Nucleophilic-Type Radical Cyclizations of Indoles: Conversion of 2-Cyano 3-Substituted Indoles to Spiro-Annelated Indolines and Tetrahydrocarbazolones

Chau-Chen Yang, Han-Ting Chang, and Jim-Min Fang*

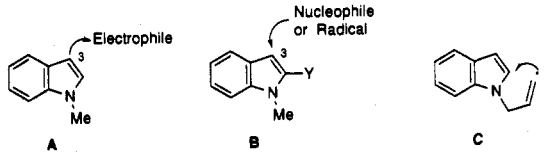
Department of Chemistry, National Taiwan University, Taipei, Taiwan 10617, Republic of China

Received October 15, 1992

Oxidative photocyclizations of appropriate 2-anilino alkenenitriles (**6**) afforded a series of indole-2-carbonitriles (**7**) having bromoalkyl substituents at the C-3 positions. Upon treatment with Bu_3SnH, these indolecarbonitriles underwent intramolecular cyclizations either by attack at the C-3 positions of the indole rings to give the spiro-annelated indolinecarbonitriles or by attack at the cyano group to give carbazolone derivatives.

Introduction

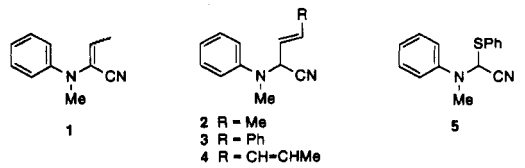
Although it is well-known that indole compounds having π-electron-rich systems react with electrophiles at C-3 (**A**),[1]



the possibility of nucleophilic addition reactions at this position (**B**) has not yet been evaluated. Many papers have described the formation of C–C bonds by means of radical additions to carbocyclic aromatic systems,[2] but only a recent report by Ziegler has demonstrated the feasibility of radical cyclizations in indole systems.[3] Ziegler used a radical reaction to form a dihydropyrrolo[1,2-*a*]-indole by cyclization onto the C-2 position of an indole ring (**C**), according to the normal polarity mode. We have investigated nucleophilic-type radical cyclizations at the C–3 position of indole derivatives such as indole-2-carbonitriles **7a–i** (Scheme I and Table I). This inverse polarity method may be applicable to the synthesis of spiro-annelated indolines and offer a route to aspidosperma alkaloids.

Results and Discussion

The requisite starting materials **6a–f** and **6h** were prepared by alkylations of the allylic anions generated from methylanilino alkenenitriles **1–4** with appropriate dihalides, 1,3-dibromopropane, *o*-bromobenzyl bromide, or 2-bromo-1-chloromethylcyclopentene.[4] The alkylations



occurred exclusively at the γ-carbons; the regioselectivity was presumably controlled by the electronic and steric effects of the anilino group.[5] Alkylation of the anion of amino(phenylthio)acetonitrile **5** with 1-bromo-4-iodobutane occurred concurrently with elimination of benzenethiol to furnish the desired alkenenitrile **6g**.[6] Irradiation of cyclohexane solutions of **6a–h** with 254-nm light under an atmosphere of oxygen afforded directly indole-carbonitriles **7a–h** in high yields. When oxygen was excluded, the photochemical reactions of **6b** and **6f** gave the corresponding 2,3-dihydro derivatives of **7b** and **7f** as the primary products.[7] The dihydro derivatives were subsequently converted to **7b** and **7f** either by further irradiation in the presence of oxygen or by a base-catalyzed autoxidation (*t*-BuOK cat., O_2, THF, rt, 3 h).[8] The

Scheme I

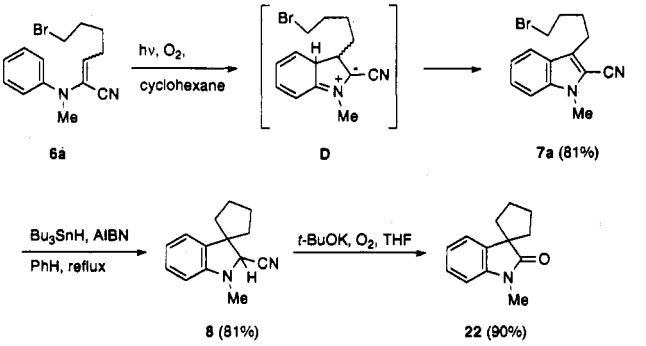


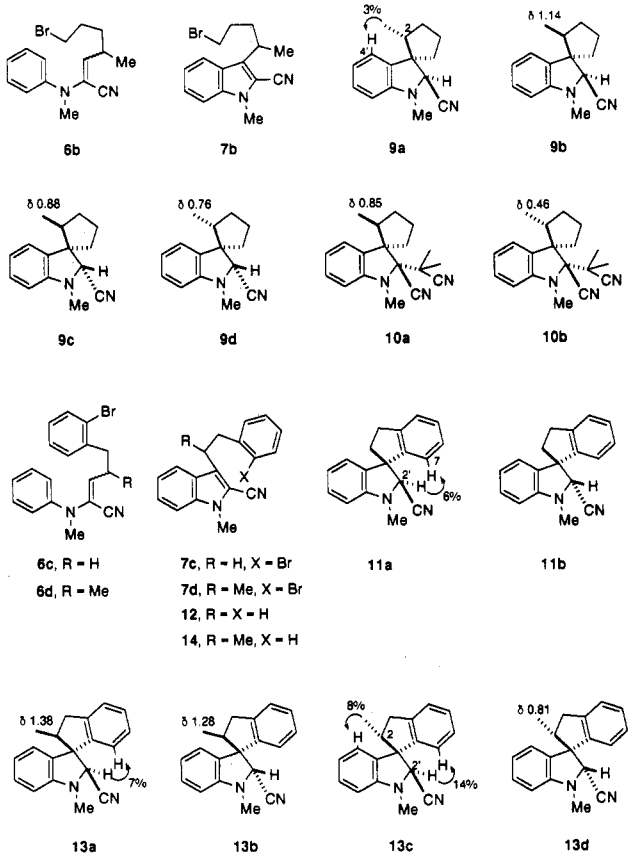
Table I. Free-Radical Cyclizations of 2-Cyanoindoles 7a–i (Bu_3SnH, AIBN, PhH, 80 °C)

substrate	Bu_3SnH/ equiv	AIBN/ equiv	products (yield/%; isomeric ratio)
7a	1.2	0.2	**8** (81)
7b	1.2	0.2	**9** (77; **a**:**b**:**d** = 46:40:16)
7b	1.2	0.4	**9** (77; **a**:**b**:**c**:**d** = 58:22:4:16) + **10** (22; **a**:**b** = 42:58)
7c	1.2	0.2	**11** (75; **a**:**b** = 30:70) + **12** (15)
7d	1.2	0.2	**13** (64; **a**:**b**:**c**:**d** = 52:10:24:14) + **14** (13)
7e	1.2	0.2	**15** (56; 28:72) + **16** (26)
7f	1.2	0.2	**17** (90)
7g	1.2	0.2	**18** (76)
7h	1.2	0.2	**19** (19) + **20** (60)
7i	1.2	0.2	**21** (78; **a**:**b** = 57:43)

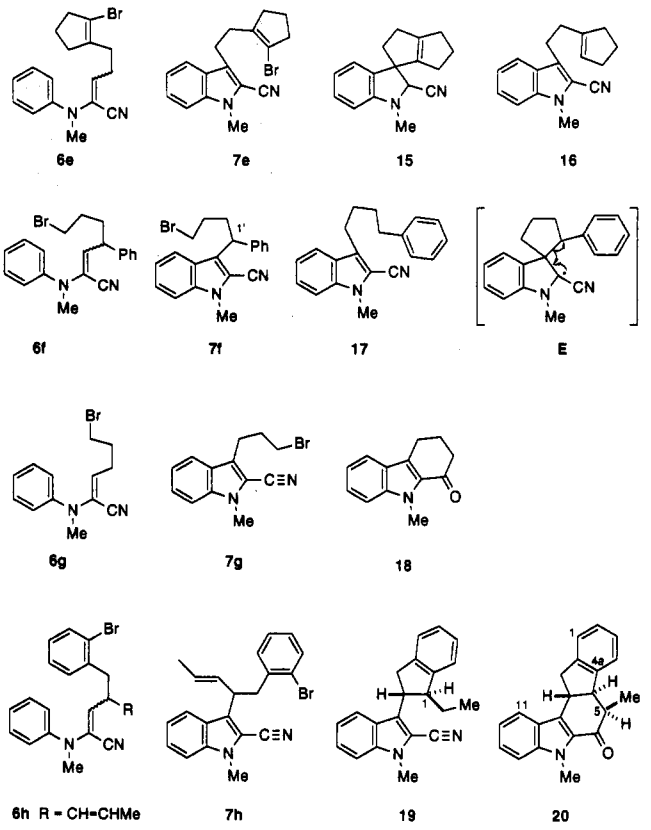
(1) Jones, R. A. In *Comprehensive Heterocyclic Chemistry*; Kartritzky, A. R., et al., Eds.; Pergamon: Oxford, 1984; Vol. 4, Chapter 3.05, pp 201–312.
(2) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon Press: Oxford, 1986; pp 210–266.
(3) Ziegler, F. E.; Jeroncic, L. O. *J. Org. Chem.* **1991**, *56*, 3479.
(4) (a) Ahlbrecht, H.; Vonderheid, C. *Synthesis* **1975**, 512. (b) Fang, J.-M.; Liao, L.-F.; Yang, C.-C. *Proc. Natl. Sci. Council (Taipei)* **1985**, *9*, 1. (c) Fang, J.-M.; Chang, H.-T.; Lin, C.-C. *J. Chem. Soc., Chem. Commun.* **1988**, 1385. (d) Yang, C.-C.; Fang, J.-M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3085.
(5) Fang, J.-M.; Chang, C.-J. *J. Chem. Soc., Chem. Commun.* **1989**, 1787.
(6) Fang, J.-M.; Chen, C.-C. *J. Chem. Soc., Perkin Trans. 1* **1990**, 3365.

0022-3263/93/1958-3100$04.00/0

photocyclizations of *N*-aryl-*N*-methylenamines related to **6** have been shown to proceed by means of a conrotatory cyclization followed by a thermally-allowed suprafacial 1,4-hydrogen migration to give 2,3-dihydroindoles.[9] A carbonyl group at the α-position is believed to stabilize the zwitterionic intermediate that corresponds to **D** and to enhance the chemical and photochemical yields of the cyclization.[9] The electron-withdrawing cyano group in **6a–h** should exert a similar beneficial effect. Direct photocyclization of **6a–h** to **7a–h** presumably involved trapping of the intermediate ylides with oxygen in a process similar to the above-mentioned base-catalyzed autoxidation.[8]



As shown in Table I, the nucleophilic radical cyclization of the indolecarbonitrile **7a**, which has a bromobutyl substituent at C-3, was carried out with tributyltin hydride in refluxing benzene to give spiro-annelated indoline **8** in 81% yield. This reaction was presumably facilitated by stabilization of an intermediate C-2′ radical by captodative substituents, i.e., the amino and cyano groups.[4c,10] Similar treatment of **7b** resulted in a 77% yield of cyclization product **9**. When a significant amount of azobisisobutyronitrile (AIBN, 0.4 equiv) was present, the reaction gave not only **9** but also derivative **10**, obtained by trapping a dimethylacetonitrile radical. The phenyl and alkenyl radicals generated from **7c**, **7d**, and **7e** also underwent intramolecular cyclizations to give annelated tetracyclic compounds **11**, **13**, and **15**, respectively, along with uncyclized reduction products **12**, **14**, and **16**.



Cyclization products **9**, **11**, **13**, and **15** exist as mixtures of diastereomers. The stereochemistry of the diastereomers was determined by analyses of the ^{1}H NMR spectra including NOE experiments. For example, the 2-CH_3 groups on the β-faces of **9b** and **9c** resonate at δ 1.14 and 0.88, respectively, whereas the corresponding groups on the α-faces of **9a** and **9d** appear at higher fields (δ 0.74 and 0.76), presumably because of the shielding effect of the indoline ring. This assignment was confirmed by the 3% enhancement of the H-4′ resonance (at δ 6.99) caused by irradiation of the 2-CH_3 resonance (at δ 0.74) in **9a**. The C-2′ protons in **11a**, **13a**, and **13c** were assigned to have α-configurations because irradiation of these resonances caused enhancements of the H-7 resonances. In these radical cyclizations, major products **9a**, **11b**, and **13a** appeared to be obtained by the trapping of a hydrogen atom from the less hindered face of the C-2′ radical.

The radical reaction of **7f**, having a phenyl group at C-1′, afforded a single indole product **17**, presumably by means of a tandem radical cyclization and cycloreversion as depicted in **E**. However, the radical reaction of indolecarbonitrile **7g** gave carbazolone **18** in 76% yield. Because **7g** has a bromopropyl substituent, the spiro-annelated indoline product would have contained a strained 4-membered ring. Presumably, cyclization at the 2,3-double bond was disfavored by the ring strain, and the radical cyclization occurred by attack at the cyano group instead.[11] Because of the reported low yields of cyclo-

(7) Chang, H.-T. M. S. Thesis, National Taiwan Univeristy, 1987. The *Z*-isomer of **6b** was irradiated in the absence of oxygen to afford two C-1′ epimers of the cis isomer of 3-(4-bromo-1-methylbutyl)-2,3-dihydro-1-methylindole-2-carbonitrile. The two epimers showed H-2 resonances at δ 4.21 (d, J = 9 Hz) and δ 4.24 (d, J = 9 Hz). Similar reaction of the *Z*-isomer of **6f** gave the cis isomers of 3-(4-bromo-1-phenylbutyl)-2,3-dihydro-1-methylindole-2-carbonitrile, which showed H-2 doublets with a coupling constant of 9 Hz, whereas the reaction of the *E*-isomers gave the corresponding *trans*-indolines, which showed H-2 signals with a small coupling constant of 2 Hz.

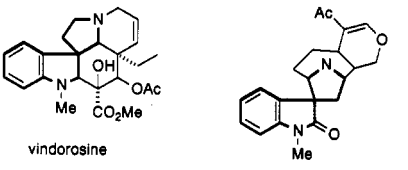
(8) Chuang, T.-H.; Yang, C.-C.; Chang, J.-C.; Fang, J.-M. *Synlett* **1990**, 733.

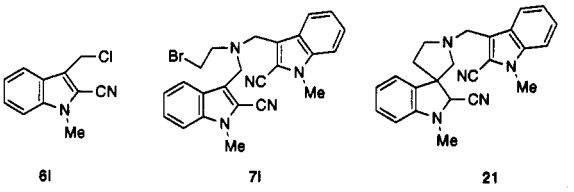
(9) (a) Chapman, O. L.; Eian, G. L.; Bloom, A.; Clardy, J. *J. Am. Chem. Soc.* **1971**, *93*, 2918. (b) Schultz, A. G.; Sha, C. K. *Tetrahedron* **1980**, *36*, 1757 and references cited therein.

(10) (a) Viehe, H. G.; Janousek, Z.; Merenyi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18*, 148. (b) Viehe, H. G.; Merenyi, R.; Janousek, Z. *Pure Appl. Chem.* **1988**, *60*, 1635.

hexanones formed by radical cyclizations,[11c] it is interesting to note that the conversion of **7g** to **18** was efficient and that no uncyclized reduction product was obtained. Compound **7h** was devised to test the differences in the reactivity of the olefinic and indole double bonds. The experiment revealed that the primary cyclization occurred selectively at the olefinic side chain. The resulting alkyl radical either absorbed a hydrogen atom to give indanylindole **19** (19%) or attacked the cyano group intramolecularly to afford novel pentacyclic compound **20** (60%). Again, the intramolecular radical cyclization onto a cyano group to form the cyclohexanone moiety was remarkably efficient in this instance. We predicted the *trans*-configuration of **19** by considering a chairlike transition state similar to those generally accepted for cyclizations of 4-substituted 5-heptenyl radicals.[4c,12] The crystal structure of **20** also clearly confirmed the (4b,5-cis)- and (4b,11c-trans)-configurations. Several models[13] have been advanced to explain stereochemical selectivities in free-radical reactions of acyclic systems; however, none of them can successfully account for the stereospecificity in the generation of the C-5 configuration of **20**.

In summary, we have expediently synthesized a series of 3-substituted indolecarbonitriles **7a–h** by oxidative photocyclization of the corresponding α-anilino alkenenitriles **6a–h**. Intramolecular radical cyclizations of **7a–h** afforded the spiro-annelated indolines and their polycyclic derivatives, which would have been difficult to assemble by other procedures. The success of these cyclizations also indicated the feasibility of nucleophilic-type radical additions to the 2,3-double bonds of indoles, provided that the C-2 position has an appropriate substituent, such as the cyano group in these examples. The cyano group was of paramount importance for the facilitation of the photocyclizations (from **6** to **7**) and the subsequent radical cyclizations. The cyano group in the indoline products could be readily removed or elaborated to other functionalities by known procedures.[14] We converted spiro-annelated indolinecarbonitrile **8** to the corresponding indolone **22** (90%) by a base-catalyzed autoxidation.[8,15] In order to utilize this spiroannelation method in the synthesis of aspidosperma alkaloids[16] such as vindorosine and alstonisine (the nucleus skeleton is shown in bold





lines), we also prepared indolecarbonitrile **7i**, which has an aminoalkyl substituent, and treated it with Bu_3SnH. The preliminary result indicated that the intramolecular radical cyclization was effective to give **21** (78%), which has a pyrrolidylindoline skeleton. The formation of new C–C bonds and additional ring closures in 2-cyanoazacycle systems are well documented.[17]

Experimental Section

Melting points are uncorrected. ^1H NMR spectra were recorded at 200 or 300 MHz; ^{13}C NMR spectra were recorded at 50 or 75 MHz. TMS was used as an internal standard. Mass spectra were recorded at an ionizing voltage of 70 eV. Merck silica gel 60F sheets were used for analytical thin-layer chromatography. Column chromatography was performed on SiO_2 (70–230 mesh); gradients of EtOAc and *n*-hexane were used as eluents. High-pressure liquid chromatography was carried out on a liquid chromatograph equipped with a refractive index detector. The samples were analyzed and/or separated on Hibar Lichrosorb Si 60 (7 μm) column (25 cm × 1 cm) with the indicated eluent with a 5 mL/min flow rate. Benzene and THF were distilled from sodium benzophenone ketyl under N_2.

3-(4-Bromobutyl)-1-methylindole-2-carbonitrile (7a). According to the known procedure,[4] a solution of 2-(*N*-methylanilino)-2-butenenitrile (172 mg, 1 mmol) in THF (5 mL) was

(11) (a) Clive, D. L. J.; Beaulieu, P. L.; Set, L. *J. Org. Chem.* **1984**, *49*, 1313. (b) Chenera, B.; Chuang, C. P.; Hart, D. J.; Hsu, L. Y. *J. Org. Chem.* **1985**, *50*, 5409. (c) Tsang, R.; Fraser-Reid, B. *J. Am. Chem Soc.* **1986**, *108*, 2116. (d) Yeung, B. W.; Contelles, J. L. M.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1989**, 1160. (e) Dickson, J. K., Jr.; Tsang, R.; Llera, J. M.; Fraser-Reid, B. *J. Org. Chem.* **1989**, *54*, 5350. (f) Knapp, S.; Gibson, F. S.; Choe, Y. H. *Tetrahedron Lett.* **1990**, *31*, 5397. (g) Snider, B. B.; Buckman, B. O. *J. Org. Chem.* **1992**, *57*, 322 and references cited therein.

(12) (a) Beckwith, A. L. *J. Chem. Soc., Chem. Commun.* **1980**, 482. (b) Beckwith, A. L.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. (c) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959. (d) Snider, B. B.; Wan, B. Y.-F.; Buckman, B. O.; Foxman, B. M. *J. Org. Chem.* **1991**, *56*, 328.

(13) For reviews, see: (a) Porter, N. A.; Giese, B.; Curran, D. P. *Acc. Chem. Res.* **1991**, *24*, 296. (b) Tsai, Y. M. *Chemistry* **1992**, *50*, 36 (in Chinese). For recent leading references, see: (c) Hart, D. J.; Huang, H.-C.; Krishnamurthy, R.; Schwartz, T. *J. Am. Chem. Soc.* **1989**, *111*, 7507. (d) Guidon, Y.; Yoakim, C.; Lemieux, R.; Boisvert, L.; Delorme, D.; Lavallee, J.-F. *Tetrahedron Lett.* **1990**, *31*, 2845. (e) Guidon, Y.; Lavallee, J.-F.; Boisvert, L.; Chabot, C.; Delorme, D.; Yoakim, C.; Hall, D.; Lemieux, R.; Simoneau, B. *Tetrahedron Lett.* **1991**, *32*, 27. (f) Guidon, Y.; Lavallee, J.-F.; Llinas-Brunet, M.; Horner, G.; Rancourt, J. *J. Am. Chem. Soc.* **1991**, *113*, 9701. (g) Hart, D. J.; *Synlett* **1991**, 412. (h) Hamon, D. P. G.; Razzino, P.; Massy-Westropp, R. A. *J. Chem. Soc., Chem. Commun.* **1991**, 332. (i) Giese, B.; Bulliard, M.; Zeitz, H.-G. *Synlett* **1991**, 425. (j) Giese, B.; Damm, W.; Wetterich, F.; Zeitz, H.-G. *Tetrahedron Lett.* **1992**, *33*, 1863. (k) Giese, B.; Carboni, B.; Gobel, T.; Muhn, R. *Tetrahedron Lett.* **1992**, *33*, 2673. (l) Beckwith, A. L. J.; Hersperger, R.; White, J. M. *J. Chem. Soc., Chem. Commun.* **1991**, 1151. (m) Chen, M. Y.; Fang, J. M.; Tsai, Y. M.; Yeh, R. L. *J. Chem. Soc., Chem. Commun.* **1991**, 1603. (n) Brandi, A.; Cicchi, S.; Goti, A.; Pietrusiewicz, K. M. *Tetrahedron Lett.* **1991**, *32*, 3265. (o) Giese, B.; Damm, W.; Dickhaut, J.; Wetterich, F.; Sun, S.; Curran, D. P. *Tetrahedron Lett.* **1991**, *32*, 6097. (p) Erdmann, P.; Schafer, J.; Springh, R.; Zeitz, H.-G.; Giese, B. *Helv. Chim. Acta* **1992**, *75*, 638. (q) Curran, D. P.; Thoma, G. *J. Am. Chem. Soc.* **1992**, *114*, 4436.

(14) For oxidative decyanation, see ref 6 and: (a) Watt, D. S. *J. Org. Chem.* **1974**, *39*, 2799. For reductive decyanation, see: (b) Yamada, S. I.; Akimoto, J. *Tetrahedron Lett.* **1969**, *3105*. (c) Bonin, M.; Romero, J. R.; Grierson, D. S.; Husson, H.-P. *Tetrahedron Lett.* **1982**, *23*, 3369. (d) Lu, Y. *Tetrahedron Asymmetry* **1990**, *32*, 4099. (e) Ogura, K. *J. Org. Chem.* **1991**, *56*, 2920. For a comprehensive reference for conversion of a cyano group to other functionalities, see: (f) Gless, R. D.; Rapoport, H. *J. Org. Chem.* **1979**, *44*, 1324.

(15) For other methods using intramolecular radical cyclizations to afford spiro-annelated indolones, see: (a) Hart, D. J.; Wu, S. C. *Tetrahedron Lett.* **1991**, *32*, 4099. For other approaches to spiro-annelated indoline derivatives, see ref 5b. (b) Remers, W. A.; Weiss, M. J. *Tetrahedron Lett.* **1968**, 81. (c) Wenkert, E.; Liu, S. *Synthesis* **1992**, 323.

(16) (a) Overman, L. E.; Sworin, M. *Alkaloids: Chemical and Biological Perspectives*; Wiley: New York, 1985; Vol. 3, p 275. (b) Kuehne, M. E.; Marko, I. Syntheses of Vinblastine-Type Alkaloids. In *The Alkaloids*; Academic Press: New York, 1990; Vol. 37, p 77. (c) Magnus, P.; Stamford, A.; Ladlow, M. *J. Am. Chem. Soc.* **1990**, *112*, 8210.

(17) For recent leading references regarding C–C bond formation and ring-closure reactions with retention of the cyano group, see a review: (a) Albright, J. D. *Tetrahedron* **1983**, *39*, 3207. For references regarding reactions with concurrent decyanation (e.g., the Bruylants reaction), see: (b) Bunnele, W. H.; Shevlin, C. G. *Tetrahedron Lett.* **1989**, *30*, 4203 and references cited therein. (c) Ahlbrecht, H.; Sommer, H. *Chem. Ber.* **1990**, *123*, 829. (d) Thaning, M.; Wistrand, L.-G. *J. Org. Chem.* **1990**, *55*, 1406. (e) Zeller, E.; Sajus, H.; Grierson, D. S. *Synlett* **1991**, 44. (f) Bonjoch, J.; Quirante, J.; Sole, D.; Castells, J.; Galceran, M.; Bosch, J. *Tetrahedron* **1991**, *47*, 4417.

treated with an LDA (1.1 mmol) solution in THF (3 mL) in the presence of HMPA (0.54 mL, 3 mmol) and subsequently alkylated with 1,3-dibromopropane (1.2 mmol) to give 7-bromo-2-(*N*-methylanilino)-2-heptenenitrile (**6a**, 79%). A solution of aminonitrile **6a** (145 mg, 0.52 mmol) in cyclohexane (60 mL) was placed in a quartz tube and purged with oxygen. The sample was irradiated under an O_2 atmosphere with 254-nm light in a Rayonet photochemical reactor (Model RPR-100) for 8 h. Complete conversion of **6a** was monitored by TLC analysis. The solvent was removed, and the residue was chromatographed on a silica gel column with EtOAc/hexane (2:98) to give **7a** (116 mg, 81% yield): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.09; IR (neat) 2214 cm^{-1} (CN); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.80–1.96 (4 H, m), 2.95 (2 H, t, J = 6.8 Hz), 3.43 (2 H, t, J = 6 Hz), 3.85 (3 H, s, NMe), 7.19 (1 H, t, J = 7 Hz), 7.35 (1 H, d, J = 7 Hz), 7.40 (1 H, t, J = 7 Hz), 7.64 (1 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.2 (t), 28.8 (t), 31.4 (q, NMe), 32.1 (t), 33.3 (t), 108.7 (s, C-3), 110.1 (d), 113.5 (s, CN), 120.5 (d), 120.6 (d), 125.6 (s), 125.9 (d), 127.5 (s), 138.1 (s); MS m/z (rel intensity) 292 (10, $[M + 2]^+$), 290 (10, $[M]^+$ for ^{79}Br), 169 (100), 115 (6), 77 (3); HRMS calcd for $C_{14}H_{15}BrN_2$ 290.0419, found 290.0429.

3-(4-Bromo-1-methylbutyl)-1-methylindole-2-carbonitrile (7b). Alkylation of 2-(*N*-methylanilino)-3-pentenenitrile with 1,3-dibromopropane gave 7-bromo-4-methyl-2-(*N*-methylanilino)-2-heptenenitrile (**6b**),[4] which was subjected to oxidative photocyclization by means of a procedure similar to the one described above to give **7b** (85%): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.1; IR (neat) 2214 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.49 (3 H, d, J = 7 Hz), 1.70–2.07 (4 H, m), 3.14–3.32 (1 H, m), 3.35 (2 H, t, J = 7 Hz), 3.83 (3 H, s), 7.15 (1 H, ddd, J = 7.4, 7.4, 1 Hz), 7.30 (1 H, dd, J = 8, 1 Hz), 7.39 (1 H, ddd, J = 8, 7.4, 1 Hz), 7.70 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 21.4 (q), 31.2 (t), 31.3 (q), 31.6 (d), 33.5 (t), 35.4 (t), 107.7 (s), 110.2 (d), 113.8 (s), 120.5 (d), 121.1 (d), 124.6 (s), 125.8 (d), 132.0 (s), 138.3 (s); MS m/z (rel intensity) 306 (8, $[M + 2]^+$), 304 (8, $[M]^+$ for ^{79}Br), 183 (100); HRMS calcd for $C_{15}H_{17}BrN_2$ 304.0576, found 304.0558.

3-[2-(2-Bromophenyl)ethyl]-1-methylindole-2-carbonitrile (7c). Alkylation of 2-(*N*-methylanilino)-2-butenenitrile with *o*-bromobenzyl bromide gave 5-(2-bromophenyl)-2-(*N*-methylanilino)-2-pentenenitrile (**6c**),[4] which was subjected to oxidative photocyclization by means of a procedure similar to the one described above to give **7c** (89%): white solid, mp 101–103 °C; TLC (EtOAc/hexane (2:98)) R_f = 0.08; IR (KBr) 2214 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.04–3.25 (4 H, m), 3.80 (3 H, s), 7.05–7.45 (6 H, m), 7.54 (1 H, dd, J = 8, 1 Hz), 7.66 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 25.6 (t), 31.3 (q), 37.3 (t), 108.7 (s), 110.0 (d), 113.2 (s), 120.6 (d, 2 C), 124.3 (s), 125.7 (s), 125.8 (d), 126.9 (s), 127.5 (d), 128.0 (d), 130.6 (d), 132.8 (d), 138.0 (s), 140.2 (s); MS m/z (rel intensity) 340 (7, $[M + 2]^+$), 338 (7, $[M]^+$ for ^{79}Br), 169 (100); HRMS calcd for $C_{18}H_{15}BrN_2$ 338.0419, found 338.0432.

3-[2-(Bromophenyl)-1-methylethyl]-1-methylindole-2-carbonitrile (7d). Alkylation of 2-(*N*-methylanilino)-3-pentenenitrile with *o*-bromobenzyl bromide gave 5-(2-bromophenyl)-4-methyl-2-(*N*-methylanilino)-2-pentenenitrile (**6d**),[4] which was subjected to oxidative photocyclization by means of a procedure similar to the one described above to give **7d** (87%): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.09; IR (neat) 2215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (3 H, d, J = 7 Hz) 3.21 (2 H, dd, J = 8, 2 Hz), 3.57–3.75 (1 H, m), 3.77 (3 H, s), 6.83–7.36 (6 H, m), 7.49 (1 H, d, J = 7.5 Hz), 7.74 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 20.0 (q), 31.2 (d), 32.0 (q), 43.3 (t), 107.2 (s), 110.1 (d), 113.7 (s), 117.2 (s), 120.4 (d), 121.2 (d), 124.8 (s), 125.7 (d), 127.0 (d), 127.8 (d), 131.2 (d), 131.8 (s), 132.8 (s), 138.0 (s), 139.3 (s); MS m/z (rel intensity) 354 (10, $[M + 2]^+$), 352 (7, $[M]^+$ for ^{79}Br), 183 (100); HRMS calcd for $C_{19}H_{17}BrN_2$ 352.0576, found 352.0549.

3-[2-(2-Bromocyclopentenyl)ethyl]-1-methylindole-2-carbonitrile (7e). Alkylation of 2-(*N*-methylanilino)-2-butenenitrile with 2-bromo-1-(chloromethyl)cyclopentene gave 5-(2-bromocyclopentenyl)-2-(*N*-methylanilino)-2-pentenenitrile (**6e**),[4] which was subjected to oxidative photocyclization by means of a procedure similar to the one described above to give **7b** (73%): white solid; mp 61–63 °C; TLC (EtOAc/hexane (2:98)) R_f = 0.14; IR (KBr) 2215 (CN), 1651 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.83–1.98 (2 H, m), 2.34 (2 H, br t, J = 6.6 Hz), 2.50–2.62 (4 H, m), 2.99 (2 H, t, J = 8 Hz), 3.80 (3 H, s), 7.17 (1 H, ddd, J = 8, 8, 1 Hz), 7.27 (1 H, dd, J = 8, 1 Hz), 7.38 (1 H, ddd, J = 8, 8, 1 Hz), 7.68 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 21.7 (t), 22.7 (t), 30.8 (t), 31.2 (q), 34.0 (t), 39.8 (t), 108.6 (s), 109.9 (d), 113.4 (s), 117.2 (s), 120.5 (d, 2 C), 125.6 (s), 125.7 (d), 127.2 (s), 137.9 (s), 139.4 (s); MS m/z (rel intensity) 330 (10, $[M + 2]^+$), 328 (10, $[M]^+$ for ^{79}Br), 169 (100); HRMS calcd for $C_{17}H_{17}BrN_2$ 328.0576, found 328.0580.

3-(4-Bromo-1-phenylbutyl)-1-methylindole-2-carbonitrile (7f). Alkylation of 2-(*N*-methylanilino)-4-phenyl-3-butenenitrile with 1,3-dibromopropane gave 7-bromo-2-(*N*-methylanilino)-4-phenyl-2-heptenenitrile (**6f**),[4] which was subjected to oxidative photocyclization by means of a procedure similar to the one described above to give **7f** (80%): yellow oil; TLC (EtOAc/hexane (5:95)) R_f = 0.15; IR (neat) 2214 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.76–1.96 (2 H, m), 2.48 (2 H, dt, J = 8, 8 Hz), 3.41 (2 H, t, J = 6.6 Hz), 3.90 (3 H, s), 4.40 (1 H, t, J = 8 Hz), 7.11–7.42 (8 H, m), 7.64 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 31.3 (t), 31.4 (q), 32.6 (t), 33.3 (t), 42.5 (d), 108.2 (s), 110.2 (d), 113.8 (s), 120.8 (d), 121.2 (d), 124.8 (s), 125.9 (d), 126.6 (d), 127.4 (d, 2 C), 128.6 (d, 2 C), 129.5 (s), 138.2 (s), 142.9 (s); MS m/z (rel intensity) 368 (9, $[M + 2]^+$), 366 (7, $[M]^+$ for ^{79}Br), 245 (100); HRMS calcd for $C_{20}H_{19}BrN_2$ 366.0702, found 366.0725.

3-(3-Bromopropyl)-1-methylindole-2-carbonitrile (7g). Alkylation of the anion of 2-(*N*-methylanilino)-2-(phenylthio)-acetonitrile with 1-bromo-4-iodobutane resulted in concurrent elimination of benzenethiol to give 6-bromo-2-(*N*-methylanilino)-2-hexenenitrile (**7g**),[6] which was subjected to oxidative photocyclization by means of a procedure similar to the one described above to give **7g** (71%): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.1; IR (neat) 2214 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.29 (2 H, tt, J = 7, 6.6 Hz), 3.10 (2 H, t, J = 7 Hz), 3.43 (2 H, t, J = 6.6 Hz), 3.85 (3 H, s), 7.20 (1 H, ddd, J = 8, 8, 1 Hz), 7.32 (1 H, d, J = 8 Hz), 7.42 (1 H, dd, J = 8, 1 Hz), 7.69 (1 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 23.4 (t), 31.4 (q), 32.7 (t), 33.2 (t), 108.9 (s), 110.1 (d), 113.3 (s), 120.5 (d), 120.8 (d), 125.6 (s), 126.0 (d), 126.2 (s), 138.0 (s); MS m/z (rel intensity) 278 (30, $[M + 2]^+$), 276 (28, $[M]^+$ for ^{79}Br), 169 (100); HRMS calcd for $C_{13}H_{13}BrN_2$ 276.0262, found 276.0268.

3-[1-(2-Bromobenzyl)-2-butenyl]-1-methylindole-2-carbonitrile (7h). Alkylation of 2-(*N*-methylanilino)-3,5-heptadienenitrile with *o*-bromobenzyl bromide gave 4-(2-bromobenzyl)-2-(*N*-methylanilino)-2,5-heptadienenitrile (**6h**),[4] which was subjected to oxidative photocyclization by means of a procedure similar to the one described above to give **7h** (82%): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.06; IR (neat) 2215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.66 (3 H, dd, J = 6, 1 Hz), 3.26 (1 H, dd, J = 13, 8 Hz), 3.42 (1 H, dd, J = 13, 7.6 Hz), 3.78 (3 H, s), 4.18–4.29 (1 H, m), 5.52 (1 H, dq, J = 15, 6 Hz), 5.95 (1 H, ddq, J = 15, 7.5, 1 Hz), 6.92–7.09 (3 H, m), 7.17 (1 H, dd, J = 7.5, 7.5 Hz), 7.28 (1 H, d, J = 7.5 Hz), 7.38 (1 H, dd, J = 7.5 Hz), 7.51 (1 H, dd, J = 7.5, 1 Hz), 7.76 (1 H, d, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 17.7 (q), 31.2 (q), 40.6 (d), 41.7 (t), 108.1 (s), 110.8 (d), 113.4 (s), 120.5 (d), 121.4 (d), 124.7 (s), 124.8 (s), 125.7 (d), 126.7 (d), 127.8 (d), 128.8 (d), 129.4 (s), 131.2 (d), 131.3 (d), 132.7 (d), 138.1 (s), 138.9 (s); MS m/z (rel intensity) 380 (10, $[M + 2]^+$), 378 (6, $[M]^+$ for ^{79}Br), 209 (100); HRMS calcd for $C_{21}H_{19}BrN_2$ 378.0732, found 378.0718.

(2-Bromoethyl)-bis[(1-methyl-2-cyanoindol-3-yl)methyl]-amine (7i). A solution of 3-(chloromethyl)-1-methylindole-2-carbonitrile[18] (194 mg, 0.95 mmol) in DMF (5 mL) was stirred with (2-bromoethyl)amine hydrobromide (230 mg, 1.1 mmol) and K_2CO_3 (300 mg, 2.2 mmol) for 12 h at room temperature. Solids were removed by filtration, and the filtrate was concentrated and chromatographed on a silica gel column with EtOAc/hexane (30:70) to give **7i** (38 mg) and 1-methyl-3-(oxazolonylmethyl)-indole-2-carbonitrile (156 mg). **7i**: TLC (EtOAc/hexane (5:95)) R_f = 0.16; IR (neat) 2216 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.03 (2 H, t, J = 7.6 Hz), 3.48 (2 H, t, J = 7.6 Hz), 3.73 (6 H, s, two NMe), 3.99 (4 H, s, two CH_2), 7.14 (2 H, dd, J = 8, 8 Hz), 7.29 (2 H, d, J = 8 Hz), 7.34 (2 H, dd, J = 8, 8 Hz), 7.72 (2 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 29.6 (t), 31.3 (q, 2 C), 49.7 (t, 2 C), 56.4 (t), 109.8 (d, 2 C), 110.2 (s, 2 C), 113.1 (s, 2 C), 120.8 (d, 2 C), 121.6 (d, 2 C), 124.0 (s, 2 C), 125.7 (s, 2 C), 125.9 (d, 2 C), 137.9 (s, 2

(18) (a) Lin, C. C. M.S. Thesis, National Taiwan University, 1989. (b) Lin, C. D. M.S. Thesis, National Taiwan University, 1992.

C); MS m/z (rel intensity) 461 (4, [M + 2]+), 459 (5, [M]+ for ^{79}Br), 169 (100); HRMS calcd for $C_{24}H_{22}N_5Br$ 459.1059, found 459.1079.

1'-Methylspiro[cyclopentane-1,3'-indoline]-2'-carbonitrile (8). The procedure described is typical for the radical cyclizations shown in Table I. Indolecarbonitrile **7a** (250 mg, 0.86 mmol) in deoxygenated anhyd benzene (20 mL) was heated to reflux under an atmosphere of N_2. A mixture of *n*-Bu_3SnH (0.28 mL, 1.2 equiv) and AIBN (28 mg, 0.2 equiv) in benzene (20 mL) was added drop-by-drop at a rate of 0.1 mL/min by means of a syringe pump. After completion of addition, the reaction mixture was kept refluxing for 6 h. The mixture was cooled and concentrated in vacuo. The residue was chromatographed on a silica gel column with hexane to remove most of the tin compounds, and subsequent elution with EtOAc gave crude cyclization product **8** in several fractions. The fractions were combined and concentrated to about 10 mL. The residue was treated with a small amount of Et_3N (0.5 mL) to precipitate out the residual tin compounds. The white precipitates were filtered off, and the filtrate was concentrated and chromatographed on a silica gel column with EtOAc/hexane (3:97) to give pure **8** (148 mg, 81%): yellow oil; TLC (EtOAc/hexane (3:97)) R_f = 0.09; IR (neat) 2216 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.78–2.08 (7 H, m), 2.24–2.31 (1 H, m), 2.87 (3 H, s, NMe), 4.01 (1 H, s, H-2), 6.55 (1 H, dd, J = 8, 1 Hz), 6.81 (1 H, ddd, J = 7, 7, 1 Hz), 7.04 (1 H, dd, J = 7, 1 Hz), 7.15 (1 H, ddd, J = 8, 7, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 24.9 (t), 25.0 (t), 34.3 (q), 36.1 (t), 39.1 (t), 55.2 (s, C-3'), 66.3 (d, C-2'), 108.3 (d), 117.0 (s), 120.0 (d), 121.8 (d), 128.1 (d), 135.9 (s), 149.4 (s); MS m/z (rel intensity) 212 (32, [M]+), 183 (8), 169 (100), 144 (13), 115 (7), 77 (6); HRMS calcd for $C_{14}H_{16}N_2$ 212.1313, found 212.1306.

2,1'-Dimethylspiro[cyclopentane-1,3'-indoline]-2'-carbonitrile (9). Isomer **9a** (major): yellow oil; TLC (EtOAc/hexane (5:95)) R_f = 0.24; IR (neat) 2214 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.74 (3 H, d, J = 7 Hz), 1.32–2.18 (6 H, m), 2.38–2.50 (1 H, m), 2.82 (3 H, s), 4.02 (1 H, s), 6.55 (1 H, dd, J = 8, 1 Hz), 6.81 (1 H, ddd, J = 7.5, 7.5, 1 Hz), 6.99 (1 H, dd, J = 7.5, 1 Hz), 7.16 (1 H, ddd, J = 8, 7.5, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 14.8 (q), 22.2 (t), 33.0 (t), 35.4 (q), 37.9 (t), 42.1 (d), 56.9 (s), 67.4 (d), 108.3 (d), 117.2 (s), 119.7 (d), 123.9 (d), 128.2 (d), 132.9 (s), 150.4 (s); MS m/z (rel intensity) 226 (26, [M]+), 169 (100); HRMS calcd for $C_{15}H_{18}N_2$ 226.1470, found 226.1469. Isomer **9b**: yellow oil; TLC (EtOAc/hexane (5:95)) R_f = 0.21; IR (neat) 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.14 (3 H, d J = 6.6 Hz), 1.84–2.30 (7 H, m), 2.85 (3 H, s), 3.84 (1 H, s), 6.58 (1 H, dd, J = 8, 1 Hz), 6.83 (1 H, ddd, J = 7, 7, 1 Hz), 7.02 (1 H, dd, J = 7, 1 Hz), 7.20 (1 H, ddd, J = 8, 7, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 14.8 (q), 22.1 (t), 32.1 (t), 34.8 (q), 38.9 (t), 44.7 (d), 58.8 (s), 65.4 (d), 108.0 (d), 117.6 (s), 120.0 (d), 128.2 (d), 132.3 (s), 150.0 (s); MS m/z (rel intensity) 226 (23, M+), 169 (100). Isomer **9c**: yellow oil; TLC (EtOAc/hexane, (5:95)) R_f = 0.21; IR (neat) 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, d, J = 6.6 Hz), 1.85–2.18 (6 H, m), 2.30–2.48 (1 H, m), 2.87 (3 H, s), 4.16 (1 H, s), 6.52 (1 H, dd, J = 8, 1 Hz), 6.79 (1 H, ddd, J = 7, 7, 1 Hz), 7.00 (1 H, dd, J = 7, 1 Hz), 7.14 (1 H, ddd, J = 8, 7, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 14.8 (q), 22.1 (t), 31.8 (q), 32.4 (t), 36.5 (t), 44.6 (d), 58.0 (s), 62.3 (d), 108.8 (d), 117.2 (s), 119.5 (d), 121.7 (d), 128.3 (d), 132.4 (s), 148.2 (s); MS m/z (rel intensity) 226 (23, [M]+), 169 (100). Isomer **9d**: yellow oil; TLC (EtOAc/hexane (5:95)) R_f = 0.15; IR (neat) 2213 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.76 (3 H, d, J = 6.6 Hz), 1.80–2.30 (7 H, m), 2.86 (3 H, s), 4.08 (1 H, s), 6.55 (1 H, dd, J = 8, 1 Hz), 6.79 (1 H, ddd, J = 7.5, 7.5, 1 Hz), 7.00 (1 H, dd, J = 7.5, 1 Hz), 7.15 (1 H, ddd, J = 8, 7.5, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 15.7 (q), 22.2 (t), 32.8 (t), 34.2 (q), 35.7 (t), 43.0 (d), 58.0 (s), 67.9 (d), 108.2 (d), 117.0 (s), 119.4 (d), 124.2 (d), 128.2 (d), 132.4 (s), 148.1 (s); MS m/z (rel intensity) 226 (21, [M]+), 169 (100).

2'-(2-Cyanoprop-2-yl)-2,1'-dimethylspiro[cyclopentane-1,3'-indoline]-2'-carbonitrile (10). Isomer **10a**: colorless solid; mp 107–107.5 °C; TLC (EtOAc/hexane (5:95)) R_f = 0.11; IR (KBr) 2231 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.87 (3 H, d, J = 7 Hz), 1.19 (3 H, s), 1.60 (3 H, s), 1.63–2.42 (6 H, m), 2.60–2.72 (1 H, m), 3.14 (3 H, s), 6.46 (1 H, dd, J = 8, 1 Hz), 6.78 (1 H, ddd, J = 8, 8, 1 Hz), 6.87 (1 H, dd, J = 8, 1 Hz), 7.13 (1H, ddd, J = 8, 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 12.0 (q), 22.2 (t), 22.3 (q), 25.6 (q), 29.6 (q), 31.3 (t), 34.6 (q), 43.0 (s), 53.4 (d), 65.3 (s), 71.9 (s), 106.6 (d), 117.3 (s), 119.8 (d), 120.0 (d), 122.4 (s), 128.7 (d), 129.2 (s), 148.7 (s); MS m/z (rel intensity) 293 (1, [M]+), 169 (100). Isomer **10b** (major): colorless solid; mp 79–81 °C; TLC (EtOAc/hexane (5:95)) R_f = 0.1; IR (KBr) 2232 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.46 (3 H, d, J = 7 Hz), 1.24 (3 H, s), 1.36–1.42 (1 H, m), 1.59 (3 H, s), 1.71–1.86 (1 H, m), 1.93–2.09 (2 H, m), 2.16–2.28 (1 H, m), 2.28–2.53 (1 H, m), 2.82–3.01 (1 H, m), 3.15 (3 H, s), 6.43 (1 H, dd, J = 8, 1 Hz), 6.75 (1 H, ddd, J = 8, 8, 1 Hz), 6.89 (1 H, dd, J = 8, 1 Hz), 7.14 (1 H, ddd, J = 8, 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 13.7 (q), 21.9 (t), 22.8 (q), 26.2 (q), 29.7 (t), 30.4 (t), 35.4 (q), 43.0 (s), 46.9 (d), 53.4 (s), 63.4 (s), 106.3 (d), 115.7 (s), 119.2 (d), 122.8 (s), 122.9 (d), 128.8 (d), 130.8 (s), 149.0 (s); MS m/z (rel intensity) 293 (2, [M]+), 169 (100); HRMS calcd for $C_{19}H_{23}N_3$ 293.1892, found 293.1889.

1'-Methylspiro[indane-1,3'-indoline]-2'-carbonitrile (11). Isomer **11a**: white solid; mp 91–93 °C; TLC (EtOAc/hexane (2:98)) R_f = 0.093; IR (KBr) 2241 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.30–2.45 (1 H, m), 2.86–2.98 (1 H, m), 2.92 (3 H, s), 3.08 (1 H, ddd, J = 14, 7, 3 Hz), 3.21–3.36 (1 H, m), 4.11 (1 H, s), 6.65 (1 H, d, J = 8 Hz), 6.75–6.90 (2 H, m), 7.05 (1 H, d, J = 7.2 Hz), 7.13–7.30 (4H, m); ^{13}C NMR ($CDCl_3$) δ 30.8 (t), 34.7 (q), 37.0 (t), 60.2 (s), 68.5 (d), 108.6 (d), 117.7 (s), 120.5 (d), 123.0 (d), 123.9 (d), 124.9 (d), 127.1 (d), 128.3 (d), 128.7 (d), 134.9 (s), 143.9 (s), 145.0 (s), 149.9 (s); MS m/z (rel intensity) 260 (100, [M]+). Anal. Calcd for $C_{18}H_{16}N_2$: C, 83.05; H, 6.19; N, 10.76. Found: C, 82.82; H, 6.30; N, 10.76. Isomer **11b** (major): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.09; IR (neat) 2246 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.20–2.36 (1 H, m), 2.57 (1 H, ddd, J = 13, 7, 3 Hz), 2.91 (3 H, s), 3.01–3.11 (2 H, m), 4.29 (1 H, s), 6.66 (1 H, d, J = 8 Hz), 6.78 (1 H, ddd, J = 7.3, 7.3, 1 Hz), 6.84 (1 H, dd, J = 7.3, 1 Hz), 7.17–7.31 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 30.3 (t), 34.2 (q), 39.4 (t), 60.8 (s), 67.7 (d), 108.5 (d), 116.3 (s), 120.3 (d), 123.0 (d), 124.5 (d), 125.7 (d), 126.9 (d), 128.5 (d), 134.4 (s), 142.7 (s), 144.0 (s), 150.2 (s); MS m/z (rel intensity) 260 (100, [M]+); HRMS calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1320.

1-Methyl-3-(2-phenylethyl)indole-2-carbonitrile (12): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.08; IR (neat) 2215 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.01 (2 H, t, J = 9 Hz), 3.22 (2 H, t, J = 9 Hz), 3.83 (3 H, s), 7.16–7.40 (8 H, m), 7.58 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 27.3 (t), 31.4 (q), 36.8 (t), 108.8 (s), 110.1 (d), 113.4 (s), 120.6 (d, 2 C), 125.6 (s), 125.8 (d), 126.2 (d), 127.3 (s), 128.4 (d, 4 C), 138.0 (s), 141.0 (s); MS m/z (rel intensity) 260 (32, [M]+), 169 (100); HRMS calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1314.

2,1'-Dimethylspiro[indane-1,3'-indoline]-2'-carbonitrile (13). Isomer **13a** (major): white solid; mp 142–144 °C; TLC (EtOAc/hexane (2:98)) R_f = 0.1; IR (KBr) 2245 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.38 (3 H, d, J = 7 Hz), 2.53–2.68 (1 H, m), 2.87 (3 H, s), 2.99 (1 H, dd, J = 16, 7.5 Hz), 3.30 (1 H, dd, J = 16, 11 Hz), 3.86 (1 H, s), 6.67 (1 H, d, J = 8 Hz), 6.80–6.93 (2 H, m), 7.08 (1 H, dd, J = 8, 1 Hz), 7.15–7.30 (4 H, m); ^{13}C NMR ($CDCl_3$) δ 12.9 (q), 35.4 (q), 38.0 (t), 48.6 (d), 62.9 (s), 65.2 (d), 108.8 (d), 116.1 (s), 120.7 (d), 123.2 (d), 124.1 (d), 124.8 (d), 127.1 (d), 128.3 (d), 128.8 (d), 133.7 (s), 144.5 (s), 145.7 (s), 151.1 (s); MS m/z (rel intensity) 274 (100, [M]+). Anal. Calcd for $C_{19}H_{18}N_2$: C, 83.18; H, 6.61; N, 10.21. Found: C, 82.85; H, 6.76; N, 9.88. Isomer **13b**: ^{1}H NMR ($CDCl_3$, inter alia) δ 1.28 (3 H, d, J = 7 Hz), 2.83 (3 H, s, NMe), 3.77 (1 H, s, H-2'). Isomer **13c**: white solid; mp 126–128 °C; TLC (EtOAc/hexane (2:98)) R_f = 0.08; IR (KBr) 2246 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (3 H, d, J = 7 Hz), 2.72 (1 H, dd, J = 15, 7 Hz), 2.93 (3 H, s), 3.06–3.24 (1 H, m), 3.32 (1 H, dd, J = 15, 8 Hz), 4.36 (1 H, s), 6.57 (1 H, dd, J = 7.5, 1 Hz), 6.64 (1 H, d, J = 8 Hz), 6.72 (1 H, ddd, J = 7.5, 7.5, 1 Hz), 7.08–7.30 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 16.3 (q), 35.4 (q), 38.9 (t), 42.3 (d), 62.5 (s), 68.1 (d), 108.7 (d), 117.2 (s), 119.8 (d), 123.6 (d), 124.8 (d), 125.0 (d), 127.0 (d), 128.2 (d), 128.7 (d), 131.0 (s), 143.4 (s), 144.4 (s), 149.9 (s); MS m/z (rel intensity) 274 (100, [M]+). Isomer **13d**: ^{1}H NMR ($CDCl_3$, inter alia) δ 0.81 (3 H, d, J = 7 Hz), 2.92 (3 H, s, NMe), 4.28 (1 H, s, H-2').

1-Methyl-3-(1-methyl-2-phenylethyl)indole-2-carbonitrile (14): while solid; mp 113–114 °C; TLC (EtOAc/hexane (2:98)) R_f = 0.08; IR (KBr) 2213 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.48 (3 H, d, J = 7 Hz), 3.00–3.20 (2 H, m), 3.43–3.57 (1 H, m), 3.78 (3 H, s), 7.08–7.25 (5 H, m), 7.28 (1 H, dd, J = 8, 1 Hz), 7.38 (1 H, dd, J = 8, 1 Hz), 7.73 (1 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 20.4 (q), 31.2 (q), 34.2 (d), 43.4 (t), 107.7 (s, C-3), 110.2 (d), 113.8 (s), 120.4 (d), 121.2 (d), 124.8 (s), 125.7 (d), 126.0 (d), 128.2 (d,

2 C), 128.9 (d, 2 C), 132.2 (s), 138.2 (s), 140.1 (s); MS *m/z* (rel intensity) 274 (9, $[M]^+$), 183 (100); HRMS calcd for $C_{19}H_{18}N_2$ 274. 1470, found 274.1467.

1′-Methylspiro[bicyclo[3.3.0]oct-2(6)-ene-1,3′-indoline]-2′-carbonitrile (15). Isomer **15a**: yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.11; IR (neat) 2213 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.81–1.95 (1 H, m), 2.01–2.31 (7 H, m), 2.35–2.43 (2 H, m), 2.86 (3 H, s), 3.95 (1 H, s), 6.56 (1 H, d, J = 8 Hz), 6.81 (1 H, dd, J = 8, 8 Hz), 6.93 (1 H, dd, J = 8, 8 Hz), 7.14 (1 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 25.8 (t), 27.9 (t), 28.0 (t), 29.7 (t), 34.9 (q), 41.4 (t), 57.6 (s), 64.6 (d), 108.4 (d), 114.5 (s), 120.2 (d), 122.6 (d), 128.3 (d), 134.4 (s), 147.0 (s), 149.2 (s), 151.3 (s); MS *m/z* (rel intensity) 250 (32, M^+), 169 (100); HRMS calcd for $C_{17}H_{18}N_2$ 250.1470, found 250.1439. Isomer **15b** (major): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.09; IR (neat) 2215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88–2.03 (1 H, m), 2.16–2.49 (7 H, m), 2.53–2.62 (2 H, m), 2.85 (3 H, s), 4.01 (1 H, s), 6.56 (1 H, d, J = 8 Hz), 6.80 (1 H, dd, J = 8, 8 Hz), 6.95 (1 H, dd, J = 8, 8 Hz), 7.14 (1 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 26.7 (t), 27.9 (t), 28.1 (t), 34.6 (q, NMe), 43.2 (t), 58.1 (s), 66.9 (d), 108.3 (d), 117.2 (s), 120.0 (d), 122.6 (d), 128.3 (d), 133.8 (s), 146.2 (s), 149.6 (s), 150.2 (s); MS *m/z* (rel intensity) 250 (100, $[M]^+$); HRMS calcd for $C_{17}H_{18}N_2$ 250.1470, found 250.1463.

3-(2-Cyclopentenylethyl)-1-methylindole-2-carbonitrile (16): yellow oil; TLC (EtOAc/hexane (2:98)) R_f = 0.11; IR (neat) 2213 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.87 (2 H, tt, J = 7.5, 7.5 Hz), 2.31 (4 H, t, J = 7.5 Hz), 2.48 (2 H, t, J = 8 Hz), 3.07 (2 H, t, J = 8 Hz), 3.84 (3 H, s), 5.37 (1 H, s), 7.18 (1 H, ddd, J = 8, 8, 1 Hz), 7.34 (1 H, dd, J = 8, 1 Hz), 7.39 (1 H, ddd, J = 8, 8, 1 Hz), 7.65 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 23.4 (t), 23.8 (t), 31.3 (q), 32.0 (t), 32.5 (t), 35.1 (t), 108.6 (s), 110.0 (d), 113.6 (s), 120.4 (d), 120.6 (d), 124.4 (d), 125.7 (s), 125.8 (d), 128.2 (s), 138.1 (s), 143.4 (s); MS *m/z* (rel intensity) 250 (32, $[M]^+$), 169 (100); HRMS calcd for $C_{17}H_{18}N_2$ 250.1470, found 250.1439.

1-Methyl-3-(4-phenylbutyl)indole-2-carbonitrile (17): oil; TLC (EtOAc/hexane (3:97)) R_f = 0.17. IR (neat) 2213 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65–1.90 (4 H, m), 2.63 (2 H, t, J = 7 Hz), 2.92 (2 H, t, J = 7 Hz), 3.77 (3 H, s), 7.10–7.36 (8 H, m), 7.59 (1 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 24.9 (t), 30.0 (t), 30.9 (t), 31.2 (q), 35.5 (t), 108.6 (s), 110.0 (d), 113.6 (s), 120.4 (d), 120.6 (d), 125.6 (d), 125.7 (d), 128.2 (d, 2 C), 128.3 (d, 2 C), 129.2 (s), 138.0 (s), 142.2 (s); MS *m/z* (rel intensity) 288 (67, $[M]^+$), 169 (100); HRMS calcd for $C_{20}H_{20}N_2$ 288.1626, found 288.1607.

1,2,3,4-Tetrahydro-9-methylcarbazol-1-one (18): white solid; mp 99–101 °C; TLC (EtOAc/hexane (5:95)) R_f = 0.11; IR (KBr) 1641 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.35–1.42 (1 H, m, H-3), 2.13–2.32 (1 H, m, H-3) 2.63 (2 H, t, J = 6 Hz, H-2), 2.99 (2 H, t, J = 6 Hz, H-4), 4.05 (3 H, s, NMe), 7.13 (1 H, ddd, J = 8, 8, 1 Hz), 7.27 (1 H, dd, J = 8, 1 Hz), 7.35 (1 H, ddd, J = 8, 8, 1 Hz), 7.64 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 21.8 (t, C-3), 24.7 (t, C-2), 31.5 (q, NMe), 39.9 (t, C-4), 110.2 (d), 119.9 (d), 121.2 (d), 124.6 (s), 126.6 (d), 129.1 (s), 130.3 (s), 139.6 (s), 192.3 (s, CO); MS *m/z* (rel intensity) 213 (2, $[M]^+$), 199 (100); HRMS calcd for $C_{13}H_{13}N_2O$ 213.1028, found 213.1031. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 77.90; H, 6.64; N, 6.93.

(1′*S,2′*R**)-3-(1-Ethylindan-2-yl)-1-methylindole-2-carbonitrile (19):** yellow oil; TLC (EtOAc/hexane (3:97)) R_f = 0.11; IR (neat) 2214 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (3 H, t, J = 7.5 Hz), 1.73–1.90 (2 H, m), 3.36 (2 H, d, J = 8 Hz), 3.58–3.80 (2 H, m), 3.87 (3 H, s), 7.02–7.40 (7 H, m), 7.47 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 10.8 (q). 26.2 (t), 31.3 (q), 39.4 (t), 42.5 (d), 52.4 (d), 108.5 (s, C-3), 110.3 (d), 113.7 (s), 120.4 (d), 121.5 (d), 123.8 (d), 124.3 (d), 124.6 (d), 125.8 (d), 126.6 (d), 126.7 (d), 131.0 (s), 138.6 (s), 142.3 (s), 145.8 (s); MS *m/z* (rel intensity) 300 (100, $[M]^+$); HRMS calcd for $C_{21}H_{20}N_2$ 300.1626, found 300.1641.

(4b*R,5*R**,11c*R**)-5,7-Dimethylindano[1,2-*c*]carbazol-6-one (20):** colorless solid; mp 171–173 °C; TLC (EtOAc/hexane (3:97)) R_f = 0.07; IR (KBr) 1645 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.21 (3 H, dd, J = 7.5, 1 Hz), 2.98–3.13 (1 H, m), 3.27–3.36 (1 H, m), 3.49–3.76 (3 H, m), 4.09 (3 H, s), 7.13–7.25 (4 H, m), 7.34–7.42 (3 H, m), 7.81 (1 H, dd, J = 8, 1 Hz); ^{13}C NMR ($CDCl_3$ δ 10.0 (q), 31.5 (q), 35.3 (t), 39.2 (d), 43.2 (d), 54.2 (d), 110.5 (d), 120.4 (d), 121.9 (d), 122.1 (d), 123.8 (s), 125.0 (d), 126.5 (d, 3 C), 129.6 (s), 129.8 (s), 139.8 (s), 142.6 (s), 144.1 (s), 195.6 (s, CO); MS *m/z* (rel intensity) 301 (100, $[M]^+$); HRMS calcd for $C_{21}H_{19}NO$ 301.1466, found 301.1480. Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.55; H, 6.28; N, 4.49.

1′-Methyl-1-[(1-methyl-2-cyano-3-indolyl)methyl]spiro[pyrrolidine-3,3′-indoline]-2′-carbonitrile (21). Isomer **21a** (major): oil; TLC (EtOAc/hexane (25:75)) R_f = 0.35; IR (neat) 2216 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20–2.34 (1 H, m), 2.44 (1 H, d, J = 9 Hz), 2.45–2.56 (1 H, m), 2.64–2.76 (1 H, m), 2.82 (3 H, s, NMe), 2.92 (1 H, d, J = 9.3 Hz), 3.00–3.09 (1 H, m), 3.85 (3 H, s, NMe), 3.92 (1 H, d, J = 15 Hz), 4.02 (1 H, d, J = 15 Hz), 4.22 (1 H, s), 6.50 (1 H, d, J = 8 Hz), 6.80 (1 H, dd, J = 8, 8 Hz), 7.09–7.24 (3 H, m), 7.30 (1 H, d, J = 8 Hz), 7.40 (1 H, dd, J = 8, 8 Hz), 7.82 (1 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 31.4 (q, NMe), 34.0 (q, NMe), 34.5 (t), 49.4 (t), 53.2 (t), 54.1 (s), 64.9 (t), 68.6 (d), 108.3 (d), 110.0 (d), 113.2 (s), 116.8 (s), 120.1 (d), 121.0 (d), 121.3 (d), 121.6 (s), 122.6 (d), 124.2 (s), 125.9 (s), 126.1 (d), 128.6 (d), 133.1 (s), 138.1 (s), 149.7 (s); MS *m/z* (rel intensity) 381 (16, $[M]^+$), 169 (100). Isomer **21b**: oil; TLC (EtOAc/hexane (25:75)) R_f = 0.31; IR (neat) 2216 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.03–2.18 (2 H, m), 2.65–2.84 (2 H, m), 2.85 (3 H, s), 2.88 (1 H, d, J = 10 Hz), 3.25 (1 H, 3, J = 10 Hz), 3.87 (3 H, s), 3.96 (1 H, d, J = 14 Hz), 4.11 (1 H, d, J = 14 Hz), 4.12 (1 H, s), 6.52 (1 H, d, J = 8 Hz), 6.81 (1 H, dd, J = 8, 8 Hz), 7.10–7.24 (3 H, m), 7.30 (1 H, d, J = 8 Hz), 7.40 (1 H, dd, J = 8, 8 Hz), 7.91 (1 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 31.5 (q), 34.1 (q), 38.5 (t), 49.6 (t), 52.7 (t), 53.6 (s), 62.8 (t), 68.6 (d), 108.3 (d), 109.6 (s), 110.0 (d), 113.3 (s), 116.5 (s), 120.2 (d), 121.0 (d), 121.6 (d), 122.6 (d), 124.4 (s), 126.0 (s), 126.1 (d), 128.6 (d), 134.2 (s), 138.2 (s), 149.5 (s); MS *m/z* (rel intensity) 381 (15, $[M]^+$), 169 (100); HRMS calcd for $C_{24}H_{23}N_5$ 381.1953, found 381.1936.

1′-Methylspiro[cyclopentane-1,3′-indolin]-2′-one (22): white solid; mp 58–59 °C; TLC (EtOAc/hexane (10:90)) R_f = 0.12; R_f = 0.12; IR (KBr) 1707 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.77–2.18 (8 H, m), 3.19 (3 H, s), 6.80 (1 H, d, J = 8 Hz), 7.01 (1 H, ddd, J = 8, 8, 1 Hz), 7.16–7.26 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 26.0 (q), 26.4 (t), 38.1 (t), 53.6 (s, C-3), 107.4 (d), 121.9 (d), 122.3 (d), 127.1 (d) 136.5 (s), 142.6 (s), 181.6 (s, CO); MS *m/z* (rel intensity) 201 (37, $[M]^+$), 160 (100); HRMS calcd for $C_{13}H_{15}NO$ 201.1154, found 201.1159. Anal. Calcd for $C_{13}H_{15}NO$: C, 77.59; H, 7.52; N, 6.96. Found: C, 77.94; H, 7.58; N, 6.84.

Acknowledgment. We are grateful to the National Science Council for financial support (Grant NSC81-0208-M002-20), to Mr. Gene-Hsiang Lee (Advanced Instrumentation Center) for the X-ray measurement, and to Professor Yeun-Min Tsai (Department of Chemistry, National Taiwan University) for helpful discussions.

Supplementary Material Available: ^{13}C NMR spectra of compounds 7-22 (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.