JOC Article

Construction of Azacycles Based on Endo-Mode Cyclization of Allenes

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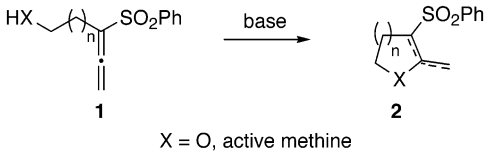
A new procedure for constructing monocyclic five- and six-membered azacycles by the endo-mode ring-closing reaction of allenylazido derivatives under neutral conditions has been developed. The azabicyclo[*m*.*n*.0] compounds were prepared by applying this newly developed procedure. The seven-membered azacycle was prepared when the allene possessing an unsubstituted carboxyl amido functionality was submitted to the basic conditions. In addition, indole and quinoline skeletons were synthesized using this procedure.

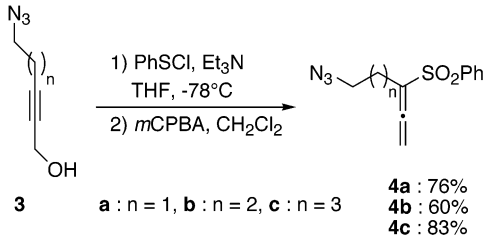
Introduction

Nitrogen-containing heterocyclic systems have attracted widespread attention in the field of organic chemistry as well as in medicinal chemistry. Many procedures for the construction of five- and six-membered azacycles[1] have been developed. Recent efforts from this laboratory[2] demonstrated that the novel endo-mode ring-closing reaction of 1-sulfonylallenes **1** (X = O)[2a] with a suitable δ-hydroxyl carbon appendage at the C_1-position underwent an endo-mode-type ring-closing reaction, resulting in the formation of the five- to eight-membered oxacycles **2** (X = O) in high yield (Scheme 1). This novel method was shown to be applicable to the construction of the carbocycles **2** (X = active methine),[2b] if the starting allenes **1** have a carbon side chain with an active methine moiety at the C_1-position. We were interested in applying this newly developed endo-mode ring-closing reaction to the preparation of the nitrogen-containing heterocycles **2** (X = nitrogen atom). In this paper, we describe the endo-mode ring-closing reaction of allenes having an azido functionality at the carbon side chain terminus.

SCHEME 1



SCHEME 2



Results and Discussion

We have devoted considerable attention to sulfonylallenes having a δ-azido-carbon tether as the starting material for this investigation, because the azido functionality of **4**, for example, would be easily reduced to the amino group under neutral conditions,[3] and the resulting primary amino functionality would immediately attack the sp-hybridized carbon center of the allenic moiety in an endo-mode manner, leading to the formation of azacycles in one operation. The required azidoallenes **4a**−**c** for the ring-closing reaction were easily prepared as follows. The azido alcohols **3a**,[4] **3b**,[5] and **3c**, derived from 3-(*tert*-butyldiphenylsiloxy)-1-propyne by conventional means, were treated with benzenesulfenyl chloride[6] at −78 °C to afford the corresponding sulfinylallenes, which were subsequently exposed to *m*-chloroperbenzoic acid (*m*CPBA) to give the sulfonylallenes **4a**−**c** (Scheme 2).

With the required allenes **4** for the ring-closure reaction in hand, we first investigated the construction of the

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(1) For leading references, see: (a) Janosik, T.; Bergman, J. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Pergamon: Amsterdam, 2003; Vol. 15, pp 140−166. (b) Coffey, D. S.; Kolis, S. P.; May, S. A. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Pergamon: Amsterdam, 2003; Vol. 15, pp 284−305.

(2) (a) Mukai, C.; Yamashita, H.; Hanaoka, M. *Org. Lett.* **2001**, *3*, 3385−3387. (b) Mukai, C.; Ukon, R.; Kuroda, N. *Tetrahedron Lett.* **2003**, *44*, 1583−1586.

(3) Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; Wiley-VCH: New York, 1999; pp 815−820.

(4) Hirschmann, R. F.; Nicolaou, K. C.; Pietranico, S.; Reisine, T. D.; Salvino, J. M.; Sprengeler, P.; Strader, C. D. PCT Int. Appl. WO 95 11686; *Chem. Abstr.* **1995**, *123*, 340754.

(5) Pearson, W. H.; Bergmeier, S. C.; Chytra, J. A. *Synthesis* **1990**, 156−159.

(6) Horner, L.; Binder, V. *Ann. Chem.* **1972**, *757*, 33−68.

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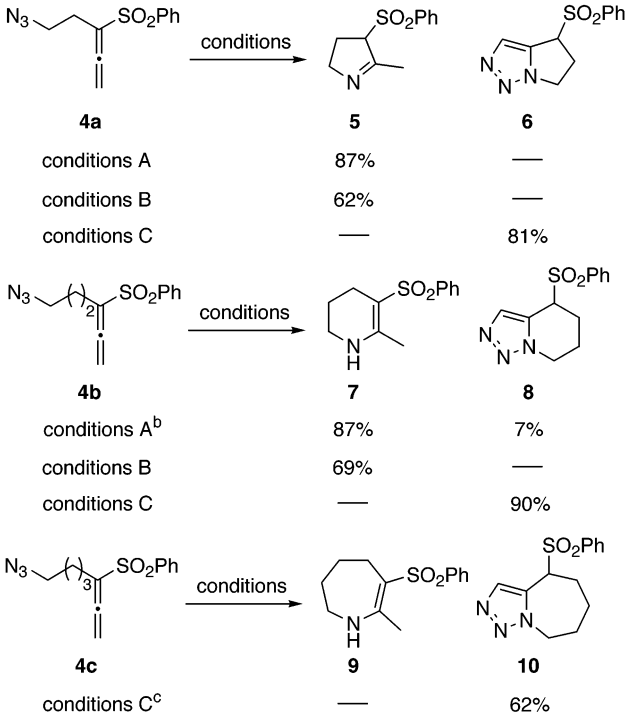
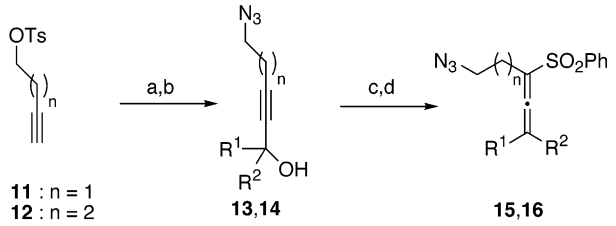
SCHEME 3[a]



[a] Reaction conditions: (conditions A) Bu_3SnH, benzene, rt; (conditions B) PPh_3, H_2O, THF, rt; (conditions C) THF, 50 °C. [b]Compound **7** was obtained in 72% yield when treated in toluene at 0 °C. [c]Compound **10** was obtained when refluxed in toluene.

five-membered azacycle. Reduction of the azido functionality was carried out by treatment of **4a** with tributyltin hydride (Bu_3SnH)[7] in benzene at room temperature (conditions A) to furnish directly the desired dihydropyrrole derivative **5**[8] as the imine in 87% yield. The formation of **5** could be interpreted to occur via reduction of the azido functionality to the primary amino group, which might immediately undergo the endo-mode ring-closing reaction at the sp-hybridized carbon, accompanied by double bond isomerization. An alternative procedure using PPh_3/H_2O[9] in THF at room temperature (conditions B) also worked well to give **5** in 62% yield. On the other hand, upon heating at 50 °C in THF (conditions C) in the absence of reducing reagents, **4a** produced the triazabicyclic derivative **6** in 81% yield (Scheme 3). The formation of **6** could be rationalized by the thermal intramolecular [2 + 3]-dipolar cycloaddition[3] of the azido functionality with the distal π-bond of the allenyl moiety, followed by double-bond migration. The ring-closing reaction of the one-carbon homologated azido derivative **4b** under conditions A provided the desired endo-mode product **7** in 87% yield as the enamine along with the triazabicyclic derivative **8** in 7% yield as the byproduct. The formation of **8** could be suppressed when the reaction was carried out in toluene at 0 °C to give exclusively **7** in 72% yield. Compound **7** was also formed in 69% yield under conditions B. The [2 + 3]-dipolar cycloaddition of the azido derivative **4b** produced the corresponding

SCHEME 4[a]



13a : n = 1, R^1 = H, R^2 = Me (54%) **15a** : n = 1, R^1 = H, R^2 = Me (82%)
13b : n = 1, R^1 = H, R^2 = Bu (44%) **15b** : n = 1, R^1 = H, R^2 = Bu (91%)
13c : n = 1, R^1 = R^2 = Me (40%) **15c** : n = 1, R^1 = R^2 = Me (76%)
14a : n = 2, R^1 = H, R^2 = Me (54%) **16a** : n = 2, R^1 = H, R^2 = Me (74%)
14b : n = 2, R^1 = H, R^2 = Bu (48%) **16b** : n = 2, R^1 = H, R^2 = Bu (85%)
14c : n = 2, R^1 = R^2 = Me (44%) **16c** : n = 2, R^1 = R^2 = Me (89%)

[a] Reaction conditions: (a) LDA, R^1COR^2, THF, −78 °C; (b) NaN_3, DMF, 60 °C; (c) PhSCl, Et_3N,THF, −78 °C; (d) *m*CPBA, CH_2Cl_2, rt.

triazabicyclic compound **8** in 90% yield. We next applied conditions A and B to prepare the seven-membered azacycle **9**. However, it was found that these procedures were not effective for construction of the larger ring-sized azacycle. In fact, when **4c** was exposed to ring-closing conditions (conditions A and B), the desired compound **9** (and/or its imine form) could never be detected in the reaction mixture. The thermal intramolecular cycloaddition of **4c** was effective in refluxing toluene to furnish the triazabicyclo[5.3.0]ring system **10** in 62% yield, although the chemical yield was somewhat lower compared to those observed in the cases of **6** and **8**.

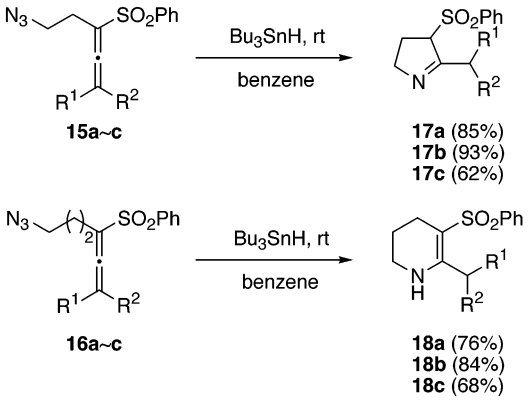
Our next efforts were directed at confirming the generality of this endo-mode ring-closing reaction of the azido derivatives. Preparation of several starting tri- and tetrasubstituted allenes **15** and **16** is summarized in Scheme 4. The acetylide, derived from 4-(tosyloxy)but-1-yne (**11**), was quenched with a suitable carbonyl compound to give **13a**−**c**, which were further converted into the corresponding allenes **15a**−**c** according to the procedures described in Scheme 4. Similarly, the carbon homologated **12** was transformed into the allenes **16a**−**c** via **14a**−**c**.

Upon treatment with Bu_3SnH in benzene (conditions A), the trisubstituted allenes **15a**,**b** underwent the ring-closing reaction in an endo-mode manner to afford the corresponding dihydropyrrole derivatives **17a**,**b** in high yield. The tetrasubstituted allene **15c** also produced the five-membered product **17c** in 62% yield. Similar treatment of **16a**−**c** furnished the tetrahydropyridine derivatives **18a**−**c** as shown in Scheme 5. Thus, the newly developed procedure was found to be applicable not only to disubstituted allenes but also to tri- and tetrasubstituted allenes, resulting in the formation of five- and six-membered azacycles possessing a carbon side chain at the C_2-position.

The next phase of this program was the application of the newly developed ring-closing reaction to the preparation of bicyclic compounds such as the azabicyclo[3.3.0]-octane, azabicyclo[4.3.0]nonane, and azabicyclo[4.4.0]-decane ring systems, because the pyrrolizidine **21** (n =1, m = 0), indolizidine **21** (n = m = 1), and quinolizidine **21** (n = 2, m = 1) skeletons are frequently found to be

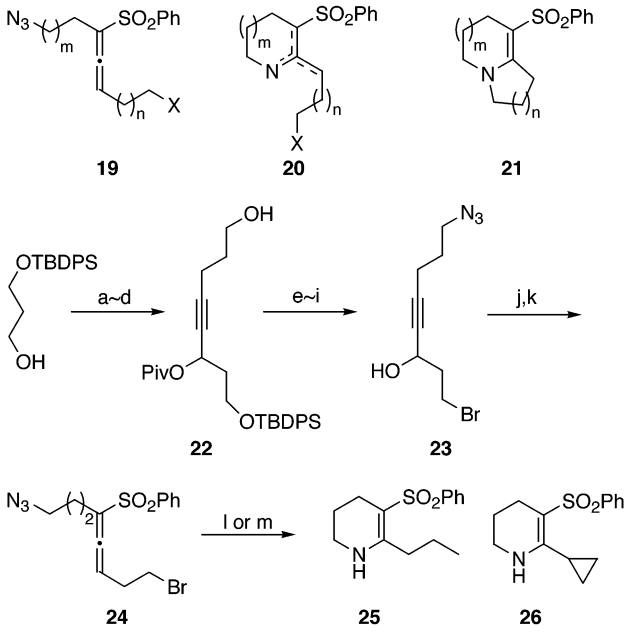
(7) Wasserman, H. H.; Brunner, R. K.; Buybak, J. D.; Carter, C. G.; Oku, T.; Robinson, R. P. *J. Am. Chem. Soc.* **1985**, *107*, 519−521.
(8) A trace amount of compound **6** was detected in the reaction mixture.
(9) Nagarajan, S.; Ganem, B. *J. Org. Chem.* **1987**, *52*, 5044−5046.

SCHEME 5[a]



[a] **a**: $R^1 = H$, $R^2 = Me$, **b**: $R^1 = H$, $R^2 = Bu$, **c**: $R^1 = R^2 = Me$.

SCHEME 6[a]

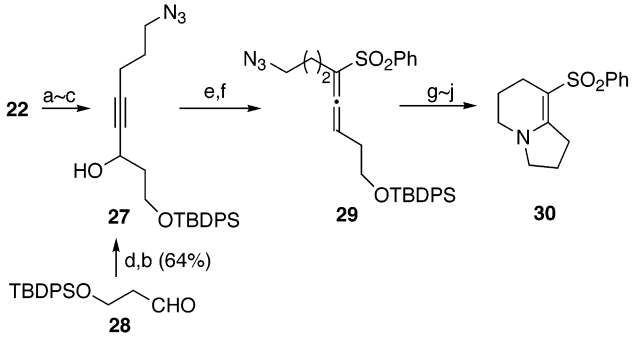


[a] Reaction conditions: (a) Dess−Martin Oxid. CH_2Cl_2, rt; (b) ^{n}BuLi, $HC{\equiv}C(CH_2)_3OTBS$, THF, −30 °C; (c) PivCl, DMAP, Pyr, CH_2Cl_2, rt; (d) PPTS, MeOH, (78%); (e) MsCl, DMAP, Et_3N, CH_2Cl_2, 0 °C; (f) NaN_3, DMF, 60 °C; (g) TBAF, AcOH, THF, rt; (h) CBr_4, PPh_3, CH_2Cl_2, 0 °C; (i) K_2CO_3, MeOH, rt, (78%); (j) PhSCl, Et_3N, THF, −78 °C; (k) *m*CPBA, CH_2Cl_2, rt, (86%); (l) Bu_3SnH, toluene, rt, **25** (49%), **26** (38%); (m) PPh_3, H_2O, THF, rt, **26** (42%).

the major components of many alkaloids. Thus, we hoped that upon exposure to conditions A and/or B, the azidoallene derivatives **19** having a suitably functionalized carbon appendage at the C_3-position would be transformed into the corresponding azacycles **20**, which might immediately undergo a further ring-closing reaction, leading to the direct formation of the azabicyclic species **21** (Scheme 6). As an initial evaluation of the direct transformation of **19** into **21**, we prepared the azidoallene derivative **24** having a bromoethyl group at the C_3-position. Oxidation of 3-(*tert*-butyldiphenylsiloxy)propanol with Dess−Martin periodinane[10] was followed by addition of the acetylide, derived from 5-(*tert*-butyldimethylsiloxy)pent-1-yne, to afford the secondary alcohol,

(10) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155−4156.

SCHEME 7[a]



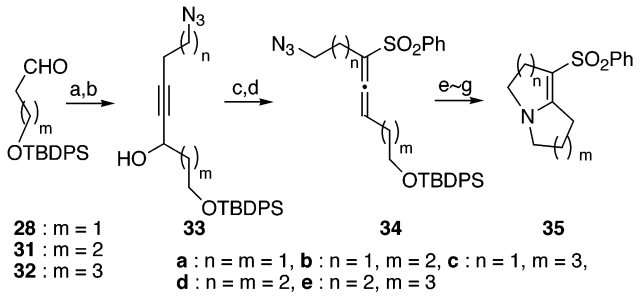
[a] Reaction conditions: (a) MsCl, DMAP, Et_3N, CH_2Cl_2, 0 °C; (b) NaN_3, DMF, 60 °C; (c) K_2CO_3, MeOH, rt, (50%); (d) LDA, $HC{\equiv}C(CH_2)_3OTs$, THF, −78 °C; (e) PhSCl, Et_3N, THF, −78 °C; (f) *m*CPBA, CH_2Cl_2, rt, (91%); (g) Bu_3SnH, toluene, rt; (h) TBAF, THF, rt; (i) CBr_4, PPh_3, Et_3N, CH_2Cl_2, rt, (64%).

which was protected with the pivaloyl group and selectively desilylated with pyridinium *p*-toluenesulfonate (PPTS) to give **22** in 78% overall yield. Compound **22** was treated with methanesulfonyl chloride (MsCl) and NaN_3 to afford the azido derivative, which was consecutively exposed to desilylation, bromination, and deacylation conditions to provide the propargyl alcohol derivative **23** in 78% overall yield. Conversion of **23** into the allene **24** (86%) was achieved using the standard conditions. Treatment of **24** with Bu_3SnH in toluene (conditions A, toluene was used instead of benzene)[11] at room temperature gave two tetrahydropyridine derivatives **25** and **26** in 49% and 38% yield, respectively. No azabicyclic derivatives such as **21** ($n = m = 1$) could be obtained. The debromination reaction of the starting **24** and/or the intermediate **20** ($n = m = 1$, X = Br) with Bu_3SnH would lead to production of **25**, while the formation of **26** could be rationalized in terms of intramolecular nucleophilic displacement of bromide by the carbanion species of **20** ($n = m = 1$). To avoid reductive debromination and the formation of a cyclopropyl ring, we performed the ring-closing reaction of **24** under conditions B (PPh_3/H_2O). However, the only isolable product from the reaction mixture was **26** (42%) and the target azabicyclic derivative **21** ($n = m = 1$) could never be found in the reaction mixture. Thus, it turned out that the cyclopropyl-ring formation by the carbanion species of **20** must be preferred over the formation of the desired azabicyclic compound **21** (displacement by the nitrogen nucleophile).

On the basis of the above experiments, we turned our efforts to the development of the stepwise procedure for the preparation of the azabicyclic compounds instead of the direct conversion method. Compound **22** was treated with MsCl and NaN_3 to give the azido derivative, which was subsequently exposed to K_2CO_3 in MeOH to afford the hydroxyl compound **27** in 50% yield. Compound **27** (64%) was prepared in fewer steps and more conveniently from the aldehyde **28** by treatment with the acetylide of 5-(tosyloxy)pent-1-yne and NaN_3. The azido derivative **27** was then converted to the sulfonylallene **29** in 91% yield by the general procedure described in Scheme 7. Treatment of **29** under conditions A (toluene was used as a

(11) Changing the solvent from benzene to toluene never affected the distribution of the products or the chemical yield.

SCHEME 8[a]



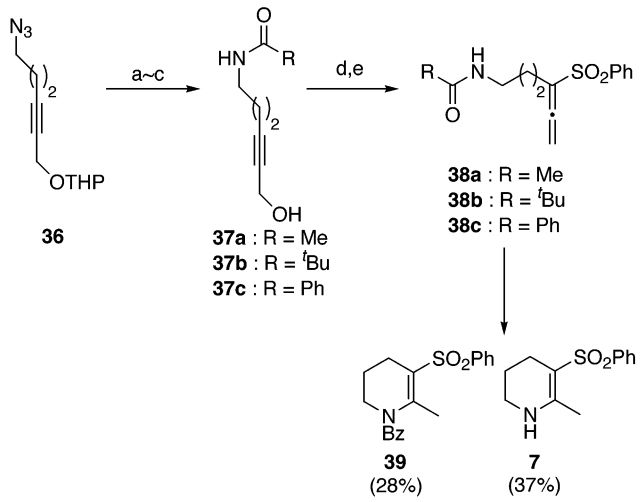
[a] Reaction conditions: (a) LDA, $HC{\equiv}C(CH_2)_nCH_2OTs$, THF, −78 °C; (b) NaN_3, DMF, 60 °C, **33a** (75%), **33b** (79%), **33c** (73%), **33d** (71%), **33e** (77%); (c) PhSCl, Et_3N, THF, −78 °C; (d) *m*CPBA, CH_2Cl_2, rt, **34a** (92%), **34b** (92%), **34c** (93%), **34d** (96%), **34e** (93%); (e) Bu_3SnH, toluene, rt; (f) TBAF, THF, rt; (g) CBr_4, PPh_3, Et_3N, CH_2Cl_2, rt,**35a** (31%), **35b** (44%), **35c** (36%), **35d** (77%), **35e** (49%).

solvent) furnished the tetrahydropyridine derivative, the silyl group of which was removed by treatment with tetrabutylammonium fluoride (TBAF). Exposure of the resulting primary hydroxyl compound to bromination conditions (CBr_4/PPh_3) effected successive bromination and construction of the azabicyclo[4.3.0]nonene skeleton to furnish **30** in 64% yield. Thus, the stepwise procedure provided the desired azabicyclic compound **30** in an acceptable yield.

We next investigated the construction of other ring-sized azabicyclic systems by taking advantage of the newly developed stepwise procedure. Reaction of the aldehydes **28**, **31**, and **32** with the acetylides provided **33**. According to the general procedure, the compounds **33** were subsequently transformed into the azido derivatives **34**, which were then submitted to the ring-closing conditions to provide the corresponding azabicyclic compounds **35**. The results are summarized in Scheme 8. Formation of the tetrahydropyridine-fused azabicyclic skeletons **30** (Scheme 7), **35d**, and **35e** (Scheme 8) occurred in moderate yield ranging from 49% to 77%. However, the azabicyclic compounds **35a**−**c** containing the dihydropyrrole moiety were formed in a rather low yield. In fact, the azabicyclo[5.3.0]decene derivative **35c** was isolated as the sole product from the reaction mixture in 36% yield. It should be mentioned that the azidoallene derivatives **34c**,**e** did not cyclize under the standard conditions at room temperature (Scheme 8). Upon refluxing in toluene in the presence of $^iPr_2NEt$ (instead of Et_3N in CH_2Cl_2 at room temperature), however, compounds **34c**,**e** afforded the corresponding cyclized products **35c**,**e** in 36% and 49% yield, respectively. Thus, this endo-mode ring-closing reaction was shown to be applicable to the construction of several azabicyclic ring systems, although it is obvious that investigation on the optimized conditions for the construction of the dihydropyrrole-fused azabicyclic derivative **35a**−**c** is still required.

In our previous paper,[2] the base-catalyzed endo-mode ring-closing reaction of allenes having a suitable *δ*-hydroxyl carbon appendage at the C_1-position was reported (Scheme 1). We could now develop an efficient procedure for the formation of five- and six-membered azacycles from the corresponding azidoallene derivatives under neutral conditions. However, we were still interested in the base-catalyzed ring-closing reaction of carbamoylallene compounds.[12] Thus, by analogy to the preparation of the aforementioned allenes (in Schemes 2 and 4), the required carbamoylallene derivatives **38** were prepared in a straightforward manner as depicted in Scheme 9. The azido derivative **36**, derived from 3-(tetrahydropyranyloxy)prop-1-yne by reaction with 1,3-dibromopropane and NaN_3, was subsequently reduced, acylated, and deprotected to afford **37**. Finally, the propargyl alcohol derivatives **37** were converted into the carbamoylallene derivatives **38** by the standard method, although the chemical yields in the conversion of **37** into **38** were somewhat lower compared to those for the formation of the azidoallene derivatives **4**, **15**, and **16**. According to the general procedure described in the previous paper,[2a] the acetyl derivative **38a** was exposed to ^{t}BuOK in ^{t}BuOH at room temperature. However, no ring-closed products could be detected in the reaction mixture and an intractable mixture was obtained. Changing solvent and/or base did not afford us a favorable result. Similarly fruitless reactions were observed when the pivaloyl derivative **38b** was submitted to the ring-closing conditions. On the other hand, the benzoyl derivative **38c** underwent the endo-mode ring-closing reaction and spontaneous debenzoylation to furnish **7** in 37% yield. When THF was used instead of ^{t}BuOH, debenzoylation could be suppressed and **39** was obtained as the sole isolable product in 28% yield. No improvement in the production of **7** or **39** was found even after screening several reaction conditions.

SCHEME 9[a]

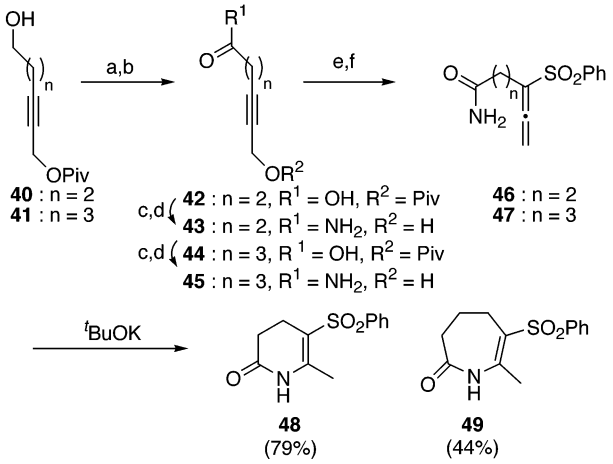


[a] Reaction conditions: (a) PPh_3, H_2O, THF; (b) acylating reagent (Ac_2O, PivCl, BzCl), Et_3N, rt; (c) *p*-TsOH, MeOH, rt, **37a** (81%), **37b** (89%), **37c** (91%); (d) PhSCl, Et_3N, THF, −78 °C; (e) *m*CPBA, CH_2Cl_2, rt, **38a** (39%), **38b** (37%), **38c** (51%).

The unsubstituted carboxamide derivative **46** was another substrate investigated to determine whether the endo-mode ring-closing reaction under basic conditions would proceed in a reasonable yield. To this end, the starting compounds **46** and **47** were prepared from **40** and **41**, respectively (Scheme 10). The chemical yields in the conversion of the propargyl alcohol derivatives **43** and **45** to **46** and **47** were again found to be lower than those

(12) An exo-mode ring-closing reaction of sulfonylallenes having a carbon side chain at the C_3-position has been reported: Gray, M.; Parsons, P. J.; Neary, A. P. *Synlett* **1993**, 281−282.

SCHEME 10[a]



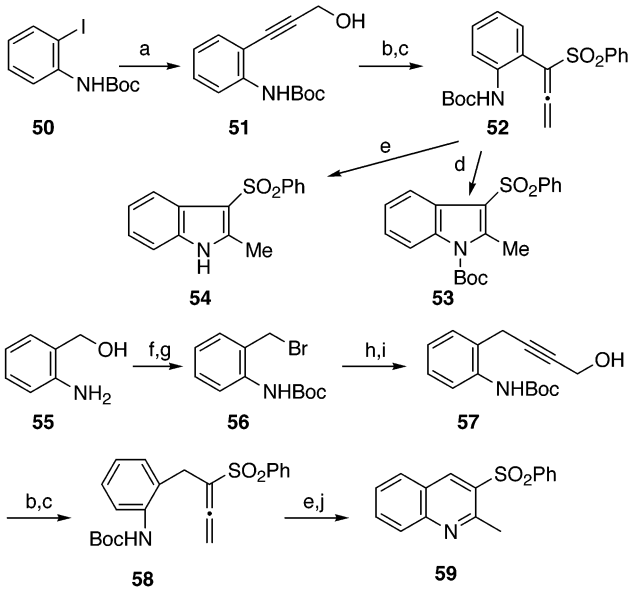
[a] Reaction conditions: (a) Dess−Martin oxidation, CH_2Cl_2, rt; (b) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^{t}BuOH, H_2O, rt, **42** (95%), **44** (95%); (c) isobutyl chloroformate, Et_3N, THF, 0 °C, then aq NH_3; (d) K_2CO_3, MeOH, rt, **43** (64%), **45** (84%); (e) PhSCl, Et_3N, THF, −78 °C; (f) *m*CPBA, CH_2Cl_2, rt, **46** (39%), **47** (37%).

for the formation of the azidoallene derivatives **4**, **15**, and **16**. After screening several reaction conditions, we found that NaH in THF at room temperature was effective in the case of **46** to produce the piperidone derivative **48** in 79% yield. When treated with ^{t}BuOK in THF, **46** also provided **48** in 64% yield. However, the NaH/THF conditions were no longer useful for the ring-closing reaction of **47**, resulting in the formation of a small amount of **49** (7%), even at reflux. The best yield so far for production of **49** (44%) was obtained when **47** was exposed to NaH in a combined solvent of CH_2Cl_2 and DMF. Thus, it was shown that the endo-mode ring-closing reaction of the unsubstituted carboxamide derivatives **46** and **47** under basic conditions was superior to that of the *N*-acylated derivatives **38**. It is noteworthy that the seven-membered lactam azacycle **49** could be obtained from **47** under basic conditions, whereas the formation of the seven-membered enamine azacycle, e.g., **9**, was never attained in more than trace amounts in the reaction of the azidoallene derivative **4c** under neutral conditions (Scheme 3).

In the last stage of this study, application of the endo-mode ring-closing reaction to the preparation of aromatic five- and six-membered azacycles was investigated (Scheme 11). The starting aniline derivatives **52** and **58** were easily prepared from the *N*-protected *o*-iodoaniline derivative **50** and *o*-aminobenzyl alcohol (**55**) by standard procedures. The endo-mode ring-closing reaction of **52** proceeded rapidly to afford the indole derivative **53** in 96% yield when treated with sodium hydride at room temperature. Upon exposure to trifluoroacetic acid (TFA), **52** underwent *N*-deprotection and spontaneous ring-closing reaction to produce **54** in 83% yield. On the other hand, treatment of the sulfonylallene **58** with TFA provided the unstable dihydroquinoline derivative, which was subsequently oxidized with salcomine/O_2[13] to give the quinoline derivative **59** in 77% yield.

In summary, we have developed a new procedure for constructing monocyclic five- and six-membered azacycles

SCHEME 11[a]



[a] Reaction conditions: (a) propargyl alcohol, $Pd(PPh_3)_2Cl_2$, CuI, $^i Pr_2NH$, THF, rt, (92%); (b) PhSCl, Et_3N, THF, −78 °C; (c) *m*CPBA, CH_2Cl_2, rt, **52** (47%), **58** (60%); (d) NaH, THF, rt, (96%); (e) CF_3CO_2H, CH_2Cl_2, rt, **54** (83%); (f) $(Boc)_2O$, THF, reflux; (g) CBr_4, PPh_3, CH_2Cl_2, 0 °C, (69%); (h) $In(C{\equiv}CCH_2OTBDMS)_3$, $Pd(dppf)Cl_2$, THF, reflux; (i) TBAF, AcOH, THF, rt, (65%); (j) salcomine, O_2, MeOH, rt, (77%).

from azidoallene derivatives under neutral conditions. This procedure was shown to be applicable to the preparation of the azabicyclo[*m*.*n*.0] ring system. The endo-mode ring-closing reaction of allenes having an unsubstituted carboxamide functionality produced not only the piperidone skeleton but also the seven-membered azacycle, which could never be obtained in the reaction of azidoallene derivatives. In addition, indole and quinoline skeletons also could be prepared using this procedure. The application of this endo-mode ring-closing reaction to the synthesis of alkaloids is now in progress.

Experimental Section

Melting points are uncorrected. IR spectra were measured in $CHCl_3$. ^{1}H NMR spectra were taken in $CDCl_3$. $CHCl_3$ (7.26 ppm) for silyl compounds and tetramethylsilane (0.00 ppm) for compounds without a silyl group were used as an internal standard. ^{13}C NMR spectra were recorded in $CDCl_3$ with $CHCl_3$ (77.00 ppm) as an internal standard. All reactions were carried out under a nitrogen atmosphere unless otherwise stated. Silica gel (silica gel 60, 230−400 mesh, Merck) was used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4.

7-Azido-2-heptyn-1-ol (3c). To a solution of LDA in THF (3.0 mL), prepared from the reaction of ^{n}BuLi (1.36 M hexane solution, 2.65 mL, 3.60 mmol) and $^i Pr_2NH$ (0.53 mL, 3.78 mmol), was added a solution of 3-(*tert*-butyldiphenylsiloxy)-prop-1-yne (883 mg, 3.00 mmol) in THF (2.0 mL) and *N*,*N*′-dimethylpropyleneurea (DMPU) (1.0 mL) and reaction mixture was stirred at 0 °C for 20 min. 1,4-Dibromobutane (0.72 mL, 6.03 mmol) was added to the reaction mixture, which was stirred at room temperature for 8 h. The reaction was quenched by addition of water and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to give the crude adduct. To a

(13) Inada, A.; Nakamura, Y.; Morita, Y. *Chem. Lett.* **1980**, 1287−1290.

solution of the crude adduct in MeOH (15 mL) was added 10% HCl (1.5 mL) at room temperature. The reaction mixture was allowed to stand for 10 h, quenched by addition of saturated aqueous $NaHCO_3$, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (3:1) to give the crude alcohol. A solution of the crude alcohol, NaN_3 (215 mg, 3.31 mmol), and NaI (450 mg, 3.00 mmol) in DMF (7.5 mL) was heated at 60 °C for 3 h, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (3:1) gave **3c** (320 mg, 70%) as a colorless oil: IR 3609, 3435, 2224, 2100 cm^{-1}; ^1H NMR δ 4.24 (2H, dt, J = 5.9, 2.4 Hz), 3.30 (2H, t, J = 6.8 Hz), 2.27 (2H, tt, J = 2.4, 7.3 Hz), 1.74−1.69 (2H, m), 1.63−1.57 (3H, m); ^{13}C NMR δ 85.5, 79.0, 51.3, 51.0, 27.9, 25.6, 18.3; FABMS m/z 154 (M^+ + 1, 100). Anal. Calcd for $C_7H_{11}N_3O$: C, 54.89; H, 7.24; N, 27.43. Found: C, 54.50; H, 7.45; N, 27.62.

5-Azido-3-phenylsulfonylpenta-1,2-diene (4a). To a solution of **3a** (275 mg, 2.20 mmol) and Et_3N (1.84 mL, 13.2 mmol) in THF (9.0 mL) was added PhSCl (954 mg, 6.60 mmol) at −78 °C. The reaction mixture was stirred for 2 h, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (2:1) to give the crude sulfoxide. To a solution of the crude sulfoxide in CH_2Cl_2 (11 mL) was added *m*CPBA (569 mg, 3.30 mmol) at room temperature. The reaction mixture was stirred for 1 h at room temperature, quenched by addition of aqueous $Na_2S_2O_3$, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (4:1) gave **4a** (417 mg, 76%) as a colorless oil: IR 2104, 1969, 1936 cm^{-1}; ^1H NMR δ 7.91−7.54 (5H, m), 5.44 (2H, t, J = 2.9 Hz), 3.41 (2H, t, J = 6.8 Hz), 2.54 (2H, tt, J = 2.9, 6.8 Hz); ^{13}C NMR δ 208.0, 139.8, 133.7, 129.2, 128.1, 110.0, 84.8, 49.0, 27.3; MS m/z 249 (M^+, 5.0). Anal. Calcd for $C_{11}H_{11}N_3O_2S$: C, 53.00; H, 4.45; N, 16.86. Found: C, 52.82; H, 4.44; N, 16.78.

Ring-Closing Reaction of 4a. Conditions A. To a solution of **4a** (25.4 mg, 0.10 mmol) in benzene (1.0 mL) was added Bu_3SnH (0.14 mL 0.52 mmol) at room temperature and the reaction mixture was stirred for 24 h. Benzene was evaporated off and chromatography of the residue with AcOEt gave 5-methyl-4-phenylsulfonyl-3,4-dihydro-*2H*-pyrrole (**5**) (19.8 mg, 87%) along with a trace amount of **6**. Compound **5** was a colorless needle: mp 74−75.5 °C (from Et_2O); IR 1645 cm^{-1}; ^1H NMR δ 7.90−7.44 (5H, m), 4.28−4.24 (1H, m), 3.78−3.73 (1H, m), 3.40−3.33 (1H, m), 2.34−2.26 (4H, m), 2.20−2.11 (1H, m); ^{13}C NMR δ 165.8, 137.4, 134.1, 129.3, 128.6, 75.1, 59.1, 27.1, 20.0; MS m/z 223 (M^+, 8.4). Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27. Found: C, 58.92; H, 5.81; N, 6.22.

Conditions B. To a solution of **4a** (25.2 mg, 0.10 mmol) in THF (1.0 mL) and H_2O (0.1 mL) was added PPh_3 (79.5 mg, 0.30 mmol) at room temperature, and the reaction mixture was stirred for 24 h. THF was evaporated off and the residue was purified by chromatography with AcOEt to afford **5** (14.0 mg, 62%).

[2 + 3]-Cycloaddition Reaction of Compound 4a. Conditions C. A solution of **4a** (25.2 mg, 0.10 mmol) in THF (1.0 mL) was heated at 50 °C for 3 days. THF was evaporated off and the residue was chromatographed with AcOEt to give 6-phenylsulfonyl-1,2,3-triazabicyclo[3.3.0]octa-2,4-diene (**6**) (20.5 mg, 81%) as a colorless needle: mp 129−130 °C (from AcOEt−hexane); ^1H NMR δ 7.77−7.57 (5H, m), 7.23 (1H, s), 4.68 (1H, dd, J = 2.4, 8.8 Hz), 4.36 (1H, ddd, J = 2.4, 9.3, 11.7 Hz), 4.17 (1H, dt, J = 11.7, 8.3 Hz), 3.36 (1H, ddt, J = 8.3, 14.7, 2.4 Hz), 3.24 (1H, ddt, J = 9.3, 14.7, 8.3 Hz); ^{13}C NMR δ 135.7, 135.6, 134.8, 129.5, 129.2, 129.0, 59.2, 45.3, 30.8; MS m/z 249 (M^+, 3.1). Anal. Calcd for $C_{11}H_{11}N_3O_2S$: C, 53.00; H, 4.45; N, 16.86. Found: C, 52.97; H, 4.42; N, 16.86.

6-Azido-3-hexyn-2-ol (13a). To a solution of **11** (224 mg, 1.00 mmol) in THF (10 mL) was added LDA (1.00 M THF solution, 1.00 mL, 1.00 mmol) at −78 °C. The reaction mixture was stirred at the same temperature for 1 h, to which acetaldehyde (0.11 mL, 1.96 mmol) was added. The reaction mixture was stirred at −78 °C for 1.5 h, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. NaN_3 (97.5 mg, 1.50 mmol) was added to a solution of the crude alcohol in DMF (5.0 mL), and the mixture was heated at 60 °C for 6 h, diluted with water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (4:1) gave **13a** (74.6 mg, 54%) as a colorless oil: IR 3603, 3433, 2245, 2110 cm^{-1}; ^1H NMR δ 4.52 (1H, tq, J = 2.0, 6.4 Hz), 3.37 (2H, t, J = 6.8 Hz) 2.51 (2H, dt, J = 2.0, 6.8 Hz), 1.79 (1H, brs), 1.44 (3H, d, J = 6.4 Hz); ^{13}C NMR δ 84.4, 80.4, 58.5, 49.8, 24.4, 19.9; FABMS m/z 162 (M^+ + Na, 5.0); FABHRMS calcd for $C_6H_{16}N_3O$ 140.0824, found 140.0823.

1-(*tert*-Butyldiphenylsiloxy)-3-(pivaloyloxy)-4-octyn-8-ol (22). To a solution of 3-(*tert*-butyldiphenylsiloxy)propan-1-ol (1.40 g, 4.45 mmol) in CH_2Cl_2 (11 mL) was added Dess−Martin periodinane (2.45 g, 5.78 mmol) at 0 °C, and the reaction mixture was allowed to stand for 30 min. The reaction was quenched by addition of aqueous $Na_2S_2O_3$ and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated. To a solution of 5-(*tert*-butyldimethylsiloxy)pent-1-yne (1.06 g, 5.34 mmol) in THF (15 mL) was added *n*-BuLi (1.40 M hexane solution, 3.81 mL, 5.33 mmol) at −30 °C, and the reaction mixture was stirred for 30 min. A solution of the crude aldehyde in THF (8.0 mL) was added to a solution of the acetylide in THF and the reaction mixture was stirred at −30 °C for 2 h. The reaction was quenched by addition of water and extracted with Et_2O, which was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (20:1) to give the crude adduct. To a solution of the crude adduct in CH_2Cl_2 (8.0 mL) and pyridine (1.0 mL) was added DMAP (48.5 mg, 0.40 mmol) and PivCl (0.73 mL, 5.93 mmol) at 0 °C. The reaction mixture was stirred for 12 h at room temperature, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (10:1) to give the crude pivaloyloxy derivative. PPTS (49.9 mg, 0.20 mmol) was added to a solution of the crude ester in MeOH (16 mL) at room temperature and the reaction mixture was stirred for 24 h. MeOH was evaporated off and the residue was chromatographed with hexane−AcOEt (4:1) to give **22** (1.66 g, 78%) as a colorless oil: IR 3628, 3443, 2245, 1724 cm^{-1}; ^1H NMR δ 7.68−7.63 (4H, m), 7.44−7.35 (6H, m), 5.57−5.53 (1H, m), 3.80−3.71 (2H, m), 3.69 (2H, t, J = 6.4 Hz), 2.29 (2H, dt, J = 2.0, 6.4 Hz), 2.09−1.95 (2H, m), 1.71 (2H, quint, J = 6.4 Hz), 1.44 (1H, brs), 1.16 (9H, s), 1.05 (9H, s); ^{13}C NMR δ 177.2, 135.6, 135.5, 133.7, 133.6, 129.6, 127.6, 85.0, 78.4, 61.6, 61.4, 59.8, 38.7, 37.9, 31.1, 27.0, 26.8, 19.2, 15.3; FABMS m/z 481 (M^+ + 1, 0.5). Anal. Calcd for $C_{29}H_{40}O_4Si$: C, 72.46; H, 8.39. Found: C, 72.16; H, 8.55.

8-Azido-1-bromo-4-octyn-3-ol (23). To a solution of **22** (929 mg, 1.93 mmol), Et_3N (0.81 mL, 5.81 mmol), and DMAP (23.6 mg, 0.19 mmol) in CH_2Cl_2 (10 mL) was added MsCl (0.22 mL, 2.84 mmol) at 0 °C. The reaction mixture was stirred for 20 min, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated. NaN_3 (188 mg, 2.89 mmol) was added to a solution of the crude mesylate in DMF (10 mL). The reaction mixture was heated at 60 °C for 5 h, diluted by addition of water, and extracted with Et_2O, which was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (20:1) to give the crude azide derivative. To a solution of the crude azide derivative in THF (6.8 mL) was successively added

AcOH (0.33 mL, 5.76 mmol) and TBAF (1.0 M THF solution, 2.90 mL, 2.90 mmol) at room temperature. The reaction mixture was stirred for 12 h. THF was evaporated off and the residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to give crude alcohol. CBr_4 (768 mg, 2.32 mmol) and Ph_3P (607 mg, 2.31 mmol) were added to a solution of the crude alcohol in CH_2Cl_2 (10 mL) at 0 °C. The reaction mixture was stirred for 1 h and CH_2Cl_2 was evaporated off. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to give the crude primary bromide. To a solution of the crude bromide, thus obtained, in MeOH (10 mL) was added K_2CO_3 (293 mg, 2.12 mmol) at room temperature. The reaction mixture was allowed to stand for 24 h, diluted by addition of water, and extracted with AcOEt, which was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (4:1) gave **23** (370 mg, 78%) as a colorless oil: IR 3607, 3420, 2224, 2100 cm^{-1}; ^1H NMR δ 4.61−4.56 (1H, m), 3.59−3.48 (2H, m), 3.40 (2H, t, J = 6.8 Hz), 2.35 (2H, dt, J = 2.0, 6.8 Hz) 2.27−2.14 (2H, m), 1.93 (1H, d, J = 4.9 Hz), 1.78 (2H, quint, J = 6.8 Hz); ^{13}C NMR δ 84.6, 81.1, 60.8, 50.2, 40.5, 28.9, 27.7, 16.0; FABMS m/z 246(M^+ + 1, 9.3), 248 (M^+ + 1, 9.1). Anal. Calcd for $C_8H_{12}BrN_4O$: C, 39.04; H, 4.91; N, 17.07. Found: C, 38.81; H, 4.97; 17.01.

Ring-Closing Reaction of 24. According to conditions A, **24** (15.3 mg, 0.04 mmol) was treated with Bu_3SnH (0.05 mL 0.19 mmol) in toluene (0.8 mL) at room temperature for 36 h to give 1,2,3,4-tetrahydro-5-phenylsulfonyl-6-propylpyridine (**25**) (5.4 mg, 49%) and 6-cyclopropyl-1,2,3,4-tetrahydro-5-phenylsulfonylpyridine (**26**) (4.1 mg, 38%). Compound **25** was a colorless oil: IR 3452, 3383 cm^{-1}; ^1H NMR δ 7.85−7.43 (5H, m), 4.19−4.13 (1H, m), 3.21−3.14 (2H, m), 2.64−2.58 (2H, m), 2.40 (2H, t, J = 5.9 Hz), 1.76 (2H, quint, J = 5.9 Hz), 1.61−1.50 (2H, m), 0.94 (3H, t, J = 7.3 Hz); ^{13}C NMR δ 154.4, 144.6, 131.5, 128.6, 126.1, 97.4, 41.3, 34.4, 23.5, 22.6, 21.3, 13.9; MS m/z 265 (M^+, 27); HRMS calcd for $C_{14}H_{19}NO_2S$ 265.1137, found 265.1140. Compound **26** was a colorless needle: mp 118−119 °C (from AcOEt−hexane); IR 3460 cm^{-1}; ^1H NMR δ 7.87−7.84 (2H, m), 7.50−7.43 (3H, m), 4.00 (1H, brs), 3.13−3.09 (2H, m), 2.79−2.73 (1H, m), 2.46 (2H, t, J = 5.9 Hz), 1.74 (2H, quint, J = 5.9 Hz), 0.80−0.75 (2H, m), 0.56−0.52 (2H, m); ^{13}C NMR δ 153.2, 144.8, 131.5, 128.6, 126.1, 99.6, 41.2, 24.0, 21.4, 12.7, 6.2; MS m/z 263 (M^+, 26). Anal.Calcd for $C_{14}H_{17}NO_2S$: C, 63.85; H, 6.51; N, 5.32. Found: C, 63.69; H, 6.56; N, 5.25.

8-Azido-1-(*tert*-butyldiphenylsiloxy)-4-octyn-3-ol (27). To a solution of 5-(tosyloxy)pent-1-yne (68.6 mg, 0.29 mmol) in THF (1.8 mL) was added LDA (0.50 M THF solution, 0.58 mL, 0.29 mmol) at −78 °C, to which a solution of 3-(*tert*-butyldiphenylsiloxy)propanal **28** (76.5 mg, 0.24 mmol) in THF (0.6 mL) was added. The reaction mixture was stirred at the same temperature for 2 h, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. NaN_3 (23.4 mg, 0.36 mmol) was added to a solution of the crude tosylate in DMF (2.4 mL). The reaction mixture was heated at 60 °C for 6 h, diluted by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (4:1) gave **27** (66.3 mg, 64%) as a colorless oil: IR 3599, 3470, 2232, 2102 cm^{-1}; ^1H NMR δ 7.71−7.67 (4H, m), 7.46−7.38 (6H, m), 4.71−4.60 (1H, m), 4.05−3.99 (1H, m), 3.86−3.81 (1H, m), 3.38 (2H, t, J = 6.8 Hz), 3.16 (1H, d, J = 6.8 Hz), 2.34 (2H, dt, J = 1.5, 6.8 Hz), 2.03−1.87 (2H, m), 1.77 (2H, quint, J = 6.8 Hz), 1.06 (9H, s); ^{13}C NMR δ 135.6, 135.5, 133.0, 129.8, 127.8, 83.5, 81.9, 61.9, 61.8, 50.2, 39.2, 27.8, 26.8, 19.1, 16.1; FABMS m/z 422 (M^+ + 1, 1.8). Anal. Calcd for $C_{24}H_{31}N_3O_2Si$: C, 68.37; H, 7.41; N, 9.97 Found: C, 68.10; H, 7.52; N, 10.12.

8-Azido-1-(*tert*-butyldiphenylsiloxy)-5-phenylsulfonyl-octa-3,4-diene (29). According to the procedure described for the preparation of **4a**, **29** (559 mg, 91%) was obtained **27** (476 mg, 1.13 mmol) as a colorless oil: IR 2100, 1962 cm^{-1}; ^1H NMR δ 7.85−7.83 (2H, m), 7.66−7.63 (4H, m), 7.58−7.54 (1H, m), 7.48−7.36 (8H, m), 5.84 (1H, sept, J = 2.9 Hz), 3.64 (2H, t, J = 6.4 Hz), 3.21 (2H, t, J = 6.4 Hz), 2.35−2.30 (4H, m), 1.74−1.62 (2H, m), 1.05 (9H, s); ^{13}C NMR δ 203.6, 140.0, 135.50, 135.48, 133.46, 133.45, 133.4, 129.77, 129.75, 129.0, 128.1, 127.74, 127.71, 112.5, 98.6, 62.7, 50.3, 31.6, 27.1, 26.8, 24.2, 19.2; FABMS m/z 546 (M^+ + 1, 1.7). Anal. Calcd for $C_{30}H_{35}N_3O_3SSi$: C, 66.02; H, 6.46; N, 7.70. Found: C, 65.88; H, 6.70; N, 7.72.

2-Phenylsulfonyl-6-azabicyclo[4.3.0]non-1-ene (30). To a solution of **29** (109 mg, 0.20 mmol) in toluene (2.0 mL) was added Bu_3SnH (0.27 mL 1.00 mmol) at room temperature, and the reaction mixture was stirred for 37 h. Toluene was evaporated off and the residue was passed through a short pad of silica gel with hexane−AcOEt (3:1) to give the crude enamine derivative. TBAF (1.0 M THF solution, 0.40 mL, 0.40 mmol) was added to a solution of the crude enamine derivative in THF (0.6 mL) at room temperature. The reaction mixture was stirred for 1.5 h, quenched by addition of water, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. To a solution of crude alcohol in CH_2Cl_2 (2.0 mL) were added Et_3N (0.11 mL, 0.79 mmol), CBr_4 (133 mg, 0.40 mmol), and Ph_3P (105 mg, 0.40 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and concentrated. Chromatography of the residue was with hexane−AcOEt (2:1) gave **30** (33.8 mg, 64%) a colorless solid: mp 90.5−91.5 °C (from AcOEt−hexane); IR 1597 cm^{-1}; ^1H NMR δ 7.82−7.79 (2H, m), 7.49−7.42 (3H, m), 3.28 (2H, t, J = 7.3 Hz), 3.14−3.10 (4H, m), 2.34 (2H, t, J = 6.4 Hz), 1.92 (2H, quint, J = 7.3 Hz), 1.82 (2H, quint, J = 6.4 Hz);^{13}C NMR δ 156.0, 144.7, 131.2, 128.6, 126.1, 92.2, 52.8, 44.6, 31.3, 22.1, 21.2, 20.1; MS m/z 263 (M^+, 31). Anal. Calcd for $C_{14}H_{17}NO_2S$: C, 63.85; H, 6.51; N, 5.32. Found: C, 63.80; H, 6.49; N, 5.26.

6-Azido-1-(tetrahydropyranyloxy)hex-2-yne (36). To a solution of 3-(tetrahydropyranyloxy)prop-1-yne (9.27 g, 66.1 mmol) in THF (60 mL) was added *n*-BuLi (1.40 M hexane solution, 52.0 mL, 72.8 mmol) at −30 °C and the reaction mixture was stirred for 1 h at the same temperature. A solution of 1,3-dibromopropane (13.4 mL, 132 mmol) in DMPU (6.0 mL) was then added to a solution of the acetylide, thus formed, in THF solution. The reaction mixture was stirred at room temperature for 2 h, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated. The residue was passed through a short pad of silica gel with hexane−AcOEt (20:1) to give the crude monobromo de4rivative. NaN_3 (6.45 g, 99.2 mmol) and NaI (991 mg, 6.61 mmol) were added to a solution of the crude bromo derivative in DMF (66 mL), which was heated at 60 °C for 10 h. The reaction was quenched by addition of water and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (20:1 to 4:1) gave **36** (4.50 g, 30%) as a colorless oil: IR 2222, 2100 cm^{-1}; ^1H NMR δ 4.78 (2H, t, J = 3.0 Hz), 4.26 (1H, dt, J = 15.5, 2.0 Hz), 4.17 (1H, dt, J = 15.5, 2.0 Hz), 3.87−3.78 (1H, m), 3.55−3.47 (1H, m), 3.39 (2H, t, J = 6.9 Hz), 2.33 (2H, tt, J = 2.0, 6.9 Hz), 1.88−1.46 (8H, m); ^{13}C NMR δ 96.7, 84.5, 77.0, 62.0, 54.5, 50.2, 30.2, 27.7, 25.3, 19.1, 16.1; FABMS m/z 224 (M^+ + 1, 3.3). Anal. Calcd for $C_{11}H_{17}N_3O_2$: C, 59.17; H, 7.67; N, 18.82. Found: C, 58.96; H, 7.76; N, 18.75.

6-Acetamido-2-hexyn-1-ol (37a). To a solution of **36** (986 mg, 5.00 mmol) in THF (10 mL) was added Ph_3P (1.57 g, 5.99 mmol) and H_2O (0.14 mL, 7.77 mmol) at room temperature. The reaction mixture was heated under reflux for 2 h and cooled to 0 °C. Et_3N (3.48 mL, 25.0 mmol) and Ac_2O (1.42 mL, 15.0 mmol) were added to the crude amine derivative in THF. After being stirred for 20 min at same temperature, the reaction mixture was diluted by addition of saturated aqueous $NaHCO_3$ and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with

AcOEt to give the crude amide. pTsOH·H_2O (86.1 mg, 0.50 mmol) was added to a solution of the crude amide in MeOH (10 mL) at room temperature and the reaction mixture was allowed to stand for 10 h. MeOH was evaporated off and the residue was chromatographed with AcOEt to afford **37a** (556 mg, 81%) as a colorless oil: IR 3449, 3331, 2235, 1663 cm^{-1}; ^1H NMR δ 6.09 (1H, brs), 4.22 (2H, t, J = 2.0 Hz), 3.34 (2H, q, J = 6.8 Hz), 3.2−2.7 (1H, brs), 2.26 (2H, tt, J = 2.0, 6.8 Hz), 1.97 (3H, s), 1.70 (2H, quint, J = 6.8 Hz); ^{13}C NMR δ 170.6, 84.7, 79.7, 50.9, 38.7, 28.0, 23.2, 16.3; MS m/z 155 (M^+, 7.5); HRMS calcd for $C_8H_{13}NO_2$ 155.0946, found 155.0948. Anal. Calcd for $C_8H_{13}NO_2 \cdot {}^1/_2H_2O$: C, 58.52; H, 8.59; N, 8.53. Found: C, 58.70; H, 8.43; N, 8.59.

6-Acetamido-3-phenylsulfonylhexa-1,2-diene (38a). According to the procedure described for the preparation of **4a**, **38a** (31.2 mg, 39%) was obtained from **37a** (44.9 mg, 0.29 mmol) as a colorless oil: IR 3449, 3402, 1971, 1936, 1666 cm^{-1}; ^1H NMR δ 7.89−7.50 (5H, m), 5.89 (1H, brs), 5.35 (2H, t, J = 3.3 Hz), 3.20 (2H, q, J = 6.6 Hz), 2.25 (2H, tt, J = 3.3, 7.6 Hz), 1.92 (3H, s), 1.66 (2H, quint, J = 7.6 Hz); ^{13}C NMR δ 207.5, 170.2, 139.7, 133.6, 129.1, 128.0, 112.4, 84.8, 38.3, 27.3, 24.0, 23.2; MS m/z 279 (M^+, 5.6); FABHRMS calcd for $C_{14}H_{18}NO_3S$ 280.1007, found 280.1008. Anal. Calcd for $C_{14}H_{18}NO_3S \cdot {}^1/_4H_2O$: C, 59.24; H, 6.21; N, 4.93. Found: C, 59.04; H, 6.28; N, 4.91.

1-Benzoyl-1,2,3,4-tetrahydro-6-methyl-5-phenylsulfonylpyridine (39). To a solution of **38c** (6.8 mg, 0.02 mmol) in THF (0.4 mL) was added ^{t}BuOK (3.4 mg, 0.03 mmol) at room temperature. The reaction mixture was stirred for 20 min, quenched by addition of water, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with AcOEt gave **39** (1.9 mg, 28%) as a colorless plate: mp 117−118 °C (from Et_2O−hexane); IR 1659 cm^{-1}; ^1H NMR δ 7.92−7.35 (10H, m), 3.63 (2H, t, J = 5.9 Hz), 2.63−2.55 (2H, m), 2.20 (3H, t, J = 2.0 Hz), 1.93−1.83 (2H, m); ^{13}C NMR δ 171.4, 148.4, 141.8, 135.7, 133.0, 131.7, 129.1, 128.6, 128.4, 127.0, 125.0, 46.3, 24.9, 23.5, 20.9; MS m/z 342 (M^+, 6.6). Anal. Calcd for $C_{19}H_{19}NO_3S$: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.72; H, 5.70; N, 4.02. When this reaction was carried out in ^{t}BuOH instead of THF, compound **7** was obtained in 37% yield.

6-(Pivaloyloxy)-4-hexyn-1-ol (40). To a solution of 5-(*tert*-butyldimethylsiloxy)pent-1-yne (2.51 g, 12.7 mmol) in THF (25 mL) was added ^{n}BuLi (1.41 M hexane solution, 10.8 mL, 15.2 mmol) at 0 °C for 30 min. Paraformaldehyde (763 mg, 25.4 mmol) was added to the reaction mixture, which was stirred at room temperature for 2 h. The reaction was quenched by addition of water and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated. To a solution of the crude adduct in CH_2Cl_2 (25 mL) and pyridine (2.5 mL) were added DMAP (155 mg, 1.27 mmol) and PivCl (2.35 mL, 19.1 mmol) at 0 °C. The reaction mixture was stirred for 10 h at room temperature, quenched by addition of water, and extracted with Et_2O. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (10:1) to give the crude pivaloyloxy derivative. pTsOH (219 mg, 1.27 mmol) was added to a solution of the crude ester in MeOH (25 mL) at room temperature and the reaction mixture was stirred for 1 h. MeOH was evaporated off and the residue was chromatographed with hexane−AcOEt (4:1) to give **40** (2.15 g, 86%) as a colorless oil: IR 3622, 3456, 2235, 1726 cm^{-1}; ^1H NMR δ 4.61 (2H, t, J = 2.4 Hz), 3.71 (2H, t, J = 6.4 Hz), 2.32 (2H, tt, J = 2.4, 6.4 Hz), 1.74 (2H, quint, J = 6.4 Hz), 1.19 (9H, s); ^{13}C NMR δ 177.9, 86.3, 74.8, 61.4, 52.7, 38.7, 31.0, 27.0, 15.3; MS m/z 198 (M^+, 4.4); HRMS calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.1255.

6-(Pivaloyloxy)-4-hexynoic Acid (42). To a solution of **40** (776 mg, 3.91 mmol) in CH_2Cl_2 (20 mL) was added Dess−Martin periodinane (2.16 g, 5.09 mmol) at room temperature. The reaction mixture was stirred for 20 min, quenched by addition of aqueous $Na_2S_2O_3$, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated. To a solution of the crude aldehyde and 2-methyl-2butene (8.0 mL) in ^{t}BuOH (20 mL) were added $NaClO_2$ (2.21 g, 19.5 mmol) and NaH_2PO_4 (2.44 g, 15.6 mmol) in H_2O (8.0 mL) at room temperature. The reaction mixture was stirred for 4 h, quenched by addition of 10% HCl, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (2:1) gave **42** (786 mg, 95%) as a colorless oil: IR 3141, 2239, 1724 cm^{-1}; ^1H NMR δ 4.62 (2H, t, J = 2.0 Hz), 2.63−2.49 (4H, m), 1.20 (9H, s); ^{13}C NMR δ 177.9, 177.6, 84.6, 75.3, 52.5, 38.7, 33.0, 27.0, 14.4; FABMS m/z 213 (M^+, 52); FABHRMS calcd for $C_{11}H_{17}O_4$ 213.1127, found 213.1126. Anal. Calcd for $C_{11}H_{16}NO_4 \cdot {}^1/_4H_2O$: C, 60.96; H, 7.67. Found: C, 61.19; H, 7.66.

6-Hydroxy-4-hexynamide (43). To a solution of **42** (1.08 g, 5.09 mmol) and Et_3N (0.85 mL, 6.10 mmol) in THF (17 mL) was added isobutyl chloroformate (0.80 mL, 6.09 mmol) at 0 °C, and the reaction mixture was stirred for 30 min. Aqueous NH_3 (28%, 0.62 mL) was added to the mixed anhydride in THF solution and the reaction mixture was stirred for 2 h. The resulting solids were filtered off, and the filtrate was concentrated. To a solution of the crude amide in MeOH (13 mL) was added K_2CO_3 (1.06 g, 7.67 mmol) at room temperature. After being stirred for 12 h at room temperature, the reaction mixture was diluted with AcOEt, and the resulting solids were filtered off. The filtrate was evaporated off and the residue was chromatographed with AcOEt−EtOH (1:0 to 10:1) to give **43** (481 mg, 74%) as a colorless needle: mp 77−79 °C (from AcOEt); IR (KBr) 3369, 3200, 22245, 1670 cm^{-1}; ^1H NMR δ 4.25 (2H, t, J = 2.0 Hz), 2.58 (2H, tt, J = 2.0, 7.3 Hz), 2.45 (2H, t, J = 7.3 Hz); ^{13}C NMR (CD_3OD) δ 177.3, 84.7, 80.7, 51.2, 35.9, 16.1; FABMS m/z 128 (M^+ + 1, 69). Anal. Calcd for $C_6H_9NO_2$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.36; H, 7.21; N, 10.73.

1,2,3,4-Tetrahydro-6-methyl-5-phenylsulfonylpyrid-2-one (48). To a solution of **46** (12.6 mg, 0.05 mmol) in THF (0.5 mL) was added NaH (60% in oil, 3.0 mg, 0.08 mmol) at room temperature, and the reaction mixture was stirred for 2.5 h. The reaction was quenched by addition of water and extracted with AcOEt, which was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (1:1) gave **48** (9.9 mg, 79%) as a colorless needle: IR 3400, 3227, 1707, 1643 cm^{-1}; ^1H NMR δ 7.86−7.52 (5H, m), 7.64 (1H, brs), 2.67 (2H, dt, J = 1.5, 8.3 Hz), 2.49 (2H, dd, J = 7.8, 8.3 Hz) 2.36 (3H, s); ^{13}C NMR δ 170.5, 144.1, 142.0, 133.1, 129.3, 126.8, 112.9, 30.0, 22.0, 17.7; MS m/z 251 (M^+, 15). Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 57.35; H, 5.21; N, 5.57. Found: C, 57.25; H, 5.32; N, 5.49.

***N*-(*tert*-Butoxycarbonyl)-2-(3-hydroxypropyn-1-yl)-aniline (51).** To a solution of **50** (957 mg, 3.00 mmol), $PdCl_2(Ph_3P)_2$ (21.1 mg, 0.03 mmol), and CuI (11.4 mg, 0.06 mmol) in THF (15 mL) were added $^i Pr_2NH$ (2.0 mL) and propargyl alcohol (0.26 mL, 4.50 mmol) at room temperature. The reaction mixture was stirred for 2.5 h, and the resulting solids were filtered off. The filtrate was concentrated to leave the residue, which was chromatographed with hexane−AcOEt (4:1) to give **51** (679 mg, 92%) as a colorless oil: IR 3603, 3408, 2230, 1726 cm^{-1}; ^1H NMR δ 8.10 (1H, d, J = 8.6 Hz), 7.37−7.29 (2H, m), 7.22 (1H, brs), 6.93(1H, dt, J = 1.0, 7.6 Hz), 4.56 (2H, d, J = 4.3 Hz), 2.50 (1H, brs), 1.54 (9H, s);^{13}C NMR δ 152.5, 139.6, 132.1, 129.8, 122.1, 117.7, 110.5, 94.1, 81.04, 80.95, 51.5, 28.3; MS m/z 247 (M^+, 22); HRMS calcd for $C_{14}H_{17}NO_3$ 247.1208, found 247.1204.

***N*-(*tert*-Butoxycarbonyl)-2-(1-phenylsulfonylprop-1,2-dien-1-yl)aniline (52).** According to the procedure described for the preparation of **4a**, **52** (35.1 mg, 47%) was obtained from **51** (49.5 mg, 0.20 mmol). Compound **52** was a colorless needle: mp 100−101 °C (from Et_2O); IR 3425, 1965, 1925, 1724 cm^{-1}; ^1H NMR δ 7.95 (1H, d, J = 8.3 Hz), 7.71−7.68 (2H, m), 7.61 (1H, tt, J = 1.3, 7.6 Hz), 7.59−7.42 (2H, m), 7.34−7.27 (1H, m), 7.22 (1H, brs), 6.87 (1H, dt, J = 1.0, 7.6 Hz), 6.71

(1H, dd, J = 1.3, 7.6 Hz), 5.53 (2H, s), 1.51 (9H, s); ^{13}C NMR δ 208.3, 152.8, 138.5, 137.6, 133.9, 131.5, 130.5, 128.9, 128.4, 122.9, 121.5, 118.7, 111.2, 83.1, 80.5, 28.3; MS m/z 371 (M^+, 11). Anal. Calcd for $C_{20}H_{21}NO_4S$: C, 64.67; H, 5.70; N, 3.77. Found: C, 64.67; H, 5.74; N, 3.64.

1-(*tert*-Butoxycarbonyl)-2-methyl-3-phenylsulfonylindole (53). To a solution of **52** (37.1 mg, 0.10 mmol) in THF (1.0 mL) was added NaH (60% NaH in oil, 6.00 mg, 0.15 mmol) at room temperature. The reaction mixture was stirred for 4 min, quenched by addition of water, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (10:1) afforded **53** (35.5 mg, 96%) as a colorless cube: mp 132−133 °C (from hexane−AcOEt); IR 1742 cm^{-1};^{1}H NMR δ 8.20−8.16 (1H, m), 8.06−7.96 (3H, m), 7.55−7.27 (5H, m), 2.98 (3H, s), 1.68 (9H, s); ^{13}C NMR δ 149.5, 143.4, 143.3, 135.1, 132.8, 129.1, 126.3, 125.3, 124.9, 124.2, 120.0, 118.3, 115.2, 85.9, 28.1, 14.3; MS m/z 371 (M^+, 15). Anal. Calcd for $C_{20}H_{21}NO_4S$: C, 64.67; H, 5.70; N, 3.77. Found: C, 64.34; H, 5.79; N, 3.72.

2-Methyl-3-phenylsulfonylindole (54). To a solution of **52** (77.5 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was added TFA (0.20 mL) at room temperature. The reaction mixture was stirred for 30 min, quenched by addition of saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−AcOEt (4:1) afforded **54** (47.5 mg, 83%) as a colorless needle: mp 174.5−176°C (from hexane−AcOEt); IR 3450 cm^{-1}; ^{1}H NMR δ 8.60 (1H, brs), 8.04−7.97 (3H, m), 7.50−7.42 (3H, m), 7.29−7.19 (3H, m), 2.74 (3H, s);^{13}C NMR δ 144.1, 141.1, 134.2, 132.4, 129.0, 126.1, 125.5, 123.2, 122.3, 119.6, 111.8, 110.9, 13.1; MS m/z 271 (M^+, 100). Anal. Calcd for $C_{15}H_{13}NO_2S\cdot{}^1/_4H_2O$: C, 65.31; H, 4.93; N, 5.08. Found: C, 65.03; H, 4.81; N, 4.94.

2-Methyl-3-phenylsulfonylquinoline (59). To a solution of **58** (56.3 mg, 0.15 mmol) in CH_2Cl_2 (0.6 mL) was added TFA (0.15 mL) at room temperature. The reaction mixture was stirred for 30 min, quenched by addition of saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated. To a solution of the crude product in MeOH (0.7 mL) was added salcomine (4.70 mg, 0.01 mmol) at room temperature under an oxygen atmosphere. The reaction mixture was stirred for 24 h at same temperature, and MeOH was evaporated off to leave the residue, which was chromatographed with hexane−AcOEt (4:1) to give **59** (31.8 mg, 77%) as a colorless needle: mp 145.5−146.5 °C (from hexane−AcOEt); ^{1}H NMR δ 9.07 (1H, s), 8.07−7.82 (5H, m), 7.67−7.50 (4H, m), 2.79 (3H, s); ^{13}C NMR δ 155.2, 149.2, 140.3, 139.3, 133.6, 133.5, 132.7, 129.3, 129.0, 128.6, 128.0, 127.4, 125.6, 24.2; MS m/z 283 (M^+, 63). Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.94. Found: C, 67.66; H, 4.71; N, 4.77.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **13a**,**b**, **16a**−**c**, **17a**,**b**, **25, 34c**, **35a**, **35b**, **35e**, **37c**, **40**, **41**, **44**, **45** and **51** and characterization data for compounds **4b**, **4c**, **7**, **8**, **10**, **13b**, **13c**, **14a-c**, **15a-c**, **16a**−**c**, **17a**−**c**, **18a**−**c**, **24**, **33a**−**e**, **34a**−**e**, **35a**−**e**, **37b**, **37c**, **38b**, **38c**, **41**, **44**, **45**, **46**, **47**, **49**, **56**, **57**, and **58**. This material is available free of charge via the Internet at http://pubs.acs.org.

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