Pergamon

Tetrahedron 58 (2002) 8067–8071

TETRAHEDRON

Study on direct benzoannelations of pyrrole and indole systems by domino reactions with 4,5-dicyanopyridazine

Donatella Giomi* and Marco Cecchi

Dipartimento di Chimica Organica 'Ugo Schiff', Polo Scientifico, Università di Firenze, Via della Lastruccia 13, I-50019 Sesto Fiorentino, Italy

Dedicated to Professor Rodolfo Nesi on the occasion of his retirement

Received 31 May 2002; revised 19 July 2002; accepted 8 August 2002

Abstract—The title pyridazine **1** was found to undergo hetero Diels–Alder [4+2] cycloadditions on the C(2)–C(3) double bond of pyrrole and indole systems; spontaneous loss of nitrogen from the primary adducts, followed by oxidation processes, afforded the corresponding fully aromatic benzoannelated skeletons in modest and reasonable yields, respectively. Competitive attacks of the same systems at the strongly electrophilic C-4 carbon of **1**, leading to substitution products, were evidenced.

1. Introduction

Although cyclisation processes of suitably substituted aromatic carbocycles still represent the methods of choice for the synthesis of indoles and carbazoles,[1] valuable alternative routes, based on cycloadditions of the title heteroaromatic systems,[2] have also been reported over the past decades. In particular, after the pioneering research of Noland and co-workers,[3] several 2- and 3-vinylindoles have been extensively employed as 4π electron components in Diels–Alder (DA) reactions with alkyne and alkene dienophiles affording dihydro- and tetrahydro-carbazoles, respectively.[4] The same reactions were extended to the conversion of 2- and 3-vinylpyrroles into indole derivatives in satisfactory yields.[4b,5] On the contrary, only few examples are known for the complementary annelation strategy involving the C(2)–C(3) double bond of the heterocyclic ring as a dienophilic moiety. Whereas some electron-deficient pyrroles and indoles were found to react with unactivated or nucleophilic dienes in normal electron-demand DA reactions,[6] *N*-methylpyrrole (**2**) and indole (**8**) were annelated with the extremely reactive tetrachlorothiophene-1,1-dioxide, which undergoes inverse electron-demand [4+2] cycloadditions followed by retro-chelotropic SO_2 extrusion.[7] The intramolecular version of both methodologies was successfully applied to the synthesis of complex indole alkaloids.[8]

Recent results from our laboratory clearly evidenced that 4,5-dicyanopyridazine (DCP) (**1**) easily enters as a strongly activated azadiene in hetero Diels–Alder (HDA) reactions. This offers with different 2π electron counterparts new and efficient approaches to carbo- and hetero-cage skeletons,[9] variously substituted phthalonitriles,[10] and dicyanocyclohexa-1,3-dienes,[11] through attractive domino processes. On this ground and in the light of preliminary data,[12] we decided to gain better insight into the possibility of exploiting **1** for direct pyrrole–indole and indole–carbazole conversions.

2. Results and discussion

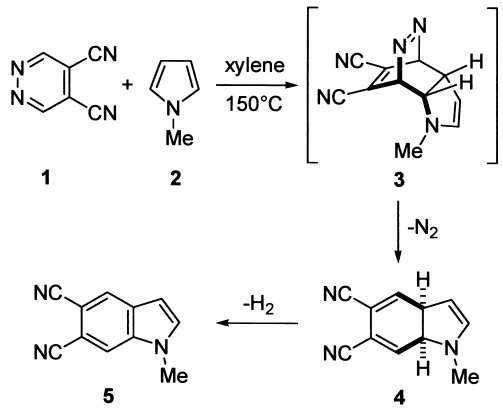
Treatment of DCP with an excess of *N*-methylpyrrole (**2**) (molar ratio 1:5) in xylene at 150°C for 48 h, afforded a very complex reaction mixture from which 5,6-dicyano-1-methylindole (**5**) was isolated as a pure product in 17% yield by careful chromatographic workup. Inverse electron-demand HDA cycloaddition of **1** on **2** leads to the labile tricyclic adduct **3**,[13] which gives rise to a retro-DA loss of nitrogen; the resulting dihydroindole **4** then evolves into **5** (Scheme 1). If the final aromatisation involves a concerted elimination of molecular hydrogen likely from a tautomeric cyclohexa-1,4-diene moiety of **4**, the benzoannelation of **2** can be regarded on the whole, apart from the protomeric equilibrium, as a three step pericyclic homodomino process.[14]

The modest yield of **5** can be accounted for bearing in mind that the starting pyrrole undergoes competitive nucleophilic displacements on the activated dicyanopyridazine **1** leading to compounds **6** and **7** (see below), that were recognised in the reaction mixture by ^{1}H NMR analysis. Moreover, the key intermediate **4** can suffer both from C(7a)–N(1)

Keywords: cycloadditions; 4,5-dicyanopyridazine; pyrrole, indole and carbazole derivatives; domino processes.

* Corresponding author. Tel.: +39-055-4573475; fax: +39-055-4573575; e-mail: donatella.giomi@unifi.it

0040–4020/02/$ - see front matter
PII: S0040-4020(02)00958-4

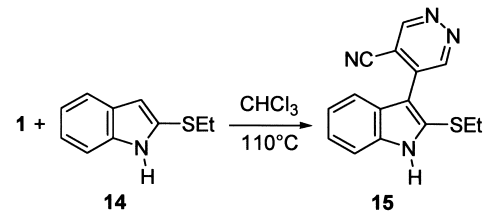


Scheme 1.

ring-opening[15] and further cycloaddition by DCP on the strongly dienophilic C(2)–C(3) double bond, affording styrene and tetrahydrocarbazole systems, respectively. The latter pathway largely predominated in the reaction of **2** with the above thiophene carbodiene, thus precluding isolation of monoannelated products.[7]

Attempts to achieve better results under different conditions failed. Replacement of xylene with chloroform allowed us to operate under milder conditions (110°C) but, after 8 days, the yield of **5** did not exceed 18%. Though the reaction was remarkably speeded up by CuI as catalyst, unfortunately we obtained only compounds **6** and **7** in 31 and 11% yields, respectively, as a consequence of an overwhelming predominance of substitution processes over the expected cycloaddition. Finally, when the reaction was performed in the presence of 10% Pd/C with the aim of favouring the final oxidation step,[16] the same regioisomers **6** and **7** were isolated as the main products together with a trace amount of **5** (Scheme 2).

On the contrary, satisfactory findings were gained on going from **2** to the more dienophilic indoles **8** and **11**. Indeed, heating of DCP with an excess of the former (molar ratio 1:2) in xylene at 150°C for 72 h, gave 2,3-dicyano-9*H*-carbazole (**9**) in 57% yield along with a minor amount (9%) of 3-(4-cyanopyridazin-5-yl)indole (**10**) (Scheme 3).



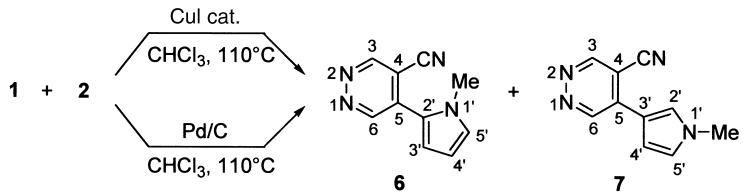
Scheme 4.

Analogously, when **1** was allowed to react with the latter (molar ratio 1:3) in chloroform at 110°C for 80 h, compounds **12** and **13** were isolated in 62 and 14% yields, respectively.

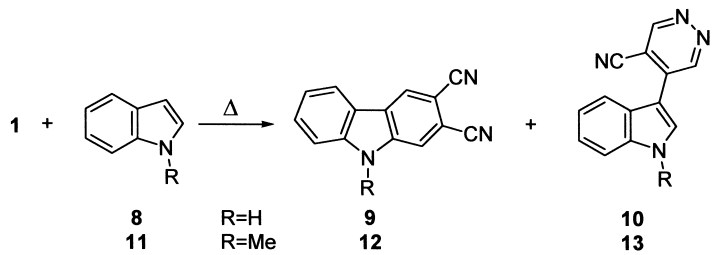
Efforts to further improve these results were unsuccessful. Although pyridine was proved to increase the reactivity of **8** as a dienophile in the cycloaddition with 2,3-bis(phenylsulfonyl)buta-1,3-diene,[17] the yield of **9** was notably reduced (23%) on behalf of **10** (32%) in the presence of the same base. On the other hand, whereas the ratio of **10** and **13** with respect to **9** and **12** was remarkably enhanced (ca. 3:1) by CuI as catalyst, the former products were obtained nearly exclusively with Pd/C as co-reagent (Section 4).

Whilst 3-acetoxy and 3-ethylthio-indole were completely inert towards DCP, compound **14** easily reacted with **1** but, unfortunately, only **15** was isolated in 92% yield (Scheme 4).

The structures of the new products **6**, **7**, **9**, **10**, **12**, **13**, and **15** followed from analytical and spectral data. In particular, even if both the H-3′ and H-2′ protons of the regioisomers **6** and **7** are strongly deshielded by the adjacent cyanopyridazine moiety with respect to the corresponding ones of **2** ($\Delta\delta$=0.99 and 1.29), they can be distinguished on the basis of the relative chemical shifts and multiplicities [δ 6.91 (dd) vs δ 7.66 (t)]. The ^{13}C NMR spectra of the carbazoles **9** and **12** are characterised by a diagnostic singlet at δ 102.7 and 102.5, respectively, for the C-3 carbon, which exhibits a remarkable upfield shift as a consequence of the electron delocalisation between the ring nitrogen and the CN group on this position. Finally, the structures of the



Scheme 2.



Scheme 3.

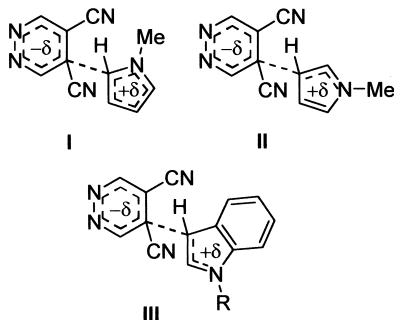


Figure 1.

3-(pyridazin-5-yl)indoles **10** and **13** rest on their ^{1}H NMR spectra showing a doublet and a singlet, respectively, at δ 8.27 for the H-2 proton; the latter was confirmed by a positive NOE effect detected between the methyl group and the same proton.

The above findings clearly show that the desired domino processes have to reckon with competitive S_NAr2 reactions on the strongly electrophilic C-4 carbon of **1**, leading to substitution products through the highly stabilised transition structures **I**–**III** of the rate determining steps (Fig. 1). Moreover, if the primary FMO controlled interactions with the soft pyrrole and indole nucleophiles can exploit the LUMO of **1** (E=0.067 eV) characterised by large coefficients at C-4 and C-5, the initial [4+2] cycloadditions must involve the corresponding LUMO+1 (E=1.636 eV) since the former shows two nodes on the C-3 and C-6 carbons.[18]

Eventually, whereas the observed effects of CuI are likely arisen from its chelation by the vicinal CN groups of **1**, the reaction patterns with Pd/C could be tentatively accounted for on the basis of concomitant or predominant metal-mediated oxidative couplings of the reagents, which certainly deserve further investigations.[19]

3. Conclusions

Although the results of this work are not so impressive as those previously obtained in the cycloaddition chemistry of DCP with other dienophiles,[9b,10] nevertheless, the transformations **2→5**, **8→9**, and **11→12** represent rare examples of direct conversion of pyrrole and indole systems into the corresponding, fully aromatic benzoannelated skeletons, simply achieved by domino reactions.

4. Experimental

4.1. General

Melting points were taken on a Büchi 510 apparatus and are uncorrected. IR spectra were measured as KBr pellets with a Perkin–Elmer 881 spectrophotometer. Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 solutions with a Varian-Gemini instrument operating at 200 and 50 MHz, respectively. Silica gel plates (Merck F_{254}) and silica gel 60 (Merck, 230–400 mesh) were used for TLC and flash chromatographies (FC), respectively; petroleum ether (PE), employed for chromatographic workup, refers to the fractions of bp 40–70°C.

4.2. Reactions of DCP (1) with compounds 2, 8, and 11. General procedure

A mixture of **1** (0.065 g, 0.5 mmol) and the reagent(s) in the specified solvent (0.5 ml) was heated under magnetic stirring in a screw-capped tube (Pyrex N. 13). The brown residue left by evaporation to dryness under reduced pressure was triturated with methanol (2×10 ml) and acetone (2×10 ml) and filtered; the solid obtained from the filtrates was subjected to FC.

4.2.1. 5,6-Dicyano-1-methylindole (5). (A) Careful chromatographic workup [PE/AcOEt (3:2 v/v)] of the solid coming from **1** and *N*-methylpyrrole (**2**) (0.203 g, 0.222 ml, 2.5 mmol) in xylene at 150°C for 48 h gave compound **5** (R_f=0.37, 0.015 g, 17%) as an ivory-coloured product: mp 257°C (after sublimation at 120–130°C/10^{-2} Torr) (lit.[20] mp 257–258°C); IR 3097, 3043, 2225, 1603, 1500 cm^{-1}; ^{1}H NMR δ 3.92 (s, 3H), 6.76 (dd, J=2.9, 0.7 Hz, 1H), 7.85 (d, J=2.9 Hz, 1H), 8.37 (s, 1H), 8.41 (d, J=0.7 Hz, 1H); ^{13}C NMR δ 33.4 (q), 103.25 (s), 103.3 (d), 104.6 (s), 117.8 (d), 117.9 (s), 117.95 (s), 128.05 (d), 130.25 (s), 136.4 (s), 136.5 (d).

(B) When the reaction was carried out in chloroform at 110°C for 8 days, compound **5** (0.016 g, 18%) was isolated.

4.2.2. 4-Cyano-5-(1-methylpyrrol-2-yl)pyridazine (6) and 4-cyano-5-(1-methylpyrrol-3-yl)pyridazine (7). (A) Chromatographic resolution [PE/AcOEt (1:1 v/v)] of the solid obtained by heating **1** and **2** (0.041 g, 0.045 ml, 0.5 mmol) in the presence of CuI (0.010 g), in $CHCl_3$ at 110°C for 24 h, afforded compound **6** (R_f=0.30, 0.029 g, 31%) as yellow crystals: mp 136–137°C (from ether); IR 3134, 3114, 2229, 1557 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 3H), 6.36 (dd, J=4.0, 2.6 Hz, 1H), 6.91 (dd, J=4.0, 1.5 Hz, 1H), 6.99 (dd, J=2.6, 1.5 Hz, 1H), 9.24 (d, J=1.1 Hz, 1H), 9.35 (d, J=1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 36.0 (q), 108.7 (s), 110.7 (d), 115.3 (s), 117.2 (d), 124.4 (s), 130.2 (d), 132.2 (s), 150.15 (d), 151.3 (d). Anal. Calcd for $C_{10}H_8N_4$: C, 65.21; H, 4.38; N, 30.42. Found: C, 65.40; H, 4.27; N, 30.19.

The following band yielded the derivative **7** (R_f=0.20, 0.010 g, 11%) as a yellow-orange solid which, after crystallisation from ether, gradually darkened above 120°C and melted at 147–148°C; IR 3112, 2227, 1563 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.78 (s, 3H), 6.77 (dd, J=2.9, 1.8 Hz, 1H), 6.83 (dd, J=2.9, 1.8 Hz, 1H), 7.66 (t, J=1.8 Hz, 1H), 9.06 (d, J=1.1 Hz, 1H), 9.43 (d, J=1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 37.0 (q), 104.7 (s), 108.4 (d), 115.6 (s), 116.5 (s), 124.8 (d), 125.0 (d), 135.1 (s), 149.3 (d), 151.2 (d). Anal. Calcd for $C_{10}H_8N_4$: C, 65.21; H, 4.38; N, 30.42. Found: C, 64.97; H, 4.40; N, 30.54.

(B) When the reaction of **1** with **2** was carried out in the presence of Pd/C (10%, 0.065 g) for 5 days, compounds **6** (0.028 g, 30%) and **7** (0.013 g, 14%) were isolated together with a trace amount of DCP.

4.2.3. 2,3-Dicyano-9*H*-carbazole (9) and 3-(4-cyanopyridazin-5-yl)indole (10). (A) The crude product from the

reaction of **1** with indole (**8**) (0.117 g, 1 mmol) in xylene at 150°C for 72 h was resolved into two components with toluene/AcOEt (5:1 v/v). The first band gave compound **9** (R_f=0.21, 0.062 g, 57%) as an ivory-coloured solid that, after crystallisation from ethanol, gradually darkened above 270°C and melted at 288°C; IR 3354, 2229, 1630, 1604 cm^{-1}; ^1H NMR δ 7.34 (ddd, J=8.0, 6.5, 1.6 Hz, 1H), 7.54–7.67 (m, 2H), 8.21 (s, 1H), 8.29 (d, J=8.0 Hz, 1H), 8.94 (s, 1H), 12.36 (br s, 1H); ^{13}C NMR δ 102.7 (s), 109.5 (s), 112.4 (d), 117.45 (s), 117.7 (d), 117.9 (s), 121.0 (s), 121.1 (d), 122.0 (d), 125.4 (s), 127.45 (d), 128.9 (d), 140.1 (s), 141.6 (s). Anal. Calcd for $C_{14}H_7N_3$: C, 77.41; H, 3.25; N, 19.34. Found: C, 77.59; H, 3.35; N, 19.28.

The following one afforded the derivative **10** (R_f=0.05, 0.010 g, 9%) as a yellow solid that, after crystallisation from AcOEt, gradually darkened above 250°C and melted at 289°C (dec.); IR 3147, 3119, 3063, 3042, 2236, 1529 cm^{-1}; ^1H NMR δ 7.19–7.35 (m, 2H), 7.56–7.63 (m, 1H), 7.89–7.96 (m, 1H), 8.27 (d, J=3.2 Hz, 1H), 9.51 (d, J=1.0 Hz, 1H), 9.78 (d, J=1.0 Hz, 1H), 12.24 (br s, 1H); ^{13}C NMR δ 107.3 (s), 107.35 (s), 113.1 (d), 116.7 (s), 119.8 (d), 121.65 (d), 123.3 (d), 124.4 (s), 130.4 (d), 136.1 (s), 137.2 (s), 151.1 (d), 151.9 (d). Anal. Calcd for $C_{13}H_8N_4$: C, 70.90; H, 3.66; N, 25.44. Found: C, 71.04; H, 3.87; N, 25.18.

(B) Chromatographic workup [PE/AcOEt (2:1 v/v)] of the solid coming from the reaction of **1** with **8** in the presence of pyridine (0.079 g, 0.081 ml, 1 mmol), under the above conditions, gave compounds **9** (R_f=0.41, 0.025 g, 23%) and **10** (R_f=0.15, 0.035 g, 32%).

(C) When DCP was allowed to react with **8** (0.059 g, 0.5 mmol) and CuI (0.010 g) in $CHCl_3$ at 110°C for 72 h, a 3:1 mixture of **10** and **9** (0.065 g, ^1H NMR) was obtained.

(D) Chromatographic workup [PE/AcOEt (1:2 v/v)] of the raw product coming from the reaction of **1** with **8** (0.059 g, 0.5 mmol) and Pd/C (10%, 0.065 g) in $CHCl_3$ at 110°C for 48 h afforded compound **10** (R_f=0.48, 0.039 g, 35%).

4.2.4. 2,3-Dicyano-9-methyl-9*H*-carbazole (12) and 3-(4-cyanopyridazin-5-yl)-1-methylindole (13). (A) The solid obtained from **1** and **11** (0.197 g, 0.192 ml, 1.5 mmol) in $CHCl_3$ at 110°C for 80 h, was resolved into two components with PE/AcOEt (7:2 v/v). The first band gave compound **12** (R_f=0.39, 0.072 g, 62%) as ivory-coloured needles: mp 232–233°C (from ethanol); IR 3062, 2225, 1624, 1590 cm^{-1}; ^1H NMR δ 3.85 (s, 3H), 7.28–7.37 (m, 1H), 7.58–7.63 (m, 2H), 8.20 (d, J=8.0 Hz, 1H), 8.29 (s, 1H), 8.77 (s, 1H); ^{13}C NMR δ 29.7 (q), 102.5 (s), 109.4 (s), 110.5 (d), 116.0 (d), 117.4 (s), 117.7 (s), 120.6 (s), 121.2 (d), 121.8 (d), 124.6 (s), 126.9 (d), 128.9 (d), 140.6 (s), 142.2 (s). Anal. Calcd for $C_{15}H_9N_3$: C, 77.91; H, 3.92; N, 18.17. Found: C, 77.88; H, 4.21; N, 17.87.

The following one yielded compound **13** (R_f=0.05, 0.016 g, 14%) as a yellow solid: mp 204–205°C (from AcOEt); IR 3110, 3050, 2234, 1614, 1555 cm^{-1}; ^1H NMR δ 3.96 (s, 3H), 7.24–7.42 (m, 2H), 7.63–7.69 (m, 1H), 7.91–7.96 (m, 1H), 8.27 (s, 1H), 9.50 (d, J=0.9 Hz, 1H), 9.75 (d, J=0.9 Hz, 1H); ^{13}C NMR δ 33.6 (q), 106.4 (s), 107.2 (s), 111.5 (d), 116.55 (s), 120.0 (d), 121.9 (d), 123.4 (d), 124.8 (s), 133.8 (d), 135.6 (s), 137.7 (s), 151.0 (d), 151.9 (d). Anal. Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30; N, 23.92. Found: C, 72.03; H, 4.22; N, 24.09.

(B) When DCP was reacted with **11** (0.066 g, 0.064 ml, 0.5 mmol) and CuI (0.010 g) in $CHCl_3$ at 110°C for 24 h, a 3:1 mixture of **13** and **12** (0.070 g, ^1H NMR) was obtained.

(C) Chromatographic resolution [PE/AcOEt (2:1 v/v)] of the solid from the reaction of **1** with **11** (0.066 g, 0.064 ml, 0.5 mmol) and Pd/C (10%, 0.065 g) in $CHCl_3$ at 110°C for 72 h, yielded compounds **12** (R_f=0.5, 0.010 g, 9%) and **13** (R_f=0.2, 0.082 g, 70%).

4.2.5. 3-(4-Cyanopyridazin-5-yl)-2-ethylthioindole (15). A mixture of DCP (0.065 g, 0.5 mmol) and 2-ethylthioindole (**14**)[21] (0.097 g, 0.55 mmol) in $CHCl_3$ (0.5 ml) was stirred at 110°C in a screw-capped tube (Pyrex N. 13) for 60 h. Chromatographic workup [PE/AcOEt (5:2 v/v)] of the residue left by evaporation to dryness, gave compound **15** (R_f=0.3, 0.129 g, 92%) as yellow-orange needles: mp 211–212°C (from $CHCl_3$); IR 3162, 3096, 3076, 2229, 1536 cm^{-1}; ^1H NMR δ 1.07 (t, J=7.3 Hz, 3H), 2.99 (q, J=7.3 Hz, 2H), 7.14–7.35 (m, 2H), 7.48–7.62 (m, 2H), 9.64 (d, J=1.0 Hz, 1H), 9.67 (d, J=1.0 Hz, 1H), 12.8 (br s, 1H); ^{13}C NMR δ 14.5 (q), 29.5 (t), 111.3 (s), 111.6 (s), 111.65 (d), 115.4 (s), 118.6 (d), 120.8 (d), 123.3 (d), 125.3 (s), 131.1 (s), 135.5 (s), 136.9 (s), 151.2 (d), 152.7 (d). Anal. Calcd for $C_{15}H_{12}N_4S$: C, 64.26; H, 4.32; N, 19.98. Found: C, 63.96; H, 4.15; N, 20.00.

Acknowledgements

We wish to thank Mrs Brunella Innocenti for the analytical data.

References

1. (a) Sundberg, R. J. Pyrroles and their Benzo Derivatives: Synthesis and Applications. *Comprehensive Heterocyclic Chemistry*, Bird, C. W., Cheeseman, G. W. H., Eds.; Pergamon: Oxford, 1984; Vol. 4, pp 313–376. (b) Sundberg, R. J. Pyrroles and their Benzo Derivatives: Synthesis. *Comprehensive Heterocyclic Chemistry II*, Bird, C. W., Ed.; Pergamon: Oxford, 1996; Vol. 2, pp 119–206. (c) Gribble, G. W. *J. Chem. Soc. Perkin Trans. 1* **2000**, 1045–1075.
2. Quinodimethane derivatives are not considered.
3. Noland, W. E.; Kuryla, W. C.; Lange, R. F. *J. Am. Chem. Soc.* **1959**, *81*, 6010–6017.
4. (a) Sundberg, R. J. Synthetic Elaboration of Indole Derivatives using Cycloaddition Reactions. *Indoles*, Meth-Cohn, O., Ed.; Academic: London, 1996; Chapter 16. (b) Hosmane, R. S.; Hiremath, S. P.; Schneller, S. W. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2450–2453. (c) Bergamasco, R.; Porter, Q. N.; Yap, C. *Aust. J. Chem.* **1977**, *30*, 1531–1544. (d) Bergamasco, R.; Porter, Q. N.; Yap, C. *Aust. J. Chem.* **1978**, *31*, 1841–1844. (e) Noland, W. E.; Wann, S. R. *J. Org. Chem.* **1979**, *44*, 4402–4410. (f) Lambert, J. D.; Porter, Q. N. *Aust. J. Chem.* **1981**, *34*, 1483–1490. (g) Reed, G. W. B.; Cheng, P. T. W.; McLean, S. *Can. J. Chem.* **1982**, *60*, 419–424.

5. (a) Jones, R. A.; Marriott, M. T. P.; Rosenthal, W. P.; Sepulveda Arques, J. *J. Org. Chem.* **1980**, *45*, 4515–4519. (b) Noland, W. E.; Kim, K. J.; Lee, C. K.; Bae, S. K.; Hahn, C. S. *J. Org. Chem.* **1980**, *45*, 4582–4584. (c) Jones, R. A.; Aznar Saliente, T.; Sepulveda Arques, J. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2541–2543. (d) Muchowski, J. M.; Scheller, M. E. *Tetrahedron Lett.* **1987**, *28*, 3453–3456.
6. (a) Wenkert, E.; Moeller, P. D. R.; Piettre, S. R. *J. Am. Chem. Soc.* **1988**, *110*, 7188–7194. (b) Kraus, G. A.; Raggon, J.; Thomas, P. J.; Bougie, D. *Tetrahedron Lett.* **1988**, *29*, 5605–5608.
7. Raasch, M. S. *J. Org. Chem.* **1980**, *45*, 856–867.
8. (a) Eberle, M. K.; Shapiro, M. J.; Stucki, R. *J. Org. Chem.* **1987**, *52*, 4661–4665. (b) Kraus, G. A.; Thomas, P. J.; Bougie, D.; Chen, L. *J. Org. Chem.* **1990**, *55*, 1624–1627.
9. (a) Nesi, R.; Giomi, D.; Turchi, S.; Paoli, P. *Tetrahedron* **1994**, *50*, 9189–9194. (b) Giomi, D.; Nesi, R.; Turchi, S.; Coppini, R. *J. Org. Chem.* **1996**, *61*, 6028–6030. (c) Giomi, D.; Nesi, R.; Turchi, S.; Mura, E. *J. Org. Chem.* **2000**, *65*, 360–364.
10. Turchi, S.; Nesi, R.; Giomi, D. *Tetrahedron* **1998**, *54*, 1809–1816.
11. (a) Turchi, S.; Giomi, D.; Capaccioli, C.; Nesi, R. *Tetrahedron* **1997**, *53*, 11711–11720. (b) Nesi, R.; Turchi, S.; Giomi, D.; Corsi, C. *Tetrahedron* **1998**, *54*, 10851–10856.
12. Nesi, R.; Giomi, D.; Turchi, S.; Falai, A. *J. Chem. Soc., Chem. Commun.* **1995**, 2201–2202.
13. The stereochemistry of **3** is portrayed arbitrarily.
14. For a proper definition and classification of domino reactions, see: Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136.
15. For a similar example, see: Benson, S. C.; Gross, J. L.; Snyder, J. K. *J. Org. Chem.* **1990**, *55*, 3257–3269.
16. A positive effect of this co-reagent was previously observed for the reaction of **1** with styrene. See Ref. 11a.
17. Padwa, A.; Gareau, Y.; Harrison, B.; Rodriguez, A. *J. Org. Chem.* **1992**, *57*, 3540–3545.
18. Hartree–Fock molecular orbital calculations were performed at the 3-21G* level of theory using the Spartan 3.1 program, Wavefunction, Inc.
19. For coupling reactions carried out under similar conditions, see: (a) Sakamoto, T.; Arakida, H.; Edo, K.; Yamanaka, H. *Heterocycles* **1981**, *16*, 965–968. (b) Sakamoto, T.; Arakida, H.; Edo, K.; Yamanaka, H. *Chem. Pharm. Bull.* **1982**, *30*, 3647–3656.
20. Duflos, J.; Dupas, G.; Quéguiner, G. *J. Heterocycl. Chem.* **1983**, *20*, 1191–1193.
21. Plate, R.; Ottenheijm, H. C. J. *Tetrahedron* **1986**, *42*, 4511–4516.