Efficient Syntheses of Substituted Carbazoles and Cyclopent[*b*]indoles from 1-Methyl-3-(benzotriazol-1-ylmethyl)indole

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1-Methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) undergoes lithiation and 1,4-addition with a variety of α,β-unsaturated ketones and aldehydes. Subsequent treatment with an acidic resin in refluxing 1,4-dioxane causes intramolecular cyclization followed by aromatization to furnish a wide range of 1,3-di-, 2,3-di-, and 1,2,3-trisubstituted carbazoles **6a**−**j** and **8** in moderate to excellent yields. NMR study is described to discriminate between structures of types **6** and **8** on the basis of $^{1}H-^{13}C$ long-range correlation. Treatment of **1** with styrenes in the presence of zinc bromide results in formal [3 + 2] cycloaddition to give cyclopent[*b*]indoles **14a**−**c** in good yields. When **1** is first lithiated and reacts with electrophiles, the resulting alkylation products undergo similar [3 + 2] additions with styrenes to give 1-functionalized cyclopent[*b*]indoles **15** and **16** with a high degree of stereoselectivity.

Introduction

Synthetic approaches to substituted carbazoles are of special interest and contemporary importance[1] since the growing variety of carbazole alkaloids isolated show antimicrobial,[2] antiviral,[3] and cytotoxic properties.[4] Major methods for the preparation of carbazoles include the following: (i) dehydrogenation of 1,2,3,4-tetrahydrocarbazoles which are usually prepared by Fischer indole syntheses,[5] (ii) reductive cyclizations of 2-nitrobiphenyls,[6] (iii) thermal,[7] photolytic,[8] and palladium-promoted[9] cyclizations of diphenylamines, (iv) iron-mediated oxidative coupling of 1,3-cyclohexadiene and arylamines,[10] and (v) [*b*]-annulations of indole skeletons.[11] Many methods of types i−iv are problematic for the synthesis of highly substituted carbazoles involving multistep preparations of appropriate precursors, harsh reaction conditions, or poor regioselectivity of the cyclization step. Accordingly, approaches *via* the [*b*]-annulation of indole skeletons are of special importance. The most important methods that fall into this category include (a) thermal-induced and photoinduced electrocyclizations of 2,3-divinylindoles,[11h] (b) 1,4-additions of indolo-2,3-quinodimethanes[11a,e] and of vinylindoles[11g] with dienophiles, and (c) addition of α-carbanions at C-2 of indoles with Michael acceptors, followed by intramolecular cyclization with the ester group at the indole 3-position.[11b,f]

The cyclopent[*b*]indole structural element occurs in a large number of indole alkaloids, including the structurally complex tremorgenic mycotoxins[12] and the monoterpenoid yuehchukene.[13] In accordance with the importance of compounds possessing this skeleton, a number of methods have been developed for its construction. However, few approaches are preparatively efficient, the most useful being the ring closure of unsaturated 3-acylindoles[14] and the [3 + 2] addition of indole-2- or 3-methanols with alkenes.[15] However, the former requires strongly acidic conditions and the latter frequently suffers from unsatisfactory yields.

Our recent work has demonstrated the versatility of benzotriazolylalkyl-substituted heterocycles for the synthesis of 1,1-bis(heteroaryl)alkanes[16] and the utility of 1-methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) for the synthesis of a wide range of 3-substituted indoles[17] and

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(1) For some excellent reviews, see: (a) Bhattacharyya, P.; Chakraborty, D. P. *Prog. Chem. Org. Nat. Prod.* **1987**, *52*, 159. (b) Chakraborty, D. P.; Roy, S. *Prog. Chem. Org. Nat. Prod.* **1991**, *57*, 71. (c) Bergman, J.; Pelcman, B. *Pure Appl. Chem.* **1990**, *62*, 1967. (d) Pindur, U. *Chimia* **1990**, *44*, 406. (e) Knölke, H.-J. *Synlett* **1992**, 371.

(2) Naid, T.; Kitahara, T.; Kaneda, M.; Nakamura, S. *J. Antibiot.* **1987**, *40*, 157.

(3) TePaske, M. R.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *J. Org. Chem.* **1989**, *54*, 4743.

(4) TePaske, M. R.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *Tetrahedron Lett.* **1989**, *30*, 5965.

(5) (a) Crum, J. D.; Sprague, P. W. *J. Chem. Soc., Chem. Commun.* **1966**, 417. (b) Chakraborty, D. P.; Chowdhury, B. K. *J. Org. Chem.* **1968**, *33*, 1265.

(6) Kureel, S. P.; Kapil, R. S.; Popli, S. P. *J. Chem. Soc., Chem. Commun.* **1969**, 1120.

(7) Islam, A.; Bhattacharyya, P.; Chakraborty, D. P. *J. Chem. Soc., Chem. Commun.* **1972**, 537.

(8) Carruthers, W. *J. Chem. Soc., Chem. Commun.* **1966**, 272.

(9) Akermark, B.; Eberson, L.; Jonsson, E.; Pettersson, E. *J. Org. Chem.* **1975**, *40*, 1365.

(10) For examples, see: (a) Birch, A. J.; Liepa, A. J.; Stephenson, G. R. *Tetrahedron Lett.* **1979**, 3565. (b) Knölker, H.-J.; Bauermeister, M. *J. Chem. Soc., Chem. Commun.* **1989**, 1468. (c) Knölker, H.-J.; Bauermerster, M. *J. Indian Chem. Soc.* **1994**, *71*, 345 and references cited therein.

(11) For recent examples, see: (a) Rao, M. V. B.; Satyanarayana, J.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* **1995**, *36*, 3385. (b) Mohanakrishnan, A. K.; Srinivasan, P. C. *Tetrahedron Lett.* **1993**, *34*, 1343. (c) Bergman, J.; Pelcman, B. *Tetrahedron Lett.* **1986**, *27*, 1939. (d) Wasserman, H. H.; van Duzer, J. H.; Vu, C. B. *Tetrahedron Lett.* **1990**, *31*, 1609. (e) Saroja, B.; Srinivasan, P. C. *Tetrahedron Lett.* **1984**, *25*, 5429. (f) Mali, R. S.; Jagtap, P. G. *Tetrahedron Lett.* **1992**, *33*, 1655. (g) Pindur, U.; Otto, C. *Chem. Lett.* **1992**, 403. (h) Kawasaki, T.; Sakamoto, M. *J. Indian Chem. Soc.* **1994**, *71*, 443 and references cited therein.

(12) Steyn, P. S.; Vleggar, R. *Fortschr. Chem. Org. Naturst.* **1985**, 1.

(13) (a) Cheng, K.-F.; Cao, G.-A.; Yu, Y.-W. *Synth. Commun.* **1994**, *24*, 65. (b) Henry, K. K. J., Jr.; Grieco, P. A. *J. Chem. Soc., Chem. Commun.* **1993**, 510. (c) Bergman, J.; Venemalm, L. *Tetrahedron* **1992**, *48*, 759. (d) Sheu, J.-H.; Chen, Y.-K.; Hong, Y.-L. V. *Tetrahedron Lett.* **1991**, *32*, 1045.

(14) (a) Bergman, J.; Venemalm, L. *Tetrahedron Lett.* **1987**, *28*, 3741. (b) Bergman J.; Venemalm, L.; Gogoll, A. *Tetrahedron* **1990**, *46*, 6067.

(15) (a) Harrison, C.-A.; Leineweber, R.; Moody, C. J.; Williams, J. M. J. *Tetrahedron Lett.* **1993**, *34*, 8527. (b) Harrison, C.-A.; Leineweber, R.; Moody, C. J.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1127.

(16) Katritzky, A. R.; Xie, L.; Fan, W.-Q. *J. Org. Chem.* **1993**, *58*, 4376.

(17) Katritzky, A. R.; Xie, L.; Cundy, D. *Synth. Commun.* **1995**, *25*, 539.

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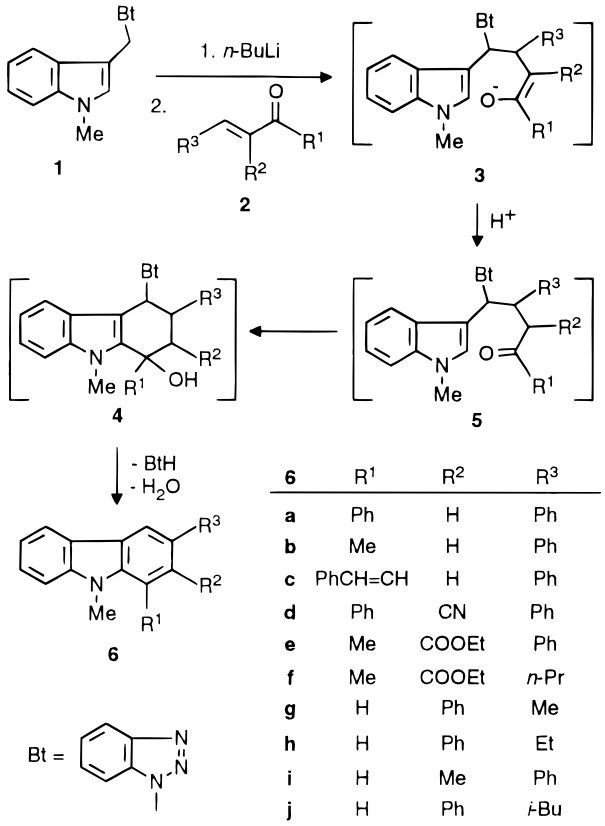
Scheme 1



6	R^1	R^2	R^3
a	Ph	H	Ph
b	Me	H	Ph
c	PhCH=CH	H	Ph
d	Ph	CN	Ph
e	Me	COOEt	Ph
f	Me	COOEt	*n*-Pr
g	H	Ph	Me
h	H	Ph	Et
i	H	Me	Ph
j	H	Ph	*i*-Bu

heterocyclo[*b*]-fused carbazoles.[18] The chemistry of compound **1** has now been further developed to provide facile and efficient routes to substituted carbazoles and cyclopenta[*b*]indoles.

Results and Discussion

Synthesis of Substituted Carbazoles. The requisite 1-methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) was readily prepared from 1-methylindole and 1-(hydroxymethyl)benzotriazole as described in our earlier work.[17] Due to the electron-withdrawing ability of the benzotriazolyl group,[17,19] compound **1** can be easily deprotonated at the side-chain CH_2 group. Thus, treatment of **1** with *n*-butyllithium at −78 °C, under argon in THF, furnished a deep green solution of the lithio derivative of **1**. Reactions of this anion with α,*β*-unsaturated ketones or aldehydes, followed by refluxing in 1,4-dioxane in the presence of an acidic resin (Amberlyst-15), formed a wide variety of 1,3-di-, 2,3-di-, or 1,2,3-trisubstituted carbazoles **6a**−**i** in moderate to excellent yields (Scheme 1). These transformations are envisioned to proceed *via* 1,4-addition of the anion of **1** to α,*β*-unsaturated carbonyl compounds to form intermediates **3**, which were protonated to ketones **5**. Acid-catalyzed cyclization of **5** followed by concurrent elimination of molecules of benzotriazole and water afforded the desired products **6** (for reviews of benzotriazole as a leaving group see refs 19 and 20).

It is well demonstrated in the literature that the alkylation of indole at C2 can occur by alkylation at C3 followed by rearrangement.[20,21] Accordingly, the ring closure of ketones **5** could have occurred directly at the indole 2-position to give intermediates **4** leading to products **6**, or first at the 3-position to give the corresponding spiro-3*H*-indolium cations of type **7** (Scheme 2), followed by the migration of either **a** or **b** bond to give in each case two regioisomers of types **6** and **8**. Interestingly, in all cases except **6j**, single regioisomers **6a**−**i** were obtained. The other expected regioisomers of type **8** were not detected, which might imply the direct C2 ring closure of **5a**−**i**. When α,*β*-unsaturated aldehyde **2j** (Scheme 2) was used as the substrate, an inseparable mixture of **6j** and **8** was obtained in a ratio of 2:3, demonstrating the existence of the intermediate **7**. However, the reason for the different behavior of intermediate **5j** from **5a**−**i** is not yet clear.

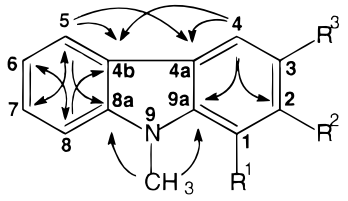
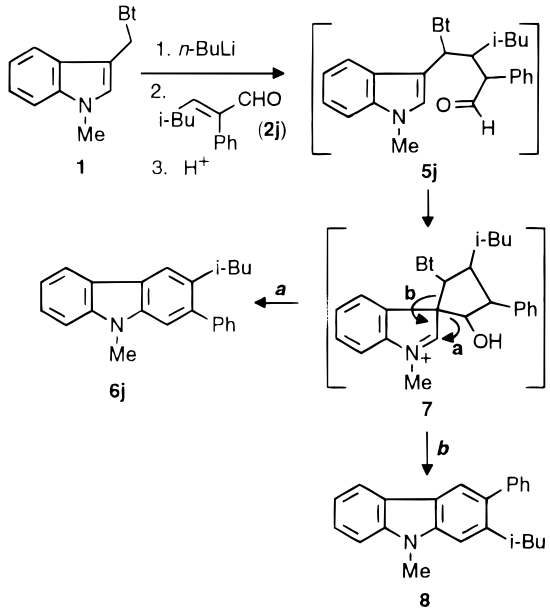


Figure 1. Position numbering and long-range polarization transfer from protons to carbons in compounds **6a**−**j** and **8**, as seen in the LRHETC spectrum.

Scheme 2



The structures of **6a**−**j** and **8** are fully supported by elemental analyses and NMR spectral data (see Experimental Section). Discrimination between structures of types **6** and **8** was made on the basis of $^1H-^{13}C$ long-range correlations between the protons/carbons of the R^1-R^3 groups and the protons/carbons at the carbazole ring (see Figure 1 and supporting information). Complete ^1H and ^{13}C chemical shift assignments were made on the basis of the $^1H-^{13}C$ direct (HETCOR) and long range (LRHETC) correlations. The HETCOR experiment was run skipping the BIRD module in the pulse sequence,

(18) Katritzky, A. R.; Xie, L. *J. Org. Chem.* **1995**, *60*, 3707.
(19) Katritzky, A. R.; Yang, Z.; Cundy, D. J. *Aldrichimica Acta* **1994**, *27*, 31.
(20) (a) Katritzky, A. R.; Rachwal, S.; Hitchings, G. J. *Tetrahedron* **1991**, *47*, 2683. (b) Katritzky, A. R.; Lan, X. *Chem. Soc. Rev.* **1994**, 363. (c) Katritzky, A. R.; Lan, X.; Fan, W.-Q. *Synthesis* **1994**, 445.
(21) (a) Joule, J. A. *Heterocyclic Chemistry*; Chapman & Hall: London, U.K.; 1995. (b) Biswas, K. M.; Jackson, A. H. *Tetrahedron* **1969,** *25*, 227. (c) Hamel, P.; Preville, P. *J. Org. Chem.* **1996**, *61*, 1573.

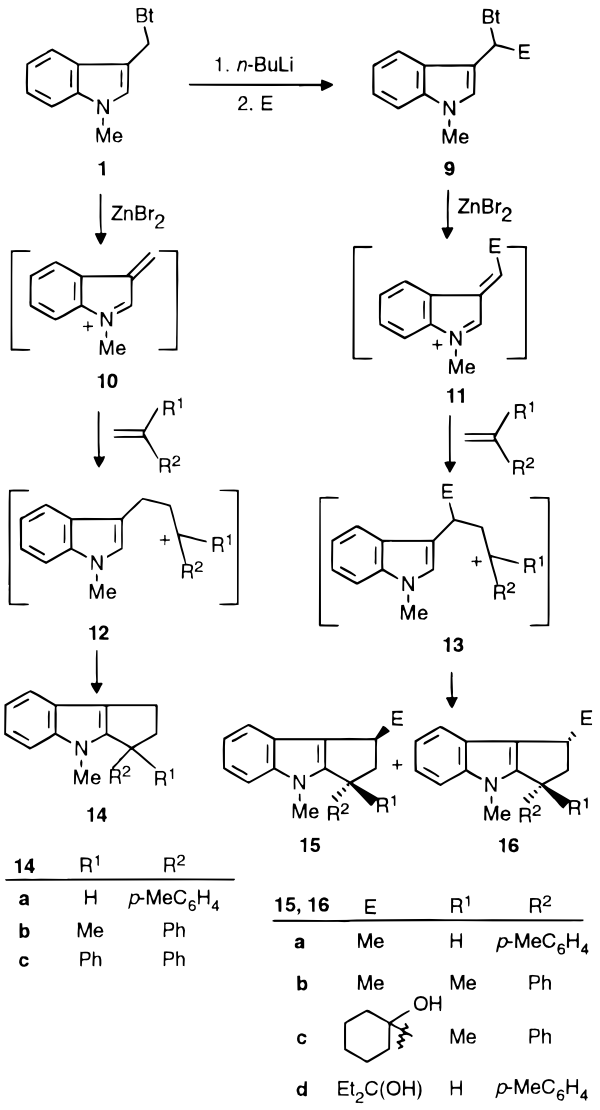
thus preserving the $^1H-^1H$ couplings in the f_1 dimension.[22] The LRHETC experiments employed the pulse sequence proposed by Krishnamurthy[23] which suppresses the direct $^1H-^{13}C$ couplings. The polarization transfers from protons to carbons as seen in the LRHETC experiment are represented by arrows in Figure 1 and supporting information. The chemical shift assignments are briefly presented below for one typical compound.

Two quaternary carbons, 8a and 9a, correlate at long range with the protons of the methyl group in position 9. The carbon in position 8a also displayed long-range correlations with the protons in positions 5 (doublet) and 7 (triplet). The ^1H and ^{13}C chemical shifts for positions 6, 8, and 4b were assigned on the basis of their mutual long-range couplings and proton multiplicity in the HETCOR spectrum. Carbon 4a was recognized on the basis of its chemical shift similar to that of 4b and on the basis of polarization transfer from proton 5. Proton 4 was identified on the basis of long-range correlations with carbons 9a, 4a, and 4b; the long-range correlation of H-4 with carbon 2 allowed the assignment of C-2. The chemical shift assignments made as described above are presented in Tables 1 (^1H) and 2 (^{13}C) (supporting information). The chemical shift assignments for groups R^1-R^3 and carbons 1 and 3 are presented in Figure 2 (supporting information), together with the long-range proton to carbon polarization transfers (over two or three bonds) which allowed discrimination between structures **6** and **8**.

In summary, a general, facile route to substituted carbazoles has been developed starting from readily available 1-methyl-3-(benzotriazol-1-ylmethyl)indole (**1**). An attractive feature of this approach is that by appropriate choice of the α,β-unsaturated ketones and aldehydes, a wide range of 1,3-di-, 2,3-di-, and 1,2,3-trisubstituted carbazoles becomes readily accessible. This route will complement the literature methods *via* the [*b*]-annulation of indole skeletons (a)−(c) already discribed. Thus, route (a) *via* 1,6-π-electrocyclization of 2,3-divinylindoles is versatile in view of the substituents incorporated into the carbazole nuclei and has been successfully used in the synthesis of many carbazole alkaloids. However, the preparation of the appropriately substituted 2,3-divinylindole precursors is often a multistep operation. Approaches (b) and (c) normally produce carbazoles substituted with electron-withdrawing substituents, especially CN and CO_2R groups. Thus, our general synthetic route to other types of substituted carbazoles from readily available starting materials should be of significant utility.

Synthesis of Cyclopent[*b*]indoles. Our earlier work demonstrated that (benzotriazolylmethyl)indoles reversibly ionize to yield the benzotriazolate anion and the corresponding indolylmethyl cations in the presence of Lewis acids or upon heating.[16−18] Due to such ionization, the benzotriazole auxiliary group can be displaced by various nucleophiles. Following a similar protocol, it seems possible that alkenes could function as nucleophiles to induce formal [2 + 3] cycloadditions with the (benzotriazolylmethyl)indoles **1** and **9**. This indeed proved to be the case, and we now report that the reaction provides a simple route to a range of cyclopent[*b*]indoles **14**−**16**.

Scheme 3



14	R^1	R^2
a	H	*p*-MeC_6H_4
b	Me	Ph
c	Ph	Ph

15, 16	E	R^1	R^2
a	Me	H	*p*-MeC_6H_4
b	Me	Me	Ph
c		Me	Ph
d	$Et_2C(OH)$	H	*p*-MeC_6H_4

Thus, treatment of compound **1** with zinc bromide followed by the addition of the appropriate styrene afforded cyclopent[*b*]indoles **14a**−**c** in 61−72% yields (Scheme 3) *via* the addition of cation **10** to styrenes and subsequent ring closure of the intermediate benzylic cations **12**. While reactions of **1** with β-unsubstituted styrenes were successful, the use of β-substituted styrenes (*e.g.* β-methylstyrene) provided no detectable cyclopent[*b*]indoles. This observation contrasts the results seen in the cycloadditions of benzylic cations with styrenes, where a β-substituent is necessary for successful cycloaddition by slowing down styrene polymerization.[24] Thus, our method extends and complements Moody's [2 + 3] cycloadditions of indole-3-methanols with β-substituted styrenes.[15]

Since compound **1** can be readily lithiated and alkylated (*vide supra*), this strategy was successfully extended to the facile synthesis of 1-functionalized cyclopent[*b*]indoles from intermediates **9**. Accordingly, treatment of **1** with 1.2 equiv of *n*-butyllithium (−78 °C, THF) followed by the addition of appropriate electrophiles (methyl iodide for **15a** + **16a** and **15b** + **16b**, cyclohexanone for **15c** + **16c**, and pentanone for **15d** + **16d**) gave the corresponding alkylation products **9**. After workup, the crude

(22) Bax, A. *J. Magn. Reson.* **1983**, *53*, 517.
(23) Krishnamurthy, V. V.; Nunlist, R. *J. Magn. Reson.* **1988**, *80*, 280.
(24) Angle, S. R.; Arnaiz, D. O. *J. Org. Chem.* **1992**, *57*, 5937.

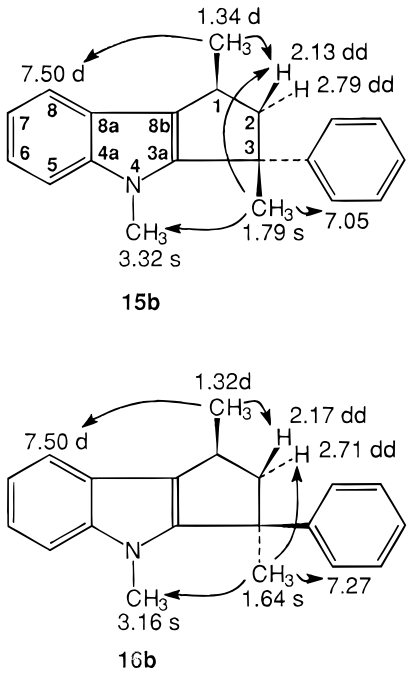


Figure 3. Position numbering NOE effects in compounds **15b** and **16b**.

compounds **9** reacted with styrenes *via* intermediates **11** and **13** in the presence of zinc bromide to furnish in each case a mixture of diastereoisomeric cyclopent[*b*]indoles (**15** and **16**) in good yields with the *trans* isomer **15** largely predominant (19:1 for **15a**/**16a**, 30:1 for **15b**/**16b**, 15:1 for **15c**/**16c**, and 18:1 for **15d**/**16d**, based on the GC−MS and NMR analyses of the crude reaction mixtures). Compounds **14**−**16** are new, and their structures were confirmed by elemental analyses and NMR spectral data (Experimental Section).

Just as for the cyclization of compounds **5** in the synthesis of carbazoles described above, ring closure of the benzylic cations (**12** and **13**) could occur either directly at the indole 2-position or first at the 3-position to give the corresponding 4-membered spiroindolenine intermediates, followed by the migration of one of the two alkyl groups. 3,3-Disubstituted indolenines have proved to be intermediates to cyclopent[*b*]indoles in some cases,[25] but this mechanism seems unlikely in the present examples since a second regioisomer would be expected and none was detected.

The regiochemistry and *cis*−*trans* stereochemistry of products **15** and **16** were clarified by NOE difference spectroscopy as exemplified by the study on **15b** and **16b**. A 2:1 mixture of **15b** and **16b**, obtained by column chromatography, showed singlet methyl signals at 3.32 ppm in **15b** and 3.16 ppm in **16b**, assigned to the NCH_3 in position 4 (Figure 3) on the basis of their chemical shifts. Irradiation of the methyl signal at 1.79 ppm (singlet, thus geminal to the phenyl substituent) in **15b** enhanced the signal at 3.32 ppm, confirming the regiochemistry given in Scheme 3. Similarly, irradiation of the singlet at 1.64 ppm in **16b** enhanced the signal at 3.16 ppm. Additional positive NOEs upon these irradiations were found for the *ortho* protons of the 3-phenyl (7.05 ppm in **15b** and 7.27 ppm in **16b**) and for one of the methylene protons (2.13 ppm in **15b** and 2.71 ppm in **16b**). Simultaneous irradiation of the doublet methyl signals (1.34 ppm in **15b** and 1.32 ppm in **16b**) enhanced the doublet at 7.50 ppm. Since the signal at 7.50 ppm was assigned to position 8 on the basis of its multiplicity and chemical shift, this again supports the assigned regiochemistry. Other notable enhancements upon the irradiation of the doublet methyl signals were for the methylene protons at 2.13 ppm in **15b** and 2.17 ppm in **16b**. For compound **15b**, irradiations of the methyl groups in positions 1 and 3 induced positive NOEs on the same methylene proton (2.13 ppm), demonstrating the *cis* relationship of these groups. In compound **16b**, irradiations of the methyl groups in positions 1 and 3 produced positive NOEs on different methylene protons (2.17 and 2.71 ppm, respectively); thus these methyl groups are *trans*.

When compared with the analogous method previously developed by Moody,[15] our approach takes advantage of the ready introduction of functionality into the 1-position of cyclopent[*b*]indoles due to the anion-stabilizing ability of the benzotriazolyl group. The readily available starting material, high stereoselectivity, convenient one-pot procedure, and reasonable yields combine to make our methodology attractive for the synthesis of substituted cyclopent[*b*]indoles.

Conclusion

1-Methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) has been shown to be a useful and efficient reagent for the construction of substituted carbazoles and cyclopent[*b*]-indoles. The convenient and versatile approaches presented in this paper should find utility in the synthesis of related natural products.

Experimental Section

General. Melting points were determined with a hot-stage apparatus and are uncorrected. NMR spectra were taken in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (300 MHz) or solvent as the internal standard for ^{13}C (75 MHz). Tetrahydrofuran was distilled under nitrogen immediately prior to use from sodium/benzophenone. All reactions with air-sensitive compounds were carried out under an argon atmosphere. Column chromatography was conducted with silica gel 230−400 mesh. 1-Methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) was prepared according to our previously reported procedure.[17]

General Procedure for the Preparation of Substituted Carbazoles 6a−j and 8. To a solution of 1-methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) (1.05 g, 4 mmol) in THF (75 mL) at −78 °C under argon was added *n*-BuLi (1.7 mL, 2.5 *M* in hexane, 4.4 mmol). After 1 h, the appropriate α,β-unsaturated aldehyde or ketone in THF (10 mL) was added. The reaction mixture was stirred at −78 °C for an additional 3 h and then allowed to warm to room temperature overnight. After the THF was distilled off under argon, 1,4-dioxane (70 mL) and amberlyst-15 (15 g) were added. The mixture was refluxed under argon for 14 h. The Amberlyst-15 was filtered off and 1,4-dioxane evaporated. The residue was dissolved in CH_2Cl_2 (60 mL), and the solution was washed with aqueous sodium hydroxide (*2* N, 30 mL) and water (20 mL). The aqueous layer was extracted with diethyl ether (2 × 30 mL). The combined organic solution was dried ($MgSO_4$) and solvent evaporated. The residue was purified by column chromatography (silica gel) to give the pure product.

1,3-Diphenyl-9-methylcarbazole (6a). Hexane/ethyl acetate (7:1) was used as the eluent to give **6a** in 83% yield as a colorless solid, mp 126−127 °C: ^1H NMR δ 8.23 (d, J = 1.9 Hz, 1H), 8.08−8.05 (d, J = 6.7 Hz, 1H), 7.66−7.63 (m, 2H), 7.47−7.43 (m, 3H), 7.40−7.32 (m, 6H), 7.24−7.14 (m, 3H), 3.27 (s, 3H); ^{13}C NMR δ 142.6, 141.7, 140.3, 137.9, 132.1, 130.1, 128.7, 128.0, 127.9, 127.4, 127.3, 126.5, 126.2, 126.1, 124.6,

(25) Ganesan, A.; Heathcock, C. H. *Tetrahedron Lett.* **1993**, *34*, 439.

123.0, 120.1, 119.0, 117.7, 109.3, 32.7. Anal. Calcd for $C_{25}H_{19}N$: C, 90.06; H, 5.74; N, 4.20. Found: C, 89.67; H, 5.54; N, 4.09.

1,9-Dimethyl-3-phenylcarbazole (6b). Hexane/ethyl acetate (6:1) was used as the eluent to give **6b** in 80% yield as colorless needles, mp 170−171 °C: ^{1}H NMR δ 8.04 (d, J = 1.4 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 7.4 Hz, 2H), 7.38−7.30 (m, 4H), 7.25−7.20(m, 2H), 7.15−7.10 (m, 1H), 3.89 (s, 3H), 2.72 (s, 3H); ^{13}C NMR δ 142.0, 141.9, 139.2, 132.4, 128.7, 128.2, 127.1, 126.3, 125.7, 124.1, 123.1, 120.5, 120.0, 119.0, 116.5, 108.6, 32.1, 20.3. Anal. Calcd for $C_{20}H_{17}N$: C, 88.52; H, 6.31; N, 5.16. Found: C, 88.89; H, 6.45; N, 5.07.

1-(2-Phenylvinyl)-3-phenyl-9-methylcarbazole (6c). Hexane/methylene chloride (6:1) was used as the eluent to give **6c** in 66% yield as a white solid, mp 174−175 °C: ^{1}H NMR δ 8.19 (d, J = 1.8 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 15.9 Hz, 1H), 7.73−7.70 (m, 3H), 7.52−7.22 (m, 11H), 6.99 (d, J = 15.9 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR δ 142.3, 141.7, 138.1, 137.5, 132.6, 131.4, 128.8, 127.7, 127.2, 126.5, 126.4, 126.2, 126.0, 124.8, 124.6, 123.0, 120.1, 119.3, 118.1, 108.8, 33.0. Anal. Calcd for $C_{27}H_{21}N$: C, 90.22; H, 5.89; N, 3.90. Found: C, 90.27; H, 5.96; N, 3.58.

1,3-Diphenyl-2-cyano-9-methylcarbazole (6d). Hexane/ethyl acetate (7:1) was used as the eluent to give **6d** in 45% yield as a colorless solid, mp 160−161 °C: ^{1}H NMR δ 8.17 (s, 1H), 8.13 (d, J = 7.9 Hz, 1H), 7.70−7.67 (m, 2H), 7.57−7.42 (m, 9H), 7.36−7.27 (m, 2H), 3.26 (s, 3H); ^{13}C NMR δ 143.5, 139.6, 136.9, 136.3, 130.4, 130.3, 129.4, 128.9, 128.5, 128.4, 127.9, 126.8, 121.7, 120.9, 120.6, 120.1, 118.4, 109.5, 109.3, 32.1. Anal. Calcd for $C_{26}H_{18}N_2$: C, 87.12; H, 5.06; N, 7.82. Found: C, 87.46; H, 5.22; N, 7.89.

1-Methyl-2-(ethoxycarbonyl)-3-phenyl-9-methylcarbazole (6e). Hexane/ethyl acetate (7:1) was used as the eluent to give a solid, which was recrystallized from ethyl acetate and hexane to give **6e** in 38% yield as a colorless solid, mp 168−169 °C: ^{1}H NMR δ 8.03 (d, J = 7.9 Hz, 1H), 7.92 (s, 1H), 7.51−7.44 (m, 3H), 7.43−7.30 (m, 4H), 7.25−7.19 (m, 1H), 4.11 (s, 3H), 4.08 (q, J = 7.2 Hz, 2H), 2.85 (s, 3H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 170.5, 142.9, 141.9, 138.9, 132.7, 131.8, 128.9, 128.1, 126.8, 126.4, 124.2, 122.5, 120.3, 119.4, 119.3, 117.9, 108.9, 61.1, 33.0, 16.8, 13.7. Anal. Calcd for $C_{23}H_{21}NO_2$: C, 80.44; H, 6.16; N, 4.08. Found: C, 80.11; H, 6.08; N, 4.00.

1,9-Dimethyl-2-(ethoxycarbonyl)-3-propylcarbazole (6f). Hexane/ethyl acetate (7:1) was used as the eluent to give **6f** in 36% yield as a colorless solid, mp 111−112 °C: ^{1}H NMR δ 7.98 (d, J = 7.8 Hz, 1H), 7.72 (s, 1H), 7.42−7.37 (m, 1H), 7.23−7.13 (m, 2H), 4.45 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 2.70 (t, J = 7.6 Hz, 2H), 2.67 (s, 3H), 1.76−1.68 (m, 2H), 1.41 (t, J = 7.1 Hz, 3H), 1.00 (t, J = 7.6 Hz, 3H); ^{13}C NMR δ 170.9, 142.6, 137.9, 133.3, 129.9, 125.9, 124.1, 122.2, 120.0, 118.9, 118.3, 116.9, 108.6, 60.9, 35.9, 32.6, 24.9, 16.6, 14.2, 14.1. Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.69; H, 7.75; N, 4.45.

2-Phenyl-3,9-dimethylcarbazole (6g). Hexane/methylene chloride (6:1) was used as the eluent to give **6g** in 62% yield as a colorless solid, mp 135−136 °C: ^{1}H NMR δ 8.00 (d, J = 7.7 Hz, 1H), 7.88 (s, 1H), 7.40−7.33 (m, 5H), 7.32−7.25 (m, 2H), 7.16 (s, 1H), 7.12 (d, J = 8.1 Hz, 1H), 3.69 (s, 3H), 2.34 (s, 3H); ^{13}C NMR δ 143.1, 141.5, 140.2, 139.6, 129.5, 128.0, 126.7, 126.0, 125.5, 122.5, 122.0, 121.3, 120.2, 118.7, 109.6, 108.3, 29.0, 20.7. Anal. Calcd for $C_{20}H_{17}N$: C, 88.52; H, 6.31; N, 5.16. Found: C, 88.52; H, 6.54; N, 5.10.

2-Phenyl-3-ethyl-9-methylcarbazole (6h). Hexane/methylene chloride (6:1) was used as the eluent to give **6h** in 60% yield as a colorless solid, mp 76−77 °C: ^{1}H NMR δ 8.08 (d, J = 7.7 Hz, 1H), 7.99 (s, 1H), 7.45−7.29 (m, 7H), 7.23−7.18 (m, 2H), 3.71 (s, 3H), 2.75 (q, J = 7.5 Hz, 2H), 1.17 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 143.1, 141.5, 140.0, 139.4, 132.6, 129.6, 128.0, 126.7, 125.5, 122.6, 122.2, 120.2, 119.7, 118.7, 109.8, 108.3, 29.0, 26.4, 16.3. Anal. Calcd for $C_{21}H_{19}N$: C, 88.38; H, 6.71; N, 4.91. Found: C, 88.38; H, 6.61; N, 4.71.

2,9-Dimethyl-3-phenylcarbazole (6i). Hexane/methylene chloride (6:1) was used as the eluent to give **6i** in 31% yield as a colorless solid, mp 115−115.5 °C: ^{1}H NMR δ 8.02 (d, J = 7.7 Hz, 1H), 7.94 (s, 1H), 7.46−7.33 (m, 7H), 7.24−7.17 (m, 2H), 3.79 (s, 3H), 2.46 (s, 3H); ^{13}C NMR δ 142.7, 141.3, 140.6, 133.6, 133.5, 129.8, 128.0, 126.4, 125.3, 122.9, 121.4, 120.9, 120.0, 118.8, 109.5, 108.4, 29.0, 21.7. Anal. Calcd for $C_{20}H_{17}N$: C, 88.52; H, 6.31; N, 5.16. Found: C, 88.18; H, 6.31; N, 5.02.

2-Phenyl-3-(2-methylpropyl)-9-methylcarbazole (6j) and 2-(2-Methylpropyl)-3-phenyl-9-methylcarbazole (8). Hexane/ethyl acetate (6:1) was used as the eluent to give an inseparable mixture of **6j** and **8** in 67% total yield in a ratio of 2:3 as a colorless oil (signals for minor isomer are quoted in brackets): ^{1}H NMR δ 7.89 [7.97] (d, J = 7.7 Hz, 1H), 7.80 [7.83] (s, 1H), 7.34−7.17 (m, 7H), 7.12−6.98 (m, 2H), 3.65 [3.59] (s, 3H), 2.58 [2.54] (d, J = 7.3 Hz, 2H), 1.66−1.23 (m, 1H), 0.66 [0.65] (d, J = 6.6 Hz, 6H); ^{13}C NMR δ 143.2 [143.3], 141.4 [141.5], 140.5 [139.4], 137.5, 134.0, 130.1 [129.7], 127.9, 126.3 [126.6], 125.4 [125.5], 122.9 [122.6], 121.6 [121.2], 120.7 [121.9], 120.0 [120.2], 118.8 [118.7], 109.2 [109.8], 108.3, 43.3 [42.5], 30.0 [30.1], 29.0 [28.9], 22.5 [22.4]. Anal. Calcd for $C_{23}H_{23}N$: C, 88.14; H, 7.40; N, 4.47. Found: C, 88.36; H, 7.50; N, 4.38.

General Procedure for the Preparation of Cyclopent-[*b*]indoles 14a−c. To a solution of 1-methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) (0.78 g, 3 mmol) in CH_2Cl_2 (60 mL) at 0 °C under nitrogen was added zinc bromide (1.35 g, 6 mmol). After 1 h, the appropriate styrene (3.15 mmol) in CH_2Cl_2 (3 mL) was added. The reaction mixture was stirred at 0 °C for an additional 3 h. After the zinc bromide was filtered off, aqueous sodium hydroxide (1 N, 20 mL) was added. The aqueous layer was extracted with diethyl ether (3 × 30 mL). The combined organic solution was dried ($MgSO_4$) and solvent evaporated. The residue was purified by column chromatography (silica gel, hexane/methylene chloride = 1:1) to give the pure product.

3-(4-Methylphenyl)-4-methyl-1,2,3,4-tetrahydrocyclopent[*b*]indole (14a): colorless solid; yield 61%; mp 108−109 °C; ^{1}H NMR δ 7.49 (d, J = 6.8 Hz, 1H), 7.18−7.01 (m, 5H), 7.00−6.94 (m, 2H), 4.31 (dd, J = 7.4 and 5.1 Hz, 1H), 3.28 (s, 3H), 3.04−2.95 (m, 2H), 2.87−2.82 (m, 1H), 2.39-2.30 (m, 1H), 2.28 (s, 3H); ^{13}C NMR δ 147.2, 141.7, 141.6, 135.9, 129.3, 127.2, 124.0, 120.3, 119.0, 118.8, 118.7, 109.4, 44.3, 40.8, 30.4, 23.9, 21.0. Anal. Calcd for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found: C, 87.32; H, 7.41; N, 5.30.

3,4-Dimethyl-3-phenyl-1,2,3,4-tetrahydrocyclopent[*b*]-indole (14b): colorless plates; yield 64%; mp 66−67 °C; ^{1}H NMR δ 7.51 (d, J = 6.9 Hz, 1H), 7.29−7.04 (m, 8H), 3.30 (s, 3H), 2.88 (t, J = 6.9 Hz, 2H), 2.73−2.55 (m, 2H), 1.76 (s, 3H); ^{13}C NMR δ 150.2, 148.0, 141.7, 128.4, 126.1, 124.0, 120.4, 119.0, 118.9, 117.7, 109.3, 50.2, 47.3, 30.1, 25.2, 22.9. Anal. Calcd for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found: C, 86.94; H, 7.51; N, 5.41.

3,3-Diphenyl-4-methyl-1,2,3,4-tetrahydrocyclopent[*b*]-indole (14c): colorless solid; yield 72%; mp 157−158 °C; ^{1}H NMR δ 7.52 (d, J = 7.0 Hz, 1H), 7.30−7.08 (m, 13H), 3.24 (t, J = 6.4 Hz, 2H), 3.21 (s, 3H), 2.93 (t, J = 6.4 Hz, 2H); ^{13}C NMR δ 148.7, 146.2, 141.8, 128.4, 128.1, 126.3, 124.0, 120.6, 119.2, 119.1, 118.6, 109.5, 57.8, 52.4, 30.6, 23.5. Anal. Calcd for $C_{24}H_{21}N$: C, 89.13; H, 6.54; N, 4.33. Found: C, 88.80; H, 6.57; N, 4.30.

General Procedure for the Preparation of 1-Substituted Cyclopent[*b*]indoles 15a−d and 16a−d. To a solution of 1-methyl-3-(benzotriazol-1-ylmethyl)indole (**1**) (0.79 g, 3 mmol) in THF (75 mL) at −78 °C under argon was added *n*-BuLi (1.3 mL, 2.5 M in hexane, 3.3 mmol). After 1 h, the appropriate electrophile (methyl iodide for **15a**, **16a**, **15b**, and **16b**; cyclohexanone for **15c** and **16d**; 3-pentanone for **15d** and **16d**) in THF (10 mL) was added. The reaction mixture was stirred at −78 °C for additional 3 h and then allowed to warm to room temperature overnight. Water (50 mL) was added, and the aqueous layer was extracted with diethyl ether (2 × 30 mL). The combined organic solution was dried ($MgSO_4$) and solvent evaporated to give the corresponding crude compound **9**, which was dissolved in CH_2Cl_2 (60 mL). To this solution at 0 °C under nitrogen was added zinc bromide (1.35 g, 6 mmol). After 1 h, the appropriate styrene (3.15 mmol) in CH_2Cl_2 (3 mL) was added. The reaction mixture was stirred at 0 °C for additional 3 h and at room temperature for 2 days. After the zinc bromide was filtered off, aqueous sodium

hydroxide (1 N, 20 mL) was added. The aqueous layer was extracted with diethyl ether (3 × 30 mL). The combined organic solution was dried ($MgSO_4$) and solvent evaporated. The residue was purified by column chromatography (silica gel) to give the pure product.

1,4-Dimethyl-3-(4-methylphenyl)-1,2,3,4-tetrahydrocyclopent[*b*]indole (15a and 16a). Hexane/methylene chloride (6:1) was used as the eluent to give **15a** and **16a** in 42% yield as a mixture of two diastereoisomers in a ratio of 11:1 as a colorless oil (GCMS analysis of the crude mixture indicated that they were formed in a ratio of 19:1) (signals for minor isomer are quoted in brackets): ^{1}H NMR δ 7.56 (d, J = 7.4 Hz, 1H), 7.21−7.02 (m, 5H), 6.99−6.95 (m, 2H), 4.41 (t, J = 6.6 Hz, 1H), 3.57−3.51 (m, 1H), 3.35 [3.26] (s, 3H), 2.56 (t, J = 6.3 Hz, 2H), 2.29 [2.31] (s, 3H), 1.38 [1.43] (d, J = 6.6 [6.8] Hz, 3H); ^{13}C NMR δ 146.4, 141.6, 141.5, 135.9, 129.3, 127.1, 123.7, 123.5, 120.3, 118.9, 118.5, 109.5, 50.1, 43.7, 32.4, 30.3, 21.5, 21.0. Anal. Calcd for $C_{20}H_{21}N$: C, 87.23; H, 7.69; N, 5.09. Found: C, 87.49; H, 7.79; N, 5.06.

1,3,4-Trimethyl-3-phenyl-1,2,3,4-tetrahydrocyclopent-[*b*]indole (15b and 16b). Hexane/methylene chloride (6:1) was used as the eluent to give **15b** and **16b** in 50% yield as a mixture of two diastereoisomers in a ratio of 2:1 (GCMS analysis of the crude mixture indicated that they were formed in a ratio of 30:1) as a colorless solid; mp 85−86 °C (signals for minor isomer are quoted in brackets): ^{1}H NMR δ 7.50 (d, J = 8.2 Hz, 1H), 7.26−7.00 (m, 8H), 3.42−3.25 (m, 1H), 3.33 [3.16] (s, 3H), 2.79 [2.71] (dd, J = 12.8 and 7.5 Hz, 1H), 2.13 [2.17] (dd, J = 12.8 and 6.0 Hz, 1H), 1.79 [1.64] (s, 3H), 1.34 [1.32] (d, J = 6.8 [5.5] Hz, 3H); ^{13}C NMR δ 149.0 [149.5], 148.1 [148.4], 141.7, 128.4, 126.3 [126.1], 126.0 [125.8], 123.7 [123.8], 122.9 [122.3], 120.4 [120.3], 119.0 [118.9], 118.7 [118.6], 109.5 [109.4], 59.4 [59.9], 47.4 [47.3], 31.6 [31.8], 30.2 [30.1], 27.4 [24.8], 21.7 [21.6]. Anal. Calcd for $C_{20}H_{21}N$: C, 87.23; H, 7.69; N, 5.09. Found: C, 87.40; H, 7.88; N, 5.04.

1-(1-Hydroxycyclohexyl)-3,4-Dimethyl-3-phenyl-1,2,3,4-tetrahydrocyclopent[*b*]indole (15c and 16c). Hexane/ethyl acetate (2:1) was used as the eluent to give **15c** in 66% yield as a single isomer, as a colorless solid (GCMS analysis of the crude mixture indicated that **15c** and **16c** were formed in a ratio of 15:1). Analysis sample was obtained by further recrystallization in ethyl acetate and hexane, mp 244−245 °C: ^{1}H NMR δ 7.69 (d, J = 7.9 Hz, 1H), 7.58−7.55 (m, 2H), 7.39−7.32 (m, 2H), 7.29−7.21 (m, 3H), 7.15−7.10 (m, 1H), 6.80 (s, 1H), 3.78−3.68 (m, 1H), 3.73 (s, 3H), 2.70 (t, J = 12.7 Hz, 1H), 2.52 (dd, J = 12.1 and 6.9 Hz, 1H), 1.90−1.81 (m, 2H), 1.79−1.68 (m, 2H), 1.65−1.56 (m, 2H), 1.61 (s, 3H), 1.46−1.37 (m, 2H), 0.93−0.78 (m, 2H); ^{13}C NMR δ 151.2, 136.9, 128.3, 127.9, 126.9, 126.0, 124.6, 121.5, 119.7, 118.8, 112.3, 109.2, 84.4, 81.5, 46.4, 45.1, 39.0, 32.7, 32.6, 32.3, 25.7, 23.5, 22.1. Anal. Calcd for $C_{25}H_{29}N$: C, 83.52; H, 8.13; N, 3.90. Found: C, 83.39; H, 8.28; N, 3.81.

1-(3-Hydroxypent-3-yl)-3-(4-methylphenyl)-4-methyl-1,2,3,4-tetrahydrocyclopent[*b*]indole (15d and 16d). Hexane/ethyl acetate (2:1) was used as the eluent to give **15d** in 50% yield as a single isomer, as a colorless oil (GCMS analysis of the crude mixture indicated that **15d** and **16d** were formed in a ratio of 18:1): ^{1}H NMR δ 7.63 (d, J = 7.7 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.25−7.07 (m, 5H), 6.80 (s, 1H), 5.04 (dd, J = 10.7 and 5.2, 1H), 3.93 (dd, J = 12.7 and 6.2 Hz, 1H), 3.64 (s, 3H), 2.51−2.45 (m, 1H), 2.35−2.27 (m, 1H), 2.33 (s, 3H), 1.99−1.92 (m, 1H), 1.71−1.58 (m, 2H), 1.20−1.13 (m, 4H), 0.79 (t, J = 7.4 Hz, 3H); ^{13}C NMR δ 140.6, 136.8, 136.5, 128.9, 128.1, 126.8, 125.7, 121.4, 119.2, 118.9, 112.8, 109.1, 86.1, 79.6, 42.6, 42.5, 32.5, 30.4, 28.8, 21.0, 8.1, 7.9; HRMS calcd for $C_{24}H_{29}NO$ 348.2327 (M + 1), found 348.2331.

Supporting Information Available: Detailed ^{1}H and ^{13}C chemical shift assignments for compounds **6a**−**j** and **8** (Figure 2, Tables 1 and 2) (4 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.

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