in 2009 from the Iowa State University exploring complex natural products synthesis. He joined the AAT Bioquest Inc. in 2009 and is involved in fluorescent dye chemistry.

Dr. Ganesh Kumar received a B.Sc. from Bharathidasan University in 1996 followed by a B. Tech from the University of Mumbai in 1999. He worked for five years in Hindustan Lever Ltd. before going to Iowa State where he received a Ph.D. in 2009. He is now a postdoctoral fellow in UT Southwestern Medical Center with Dr. John Falck.



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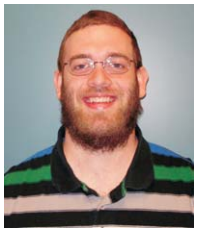
Divya Chaudhary received a B.S. in chemistry (Honors) from Sri Venkateswara College, University of Delhi (New Delhi, India) in 2005 and an M.S. from University of Delhi in 2007. She is currently a second-year graduate student in the laboratory of Dr. George A. Kraus in the Department of Chemistry.



Jonathan Beasley got his B.S. in chemistry from the Southeast Missouri State University. He is currently a graduate student at Iowa State University, studying organic chemistry in Dr. Kraus's research group.

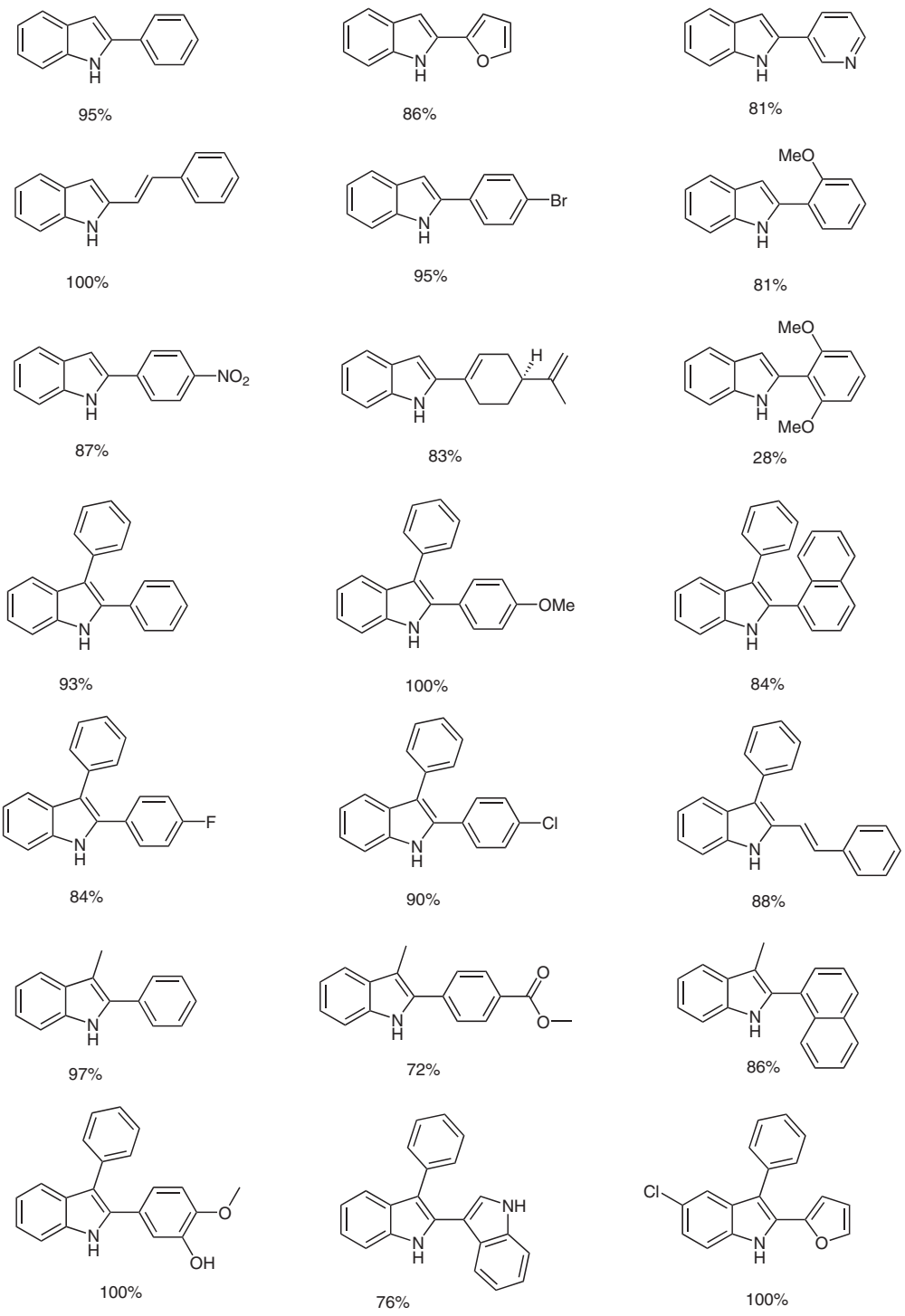
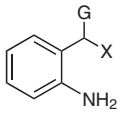


Figure 1 Indoles prepared using aniline **1**



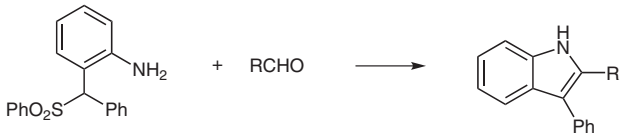
2: G = SO_2Ph, X = Ph
3: G = CN, X = H
4: G = $PO(OEt)_2$, X = H
5: G = SPh, X = H
6: G = SMe, X = SMe

Figure 2 Anilines bearing a benzylic activating group

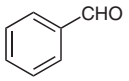
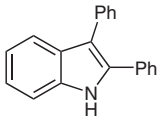
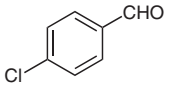
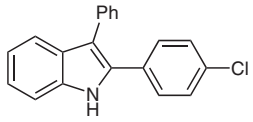
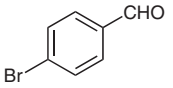
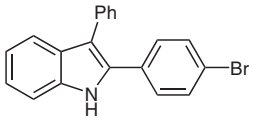
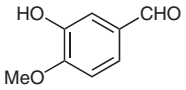
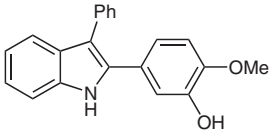
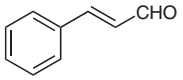
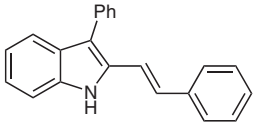
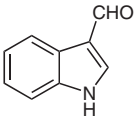
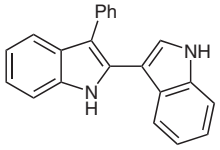
anoindoles in good to excellent yields. Instead of the elimination of cyanide, oxidation to a 3-cyanoindole occurred, presumably via deprotonation of the benzylic hydrogen with base followed by reaction with oxygen. Although this was not the expected product, it represents a convenient route to 3-cyanoindoles. The results with representative aldehydes are illustrated below in Table 2.

Phosphonate **4** was prepared from *o*-nitrobenzyl bromide by reaction with triethyl phosphite followed by reduction of the nitro group.[11] The reaction of **4** with benzaldehyde generated the required imine; however, the imine did not undergo ring closure. We then synthesized the sulfide **5**.[12]

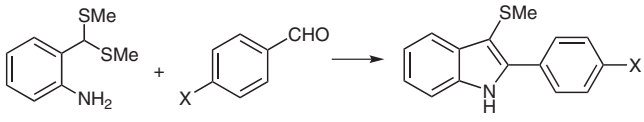
Table 1 Reaction of **2** with Aldehydes to Generate Indoles



2 **7**

Entry	Aldehyde	Product		Isolated yield (%)
1			**7a**	85
2			**7b**	81
3			**7c**	68
4			**7d**	71
5			**7e**	74
6			**7f**	68

Although the required intermediate formed readily, the reaction of the imine with base returned the starting imine. Therefore, lithium diisopropylamide was used in place of potassium *tert*-butoxide, resulting in cyclization and elimination of the phenylthio group. We then prepared the known thioacetal **6** in 68% yield in one step from aniline by the method of Setzer.[13] Imine formation followed by treatment with base afforded 3-methylthio-2-phenylindole (**9**)[14] in 42% yield. Indole **10** was synthesized from **6** in 78% yield (Scheme 3).



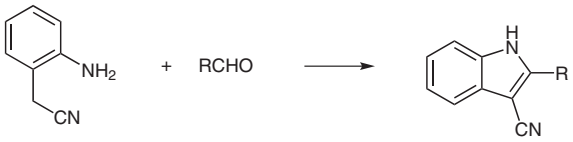
6 **9**: X = H
10: X = Br

Scheme 3

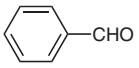
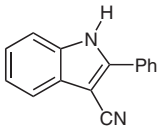
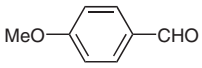
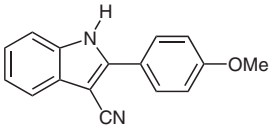
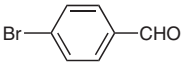
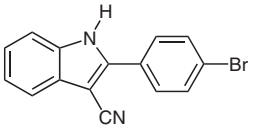
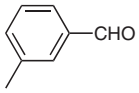
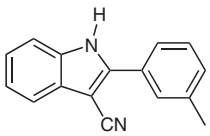
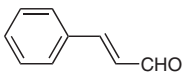
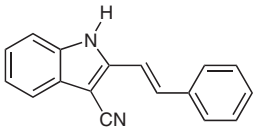
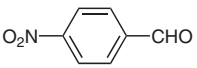
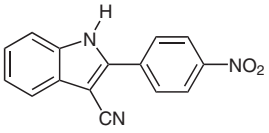
Mechanism

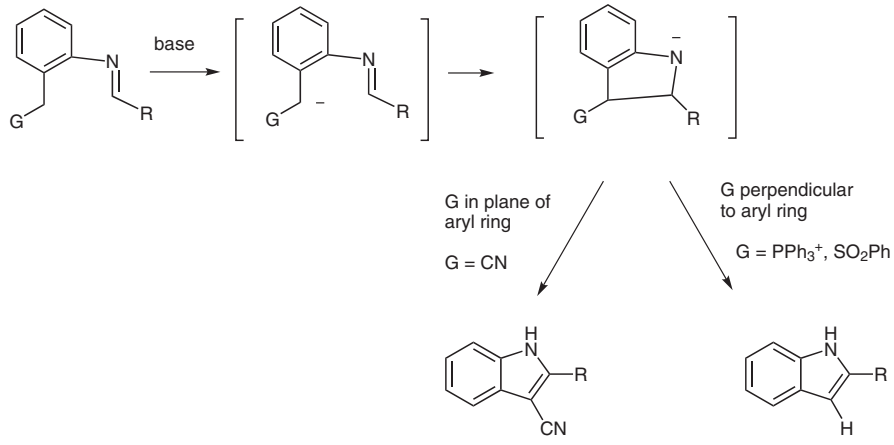
We believe that these cyclizations proceed by imine formation, followed by a base-mediated electrocyclic ring closure and a 1,5-hydrogen atom shift. Our rationale for the generation of two types of products is shown in Scheme 4. If G is bulky, it is likely to adopt an orientation perpendicular to the aromatic ring to minimize nonbonded interactions and therefore would be well aligned to eliminate to form an intermediate that would undergo a rapid 1,5-hydrogen atom shift to provide the indole. If G is a small group such as a nitrile, it is likely to adopt a wider range of conformations. In the conformation with the cyano group in the plane of the ring, the benzylic hydrogen alpha to the nitrile would be very acidic, allowing deprotonation and oxidation to generate the 3-cyanoindole.

Table 2 Reaction of **3** with Aldehydes to Generate Indoles



3 **8**

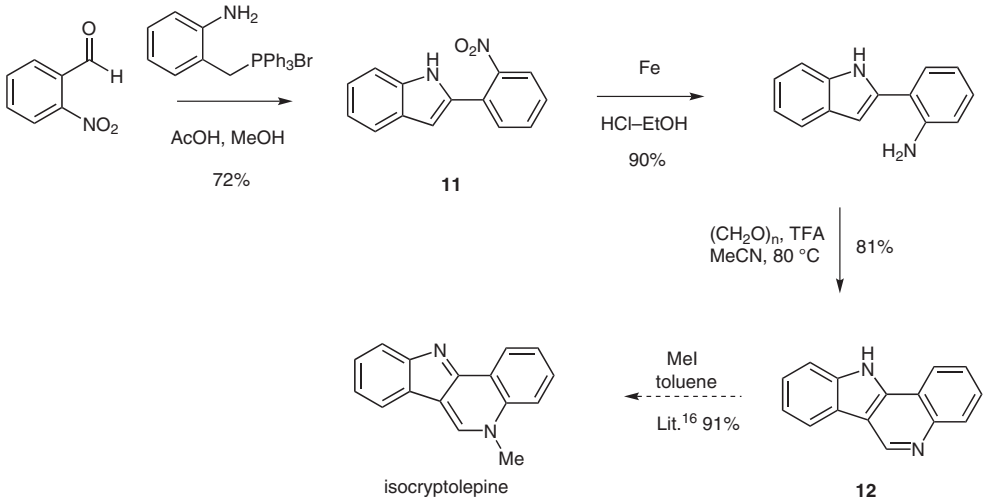
Entry	Aldehydes	Product		Isolated yield (%)
1			**8a**	97
2			**8b**	78
3			**8c**	83
4			**8d**	87
5			**8e**	74
6			**8f**	85



Scheme 4

Extension to Heterocyclic Synthesis

The indolo[2,3-*b*]quinoline alkaloid, isocryptolepine, was isolated from the roots of *Cryptolepis sanguinolenta*. This compound exhibits potent antiplasmodial activity.[15] A number of syntheses of isocryptolepine have been reported.[16] The most common approach involves organopalladium-mediated coupling of substituted quinolines.[17] We report herein a direct and strategically different approach starting from *o*-nitrobenzaldehyde.



Scheme 5

As shown in Scheme 5, the nitro group in the nitrophenyl indole **11** can be readily reduced using iron and hydrochloric acid in aqueous ethanol. Formaldehyde and trifluoroacetic acid introduced the aldehyde group into the 3-position of the indole, which rapidly cyclized to generate the tetracyclic ring system **12** in 81% yield. Since Kundu and co-workers have already accomplished the N-methylation using methyl iodide in toluene,[16] the synthesis of indoloquinoline **12** constitutes a formal total synthesis of isocryptolepine.

The indolo[2,1-*a*]isoquinolines are a family of compounds that have shown potent inhibitory activity against tumors.[18] The synthesis of **14** was achieved from aldehyde **13**, readily available from indene.[19] Indole formation provided a mixture of the expected indole ester and **14**. Treatment of this mixture with PTSA[20] afforded **14** in 79% yield (Scheme 6).

In conclusion, the synthesis of indoles using aminobenzyl phosphonium salts or sulfones or nitriles is a direct and flexible strategy. This strategy is compatible with a wide range of functional groups. It has already been successfully applied to several natural products, including rutaecarpine, arcyriacyanin A, and isocryptolepine.

Microwave reactions were conducted in a capped vial using a CEM Discover System. The reaction temperature was measured by the build-in temperature control system in CEM Discover Microwave reactor.

2,3-Disubstituted Indoles from Active 2-Aminobenzyl Compounds; General Procedure

In a 10 mL microwave reaction vessel (CEM Discover System) equipped with a magnetic stir bar, the active 2-aminobenzyl compound **3**, **6**, or the 2-aminobenzyl phosphonium salt **1** (0.5 mmol), the respective aldehyde (0.5 mmol), and glacial AcOH (11.4 μL, 0.2 mmol) were added to distilled MeOH (3 mL). The vial was capped properly and placed in the microwave. Microwave irradiation was carried out at 80 °C for 10 min (temperature fixed). After cooling the vial to r.t., MeOH was removed under vacuum. All MeOH must be removed before the next step. THF (4 mL) was added to the mixture, followed by dropwise addition of a 1 M *t*-BuOK solution in THF (0.8 mL). The resulting mixture was stirred at 25 °C under argon for 1 h. Sat. aq NH_4Cl (10 mL) was added to quench the reaction and the aqueous layer was extracted with EtOAc (3 × 10 mL). The organic layers were combined and washed with brine (2 × 10 mL), dried ($MgSO_4$), and filtered. The filtrate was concentrated under vacuum and the residue was purified by silica gel column chromatography using a mixture of EtOAc and hexanes as the eluent.

3-Cyano-2-phenyl-1*H*-indole (8a)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.83 (s, 1 H), 7.89 (d, *J* = 8 Hz, 2 H), 7.78 (d, *J* = 8 Hz, 1 H), 7.55–7.45 (m, 4 H), 7.34–7.28 (m, 2 H).

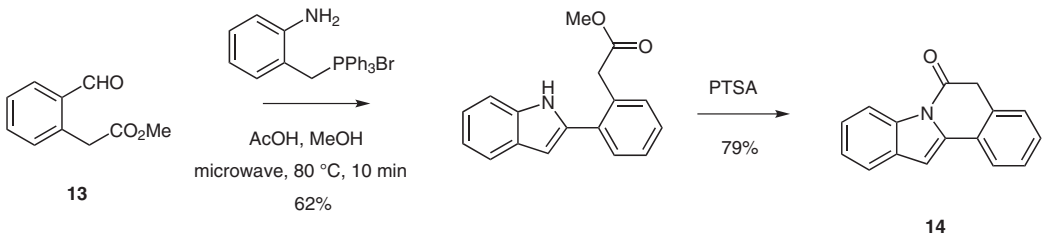
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.4, 136.4, 135.9, 128.9, 128.2, 128.1, 124.6, 124.1, 123.8, 122.8, 119.2, 115.9, 112.9, 54.3.

MS: *m*/*z* = 218, 190, 164, 96, 83, 71, 69, 57, 52.

HRMS: *m*/*z* calcd for $C_{15}H_{10}N_2$ [M^+]: 218.084; found: 218.084.

3-Cyano-2-(4-methoxyphenyl)-1*H*-indole (8b)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1 H), 7.84 (d, *J* = 8 Hz, 2 H), 7.74 (d, *J* = 8 Hz, 2 H), 7.43 (d, *J* = 8 Hz, 1 H), 7.33–7.22 (m, 2 H), 7.04 (d, *J* = 8 Hz, 1 H), 3.88 (s, 3 H).



Scheme 6

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2, 145.1, 135.1, 129.1, 128.5, 122.1, 119.6, 115.1, 111.6, 67.5, 60.1, 55.7.

MS: *m*/*z* = 248, 233, 205, 178, 151, 124, 105, 86, 84, 49.

HRMS: *m*/*z* calcd for $C_{16}H_{12}N_2O$ [M$^+$]: 248.096; found: 248.095.

2-(4-Bromophenyl)-3-cyano-1*H*-indole (8c)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (s, 1 H), 7.98 (d, *J* = 8 Hz, 2 H), 7.73 (d, *J* = 8 Hz, 2 H), 7.52 (d, *J* = 8 Hz, 1 H), 7.43 (t, *J* = 8 Hz, 1 H), 7.32 (t, *J* = 8 Hz, 1 H), 7.27 (d, *J* = 8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 149.5, 135.7, 132.2, 130.9, 129.6, 129.3, 129.1, 127.0, 126.3, 125.8, 118.4, 118.1, 65.2.

MS: *m*/*z* = 298, 296, 219, 190, 165, 143, 116, 89.

HRMS: *m*/*z* calcd for $C_{15}H_{19}BrN_2$ [M$^+$]: 295.995; found: 295.995.

3-Cyano-2-(3-methylphenyl)-1*H*-indole (8d)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (s, 1 H), 7.77 (d, *J* = 8 Hz, 1 H), 7.69 (d, *J* = 8 Hz, 2 H), 7.46–7.41 (m, 2 H), 7.32–7.29 (m, 3 H), 2.44 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.1, 139.5, 135.1, 129.6, 127.6, 122.6, 119.8, 116.9, 111.8, 67.2, 21.7.

MS: *m*/*z* = 232, 204, 190, 115.

HRMS: *m*/*z* calcd for $C_{16}H_{12}N_2$ [M$^+$]. 232.100; found: 232.100.

3-Cyano-2-(styryl)-1*H*-indole (8e)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1 H), 7.72 (d, *J* = 8 Hz, 1 H), 7.57 (d, *J* = 8 Hz, 2 H), 7.43–7.24 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.3, 135.6, 135.5, 133.2, 129.5, 129.2, 128.4, 127.3, 125.0, 122.6, 119.7, 116.2, 115.5, 115.3, 111.6, 86.6.

MS: *m*/*z* = 244, 243, 231, 217, 191, 189, 115, 105, 84, 56, 49.

HRMS: *m*/*z* calcd for $C_{17}H_{12}N_2$ [M$^+$]: 244.100; found: 244.101.

3-Cyano-2-(4-nitrophenyl)-1*H*-indole (8f)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (s, 1 H), 8.49 (d, *J* = 8 Hz, 2 H), 8.30 (d, *J* = 8 Hz, 2 H), 7.75 (d, *J* = 8 Hz, 1 H), 7.62 (d, *J* = 8 Hz, 1 H), 7.40 (t, *J* = 8 Hz, 1 H), 7.35 (t, *J* = 8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.1, 137.6, 135.1, 130.1, 129.5, 129.0, 127.2, 124.3, 122.3, 118.9, 116.5, 112.6, 57.0.

MS: *m*/*z* = 264, 263, 247, 241, 217, 211, 190, 163, 150, 123, 102.

HRMS: *m*/*z* calcd for $C_{15}H_9N_3O_2$ [M$^+$]: 263.069; found: 263.069.

3-(Methylthio)-2-phenyl-1*H*-indole (9)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.30 (br s, 1 H), 7.83 (m, 3 H), 7.48 (t, *J* = 6 Hz, 2 H), 7.39 (m, 2 H), 7.24 (m, 2 H), 2.29 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.7, 135.6, 131.9, 130.9, 128.6, 128.3, 128.1, 123.0, 120.6, 119.6, 111.1, 104.9, 19.72, 19.70.

HRMS: *m*/*z* calcd for $C_{15}H_{13}NS$ [M$^+$]: 239.07687; found: 239.07719.

2-(4-Bromophenyl)-3-(methylthio)-1*H*-indole (10)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.31 (br s, 1 H), 7.80 (dd, *J* = 6.5, 2.2 Hz, 1 H), 7.71 (dt, *J* = 8.4, 2.4 Hz, 2 H), 7.59 (dt, *J* = 8.4, 1.8 Hz, 2 H), 7.37 (dd, *J* = 6.9, 2.4 Hz, 1 H), 7.24 (m, 2 H), 2.28 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 135.6, 131.8, 130.82, 130.76, 129.5, 123.3, 122.4, 120.8, 119.7, 111.1, 105.5, 19.7, 19.6.

HRMS: *m*/*z* calcd for $C_{15}H_{12}BrNS$ [M$^+$]: 316.98738; found: 316.98779.

2-(2-Nitrophenyl)indole (11)
^{1}H NMR (400 MHz, acetone-d_6): δ = 10.65 (br s, 1 H), 7.90 (d, *J* = 8 Hz, 1 H), 7.81 (d, *J* = 6.8 Hz, 1 H), 7.71 (t, *J* = 15.2 Hz, 1 H), 7.64 (d, *J* = 8 Hz, 1 H), 7.57 (t, *J* = 14 Hz, 1 H), 7.48 (d, *J* = 8 Hz, 1 H), 7.20 (t, *J* = 14.4 Hz, 1 H), 7.10 (t, *J* = 15.6 Hz, 1 H), 6.68 (s 1 H).

^{13}C NMR (acetone-d_6): δ = 205.8, 149.4, 137.8, 132.9, 132.5, 131.5, 129.1, 129.0, 127.1, 122.8, 120.9, 120.1, 111.6, 102.7.

HRMS: *m*/*z* calcd for $C_{14}H_{10}N_2O_2$ [M$^+$]: 238.07422; found: 238.07453.

Indolo[2,3-*b*]quinoline (12)
^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.68 (br s, 1 H), 9.58 (s, 1 H), 8.51 (dd, *J* = 1.0, 7.5 Hz, 1 H), 8.30 (d, *J* = 7.7 Hz, 1 H), 8.11 (d, *J* = 8.4 Hz, 1 H), 7.75–7.64 (m, 3 H), 7.47 (d, *J* = 8.2 Hz, 1 H), 7.32 (d, *J* = 7.1 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 145.8, 145.1, 140.0, 139.3, 130.0, 128.6, 126.5, 125.9, 122.3, 122.1, 121.0, 120.6, 117.4, 114.9, 112.0.

HRMS: *m*/*z* calcd for $C_{15}H_{10}N_2$ [M$^+$]: 218.0844; found: 218.0854.

Indolo[2,1-*a*]isoquinolin-6(5*H*)-one (14)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (d, *J* = 7.6 Hz, 1 H), 7.84 (d, *J* = 6.4 Hz, 1 H), 7.59 (d, *J* = 6.8 Hz, 1 H), 7.31–7.36 (m, 5 H), 7.03 (s, 1 H), 4.10 (s, 2 H).

^{13}C NMR ($CDCl_3$): δ = 167.0, 135.3, 134.2, 130.6, 130.2, 129.8, 128.7, 128.1, 127.8, 125.5, 124.8, 124.1, 120.7, 116.8, 103.5, 37.8.

HRMS: *m*/*z* calcd for $C_{16}H_{11}NO$ [M$^+$]: 233.08406; found: 233.08431.

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References

(1) Gribble, G. W. *Comprehensive Heterocyclic Chemistry II*, Vol. 2; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon Press: Oxford, **1996**, 207.
(2) Sundberg, R. J. *Indoles*; Academic Press: New York, **1996**.
(3) Robinson, B. *Chem. Rev.* **1969**, *69*, 227.
(4) Phillips, R. R. *Org. React.* **1959**, *10*, 143.
(5) (a) Larock, R. C.; Yum, E. K.; Refvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652. (b) Bressy, C.; Alberico, D.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 13148. (c) Grimster, N. P.; Gauntlett, C.; Godfrey, C. R. A.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2005**, *44*, 3125. (d) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972.
(6) Li, J. J.; Gribble, G. W. In *Palladium in Heterocyclic Chemistry*, Vol. 20; Baldwin, J. E.; Williams, M. R., Eds.; Pergamon Press: New York, **2000**, 73–181.
(7) Houlihan, W. J.; Uike, Y.; Parrino, V. A. *J. Org. Chem.* **1981**, *46*, 4511.
(8) Sridharan, V.; Perumal, S.; Avendaño, C.; Menéndez, J. C. *Synlett* **2006**, 91.
(9) Kraus, G. A.; Guo, H. T. *Org. Lett.* **2008**, *10*, 3061.
(10) Koutek, B.; Pavlickova, L.; Soucek, M. *Synth. Commun.* **1976**, *6*, 305.
(11) Khartulyari, S. A.; Kapur, M.; Maier, E. M. *Org Lett.* **2006**, *8*, 5833.
(12) Gassman, P. G.; Drewes, H. R. *J. Am. Chem. Soc.* **1974**, *96*, 3002.
(13) Claus, P. K.; Jager, E.; Setzer, A. *Monastsh. Chem.* **1985**, *116*, 1017.

(14) Park, K. H.; Gray, G. A.; Daves, G. D. Jr. *J. Am. Chem. Soc.* **1978**, *100*, 7475.
(15) Van Miert, S.; Hostyn, S.; Maes, B. U. W.; Cimanga, K.; Brun, R.; Kaiser, M.; Matyus, P.; Dommisse, R.; Lemiere, G.; Vlietinck, A.; Pieters, L. *J. Nat. Prod.* **2005**, *68*, 674.
(16) Agarwal, P. K.; Sawant, D.; Sharma, S.; Kundu, B. *Eur. J. Org. Chem.* **2009**, 292.
(17) Jonckers, T. H. M.; Maes, B. U. W.; Lemiere, G. L. F.; Rombouts, G.; Pieters, L.; Haemers, A.; Dommisse, R. A. *Synlett* **2003**, 615.
(18) Ambros, R.; Von Angerer, S.; Wiegrebe, W. *Arch. Pharm. (Weinheim, Ger.)* **1988**, *321*, 481.
(19) Claus, R. E.; Schreiber, S. L. *Org. Synth.* **1984**, *64*, 150.
(20) Reboredo, F. J.; Treus, M.; Estevez, J. C.; Castedo, L.; Estevez, R. J. *Synlett* **2003**, 1603.