Inter- and Intramolecular Addition/Cyclizations of Sulfonamide Anions with Alkynyliodonium Triflates. Synthesis of Dihydropyrrole, Pyrrole, Indole, and Tosylenamide Heterocycles

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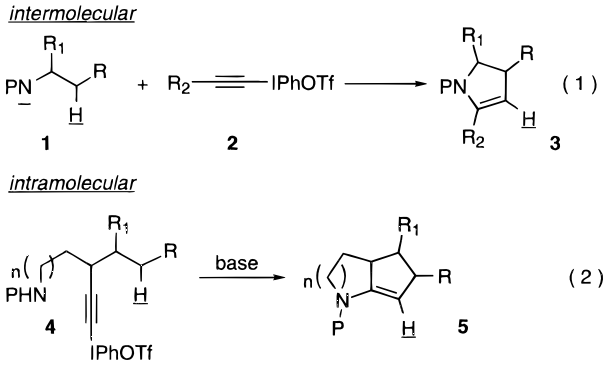
The synthesis of dihydropyrroles, pyrroles, and indoles through [3-atom + 2-atom] combination of ethyl or aryl tosylamide anions with phenyl(propynyl)iodonium triflate, and the base-mediated intramolecular bicyclization of alkynyliodonium-bearing tosylamide or tosylimide substrates to furnish bicyclic and tricyclic tosylenamide (-enimide) products, is described. A detailed discussion of the scope, limitations, byproduct formation, and the basis for observed diastereoselectivity is presented.

The unique reactivity of alkynyliodonium salts **2** suggests that they may serve as versatile reagents in heterocycle synthesis.[1] In particular, combination of nitrogen-bearing substrates with alkynyliodonium species (eqs 1 and 2) might provide products congruent with substructures contained within several alkaloid families. The reduction of the strategy described in eqs 1 and 2 to practice could permit access to five-membered ring products with either endocyclically (e.g., **3**) or exocyclically disposed nitrogen atoms (e.g., **5**).[2]



These two-step transformations initiate with nucleophilic capture by the iodonium salt. The potent electrophilicity of the alkynyliodonium species **6** has been well documented with a host of *soft* nucleophiles (malonates and related β-dicarbonyls,[1c,i,j,p] sulfinate,[1e,k] thiolate,[1r] and thiocyanate,[1b] carboxylate/phosphate/sulfonate,[1d,q] and azide,[1l,o] inter alia); however, clear limitations prevent extension to more nucleophilic species.[1n] Amine-derived substrates represent a notable omission.[1f] Upon nucleophilic addition to the β-carbon of the alkynyliodonium salt, an intermediate alkylidene carbene **8** of orthogonal reactivity is generated, Scheme 1. This reactive and mildly electrophilic singlet carbene has four conceivable fates:[3] (1) rearrangement (1,2 shift, path a), (2) C−H insertion (path b), (3) cycloaddition (path c), and (4) dimerization (not shown). The relative rates of these options depend upon the nature of R and Nu, and scattered reactivity data allow deduction of qualitative rankings for these paths. 1,2-Shifts of hydrogen ($t_{1/2}$ <1 ps for the parent ethylidene),[3k] aryl, and TMS groups apparently proceed more rapidly than any other options, and alkyne formation (path a) will predominate in these cases. Both 1,5 C−H insertion (path b) and alkene cycloaddition (path c) can compete with 1,2-*alkyl* shifts, and it is this key observation that opens a window of opportunity for synthesis. 1,5 C−H insertion appears to prevail over either inter- or intramolecular alkene cycloaddition, which is, in turn, faster than 1,2-alkyl shifts. Of course it is possible that exceptions to these generalizations will emerge as more data becomes available.

The results shown in Table 1 demonstrate that the yield of the dihydropyrrole product **16** from combination of anion **14** with the prototype iodonium salt **15**[1s] is extremely sensitive to the nature of the protecting group P, eq 3. No conditions were found which permitted either the lithium amide **14a** (or the parent amine) or the weakly acidic benzamide **14b** to participate in N−C bond formation. The much more acidic triflamide **14c** and trifluoroacetamide **14d** did furnish modest amounts of

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(1) (a) Stang, P. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 285 and references cited therein. (b) Fischer, D. R.; Williamson, B. L.; Stang, P. J. *Synlett* **1992**, 535. (c) Bachi, M. D.; Bar-Ner, N.; Crittell, C. M.; Stang, P. J.; Williamson, B. L. *J. Org. Chem.* **1991**, *56*, 3912. (d) Stang, P. J. *Russ. Chem. Bull.* **1993**, *42*, 12. (e) Williamson, B. L.; Tykwinski, R. R.; Stang, P. J. *J. Am. Chem. Soc.* **1994**, *116*, 93. (f) March, P.; Williamson, B. L.; Stang, P. J. *Synthesis* **1994**, 1255. (g) Tykwinski, R. R.; Whiteford, J. A.; Stang, P. J. *J. Chem. Soc., Chem. Commun.* **1993**, 1800. (h) Ochiai, M., In *Reviews on Heteroatom Chemistry, Volume 2*; Oae, S., Ed.; MYU: Tokyo, 1989; p 92. (i) Ochiai, M.; Kunishima, M., Nagao, Y.; Fuji, K.; Shiro, M.; Fujita, E. *J. Am. Chem. Soc.* **1986**, *108*, 8281. (j) Ochiai, M.; Ito, T.; Takaoka, Y.; Kunishima, M.; Tani, S.; Nagao, Y. *J. Chem. Soc. Chem. Commun.* **1990**, 118. (k) Ochiai, M.; Kunishima, M.; Tani, S.; Nagao, Y. *J. Am. Chem. Soc.* **1991**, *113*, 3135. (l) Ochiai, M.; Kunishima, M.; Fuji, K.; Nagao, Y. *J. Org. Chem.* **1988**, *53*, 6144. (m) Ochiai, M.; Takaoka, Y.; Nagao, Y. *J. Am. Chem. Soc.* **1988**, *110*, 6565. (n) Margida, A.; Koser, G. F. *J. Org. Chem.* **1984**, *49*, 4703. (o) Kitamura, T.; Stang, P. J. *Tetrahedron Lett.* **1988**, *29*, 1887. (p) Tykwinski, R. R.; Stang, P. J.; Peisky, N. E. *Tetrahedron Lett.* **1994**, *35*, 23. (q) Stang, P. J. *Acc. Chem. Res.* **1991**, *24*, 304. (r) Stang, P. J.; Zhdankin, V. V. *J. Am. Chem. Soc.* **1991**, *113*, 4571. (s) Zhdankin, V. V.; Scheuller, M. C.; Stang, P. J. *Tetrahedron Lett.* **1993**, *34*, 6853.

(2) (a) Schildknegt, K.; Bohnstedt, A. C.; Feldman, K. S.; Sambandam, A. *J. Am. Chem. Soc.*, **1995**, *117*, 7544. (b) Feldman, K. S.; Bruendl, M. M.; Schildknegt, K. *J. Org. Chem.* **1995**, *60*, 7722.

(3) (a) Stang, P. J. *Acc. Chem. Res.* **1982**, *15*, 348, and references cited therein. (b) Stang, P. J. *Chem. Rev.* **1978**, 383. (c) Stang, P. J. *Isr. J. Chem.* **1981**, *21*, 119. (d) Stang, P. J. *Acc. Chem. Res.* **1978**, *11*, 107. (e) Taber, D. F.; Meagley, R. P. *Tetrahedron Lett.* **1994**, *35*, 7909. (f) Gilbert, J. C.; Giamalva, D. H.; Weerasooriya, U. *J. Org. Chem.* **1983**, *48*, 5251. (g) Gilbert, J. C.; Giamalva, D. H.; Baze, M. E. *J. Org. Chem.* **1985**, *50*, 2557. (h) Baird, M. S.; Baxter, A. G. W.; Hoorfar, A.; Jefferies, I. *J. Chem. Soc., Perkin Trans. 1*, **1991**, 2575. (i) Karpf, M.; Huguet, J.; Dreiding, A. S. *Helv. Chim. Acta* **1982**, *65*, 13. (j) Kim, S.; Cho, C. M. *Tetrahedron Lett.* **1994**, *35*, 8405. (k) Gallo, M. M.; Hamilton, T. P.; Schaeffer, H. F., III. *J. Am. Chem. Soc.* **1990**, *112*, 8714, and references cited therein. (l) Fisher, R. H.; Baumann, M.; Köbrich, G. *Tetrahedron Lett.* **1974**, 1207.

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Scheme 1

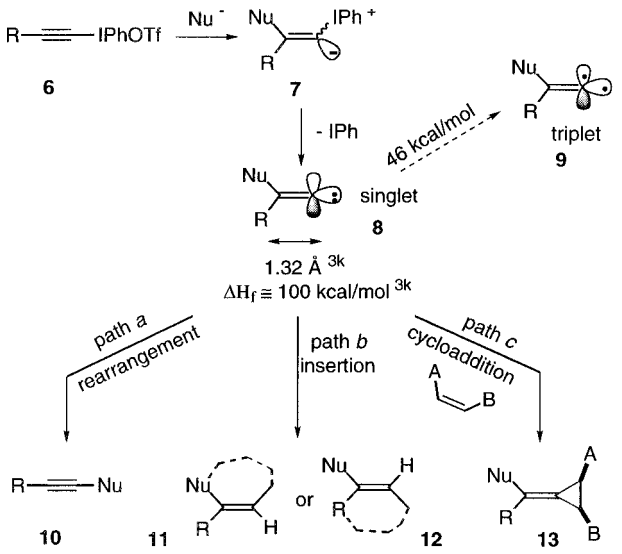
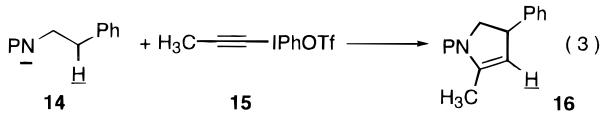


Table 1. Yield of Dihydropyrrole 16 as a Function of Protecting Group P

entry	P in **14**	est pK_a of P*H*N	yield of **16** (%)
a	H	41[5a]	–
b	PhCO	23[5b]	–
c	CF_3SO_2	10[5c]	16
d	CF_3CO	17[5d]	28
e	$tolSO_2$	16[5e]	67
f	$TMS(CH_2)_2SO_2$	17[5f]	9

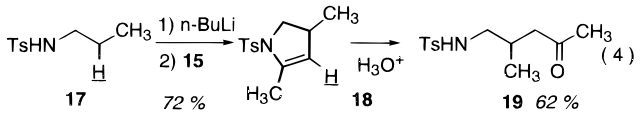
the [3 + 2] dihydropyrrole adducts **16c** and **16d**, respectively. However, the highest yields consistently attended the tosylamide substrate **14e**. Optimization studies probing the effects of solvent (THF, Et_2O, DME, PhH, CH_2Cl_2), metal counterion (Li, Na, K, Ce), reagent ratios, temperature (−78 °C to 60 °C), sequence (and rate) of addition, and concentration (0.001 to 0.1 M in **14e**) converged on the reaction parameters shown with eq 3 for best yield. It is notable that these conditions require no more than 1 equiv of each component for optimum yields. Some of the product tosylenamides **16** proved to be quite hydrolytically labile,[4] and minimizing exposure to acid upon workup and chromatographic isolation (Et_3N in the eluent) was essential to suppress hydrolysis (vide infra). It is apparent from the data in Table 1 that pK_a (DMSO) is not the sole determinant of successful reaction in this series.



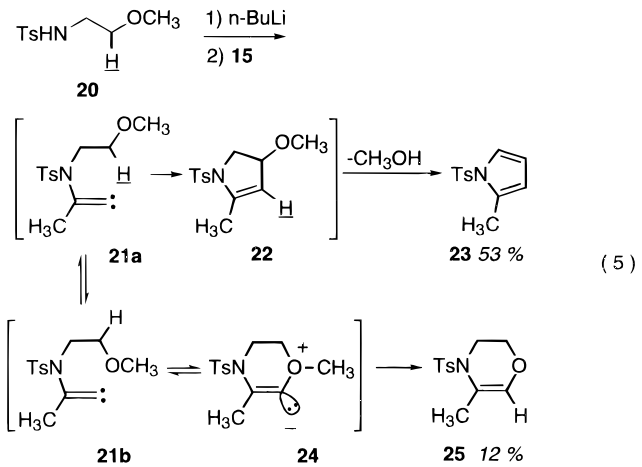
best conditions: P = $tolSO_2$, THF solvent, n-BuLi base, 0.01 M in **14**, 25 °C

Several readily available substrates **17**, **20**, **26**, **33**, and **36a**/**b** were examined for their capacity to participate in this reaction. The first two species, **17** and **20**, test the question of functional group compatibility at the C−H insertion site, while the latter four substrates, which bear substituents at both the α and *β* positions, examine the diastereoselectivity of alkylidene carbene C−H insertion.

n-Propyltosylamide **17** furnished dihydropyrrole product **18** in good yield if careful attention was paid to workup conditions. This methyl-substituted product **18** hydrolyzed more readily than the phenyl analog **16e** to furnish the ketoamide **19**, eq 4. The relatively indiscriminate nature of the highly energetic alkylidene carbene intermediate is emphasized by the equally facile insertion into the secondary C−H bond of **17** (BDE ∼ 95 kcal/mol) as compared to the slightly activated benzylic position (BDE ∼ 85 kcal/mol) of **14e**.



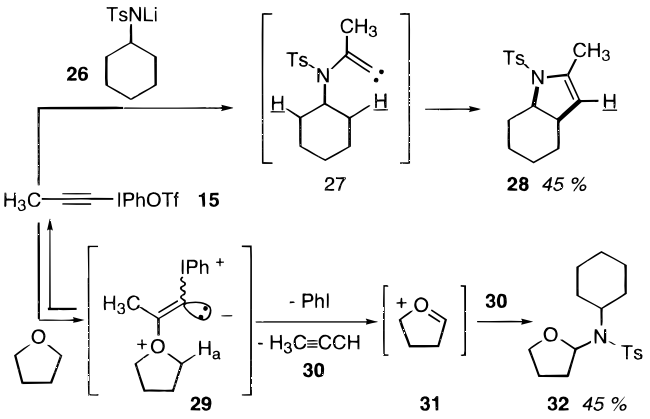
The *β*-methoxylated substrate **20** participated in the [3 + 2] addition with phenyl(propynyl)iodonium triflate (**15**) as well, although two unexpected products were isolated after workup, eq 5. The major adduct, pyrrole **23**, logically follows through ready elimination of methanol from the putative (but never observed) dihydropyrrole intermediate **22**. The second, minor product exhibits spectral data consistent with the heterocycle **25**. The formation of this product could involve initial carbene trapping by the nucleophilic ether oxygen to furnish an intermediate ylide **24**. Formal demethylation of this species by some extant nucleophile such as triflate, tosylamide anion, or methoxide followed by protonation of the resultant vinyl anion, perhaps by dihydropyrrole **22**, yields **25**. A similar DME adduct has been observed by Stang upon treatment of *tert*-butyl(phenyl)iodonium tosylate with sodium azide in that solvent.[1o]



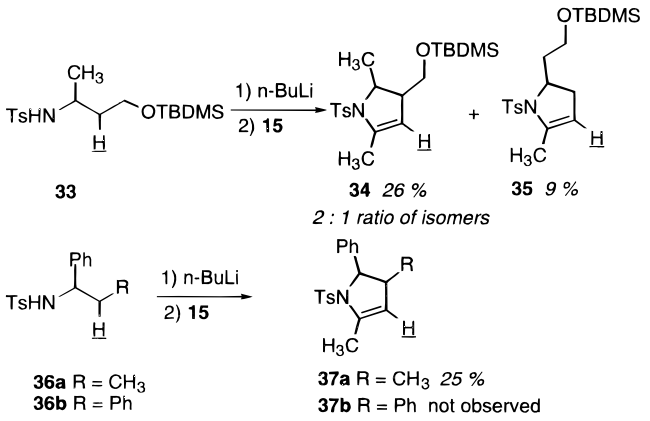
The lithiated cyclohexyltosylamide substrate **26** differs from the previous entries in that it features both a substituted α-position and diastereotopic hydrogens available for C−H insertion by the intermediate carbene. Treatment of anion **26** with phenyl(propynyl)iodonium triflate (**15**) affords moderate amounts of dihydropyrrole product **28** as a single cis-fused diastereomer, Scheme 2. In this case, addition of the iodonium salt **15** to a refluxing solution of amide anion was critical in elevating the yield; reaction at 25 °C under otherwise identical conditions afforded only 22% of **28**. In addition to formation of the expected dihydropyrrole product, an equal amount (45%) of the curious THF adduct **32** was isolated. Apparently, a formal oxidation of THF has occurred, perhaps with concomitant reduction of the alkynyliodonium salt to the parent alkyne **30** (undetected). A plausible mechanistic interpretation of this transformation is suggested in Scheme 2. Formation of

(4) (a) Hegedus, L. S.; Holden, M. S. *J. Org. Chem.* **1986**, *51*, 1171. (b) Hegedus, L. S.; McKearin, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 2444.

Scheme 2



Scheme 3



the key THF-derived electrophile **31** might result from initial (reversible) nucleophilic capture of salt **15** by THF, followed by elimination of the elements of propyne and PhI. The base **26** may play a role in siphoning off the THF adduct **29** by deprotonation of H_a. Isolation of this particular byproduct is unique to the cyclohexyltosylamide substrate and may simply be a reflection of both the higher temperature (60 °C) employed compared to the other cases (~ 25 °C) and the inherent sluggishness of the α-substituted tosylamide in direct nucleophlic addition to **15** (vide infra).[6] Further studies are in progress to test this mechanistic proposal and to probe the generality of this THF oxidation/nucleophile-trapping sequence.

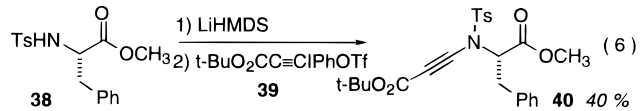
Further attempts to discern diastereoselective C−H insertion with the α and *β* substituted ethyltosylamide substrates **33** and **36a**/**b** did not furnish encouraging results, Scheme 3. In each case, optimization studies could not improve the yields past the values shown, and recovered starting tosylamide accounted for the majority of the material isolated. Three dihydropyrroles resulted from reaction of the silyl ether **33** with iodonium salt **15**. Thus, only modest regioselectivity favoring alkylidene carbene insertion into a secondary C−H bond (**34**) over a primary C−H bond (**35**), and minimal diastereoselectivity in the secondary C−H insertion species **34**, was observed. The α-phenylated substrates **36a** and **36b** remove the regiochemical ambiguity noted above as only

Table 2. Tosylindole Synthesis from Tosylanilides 43 and Alkynyliodonium Salt 15

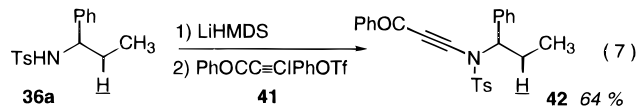
entry	R in **43**	yield of **45**/**46**(%)	**45**:**46** ratio
a	H	66	–
b	CH_3	59	1:1
c	OCH_3	61	1.4:1
d	CO_2CH_3	51	1.2:1
e	CO_2t-Bu	46	1.3:1

insertion into the benzylic C−H position is possible. Unfortunately, only minor amounts of dihydropyrrole product **37a** was observed in the former case. These substrates reveal a significant limitation of this approach to dihydropyrrole synthesis: substituents at the α position are barely tolerated, and in any event 1,2-relative asymmetric induction is modest at best.

The use of more electrophilic alkynyliodonium salts to overcome the sluggish reactivity of α-substituted ethyltosylamides was briefly examined with the propiolate and propynylphenone species **39** and **41**,[7] respectively. In both cases (eqs 6 and 7), moderate amounts of the alkynylated species **40** and **42** were obtained to the exclusion of 1,5 C−H insertion products. It is unclear at present whether these transformations followed the alkylidene carbene/1,2-shift mechanism (Scheme 1) or a more orthodox conjugate addition/iodonium salt elimination sequence initiated by amide anion addition to the iodonium-bearing carbon of the alkyne electrophile.

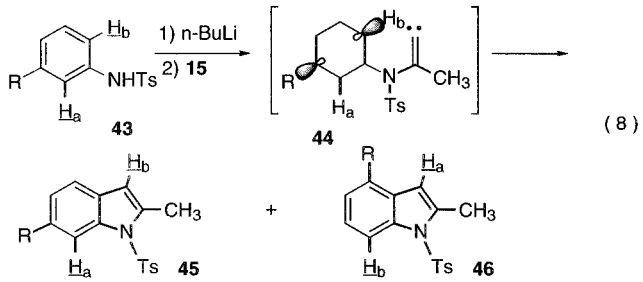


(6)



(7)

Extension of this [3-atom + 2-atom] nitrogen heterocycle synthesis to indole targets would require tosylanilides as the three-atom component. In this instance, alkylidene carbene insertion into a much more refractory aryl C−H bond (BDE ~ 103 kcal/mol) would be necessary to secure the indole product, a transformation which enjoys scant precedent.[1g] However, the ready availability of the precursor tosylanilides and the lack of a prerequisite for further aryl ring activation suggested that successful realization of this strategy might provide a novel and useful complement to current art.[8] In fact, treatment of the lithium salt of tosylanilide itself with phenyl(propynyl)iodonium triflate (**15**) furnished the desired 2-methylindole nucleus **45a** in 66% yield, eq 8 and Table 2, entry a.



(8)

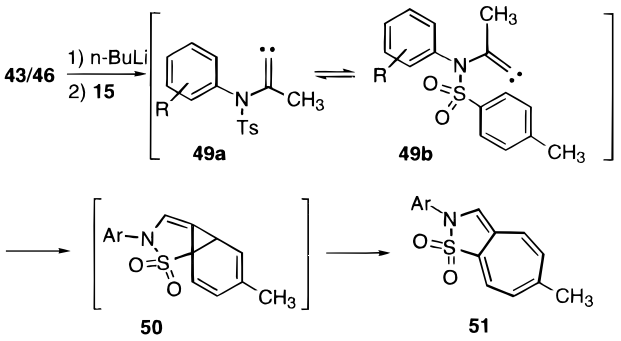
(5) All pK_a data were taken from Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456. The following model compounds (in DMSO) were used for comparison: (a) NH_3 41; (b) $PhCONH_2$ 23.4; (c) $F_3CSO_2NH_2$ 9.7; (d) F_3CCONH_2 17.2; (e) $PHSO_2NH_2$ 16.1; (f) $CH_3SO_2NH_2$ 17.5.

(6) Control experiments demonstrated that alkynyliodonium salt **15** remains unchanged for 72 h at rt in THF-d_8 and only suffers ~20% decomposition (to unidentified materials) after 7 h at 60 °C in THF-d_8.

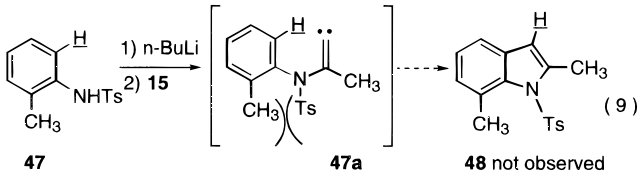
(7) Williamson, B. L.; Stang, P. J.; Arif, A. M. *J. Am. Chem. Soc.* **1993**, *115*, 2590.

(8) Gribble, G. W. *Contemp. Org. Synth.* **1994**, *1*, 145.

Scheme 4

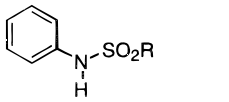


Meta substituents on the tosylanilide ring introduce an issue of regioselectivity upon carbene C−H insertion. The meta-functionalized substrates **43b**−**43e** were examined in this indole synthesis to test the premise that the facility of C−H insertion might be modulated by the through space orbital interaction shown in **44**. In practice, only modest and unidirectional selectivity for insertion into the least sterically encumbered C−H_b bond, irrespective of the electronic character of the cognate R−Ar bond, was detected (Table 2, entries b−e). Indole formation from iodonium salt **15** and *o*-methyltosylanilide (**47**) did not proceed in any detectable amount, plausibly due to the repulsive peri-type steric interactions indicated in **47a** which would be unavoidable as the carbene approaches the C−*H* bond, eq 9.

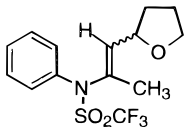


In each instance, and especially with **47**, indole formation was accompanied by substantial quantities (10−30%) of a highly colored, purple, unstable product which displayed characteristic signals in the ^{1}H and ^{13}C NMR spectra of the crude reaction mixtures. Although these byproducts defied all attempts at purification/isolation, the spectral evidence in hand, coupled with literature precedent and subsequent results in the intramolecular series (vide infra) suggests an "azulene"-type structural assignment **51**, Scheme 4.[9] These products **51** might arise through a mechanistic pathway that features alkylidene carbene *addition* to an alkene in the toluene ring of the tosyl unit, followed by electrocyclic opening of the exceedingly strained norcaradiene intermediate **50**. Thus, the penalty for relying on a relatively slow aryl−H insertion appears to be the emergence of a normally uncompetitive C═C addition.

Attempts to suppress this unwanted addition process focused on either removing, or at least hindering, the offending tolyl unit. Toward this end, substrates **52a**−**52c** were combined with phenyl(propynyl)iodonium triflate (**15**) under standard conditions, but no useful results were forthcoming. The steric hindrance strategy (mesityl **52a** or trisyl **52b**) did not afford any characterizable products, while complete replacement of the tolyl ring with CF_3 (**52c**) furnished only modest amounts of indole (~30%) along with the THF−alkylidene carbene intermolecular insertion product **53** in similar yield. This example is the only instance throughout the entire study in which intermolecular insertion into solvent was seen. The basis for this unusual reactivity in the triflamide case remains obscure.

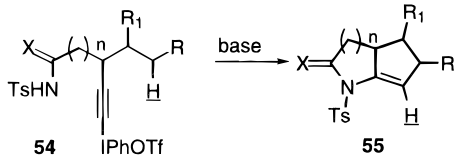


52a R = 1,3,5-trimethylphenyl
52b R = 1,3,5-triisopropylphenyl
52c R = CF_3



53

The intramolecular variant of this tosylamide/iodonium salt combination is particularly well suited to the construction of (at least) bicyclic nitrogen-containing skeleta which are related to several cyclopentylamine-containing naturally occurring alkaloids. At the outset, this chemistry was not without its risks: (1) preparation of the sensitive alkynyliodonium unit from its alkynylstannane precursor requires a very reactive electrophilic iodinating reagent which might be incompatible with the tosylamide moiety, and (2) activation of the cyclization precursor (e.g. **54**) with base raises the specter of untoward reaction with the alkynyliodonium unit (addition, propargyl deprotonation?) in competition with tosylamide deprotonation. Nevertheless, this cyclization sequence proceeds smoothly and normally in higher yields than the intermolecular cases to afford annelated cyclopentenyltosylamide products in which the size of the nitrogen bearing ring depends upon the tether length connecting nucleophile with electrophile. The initial studies focused on three key issues (eq 10): (1) What tether length *n* is acceptable? (2) What functionality (X, R, R_1) are tolerated/beneficial? (3) What level of diastereoselectivity can be achieved?



The substrates designed to probe these questions, **59a**−**f**, **62**, **63**, and **66**, were assembled via standard propargyl anion chemistry where appropriate, Scheme 5. The tosylamide functionality was introduced by the method of Weinreb.[10] The eight-membered ring cyclization precursor tosylamide **66** was prepared by a slightly different route, starting with ester **64**, which relied on alkyne introduction through a Corey−Fuchs procedure[11] as the requisite parent alkynol was not readily available. These cyclization substrates were stored as their alkynylstannanes, which themselves were rather labile and only survived chromatography if the silica gel was first deactivated with 10−20% H_2O and ~0.1% Et_3N was included in the eluant. The alkynyliodonium salts were generated in situ as required and used immediately in cyclization experiments.

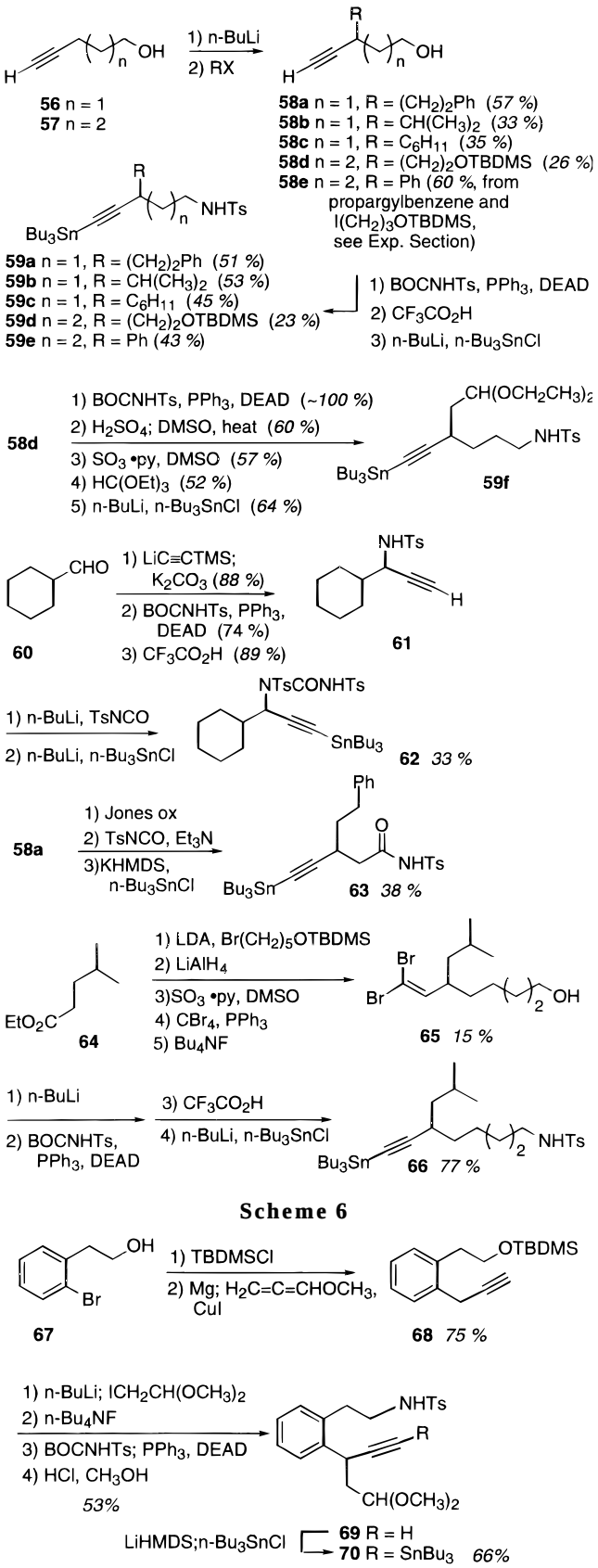
The tosylurea substrate **62** was prepared from cyclohexanecarboxaldehyde (**60**) as shown in Scheme 5. It is notable that stannylation of the dianion derived from double deprotonation of the tosylurea alkyne precursor to **62** only occurred on carbon. Tosyl*imide* **63** was readily

(9) Gilbert, J. C.; Blackburn, B. K. *Tetrahedron Lett.* **1990**, *31*, 4727.

(10) Henry, J. R.; Marcin, L. R.; McIntosh, M. C.; Scola, P. M.; Harris, G. D., Jr.; Weinreb, S. M. *Tetrahedron Lett.* **1989**, *30*, 5709.

(11) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

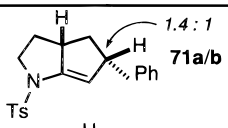
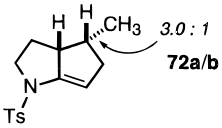
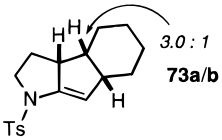
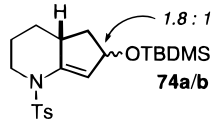
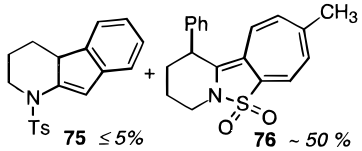
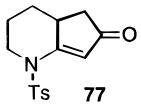
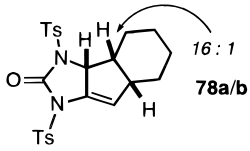
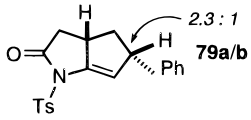
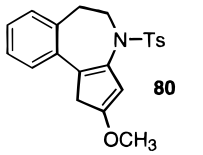
Scheme 5



Scheme 6

available from the precursor **58a** already in hand. Again, stannylation proceeded exclusively on carbon. The preparation of the final cyclization substrate, **70**, was slightly more involved and is detailed in Scheme 6. Nevertheless, both propargyl anion alkylation and Mitsunobu-based introduction of the tosylamide functionality proved reliable and the requisite stannane **70** was obtained without event.

Table 3. Base-Mediated Bicyclization of Alkynyliodonium Tosylamides and Tosylimides

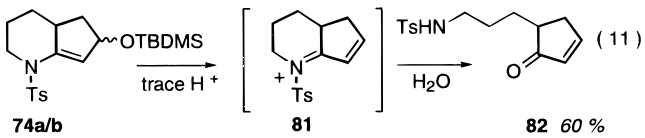
Entry	Substrate	yield (%)	Bicyclization Products
a	**59a**	*73*	 1.4 : 1 **71a/b**
b	**59b**	*66*	 3.0 : 1 **72a/b**
c	**59c**	*69*	 3.0 : 1 **73a/b**
d	**59d**	*64*	 1.8 : 1 **74a/b**
e	**59e**		 **75** ≤5% **76** ~ 50 %
f	**59f**	*50*	 **77**
g	**62**	*44*	 16 : 1 **78a/b**
h	**63** (Et_3N base)	*54*	 2.3 : 1 **79a/b**
i	**66**		no cyclization products
j	**70**	*56*	 **80**

The prototype case **59a**, Table 3, entry a, established that the transformation proceeds as desired to furnish bicyclic tosylenamide products **71a/b**. Optimization studies with **59a** converged on a set of "best" parameters (THF solvent, 0.08 M, 1 equiv of t-BuOK, −40 °C → rt) similar to those derived for the intermolecular case. The intermediate alkynyliodonium salt did not share the stability of its lower molecular weight analogs (e.g., **15**), and decomposition often foiled attempts at isolation and purification. Accordingly, an experimental protocol was devised which limited the exposure of these fragile intermediates to adventitious moisture or warm temperatures (see Experimental Section).

Examination of the bicyclization results summarized in Table 3 indicates that five- and six-membered rings are readily accessible through intramolecular addition of

tosylamide or tosylimide anions to alkynyliodonium salts. At least in the one constrained case examined, a seven-membered ring can be formed (entry j). All efforts directed toward eight-membered ring synthesis with substrate **66** failed.

Tosylamide, tosylimide, and tosylurea moieties are equally efficient nucleophilic cyclization initiators based on this limited data set. At the C−H insertion end, the results of this study mirror prior efforts to delineate the reactivity patterns of alkylidene carbenes. Primary (entry b), secondary (entries *c*, *d*, and *g*) benzylic (entries a and h), and tertiary (entries f and j) C−H bonds all react with similar facility. In addition, ether functionality at the insertion site (entries d, f, and j) is compatible with the reactive carbenic intermediate (compare **21b**), with the proviso that product lability may thwart isolation of the first formed adduct. Thus, the silyl ether **74a**/**b** readily hydrolyzes upon chromatography to furnish the ring-opened product **82**, eq 11. Similarly, while the ketal products derived from **59f** and **70** can be detected in the ^{1}H NMR spectrum of the crude reaction product, exposure to (deactivated) silica gel led to nitrogen-assisted solvolysis and delivered either hydrolysis (e.g., **77**) or elimination products (e.g., **80**). The tosylimide (urea) products **78a**/**b** and **79a**/**b** appear more resistant in general to silica gel-mediated hydrolysis of the enimide functionality.

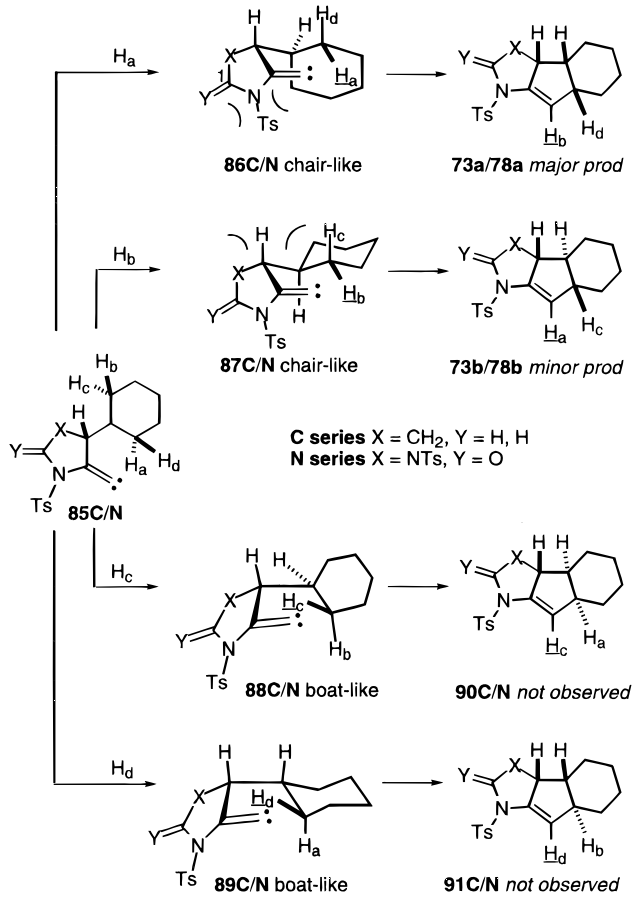


Attempts to effect alkylidene carbene/Ar−H insertion with substrate **59e** afforded only trace amounts of the desired indenyltosylamide **75**. Rather, formal *addition* of the carbene to the tolyl ring led, via a putative norcaradiene intermediate (cf. **50**), to an azulene-type product **76** related to those observed in the indole series. Why the alkylidene carbene intermediate derived from **59e** scarcely participates in aryl C−H insertion while the related carbene **49** does so with facility remains a matter of speculation.

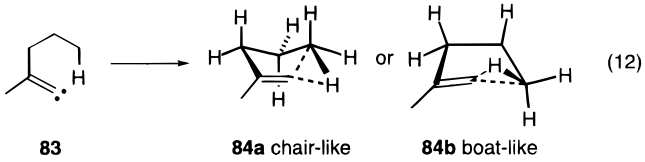
The levels of 1,2 and 1,3 diastereoselectivity attainable in this bicyclization sequence are highly variable and it is difficult to draw generalizations from these limited examples. The prototype case **59a** (entry a) shows only a barely discernable preference for the 1,3 syn product with R = Ph, similar to that seen with both the related imide substrate **63** (entry h) and **59d** (R = OTBDMS, entry d). Matters improve for those substrates designed to test 1,2 relative asymmetric induction (entries b, c, and g). In these instances, selectivity ranges from 3−3.5:1 favoring the 1,2 syn isomers (entries b and c) to as much as 16:1 with the similar (to **59c**) tosylurea substrate **62** (entry g).

A framework for discussing these stereochemical results can be developed from the seminal model for alkylidene carbene C-H 1,5 insertion proposed by Gilbert.[3g] The question of diastereoselectivity in these transformations has been subject to only scattered experimental inquiry[3e] and no theoretical examination. A priori, two diastereotopic transition states featuring flattened chairlike (**84a**) and boatlike (**84b**) conformations can be posited for insertion of the archetype alkylidene carbene **83**, eq 12. Within this context, attachment of substituents along

Scheme 7



the molecular periphery will engender differential steric interactions which will influence the energies of these diastereomeric transition states. Application of this model only to the intramolecular bicyclizations is warranted at present as the intermolecular dihydropyrrole series did not afford meaningful results with α,β-disubstituted ethyltosylamide substrates.



This simple two-state model can be expanded to rationalize the striking difference in diastereoselectivity between the similar examples **73a**/**b** and **78a**/**b**. In both cases, nitrogen nucleophile cyclization into the tethered alkynyliodonium salt presumably affords similar alkylidene carbene intermediates **85C** and **85N**, respectively, Scheme 7. In principle, all four 1,5-disposed hydrogens H_a−H_d in **85** are available for insertion through the transition states approximated by **86C**/**N**−**89C**/**N**. Two of these species (**88** and **89**) have boatlike dispositions and none of the observed products **73a**/**b** or **78a**/**b** could have derived from them. Rather, the observed stereochemical outcome of these cyclizations is only consistent with reaction through the chairlike alternatives **86C**/**N** and **87C**/**N**. The structural rigidity in **85** permits identification of salient transannular steric interactions in the bicyclization series that are not so apparent in the more flexible intermolecular cases. In the two chairlike constructs **87C** and **87N**, a syn pentane-like collision

between a hydrogen (**C** series) or tosyl group (**N** series) and the indicated cyclohexyl methylene is evident. In the alternative chairlike conformer **86C** only, a transannular interaction between the α-oriented hydrogen on C(1) (Y = H,H) and the indicated cyclohexyl methylene appears prominant. This interaction is absent in the tosylurea series **86N** (Y = O). The observed results with **59c** suggest that, to the extent that this model is applicable, the interaction shown in **87C** is more penalizing than that in **86C**, and so **73a** is favored. This difference is amplified in the tosylimide series **62**, as the former interaction now involves the much larger tosyl group (in **87N**), while the latter interaction (in **86N**) is removed along with the offending α-hydrogen. Hence, the observed diastereoselectivity with **62** is enhanced compared with **59c**. While this model provides a post facto rationale for the observed selectivity, only further testing will determine if it has any predictive value.

In summary, the tandem nucleophile addition/carbene insertion sequence characteristic of alkynyliodonium salts has been extended to include sulfonamide and sulfonimide nucleophiles. Intermolecular combination leads to a [3-atom + 2-atom] strategy for dihydropyrrole, pyrrole, and indole synthesis. An intramolecular version demonstrates for the first time that the reactive alkynyliodonium electrophile can be generated in the presence of the (pre)nucleophile. The cyclopentenyltosylamide and -imide products of these bicyclizations are formed with varying (and only sketchily understood) levels of diastereoselectivity.

Experimental Section

Tetrahydrofuran (THF), dimethoxyethane (DME), and diethyl ether (Et_2O) were dried by distillation from sodium/benzophenone under argon (Ar). Benzene and methylene chloride (CH_2Cl_2) were dried by distillation from CaH_2 under Ar. Liquid (flash)[12] chromatography was carried out using 32−63 μm silica gel and the indicated solvent system. Hexane, Et_2O, petroleum ether, and pentane used in flash chromatography were distilled from CaH_2 prior to use. All moisture and air sensitive reactions were carried out in predried glassware under an inert atmosphere of Ar. All melting points are uncorrected. Low and high resolution mass spectra (EIMS, HRMS) were obtained at 50−70 eV by electron impact. Chemical impact mass spectra (CIMS) were obtained with isobutane as the reagent gas. Combustion analyses were performed by Midwest Microlabs, Indianapolis, IN. ^{13}C NMR spectra are provided in the supporting information to establish purity for those compounds which were not subject to combustion analyses.

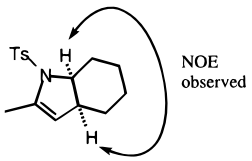
General Procedure A (Intermolecular Tosylamide/Alkynyliodonium Additions). *n*-BuLi (1 equiv) in hexane was added dropwise over several minutes to a deoxygenated, stirring solution of the appropriate sulfonamide in THF (∼0.01 M) at −78 °C. The reaction was warmed either to rt or reflux (as indicated) and phenyl(propynyl)iodonium triflate (**15**) (∼1.04 equiv) was added dropwise via syringe over 15 min as a ∼0.10 M solution in deoxygenated THF. Stirring was maintained for the indicated time, at which point the solution was diluted with an equal volume of Et_2O and poured into an equal volume of ice/brine. The aqueous layer was extracted with Et_2O (3×), and the combined organic phases were washed with H_2O and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resulting residue was purified via flash chromatography on silica gel with the indicated solvent system.

(12) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(13) Stang, P. J.; Williamson, B. L.; Zhdankin, V. V. *J. Am. Chem. Soc.* **1991**, *113*, 5780.

2,3-Dihydro-5-methyl-3-phenyl-1-[(trifluoromethyl)sulfonyl]pyrrole (16c). A solution of *n*-BuLi (2.5 M in hexane, 0.41 mL, 1.0 mmol, 2 equiv) was added dropwise to a deoxygenated 0 °C solution of *N*-(2-phenylethyl)trifluoromethanesulfonamide (0.26 g, 1.0 mmol, 2 equiv) in 50 mL of THF. After 15 min the solution was charged with phenyl(propynyl)iodonium triflate (**15**) (0.20 g, 0.51 mmol) and stirred at rt for 20 h. The reaction solution was then concentrated in vacuo, and the crude product residue was purified by flash column chromatography, eluting with hexane−Et_2O (9:1, with 0.1% triethylamine), to give 41 mg (28%) of pure **16c** as a light yellow oil: IR (thin film) 1223 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.10−6.80 (m, 5 H), 4.48 (q, *J* = 1.3 Hz, 1 H), 3.91 (m, 1 H), 3.57 (ddd, *J* = 10.9, 6.9, 1.0 Hz, 1 H), 3.39 (m, 1 H), 1.81 (dd, *J* = 2.1, 1.5 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 142.0, 138.8, 128.9, 127.4, 127.1, 120.1 (q, *J* = 324.8 Hz), 115.1, 59.2, 45.2, 14.1; EIMS *m/z* (relative intensity) 291 (M^+, 100), 158 (52), 105 (40); HRMS calcd for $C_{12}H_{12}F_3NO_2S$ 291.0541, found 291.0562.

Reaction of *N*-[(4-Methylphenyl)sulfonyl]cyclohexylamine. Following general procedure A, *n*-BuLi (2.5 M in hexane, 0.30 mL, 0.75 mmol, 1 equiv) was added to cyclohexanesulfonamide (0.19 g, 0.75 mmol) in 75 mL of THF at −78 °C. The reaction was heated to reflux, followed by addition of phenyl(propynyl)iodonium triflate (**15**) (0.31 g, 0.78 mmol, 1.04 equiv) in 8 mL of THF. After 3 h at reflux, the reaction was cooled to rt. Purification of the crude product by flash chromatography with 4% Et_2O/petroleum ether (with 0.1% Et_3N) as eluent afforded 0.10 g of **28** as a colorless oil (45%) and 0.11 g of **32** as a colorless oil (45%).

***cis*-3a,4,5,6,7,7a-Hexahydro-2-methyl-1-[(4-methylphenyl)sulfonyl]indole (28).** Spectral data obtained matches that reported in the literature.[4b] IR (CCl_4) 1357, 1168 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.77 (d, *J* = 8.3 Hz, 2 H), 6.82 (d, *J* = 8.0 Hz, 2 H), 4.46 (s, 1 H), 4.12 (dt, *J* = 6.3, 2.5 Hz, 1 H), 2.25 (m, 1 H), 2.11 (dd, *J* = 2.7, 1.4 Hz, 3 H), 2.02 (m, 1 H), 1.91 (s, 3 H), 1.68 (m, 1 H), 1.40 (m, 1 H), 1.31−0.86 (m, 5H); ^{13}C NMR (75 MHz, C_6D_6) δ 142.8, 139.6, 138.2, 129.6, 127.4, 117.9, 63.0, 39.8, 28.9, 26.0, 21.4, 21.1, 21.0, 16.3; EIMS *m/z* (relative intensity) 291 (M^+, 16.2), 136 (100); HRMS calcd for $C_{16}H_{21}NO_2S$: 291.1293, Found 291.1299.



4-Methyl-*N*-cyclohexyl-*N*-(2-tetrahydrofuryl)benzenesulfonamide (32): IR ($CDCl_3$) 1329, 1159 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 8.07 (d, *J* = 8.3 Hz, 2 H), 6.83 (d, *J* = 7.9 Hz, 2 H), 5.48 (t, *J* = 6.7 Hz, 1 H), 3.86 (m, 1 H), 3.46 (dt, *J* = 5.0, 7.8 Hz, 1 H), 3.35 (m, 1 H), 1.88 (s, 3 H), 2.27−0.85 (m, 14H); ^{13}C NMR (75 MHz, C_6D_6) δ 142.2, 141.4, 129.3, 127.8, 89.0, 67.8, 57.7, 34.1, 31.7, 31.4, 26.8, 25.5, 25.4, 21.1; CIMS *m/z* (relative intensity) 324 (MH^+, 100); HRMS calcd for $C_{17}H_{25}NO_3S$: 323.1555, found 323.1546.

Tosylynamide 40. Sulfonamide **38** (218 mg, 0.654 mmol) dissolved in 3 mL of THF was cooled to −78 °C and treated with 2.5 M BuLi in hexanes (262 μL, 0.654 mmol, 1 equiv). After 5 min, (*tert*-butyloxy)[phenyl[[(trifluoromethyl)sulfonyl]oxy]iodo]acetylene (**39**) (313 mg, 0.654 mmol, 1 equiv) was added in one portion, and the reaction was stirred for 1 h without external cooling. The solution was diluted with 25 mL of Et_2O and poured into a saturated NH_4Cl solution. The organic phase was washed once with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (20% Et_2O in hexanes, silica gel pretreated with 1% Et_3N (w/v) in hexanes) of the resulting residue gave 121 mg of ynamide **40** as a colorless oil (40%). IR (CCl_4) 2214, 1749, 1702 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.3 Hz, 2H), 7.35−7.10 (m, 7H), 4.78 (dd, *J* = 11.0, 4.4 Hz, 1H), 3.69 (s, 3H), 3.34 (dd, *J* = 14.5, 4.4 Hz, 1H), 3.08 (dd, *J* = 14.4, 11.0

Hz, 1H), 2.41 (s, 3H), 1.51 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.8, 153.0, 145.1, 135.4, 133.6, 129.6, 129.0, 128.6, 127.9, 127.0, 82.9, 77.5, 71.9, 62.9, 52.8, 35.9, 28.2, 21.6; EIMS *m/z* (relative intensity) 457 (M^+, 6), 401 (36); HRMS calcd for $C_{24}H_{27}NO_6S$ 457.1559, found 457.1571.

Tosylynamine 42. Sulfonamide **36a** (119 mg, 0.411 mmol) and benzoyl[phenyl[[(trifluoromethyl)sulfonyl]oxy]iodo]acetylene **41** (198 mg, 0.411 mmol) gave 109 mg of the title compound as a colorless oil via the same procedure as employed for the synthesis of tosylynamide **42** (64%). IR (CCl_4) 2194, 1638 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.15 (dt, J = 6.0, 1.2 Hz, 2H), 7.70−7.40 (m, 5H), 7.30−7.20 (m, 5H), 7.13 (d, J = 8.2 Hz, 2H), 4.87 (dd, J = 8.7, 6.8 Hz, 1H), 2.35 (s, 3H), 2.30−1.95 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 176.8, 145.2, 138.3, 137.0, 134.6, 133.5, 129.6, 129.0, 128.6, 128.5, 128.3, 127.7, 126.9, 89.2, 79.4, 66.1, 27.7, 21.6, 11.0; EIMS *m/z* (relative intensity) 417 (M^+, 4), 299 (3); HRMS, calcd for $C_{25}H_{23}NO_3S$ 417.1399, found 417.1397.

General Procedure B. Alkylations of Trilithiated 4-Pentyn-1-ol and 5-Hexyn-1-ol. 4-Pentyn-1-ol or 5-hexyn-1-ol (1 equiv) was added to a −78 °C solution of *n*-BuLi (2.5 M in hexanes, ∼3.7 equiv) in deoxygenated THF (∼0.6 M based on alkynol). This solution was stirred without external cooling for the indicated time and then cooled (0 °C or −78 °C, see below), and the alkyl halide (1−1.6 equiv) was added. The reaction was once again stirred without external cooling for the indicated time and then cautiously poured into saturated NH_4Cl, extracted with Et_2O, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. α-Alkylated acetylenes were isolated by flash column chromatography of the crude product residue on silica gel. In some cases distillation of starting material from the crude product residue preceded chromatography.

General Procedure C. Mitsunobu Reaction of *N*-(*t*-Butoxycarbonyl)-*p*-toluenesulfonamide with Alcohols. Adapted from the method of Weinreb.[10] Diethyl azodicarboxylate (2.6 equiv) was added dropwise to a deoxgenated rt solution of alkynol substrate (1 equiv), N-BOC *p*-toluenesulfonamide (1.5 equiv), and triphenylphosphine (3 equiv) in THF (∼0.1 M based on alkynol). After the indicated time, the reaction was concentrated in vacuo and the crude product residue was purified by flash column chromatography on silica gel.

General Procedure D. Deprotection of BOC-Tosylamides. A ∼0.1 M deoxygenated rt solution of substituted N-BOC *p*-toluenesulfonamide in CH_2Cl_2 was acidified with trifluoroacetic acid (5−10 equiv, see below). After the indicated time the reaction solution was poured into saturated $NaHCO_3$, extracted with CH_2Cl_2, washed with water, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Secondary *p*-toluenesulfonamides were isolated by flash column chromatography of the crude product residue on silica gel.

General Procedure E: Stannylation of Lithiated Acetylenes with Tributyltin Chloride. A deoxygenated −78 °C, ∼0.06 M solution of terminal alkyne substrate in THF was treated with a 2.5 M hexane solution of *n*-BuLi (2 equiv based on alkyne). The reaction was kept at −78 °C or warmed to 0 °C for the indicated time, and then n-Bu_3SnCl was added (1 equiv based on alkyne). The reaction solution was then stirred without external cooling and, after the indicated time, poured over saturated NH_4Cl solution, extracted with Et_2O, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Stannylated alkynes were isolated by flash column chromatography of the crude product residue on silica gel.

Tosylamide 59f. A solution of sulfur trioxide−pyridine complex (1.16 g, 7.29 mmol, 3 equiv) in 5 mL of DMSO was combined with a solution of the hydroxytosylamide derived from **58d** (0.72 g, 2.4 mmol) and triethylamine (3.63 g, 35.9 mmol, 15 equiv) in 5 mL of DMSO. After 1.5 h the reaction solution was poured over ice/1 M HCl (1:1) and extracted with CH_2Cl_2. The organic layer was washed with water, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (1:1), gave 0.41 g (57%) of pure aldehyde as a clear oil: IR (thin film) 3284, 1723 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.75 (t, J = 1.6 Hz, 1 H), 7.75 (d, J = 8.3 Hz, 2 H), 7.31 (d, J = 8.0 Hz, 2 H), 4.90 (m, 1 H), 2.97 (q, J = 6.5 Hz, 2 H), 2.82 (m, 1 H), 2.55 (td, J = 6.7, 1.6 Hz, 2 H), 2.43 (s, 3 H), 2.09 (d, J = 2.4 Hz, 1 H), 1.80−1.30 (m, 4 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 200.3, 143.4, 136.8, 129.7, 127.0, 84.9, 70.8, 48.2, 42.6, 31.2, 27.0, 25.1, 21.4; CIMS *m/z* (relative intensity) 294 (MH^+, 100), 276 (23), 184 (63).

This aldehyde (0.64 g, 2.2 mmol) and triethyl orthoformate (0.36 g, 2.4 mmol, 1.1 equiv) were heated at 50 °C in 0.30 mL of ethanol. After 3 h the reaction was poured over ice/brine (1:1), extracted with Et_2O, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (1:1), gave 0.42 g (52%) of pure tosylamide diethyl acetal as a clear oil: IR (thin film) 3283 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2 H), 7.30 (d, J = 8.6 Hz, 2 H), 4.80 (bs, 1 H), 4.70 (m, 1 H), 3.76−3.43 (m, 4 H), 2.95 (q, J = 6.6 Hz, 2 H), 2.43 (m, 1 H), 2.42 (s, 3 H), 2.04 (d, J = 2.4 Hz, 1 H), 1.77−1.34 (m, 6 H), 1.20 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C*, 143.3, 136.9, 86.2; *C*H, 129.6 (2), 127.0 (2), 101.3, 70.2, 27.2; *C*H_2, 62.1, 61.2, 42.9, 38.9, 31.7, 27.1; *C*H_3, 21.4, 15.3, 15.2; EIMS *m/z* (relative intensity) 367 (M^+, 0.5), 322 (9), 103 (100); HRMS calcd for $C_{19}H_{29}NO_4S$ 367.1817, found 367.1836.

Following general procedure E, a −78 °C solution of this tosylamide (0.42 g, 1.1 mmol, 1.0 equiv) in 20 mL of THF was treated with 2.5 M *n*-BuLi (1.00 mL, 2.50 mmol, 2.2 equiv). This solution was warmed at 0 °C for 20 min, and then n-Bu_3-SnCl (0.37 g, 1.1 mmol, 1 equiv) was added. The resulting solution was allowed to react at rt for 1 h. Following the indicated workup, purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (2.3:1), gave 0.48 g (64%) of pure **59f** as a clear oil: IR (thin film) 3279 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2 H), 7.30 (d, J = 7.9 Hz, 2 H), 4.74 (m, 1 H), 4.63 (t, J = 6.1 Hz, 1 H), 3.78−3.42 (m, 4 H), 2.95 (q, J = 6.6 Hz, 2 H), 2.45 (m, 1 H), 2.42 (s, 3 H), 1.80−1.44 (m, 9 H), 1.44−1.14 (m, 15 H), 1.00−0.83 (m, 15 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C*, 143.2, 136.9, 113.2, 83.5; *C*H, 129.6 (2), 127.0 (2), 101.8, 28.7; *C*H_2, 62.6, 61.1, 43.0, 39.5, 32.2, 28.8 (3), 27.1, 26.8 (3), 10.9 (3); *C*H_3, 21.4, 15.3, 15.2, 13.6 (3); CIMS *m/z* (relative intensity) 658 (MH^+, 38), 612 (80), 554 (49). Anal. Calcd for $C_{31}H_{55}NO_4SSn$: C, 56.71; H, 8.44; N, 2.13; S, 4.88. Found: C, 56.46; H, 8.13; N, 2.24; S, 4.79.

Tosylamide 61. A solution of 2.5 M *n*-BuLi in hexanes (14.20 mL, 35.50 mmol, 1 equiv) was added over 5 min to a 0 °C solution of (trimethylsilyl)acetylene (3.47 g, 35.4 mmol) in 100 mL of deoxygenated THF. After 15 min the solution was charged with cyclohexanecarboxaldehyde (**60**) (3.19 g, 28.5 mmol, 0.8 equiv) and stirred at rt for 2 h. The reaction solution was then poured over ice/saturated NH_4Cl (1:1), extracted with Et_2O, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was diluted with 200 mL of methanol and treated with solid K_2CO_3 (∼2 g). After 2 h the reaction was poured over ice/saturated NH_4Cl solution/1 M HCl (1:1:1), extracted with Et_2O, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give 3.44 g (88%) of the pure acetylenated alcohol as a clear oil: IR (thin film) 3379, 3300 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.16 (m, 1 H), 2.47 (d, J = 2.2 Hz, 1 H), 2.01 (d, J = 5.5 Hz, 1 H), 1.88−1.76 (m, 4 H), 1.70 (m, 1 H), 1.59 (m, 1 H), 1.39−0.98 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C*, 83.9; *C*H, 73.6, 67.0, 43.8; *C*H_2, 28.3, 27.9, 26.3, 25.8, 25.76; CIMS *m/z* (relative intensity) 139 (MH^+, 4), 121 (100), 93 (63).

Following general procedure C, diethyl azodicarboxylate (1.66 g, 9.52 mmol, 2.6 equiv) was added dropwise to a deoxygenated rt solution of this alcohol (0.50 g, 3.6 mmol), N-BOC *p*-toluenesulfonamide (1.50 g, 5.53 mmol, 1.5 equiv), and triphenylphosphine (2.85 g, 10.9 mmol, 3 equiv) in 100 mL of THF. After 20 h the reaction was concentrated in vacuo, and the crude product residue was purified by flash column chromatography, eluting with hexane−Et_2O (4:1), to give 1.05 g (74%) of pure BOC-protected tosylimide as a clear oil that crystallized upon standing: mp 130−132°; IR (CCl_4) 3312,

1737 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 8.04 (d, J = 8.3 Hz, 2 H), 6.77 (d, J = 8.4 Hz, 2 H), 5.31 (dd, J = 10.4, 2.5 Hz, 1 H), 2.53 (m, 1 H), 2.23 (m, 2 H), 2.05 (d, J = 2.5 Hz, 1 H), 1.85 (s, 3 H), 1.65 (m, 2 H), 1.47 (m, 1 H), 1.19 (s, 9 H), 1.31−0.86 (m, 5 H); ^{13}C NMR (75 MHz, C_6D_6, DEPT) δ *C*, 150.5, 143.7, 138.6, 83.9, 81.8; *C*H, 129.2 (2), 128.4 (2), 72.7, 55.7, 41.2; *C*H_2, 31.5, 29.9, 26.3, 26.1, 25.9; *C*H_3, 27.8 (3), 21.1; CIMS *m/z* (relative intensity) 391 (M^+, 5), 336 (100), 182 (78). Anal. Calcd for $C_{21}H_{29}NO_4S$: C, 64.42; H, 7.47; N, 3.58; S, 8.19. Found: C, 64.53; H, 7.61; N, 3.56; S, 8.18.

Following general procedure D, a rt solution of this BOC-protected tosylamide (1.84 g, 4.71 mmol) in 100 mL of CH_2Cl_2 was acidified with trifluoroacetic acid (5.32 g, 46.7 mmol, 10 equiv) and allowed to react for 20 h. Following the indicated workup, the crude product residue was purified by flash column chromatography, eluting with hexane−Et_2O (4:1), to give 1.22 g (89%) of pure **61** as a white solid: mp 132−134 °C; IR (CCl_4) 3311, 3289 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.82 (d, J = 8.3 Hz, 2 H), 6.79 (d, J = 8.5 Hz, 2 H), 4.42 (d, J = 9.4 Hz, 1 H), 3.97 (ddd, J = 9.4, 6.1, 2.4 Hz, 1 H), 1.89 (s, 3 H), 1.70−1.40 (m, 5 H), 1.58 (d, J = 2.2 Hz, 1 H), 1.30 (m, 1 H), 1.06−0.84 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C*, 143.4, 137.3, 80.8; *C*H, 129.5 (2), 127.4 (2), 73.1, 50.7, 42.9; *C*H_2, 28.9, 28.0, 26.0, 25.7, 25.6; *C*H_3, 21.5; CIMS *m/z* (relative intensity) 292 (MH^+, 5), 200 (100), 184 (10).

Tosylated Urea 62. A deoxygenated 0 °C solution of secondary tosylamide **61** (1.00 g, 3.44 mmol) in 60 mL of THF was treated sequentially with a solution of 2.5 M *n*-BuLi (1.40 mL, 3.50 mmol, 1 equiv) followed after 20 min by *p*-toluenesulfonyl isocyanate (0.68 g, 3.4 mmol, 1 equiv). The reaction solution was stirred at rt for 1 h and then poured into ice-cold brine and extracted with EtOAc. The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification of the crude product residue by flash column chromatography, eluting with hexane−EtOAc (1:1) followed by EtOAc, gave 1.10 g (65%) of the pure urea derivative as a white solid: mp 150−152°; IR (KBr), 3278, 1605 cm^{-1}; ^1H NMR (200 MHz, $(D_3C)_2CO$) δ 7.91 (d, J = 8.4 Hz, 2 H), 7.52 (d, J = 8.2 Hz, 2 H), 7.16 (d, J = 8.1 Hz, 2 H), 7.07 (d, J = 8.0 Hz, 2 H), 5.18 (d, J = 10.4 Hz, 1 H), 2.73 (d, J = 2.5 Hz, 1 H), 2.39 (m, 1 H), 2.31 (s, 6 H), 2.14 (m, 1 H), 1.91−1.48 (m, 4 H), 1.34−1.00 (m, 3 H), 1.00−0.70 (m, 2 H); ^{13}C NMR (50 MHz, D_3COD) δ 157.8, 144.4, 142.5, 142.3, 140.1, 129.7, 129.5, 129.4, 127.5, 83.5, 73.6, 56.1, 42.3, 32.5, 30.6, 27.4, 26.9, 26.8, 21.5, 21.4; CIMS *m/z* (relative intensity) 489 (MH^+, 4), 335 (6), 292 (100).

A 0 °C deoxygenated solution of this urea derivative (0.343 g, 0.704 mmol) in 30 mL of THF was treated with a 1 M THF solution of lithium bis(trimethylsilyl)amide (1.60 mL, 1.60 mmol, 2.3 equiv). After 20 min, n-Bu_3SnCl (0.240 g, 7.37 mmol, 1.04 equiv) was added, and the resulting solution was allowed to stir at rt for 40 min. The reaction solution was then poured into ice-cold brine and extracted with Et_2O. The organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the crude product residue by flash column chromatography, eluting with hexane−EtOAc (1:2), gave 0.28 g (51%) of pure **62** as a light yellow oil: IR (CCl_4) 3534, 1598 cm^{-1}; ^1H NMR (200 MHz, $(D_3C)_2CO$) δ 8.01 (d, J = 8.2 Hz, 2 H), 7.55 (d, J = 8.0 Hz, 2 H), 7.18 (d, J = 8.1 Hz, 2 H), 7.11 (d, J = 8.1 Hz, 2 H), 5.28 (bs, 1 H), 2.39−2.15 (m, 3 H), 2.34 (s, 6 H), 1.92−1.50 (m, 10 H), 1.48−1.25 (m, 8 H), 1.20−0.98 (m, 9 H), 0.88 (t, J = 7.2 Hz, 9 H); ^{13}C NMR (75 MHz, $(D_3C)_2CO$) δ 158.1, 143.4, 142.4, 141.8, 139.8, 129.5, 129.3, 129.2, 126.8, 109.7, 86.9, 56.5, 42.5, 32.2, 29.9, 29.6, 27.6, 26.9, 26.6, 26.3, 21.5, 21.3, 13.9, 11.5; FABMS *m/z* (relative intensity) 778 (MH^+, 18), 721 (68), 524 (100).

Tosylimide 63. Alcohol **58a** (1.23 g, 6.53 mmol) in 20 mL of acetone was cooled to 0 °C and treated with Jones reagent in 1 mL portions until TLC indicated the absence of starting material. The mixture was diluted with 70 mL of EtOAc and washed with H_2O until the aqueous and organic phases were nearly colorless. The organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (383:16:1 CH_2Cl_2:MeOH:HOAc) of the resulting residue gives 0.85 g of the derived acid as a pale yellow oil (64%). IR (thin film) 2115, 1713 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35 (m, 5H), 2.95−2.43 (m, 5H), 2.17 (d, J = 2.4 Hz, 1H), 1.87−1.73 (m, H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 177.7, 141.2, 128.4, 126.0, 85.1, 70.7, 39.7, 36.0, 33.2, 27.4; EIMS *m/z* (relative intensity) 202 (M^+, 10), 157 (15); HRMS calcd for $C_{13}H_{14}O_2$ 202.0994, found 202.1009.

This acid (0.85 g, 4.2 mmol) in 5 mL of THF was treated with TsNCO (0.70 mL, 4.6 mmol, 1.1 equiv) and then Et_3N (0.59 mL, 4.2 mmol, 1 equiv), which caused the immediate evolution of CO_2. After 0.5 h at rt, 1 mL of H_2O and 50 mL of Et_2O were added, and the solution was washed once with 50 mL of 1 N HCl and once with brine. Drying (Na_2SO_4) of the organic phase, filtration, solvent evaporation, and flash chromatography of the residue (50% Et_2O in hexane) gave 1.40 g of the derived tosylimide as a viscous oil (94%). IR (CCl_4) 2116, 1727 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.94 (d, J = 8.4 Hz, 2H), 7.35−7.05 (m, 7H), 2.90−2.53 (m, 3H), 2.53−2.40 (m, 2H), 2.39 (s, 3H), 2.16 (d, J = 2.4 Hz, 1H), 1.78−1.60 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.7, 145.1, 140.9, 135.3, 129.5, 128.3, 125.9, 84.9, 71.6, 41.5, 35.7, 33.0, 27.2, 21.6; EIMS *m/z* (relative intensity) 355 (M^+, 4), 264 (2); HRMS calcd for $C_{20}H_{21}NO_3S$ 355.1242, found 355.1243.

To this sulfonimide (1.40 g, 3.94 mmol) in 15 mL of THF at −78 °C was added KHMDS (2.36 gm, 11.8 mmol, 3 equiv) followed by n-Bu_3SnCl (1.28 mL, 4.72 mmol, 1.2 equiv). The reaction solution was treated 0.5 h later with saturated aqueous NH_4Cl and then diluted with 100 mL of Et_2O. The organic phase was washed once with 100 mL of H_2O and once with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo at rt. Flash chromatography (30% Et_2O/hexane) of the residue using wet silica (20% w/w H_2O) yielded 1.61 g of alkynylstannane **63** as a clear colorless oil (63%). IR (thin film) 3241, 2143 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.37 (bs, 1H), 7.93 (d, J = 8.3 Hz, 2H), 7.35−7.10 (m, 7H), 2.87−2.60 (m, 3H), 2.41 (m, 2H), 2.40 (s, 3H), 1.75−1.20 (m, 14H), 1.09 (t, J = 7.9 Hz, 6H), 0.93 (t, J = 7.2 Hz, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.6, 144.8, 141.0, 135.8, 129.4, 128.4, 128.3, 126.0, 112.1, 88.6, 42.3, 36.2, 33.1, 28.9, 28.7, 27.0, 21.6, 13.6, 11.1; EIMS m/z (relative intensity) 645 (M^+, 2), 588 (100); HRMS calcd for $C_{32}H_{47}NO_3SSn$ (M^+ − Bu) 588.1593, found 588.1644.

1,1-Dibromoalkenyl Alcohol 65. To a deoxygenated −78 °C solution of LDA (38.1 mmol, 1.1 equiv) in 125 mL of THF was added 60 mL of DMPU followed after 10 min by ethyl 4-methylpentanoate (5.00 g, 34.7 mmol). This solution was held at −78 °C for 1 h, and then 1-bromo-5-(*tert*-butyldimethylsilyloxy)pentane (12.7 g, 45.2 mmol, 1.3 equiv) was added. The resulting solution was allowed to react at rt for 2 h and then poured over ice-cold 1 M HCl/brine (1:1), extracted with Et_2O, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The resulting crude product residue was added to a deoxygenated 0 °C suspension of $LiAlH_4$ (1.63 g, 43.0 mmol, 1.2 equiv) in 100 mL of Et_2O. This mixture was heated at reflux for 1 h and then recooled to 0 °C, quenched with ice, and filtered, and the precipitate was rinsed with Et_2O. The filtrate was washed with water and then with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (4:1), gave 4.26 g (41%) of pure alkylated alcohol as a clear oil. IR (thin film) 3334 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.60 (t, J = 6.5 Hz, 2 H), 3.51 (m, 2 H), 1.75−1.60 (m, 2 H), 1.60−1.45 (m, 3 H), 1.32 (m, 5 H), 1.25−1.04 (m, 3 H), 0.89 (s, 9 H), 0.88 (m, 6 H), 0.05 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.7, 63.2, 40.6, 38.0, 32.8, 31.2, 26.5, 26.2, 25.9, 25.3, 22.9, 18.3, −5.3; EIMS *m/z* (relative intensity) 302 (M^+, 1), 245 (7), 97 (100).

A solution of sulfur trioxide−pyridine complex (4.78 g, 30.0 mmol, 2 equiv) in 20 mL of DMSO was combined with a solution of the above alcohol (4.11 g, 13.6 mmol) and triethylamine (6.53 g, 64.6 mmol, 4.7 equiv) in 10 mL of DMSO. After 1.5 h the reaction solution was poured over ice/1 M HCl (1:1) and extracted with CH_2Cl_2. The organic layer was washed with water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude aldehyde product was added as a solution in 5 mL of CH_2Cl_2 to a deoxygenated 0 °C solution of triphenylphosphine (7.45 g, 28.4 mmol, 2.1 equiv) and carbon tetrabromide (4.71 g, 14.2 mmol, 1 equiv) in 40 mL of

CH_2Cl_2. The solution was stirred at 0 °C for 1 h and then diluted with pentane, and the resulting mixture was filtered, rinsing the precipitate with pentane. Concentration of the filtrate in vacuo and purification of the resulting residue by flash column chromatography, eluting with hexane, gave 2.77 g of a clear oil that was immediately treated with a 1 M THF solution of n-Bu_4NF (12 mL, 12 mmol) and stirred at rt for 1 h. The reaction solution was then poured over ice-cold 1 M HCl/brine (1:1), extracted with Et_2O, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (4:1) and then with hexane−Et_2O (1:1), gave 1.74 g (37%) of pure **65** as a clear oil. IR (thin film) 3334 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.09 (d, J = 9.8 Hz, 1 H), 3.64 (t, J = 6.6 Hz, 2 H), 2.46 (m, 1 H), 1.66−1.50 (m, 4 H), 1.50−1.14 (m, 8 H), 0.89 (dd, J = 6.6, 4.0 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 87.5, 62.8, 44.0, 41.7, 34.8, 32.6, 26.8, 25.8, 25.7, 23.4, 22.3.

Tosylamide 66. A −78 °C solution of the 1,1-dibromovinyl alcohol **65** (1.66 g, 4.85 mmol) in 25 mL of THF was treated with 2.5 M *n*-BuLi (6.2 mL, 15 mmol, 3.2 equiv). This solution was stirred at −78 °C for 1 h and then warmed to rt and held there for 1 h. The reaction was then poured over ice-cold 1 M HCl/brine (1:1), extracted with Et_2O, washed with water and then with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The resulting residue was dissolved in a solution of N-BOC *p*-toluenesulfonamide (1.97 g, 7.26 mmol, 1.5 equiv) and triphenylphosphine (3.80 g, 14.5 mmol, 3 equiv) in 50 mL of THF and treated with dropwise addition of diethyl azodicarboxylate (3.43 g, 19.7 mmol, 2.6 equiv). After 20 h the reaction was concentrated in vacuo, and the crude product residue was purified by flash column chromatography, eluting with hexane−Et_2O (5:1), to give 1.82 g (86%) of pure BOC-protected tosylimide as a clear thick oil. IR (thin film) 3306, 1728 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 2 H), 7.30 (d, J = 8.3 Hz, 2 H), 3.81 (m, 2 H), 2.44 (s, 3 H), 2.40 (m, 1 H), 2.03 (d, J = 2.4 Hz, 1 H), 1.95−1.65 (m, 3 H), 1.55−1.10 (m, 8 H), 1.33 (s, 9 H), 0.90 (m, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 151.0, 143.9, 137.6, 129.2, 127.8, 87.9, 83.9, 69.0, 47.1, 44.2, 35.2, 30.1, 29.4, 27.9, 26.8, 26.6, 25.8, 23.3, 21.6, 21.5.

Following general procedure D, a rt solution of the BOC-protected tosylimide (1.77 g, 4.07 mmol) in 100 mL of CH_2Cl_2 was acidified with trifluoroacetic acid (4.59 g, 40.2 mmol, 10 equiv) and allowed to react for 20 h. The indicated workup afforded 1.31 g (96%) of the pure tosylamide as a yellow oil. IR (thin film) 3286 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2 H), 7.30 (d, J = 8.5 Hz, 2 H), 4.86 (bt, J = 6.0 Hz, 1 H), 2.92 (q, J = 6.7 Hz, 2 H), 2.42 (s, 3 H_3), 2.35 (m, 1 H), 2.00 (d, J = 2.4 Hz, 1 H), 1.82 (m, 1 H), 1.58−1.02 (m, 10 H), 0.89 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 136.9, 129.6, 127.0, 87.6, 69.1, 44.1, 43.1, 35.0, 29.35, 29.3, 26.6, 26.3, 25.7, 23.2, 21.6, 21.4.

Following general procedure E, a −78 °C solution of this tosylamide (1.24 g, 3.70 mmol) in 75 mL of THF was treated with 2.5 M *n*-BuLi (3.10 mL, 7.75 mmol, 2.1 equiv). This solution was warmed to 0 °C and held there for 1 h, and then n-Bu_3SnCl (1.20 g, 3.69 mmol, 1 equiv) was added. The resulting solution was allowed to react at rt for 1 h. The indicated workup afforded 2.20 g (93%) of pure **66** as a light yellow oil. IR (thin film) 3280 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2 H), 7.30 (d, J = 8.1 Hz, 2 H), 4.73 (bs, 1 H), 2.92 (m, 2 H), 2.42 (s, 3 H), 2.36 (m, 1 H), 1.70−1.15 (m, 23 H), 1.00−0.75 (m, 21 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.1, 137.1, 129.6, 127.0, 115.1, 81.9, 44.8, 43.2, 35.6, 30.9, 29.5, 28.9, 27.8, 26.8, 26.5, 25.9, 23.3, 21.6, 21.4, 13.6, 11.0; EIMS *m/z* (relative intensity) 623 (M^+, 0.6), 569 (73), 91 (100).

Silyl Ether 68. Alcohol **67** (5.92 g, 29.4 mmol) was dissolved in 30 mL of DMF and treated with imidazole (4.01 g, 58.9 mmol, 2.0 equiv) and TBDMSCl (4.88 g, 32.4 mmol, 1.1 equiv) at 0 °C. The reaction solution was warmed to rt and stirred for 24 h and then diluted with 100 mL of Et_2O. This mixture was washed twice with 100 mL portions of 1 N HCl and once with 100 mL of brine. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (3% Et_2O/hexane) afforded 9.01 g of the silyl ether (97%) as a colorless oil. ^1H NMR (200 MHz, $CDCl_3$) δ 7.50 (d, J = 7.9 Hz, 1 H), 7.27−7.19 (m, 2 H), 7.16−6.92 (m, 1 H), 3.82 (t, J = 7.0 Hz, 2 H), 2.97 (t, J = 6.9 Hz, 2 H), 0.86 (s, 9 H), −0.03 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 138.4, 132.6, 131.7, 127.9, 127.1, 124.6, 62.5, 39.6, 25.9, 18.3, −5.4; CIMS *m/z* (relative intensity) 315 (MH^+, 34), 299 (10), 257 (97), 185 (90). Anal. Calcd for $C_{14}H_{23}BrOSi$: C, 53.33; H, 7.35. Found: C, 53.28; H, 7.58.

A flask containing Mg turnings (2.05 g, 84.2 mmol) was flame dried under an argon stream, cooled, and charged with 25 mL of Et_2O followed by 250 μL of 1,2-dibromoethane. After the initiation reaction subsided, the silyl ether (13.3 g, 42.1 mmol) was added dropwise so as to maintain a gentle reflux. After addition of this compound was complete, the reaction was refluxed for 1 h and cooled to 0 °C, and methoxyallene (6 mL, 70 mmol, 1.7 equiv) in 15 mL of Et_2O and CuI (135 mg, 0.71 mmol, 0.02 equiv) were added over 5 min. Over the next 10 min, an exothermic reaction took place which was controlled by maintaining the ice bath. The resulting light brown slurry was allowed to slowly warm to rt and stirred there for 10 h. The reaction was then cooled to 0 °C and slowly treated with 30 mL of aqueous KCN (0.4g)/NH_4Cl (4.0 g). Et_2O was added (100 mL), and the organic phase was washed twice with 100 mL portions of 1 N HCl and once with 100 mL of brine. Drying of the organic layer over Na_2SO_4, solvent evaporation, and flash chromatography of the residue (1% Et_2O/hexane) gave 8.95 g (77%) of silyl ether **68** as a colorless oil. IR (thin film) 3311, 2120 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.50−7.40 (m, 1 H), 7.27−7.18 (m, 3 H), 3.83 (t, J = 7.0 Hz, 2 H), 3.64 (d, J = 2.7 Hz, 2 H), 2.89 (t, J = 7.0 Hz, 2 H), 2.18 (t, J = 2.7 Hz, 1 H), 0.87 (s, 9 H), −0.02 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.9, 134.6, 130.1, 128.6, 126.9, 126.7, 82.1, 70.6, 63.9, 36.1, 25.9, 22.6, 18.3, −5.5; CIMS *m/z* (relative intensity) 275 (MH^+, 8), 217 (36).

Tosylamide Acetal 69. Alkyne **68** (1.86 g, 6.78 mmol) dissolved in 12 mL of THF was cooled to −78 °C and treated with *n*-BuLi (6.0 mL of 2.5 M in hexanes, 14.9 mmol, 2.2 equiv). After stirring for 15 min at −78 °C and 30 min at rt, the resulting dilithiated intermediate was cooled to −78 °C, and 2 mL of HMPT was added followed by 2-iodoacetaldehyde dimethyl acetal (1.6 mL, 14 mmol, 2.0 equiv). The reaction was allowed to slowly warm to rt over 4 h and stirred an additional 4 h. Residual carbanions were quenched at 0 °C by the addition of 10 mL of saturated NH_4Cl and the solution was diluted with 100 mL of Et_2O. The organic phase was washed twice with 100 mL portions of 1 N HCl and once with 100 mL of brine. Drying (Na_2SO_4) of the organic phase, solvent evaporation, and flash chromatography of the residue (5% Et_2O/hexane as eluent) gave 2.00 g of the alkylated alkyne (81%) as a colorless oil. IR (thin film) 3309, 2115 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.53−7.45 (m, 1 H), 7.25−7.10 (m, 3 H), 4.58 (dd, J = 6.9, 4.7 Hz, 1 H), 4.17−4.08 (m, 1 H), 3.80 (t, J = 7.3 Hz, 2 H), 3.39 (s, 3 H), 3.31 (s, 3 H), 3.10−2.75 (m, 2 H), 2.20 (d, J = 2.5 Hz, 1 H), 2.10−2.02 (m, 2 H), 0.88 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 135.9, 130.6, 127.5, 126.9, 126.8, 102.7, 85.9, 70.5, 64.1, 53.8, 52.5, 40.4, 36.0, 29.3, 25.9, 18.3, −5.4, −5.5; CIMS *m/z* (relative intensity) 361.1 ($(M - H)^+$, 8), 331.1 (42), 299.1 (21), 273.1 (38). Anal. Calcd for $C_{21}H_{34}O_3Si$: C, 69.56; H, 9.45. Found: C, 69.37; H, 9.56.

This silyl ether (2.26 g, 6.23 mmol) in 10 mL of THF was cooled to 0 °C and treated with 9.4 mL of a 1.0 M n-Bu_4NF in THF solution (9.4 mmol, 1.5 equiv). After 2 h at 0 °C, 50 mL of Et_2O was added, and the mixture was washed twice with 50 mL portions of water. Drying (Na_2SO_4) of the organic phase, solvent evaporation, and flash chromatography of the residue (50% EtOAc/hexane) gave 1.39 g of the desilylated alcohol (90%) as a viscous oil. IR (CCl_4) 3632, 3311, 2290 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.55−7.50 (m, 1 H), 7.29−7.19 (m, 3 H), 4.55 (dd, J = 7.0, 4.7 Hz, 1 H), 4.08−3.99 (m, 1 H), 3.88 (t, J = 6.7 Hz, 2 H), 3.39 (s, 3 H), 3.31 (s, 3 H), 3.10−2.80 (m, 2 H), 2.22 (d, J = 2.7 Hz, 1 H), 2.15−1.90 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5, 135.4, 130.2, 127.8, 127.2, 127.1, 102.7, 85.8, 70.5, 63.3, 53.9, 52.5, 40.3, 35.6, 29.2; CIMS

m/*z* (relative intensity) 248.2 (M^+, 3), 231.2 (8), 217.2 (13). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.44; H, 8.12.

Following general procedure C, this alcohol (3.16 g, 12.7 mmol), BOC-*p*-toluenesulfonamide (3.79 g, 14.0 mmol, 1.1 equiv), and triphenylphosphine (6.66 g, 25.4 mmol, 2.0 equiv) were dissolved in 50 mL of THF. Diethyl azodicarboxylate (3.40 mL, 21.6 mmol, 1.7 equiv) was added and the reaction solution was stirred at rt for 10 h. The volatiles were evaporated in vacuo and flash chromatography of the residue (25% Et_2O/hexane) furnished 5.69 g (89%) of the BOC-protected tosylimide as a viscous oil. IR (CCl_4) 3312, 2116, 1724 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 2 H), 7.55 (d, J = 7.7 Hz, 1 H), 7.31−7.20 (m, 5 H), 4.53 (dd, J = 6.7, 4.8 Hz, 1 H), 4.22−4.11 (m, 1 H), 4.02−3.89 (m, 2 H), 3.38 (s, 3 H), 3.32 (s, 3 H), 3.68−2.95 (m, 2 H), 2.43 (s, 3 H), 2.22 (d, J = 2.6 Hz, 1 H), 2.20−1.92 (m, 2 H), 1.38 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.7, 144.0, 139.5, 137.3, 135.1, 130.5, 129.2, 127.9, 127.7, 127.4, 127.2, 102.6, 86.0, 84.2, 70.4, 53.9, 52.3, 47.9, 40.6, 33.4, 29.1, 27.8, 21.5; CIMS *m*/*z* (relative intensity) 501.1 (M^+, 8), 470.2 (10), 414.2 (22). Anal. calcd for $C_{27}H_{35}NO_6S$: C, 64.65; H, 7.03; N, 2.79. Found: C, 64.47; H, 7.20; N, 2.90.

This tosylimide (5.69 g, 11.4 mmol) was dissolved in 50 mL of dry MeOH and 35 mL of trimethyl orthoformate. Acetyl chloride (14 mL) was added slowly, and the mixture was brought to reflux and held there for 5 h. The reaction solution was cooled to 0 °C, and 20 g of $NaHCO_3$ was carefully added. The resulting mixture was diluted with 150 mL of water and extracted twice with 150 mL portions of CH_2Cl_2. Drying (Na_2SO_4) of the organic layer, solvent evaporation, and flash chromatography of the residue (50% Et_2O/hexane) afforded 3.89 g of **69** (85%) as a viscous oil. IR (CCl_4) 3302, 2116 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.71 (d, J = 8.3 Hz, 2 H), 7.46 (dd, J = 7.6, 1.7 Hz, 1 H), 7.35−7.00 (m, 5 H), 4.56 (t, J = 6.2 Hz, 1 H), 4.47 (dd, J = 7.0, 4.6 Hz, 1 H), 3.90−3.81 (m, 1 H), 3.36 (s, 3 H), 3.27 (s, 3 H), 3.30−3.12 (m, 2 H), 3.02−2.70 (m, 2 H), 2.41 (s, 3 H), 2.17 (d, J = 2.5 Hz, 1 H), 2.13−1.83 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 139.0, 136.8, 134.8, 129.9, 129.5, 127.7, 127.2, 127.1, 126.9, 102.4, 85.5, 70.6, 53.7, 52.4, 43.7, 40.0, 32.4, 29.0, 21.3; CIMS *m*/*z* (relative intensity) 401.6 (M^+, 1), 370.6 (100), 338.6 (96). Anal. Calcd for $C_{22}H_{27}NO_4S$: C, 65.81; H, 6.78; N, 3.49. Found: C, 65.60; H, 6.83; N, 3.50.

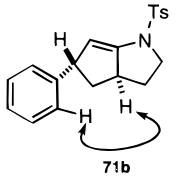
Tosylamide 70. To tosylamide **69** (147 mg, 0.366 mmol) in 3 mL of THF at 0 °C was added 1.1 mL of a 1 M LiHMDS solution in THF (1.1 mmol, 3 equiv) followed by 119 μL of Bu_3SnCl (0.439 mmol, 1.2 equiv). The reaction solution was treated 0.5 h later with saturated aqueous NH_4Cl and then diluted with 20 mL of Et_2O. The organic phase was washed once with 20 mL of H_2O, dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography (35% Et_2O/hexane) of the residue using wet silica (12% w/w H_2O) yielded 166 mg of **70** (66%) as a clear, colorless oil. IR (thin film) 3279, 2145 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.71 (d, J = 8.3 Hz, 2 H), 7.54 (dd, J = 7.7, 1.5 Hz, 1 H), 7.27 (d, J = 7.3 Hz, 2 H) 7.22−6.99 (m, 3 H), 4.61−4.53 (m, 2 H), 3.86 (dd, J = 9.6, 5.5 Hz, 1 H), 3.38 (s, 3 H), 3.26 (s, 3 H), 3.31−3.12 (m, 2 H), 2.98−2.70 (m, 2 H), 2.41 (s, 3 H), 2.08−1.83 (m, 2 H); 1.70−1.50 (m, 6 H), 1.45−1.25 (m, 6 H), 1.05−0.90 (m, 6 H), 0.90 (t, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 140.3, 137.2, 134.6, 129.7, 128.2, 127.3, 127.1, 127.0, 112.0 103.1, 85.0, 54.4, 52.3, 43.7, 41.3, 32.3, 30.9, 28.9, 26.9, 21.5, 13.7, 11.1; CIMS *m*/*z* (relative intensity) 692.5 (MH^+, 3), 690.1 (3), 634.4 (4). Anal. Calcd for $C_{34}H_{53}NO_4SSn$: C, 59.14; H, 7.74; N, 2.03. Found: C, 58.69; H, 7.77; N, 2.20.

General Procedure F. Intramolecular Tandem Conjugate Addition−Carbene Insertion Reactions. Cyano(phenyl)iodonium triflate[13] (1 equiv) was added to a −40 °C deoxygenated ~0.08 M solution of alkynylstannane (1 equiv) in CH_2Cl_2. After 45 min the reaction solution was diluted with three times its volume of hexane, the solvent layer was quickly decanted, and the remaining alkynyl(phenyl)iodonium triflate residue was washed with an additional 1 volume of hexane and dried in vacuo in an ice bath. The purity of the resulting alkynyl(phenyl)iodonium triflate salt may be assayed by ^1H NMR. In practice, however, this intermediate was recooled to −40 °C, dissolved in precooled THF (~0.08 M), and charged with potassium *tert*-butoxide (~1 equiv based on iodonium salt). The resulting solution was allowed to warm to rt and, after the indicated time, was poured over ice/brine (1:1), extracted with Et_2O, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Product heterocycles were isolated by flash column chromatography of the crude product residue on silica gel.

Conversion of 59a into 71a/71b. Following general procedure F, cyano(phenyl)iodonium triflate (0.298 g, 0.787 mmol, 1 equiv) was added to a deoxygenated −40 °C solution of alkynylstannane **59a** (0.496 g, 0.787 mmol) in 10 mL of CH_2Cl_2. After 45 min the solution was diluted with 30 mL of hexane, the solvent layer was quickly decanted off, and the remaining residue was rinsed with 10 mL of hexane and dried in vacuo to yield 0.491 g (0.680 mmol, 86% yield—corrected (^1H NMR) for 4% residual hexane) of alkynyl(phenyl)iodonium triflate as a white foam. ^1H NMR (200 MHz, $CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 2 H), 7.71 (d, J = 8.2 Hz, 2 H), 7.59 (m, 1 H), 7.46 (m, 2 H), 7.33−7.12 (m, 5 H), 7.04 (d, J = 7.7 Hz, 2 H), 5.85 (bs, 1 H), 3.00 (m, 2 H), 2.86 (m, 1 H), 2.59 (m, 2 H), 2.36 (s, 3 H), 1.71 (m, 4 H). This salt was cooled to −40 °C, dissolved in 10 mL of THF, charged with potassium *tert*-buoxide (79 mg, 0.71 mmol, 1.04 equiv based on iodonium intermediate), and allowed to react at rt for 1 h. Following the indicated workup, purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (4:1, with 0.1% triethylamine), gave 0.167 g (73% yield) of the fused phenyl-substituted enamides **71a**/**71b** as a 1.4:1 mixture of diastereoisomers by ^1H NMR integration. EIMS *m*/*z* (relative intensity) 339 (M^+, 12), 262 (5), 184 (63); HRMS calcd for $C_{20}H_{21}NO_2S$ 339.1293, found 339.1271. Each isomer was partially purified from this mixture by additional flash column chromatography, eluting with hexane−EtOAc (19:1, with 0.1% triethylamine).

71a. ^1H NMR (200 MHz, C_6D_6) δ 7.81 (d, J = 8.3 Hz, 2 H), 7.26−7.05 (m, 5 H), 6.80 (d, J = 8.5 Hz, 2 H), 5.48 (t, J = 1.9 Hz, 1 H), 4.04 (m, 1 H), 3.80 (dd, J = 10.3, 8.1 Hz, 1 H), 3.35 (m, 1 H), 2.46 (m, 1 H), 2.01 (m, 1 H), 1.88 (s, 3 H), 1.26−1.02 (m, 2 H), 0.82 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 148.4, 146.2, 143.3, 129.8, 128.8, 128.7, 127.4, 127.0, 126.6, 104.6, 55.9, 49.4, 47.7, 42.0, 29.5, 21.2.

71b. ^1H NMR (300 MHz, C_6D_6) δ 7.82 (d, J = 8.3 Hz, 2 H), 7.38−7.12 (m, 7 H), 5.35 (t, J = 2.9 Hz, 1 H), 4.19 (bd, J = 8.2 Hz, 1 H), 4.05 (dd, J = 10.0, 8.0 Hz, 1 H), 3.70 (ddd, J = 11.5, 10.2, 5.5 Hz, 1 H), 3.02 (m, 1 H), 2.47 (s, 3 H), 2.04−1.86 (m, 3 H), 1.40 (dq, J = 11.7, 8.0 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 149.0, 145.5, 143.5, 136.1, 129.5, 128.6, 127.9, 127.5, 126.4, 103.8, 55.9, 55.5, 47.9, 39.1, 29.4, 21.1.



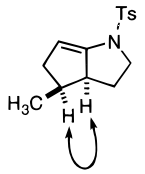
71b

NOESY

Conversion of 59b into 72a/72b. Following general procedure F, cyano(phenyl)iodonium triflate (0.316 g, 0.834 mmol, 1 equiv) was added to a −40 °C deoxygenated solution of alkynylstannane **59b** (0.473 g, 0.834 mmol) in 10 mL of CH_2Cl_2. After 45 min, the solution was diluted with 30 mL of hexane, the solvent layer was quickly decanted off, and the remaining residue was rinsed with 10 mL of hexane and dried in vacuo to yield 0.477 g (0.726 mmol, 87% yield—corrected (^1H NMR) for 4% residual hexane) of alkynyl(phenyl)iodonium triflate as a white foam. ^1H NMR (200 MHz, $CDCl_3$) δ 8.05 (d, J = 7.5 Hz, 2 H), 7.73 (d, J = 8.3 Hz, 2 H), 7.62 (m, 1 H), 7.48 (m, 2 H), 7.27 (d, J = 8.1 Hz, 2 H), 5.85 (bs, 1 H), 3.00 (bs, 2 H), 2.77 (m, 1 H), 2.39 (s, 3 H), 1.68 (m, 3 H), 0.85 (m,

6 H). This salt was cooled to −40 °C, dissolved in 10 mL of THF, charged with potassium *tert*-butoxide (85 mg, 0.76 mmol, 1.05 equiv based on iodonium intermediate), and allowed to react at rt for 1 h. Following the indicated workup, purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (4:1, with 0.1% triethylamine), gave 0.133 g (66%) of the methyl-substituted bicyclic enamides **72a**/**72b** as a 3:1 mixture of diastereoisomers by ^{1}H NMR integration: EIMS *m*/*z* (relative intensity) 277 (M^+, 34), 262 (64), 183 (39); HRMS calcd for $C_{15}H_{19}NO_2S$ 277.1136, found 277.1134. A purified sample of the major isomer **72a** was separated from this mixture by additional flash column chromatography, eluting with hexane−EtOAc (19:1, with 0.1% triethylamine).

72a. ^{1}H NMR (300 MHz, C_6D_6) δ 7.82 (d, J = 8.3 Hz, 2 H), 6.79 (d, J = 8.0 Hz, 2 H), 5.34 (s, 1 H), 3.78 (dd, J = 10.0, 8.0 Hz, 1 H), 3.33 (ddd, J = 11.6, 10.1, 5.6 Hz, 1 H), 2.46 (ddd, J = 14.5, 7.3, 2.8 Hz, 1 H), 2.21 (dddd, J = 14.5, 9.5, 3.0, 1.6 Hz, 1 H), 2.10 (m, 1 H), 1.87 (s, 3 H), 1.64 (m, 1 H), 1.20 (pentet, J = 6.0 Hz, 1 H), 0.82 (qd, J = 11.6, 8.1 Hz, 1 H), 0.75 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (50 MHz, C_6D_6) δ 146.9, 143.4, 136.2, 129.5, 100.2, 56.3, 55.6, 44.7, 41.6, 28.4, 21.1, 18.0.



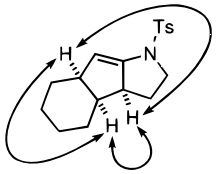
72a

NOESY

72b. ^{1}H NMR (200 MHz, C_6D_6) δ 7.80 (d, J = 8.4 Hz, 2 H), 6.86 (d, J = 8.0 Hz, 2 H), 5.31 (s, 1 H), 3.81 (m, 1 H), 3.36 (ddd, J = 11.6, 10.1, 5.6 Hz, 1 H), 2.78 (m, 1 H), 2.56 (m, 1 H), 1.96 (m, 1 H), 1.92 (s, 3 H), 1.65 (m, 1 H), 1.27 (pentet, J = 6.0 Hz, 1 H), 1.06 (m, 1 H), 0.51 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (50 MHz, C_6D_6) δ 145.5, 135.9, 129.6, 98.2, 55.9, 52.4, 44.4, 32.3, 23.0, 15.9.

Conversion of 59c into 73a/73b. Following general procedure F, cyano(phenyl)iodonium triflate (0.308 g, 0.812 mmol, 1 equiv) was added to a −40 °C deoxygenated solution of alkynylstannane **59c** (0.494 g, 0.812 mmol, 1 equiv) in 10 mL of CH_2Cl_2. After 45 min, the solution was diluted with 30 mL of hexane, the solvent layer was quickly decanted off, and the remaining residue was rinsed with 10 mL of hexane and dried in vacuo to yield 0.488 g (0.684 mmol, 84% yield—corrected (^{1}H NMR) for 6% residual hexane) of alkynyl(phenyl)iodonium triflate as a white foam. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.05 (d, J = 8.6 Hz, 2 H), 7.73 (d, J = 8.2 Hz, 2 H), 7.62 (m, 1 H), 7.49 (m, 2 H), 7.27 (d, J = 8.2 Hz, 2 H), 5.81 (bs, 1 H), 3.00 (m, 2 H), 2.74 (m, 1 H), 2.39 (s, 3 H), 1.80−1.45 (m, 7 H), 1.23−0.95 (m, 6 H). This salt was cooled to −40 °C, dissolved in 10 mL of THF, charged with potassium *tert*-butoxide (81 mg, 0.73 mmol, 1.06 equiv based on iodonium intermediate), and allowed to react at rt for 1 h. Following the indicated workup, purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (4:1, with 0.1% triethylamine), gave 0.150 g (69%) of the fused tricyclic eneamides **73a**/**73b** as a 3.5:1 mixture of diastereoisomers by ^{1}H NMR integration: EIMS *m*/*z* (relative intensity) 317 (M^+, 24), 253 (100), 91 (63); HRMS Calcd for $C_{18}H_{23}NO_2S$ 317.1449, found 317.1466. A purified sample of the major isomer **73a** was separated from this mixture by additional flash column chromatography, eluting with hexane−EtOAc (19:1, with 0.1% triethylamine).

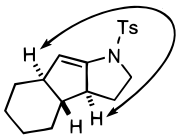
73a. ^{1}H NMR (300 MHz, C_6D_6) δ 7.82 (d, J = 8.3 Hz, 2 H), 6.83 (d, J = 8.5 Hz, 2 H), 5.43 (d, J = 0.6 Hz, 1 H), 3.81 (dd, J = 10.0, 8.2 Hz, 1 H), 3.32 (ddd, J = 11.7, 10.1, 5.7 Hz, 1 H), 2.30 (m, 1 H), 2.11 (m, 1 H), 1.90 (s, 3 H), 1.85 (m, 1 H), 1.58 (m, 2 H), 1.45 (m, 1 H), 1.26 (m, 1 H), 1.20−0.98 (m, 5 H), 0.89 (qd, J = 11.6, 8.2 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6, DEPT) δ *C*, 147.8, 143.4, 136.2; *C*H, 129.5 (2), 127.6 (2), 105.5, 56.6, 55.6, 53.6; CH_2, 55.5, 31.7, 28.8, 27.8, 26.7, 26.5; CH_3, 21.1.



73a

NOESY

73b. ^{1}H NMR (300 MHz, C_6D_6) δ 7.82 (d, J = 8.3 Hz, 2 H), 6.83 (d, J = 8.5 Hz, 2 H), 5.18 (m, 1 H), 3.81 (dd, J = 10.0, 8.2 Hz, 1 H), 3.32 (ddd, J = 11.7, 10.1, 5.7 Hz, 1 H), 3.02 (m, 1 H), 2.51 (m, 1 H), 1.90 (s, 3 H), 1.85 (m, 1 H), 1.58 (m, 2 H), 1.45 (m, 1 H), 1.26 (m, 1 H), 1.20−0.98 (m, 5 H), 0.89 (qd, J = 11.6, 8.2 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 146.5, 143.5, 135.9, 129.6, 126.8, 103.8, 67.3, 57.7, 55.3, 53.4, 40.6, 29.0, 28.7, 28.3, 24.6, 21.2.



73b

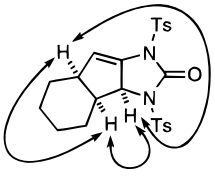
NOESY

Conversion of 59d into 74a/74b. Following general procedure F, cyano(phenyl)iodonium triflate (0.114 g, 0.302 mmol, 1 equiv) was added to a −40 °C deoxygenated solution of alkynylstannane **59d** (0.210 g, 0.302 mmol) in 4 mL of CH_2Cl_2. After 45 min, the solution was diluted with 12 mL of hexane, the solvent layer was quickly decanted off, and the remaining residue was rinsed with 4 mL of hexane and dried in vacuo to yield 0.143 g (0.177 mmol, 59% yield—corrected (^{1}H NMR) for 6% residual hexane) of alkynyl(phenyl)iodonium triflate as a white foam. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 2 H), 7.79 (d, J = 8.3 Hz, 2 H), 7.70 (m, 1 H), 7.56 (m, 2 H), 7.33 (d, J = 8.0 Hz, 2 H), 5.56 (bt, J = 6.1 Hz, 1 H), 3.63 (m, 2 H), 2.95 (m, 3 H), 2.46 (s, 3 H), 1.88−1.50 (m, 6 H), 0.87 (s, 9 H), 0.01 (s, 6 H). This salt was cooled to −40 °C, dissolved in 4 mL of THF, charged with potassium *tert*-butoxide (21 mg, 0.19 mmol, 1.06 equiv based on iodonium intermediate), and allowed to react at rt for 1 h. Following the indicated workup, purification of the crude product residue by flash column chromatography, eluting with hexane−Et_2O (9:1, with 0.1% triethylamine), gave 47 mg (64%) of the fused bicyclic eneamides **74a**/**74b** as a 1.8:1 mixture of unassigned diastereoisomers by ^{1}H NMR integration. The product mixture proved to be unstable and underwent facile hydrolysis upon standing to yield 20 mg (60%) of the cyclopentenone derivative **82** as a light yellow oil: IR (thin film) 3274, 1692 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2 H), 7.66 (m, 1 H), 7.30 (d, J = 8.4 Hz, 2 H), 6.15 (dt, J = 5.7, 2.1 Hz, 1 H), 4.80 (bs, 1 H), 2.94 (m, 2 H), 2.80 (m, 1 H), 2.43 (s, 3 H), 2.35−2.20 (m, 2 H), 1.85−1.30 (m, 4 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 212.0, 163.6, 143.4, 136.9, 133.7, 129.7, 127.1, 44.0, 43.0, 35.6, 28.1, 27.1, 21.5; CIMS *m*/*z* (relative intensity) 294 (MH^+, 100), 138 (35), 123 (47).

Conversion of 59f into 77. Following general procedure F, cyano(phenyl)iodonium triflate (0.156 g, 0.410 mmol, 1 equiv) was added to a −40 °C deoxygenated solution of alkynylstannane **59f** (0.269 g, 0.410 mmol) in 5 mL of CH_2Cl_2. After 45 min, the solution was diluted with 15 mL of hexane, the solvent layer was quickly decanted off, and the remaining residue was rinsed with 5 mL of hexane and dried in vacuo to yield 0.236 g (0.318 mmol, 77% yield—corrected (^{1}H NMR) for 3% residual hexane) of alkynyl(phenyl)iodonium triflate as a white foam. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.05 (d, J = 7.8 Hz, 2 H), 7.73 (d, J = 8.1 Hz, 2 H), 7.65 (m, 1 H),

7.52 (m, 2 H), 7.28 (d, J = 8.9 Hz, 2 H), 5.28 (m, 1 H), 3.57 (m, 3 H), 2.87 (m, 4 H), 2.41 (s, 3 H), 2.35 (m, 1 H), 1.80−1.42 (m, 6 H), 0.82 (m, 6 H). This salt was cooled to −40 °C, dissolved in 5 mL of THF, charged with potassium *tert*-butoxide (37 mg, 0.33 mmol, 1.03 equiv based on iodonium intermediate), and allowed to react at rt for 1 h. The reaction solution was then diluted with 1 mL of water, acidified with oxalic acid (0.100 g, 1.11 mmol, 3.4 equiv), and allowed to react at rt for 20 h. Following the described workup, purification of the crude product residue by flash column chromatography, eluting with hexane−EtOAc (1:1, with 0.1% triethylamine), gave 48 mg (50%) of pure enone **77** as a white solid: mp 142−144 °C; IR (CCl_4) 1711 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2 H), 7.35 (d, J = 8.3 Hz, 2 H), 6.02 (m, 1 H), 3.90−3.65 (m, 2 H), 2.86 (m, 1 H), 2.53 (dd, J = 18.0, 6.7 Hz, 1 H), 2.45 (s, 3 H), 2.23−1.82 (m, 4 H), 1.25 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 204.4, 170.9, 145.2, 134.2, 130.0, 127.4, 112.2, 45.6, 40.2, 38.1, 26.1, 22.4, 21.6; CIMS *m*/*z* (relative intensity) 292 (MH^+, 81), 157 (61), 138 (100); HRMS calcd for $C_{15}H_{17}NO_3S$ 291.0929, found 291.0917.

Conversion of 62 to 78a/b. Following general procedure F, cyano(phenyl)iodonium triflate (0.302 g, 0.796 mmol, 1 equiv) was added to a −40 °C deoxygenated solution of alkynylstannane **62** (0.619 g, 0.796 mmol) in 10 mL of CH_2Cl_2. After 45 min, the solution was diluted with 30 mL of hexane, the solvent layer was quickly decanted off, and the remaining residue was rinsed with 10 mL of hexane and dried in vacuo to yield 0.528 g (0.591 mmol, 74% yield−corrected (^1H NMR) for 6% residual hexane) of alkynyl(phenyl)iodonium triflate as a white foam. ^1H NMR (200 MHz, $CDCl_3$) δ 8.17 (d, J = 7.4 Hz, 2 H), 8.05 (d, J = 8.3 Hz, 2 H), 7.83 (d, J = 8.1 Hz, 2 H), 7.71 (d, J = 7.5 Hz, 2 H), 7.57 (m, 1 H), 7.50 (d, J = 7.9 Hz, 2 H), 7.40 (d, J = 7.4 Hz, 2 H), 5.81 (s, 1 H), 5.31 (s, 1 H), 4.76 (m, 1 H), 2.50 (s, 6 H), 1.76−1.44 (m, 8 H), 1.40−1.06 (m, 2 H). This salt was cooled to −40 °C, dissolved in 10 mL of THF, charged with potassium *tert*-butoxide (70 mg, 0.63 mmol, 1.06 equiv based on iodonium intermediate), and allowed to react at rt for 1 h. Purification of the crude product residue by flash column chromatography, eluting with hexane−EtOAc (4:1, with 0.1% triethylamine), gave 0.126 g (44%) of two compounds in a 16:1 ratio. The major compound proved to be cyclic urea **78a**. mp 158−160°; IR (CCl_4) 1774 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.4 Hz, 2 H), 7.88 (d, J = 8.4 Hz, 2 H), 7.34 (d, J = 8.2 Hz, 2 H), 7.33 (d, J = 8.2 Hz, 2 H), 5.45 (m, 1 H), 4.60 (m, 1 H), 3.06 (bs, 1 H), 2.70 (m, 1 H), 2.46 (s, 3 H), 2.44 (s, 3 H), 1.94 (m, 1 H), 1.70−1.45 (m, 3 H), 1.18−1.00 (m, 3 H), 0.88 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C*, 150.8, 146.2, 145.8, 133.7, 133.5, 132.9; *C*H, 129.9 (2), 128.5, 128.0, 110.0, 67.0, 45.9, 43.0; *C*H_2, 27.4, 23.3, 21.9, 21.2; *C*H_3, 21.7, 21.68; EIMS *m*/*z* (relative intensity) 486 (M^+, 23), 331 (21), 91 (100); HRMS Calcd for $C_{24}H_{26}N_2O_5S_2$ 486.1283, found 486.1278.

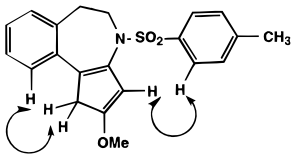


78a

DNOE

Conversion of 63 into 79a/b. To alkynylstannane **63** (141 mg, 0.219 mmol) in 3.5 mL of CH_2Cl_2 at −40 °C was added cyano[[(trifluoromethyl)sulfonyl]oxy]iodobenzene (83 mg, 0.22 mmol, 1 equiv) in one portion, and the reaction was stirred at −40 °C for 0.5 h to furnish a clear solution. Triethylamine (62 μL, 0.44 mmol, 2 equiv) was added, and external cooling bath was removed. The reaction solution was stirred for 0.5 h at rt and then diluted with 50 mL of Et_2O. The organic phase was washed once with aqueous KF and once with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography of the residue (25% Et_2O in hexanes, silica gel pretreated with 1% Et_3N (w/v) in hexanes) provided 42 mg (54%) of the bicyclic enimides **79a**/**b** as a 2.3:1 mixture of diastereomers. The relative stereochemistries of **79a**/**b** were assigned by comparison of the alkene-H region of the ^1H NMR spectrum of the mixture with the nearly identical signals in the analogous and stereochemically well-characterized system **71a**/**b**. IR (CCl_4) 1766 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 2H, minor diastereomer), 7.97 (d, J = 8.3 Hz, 2H, major diastereomer), 7.40−7.10 (m, 7H), 5.75 (t, J = 3.0 Hz, 1H, minor diastereomer), 5.67 (t, J = 2.1 Hz, 1H, major diastereomer), 4.25−4.05 (m, 1H), 3.30−3.05 (m, 1H), 2.75−2.40 (m, 1H), 2.46 (s, 3H), 2.40−2.00 (m, 2H), 1.50−1.30 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.7, 174.5, 145.6, 144.2, 143.3, 142.7, 142.5, 135.0, 134.9, 129.74, 129.72, 128.54, 128.48, 128.1, 127.1, 127.0, 126.7, 126.5, 108.9, 107.4, 52.2, 51.7, 42.2, 42.0, 40.5, 39.7, 39.0, 21.7; EIMS *m*/*z* (relative intensity) 353 (M^+, 26); HRMS calcd for $C_{20}H_{19}NO_3S$ 353.1086, found 353.1104.

Conversion of 70 into Diene 80. To alkynylstannane **70** (77 mg, 0.11 mmol) in 2 mL of CH_2Cl_2 at −50 °C was added cyano(phenyl)iodonium triflate (42 mg, 0.11 mmol, 1.0 equiv) in one portion, and the reaction was stirred at −40 °C for 0.5 h to furnish a clear solution. Hexanes (10 mL) was added, leading to a white precipitate. The supernatant was quickly decanted, and the solid was washed once with 3 mL of hexane and dried in vacuo. The crude iodonium salt was cooled to −78 °C, and 5 mL of THF was added followed by 110 μL of a 1.0 M LiHMDS in THF solution (0.11 mmol, 1.0 equiv). The reaction solution was warmed to rt and stirred there for another 12 h. The solution was diluted with 25 mL of Et_2O and then treated with 10 mL of brine. The organic phase was washed once with water, dried over Na_2SO_4, and the residue was purified by flash chromatography (30% Et_2O/hexane containing 0.5% triethylamine) to provide 23 mg (56%) of diene **80** as a white solid. mp 161−163° dec; IR (CCl_4) 2360 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.72 (d, J = 8.3 Hz, 2 H), 6.90−6.87 (m, 2 H), 6.80−6.75 (m, 1 H), 6.67 (d, J = 7.6 Hz, 1 H), 6.62 (d, J = 8.2 Hz, 2 H), 6.42 (s, 1 H), 3.86−3.82 (m, 2 H), 3.30 (s, 3 H), 3.23 (s, 2 H), 2.56−2.53 (m, 2 H), 1.71 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6, DEPT) δ *C*, 165.8, 143.2, 139.1, 137.7, 134.6, 114.0, 65.9; *C*H, 129.6, 129.3, 127.5, 126.6, 126.3, 124.5, 102.5; *C*H_2, 49.7, 40.6, 36.5; *C*H_3, 56.8, 21.0; CIMS *m*/*z* (relative intensity) 368.4 (MH^+, 41), 367.4 (32). Anal. Calcd for $C_{21}H_{21}NO_3S$: C, 68.64; H, 5.76; N, 3.81. Found: C, 68.47; H, 5.79 ; N, 3.74.



DNOE **80**

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Supporting Information Available: Experimental procedures and characterization data for **16d**, **16e**, **18**, **19**, **23**, **25**, **34**, **35**, **37a**, **45a**−**e**, **46b**−**e**, **53**, **58a**−**e**, and **59a**−**e**, and copies of ^{13}C NMR spectra for **16c**, **32**, **40**, **42**, **61**, **62**, **63**, **65**, **66**, **68**, **71b**, **72a**/**b**, **73a**/**b**, **77**, **78a**, **79a**/**b**, and **82** (33 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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