Synthesis of Benzo-Fused 1-Azabicyclo[*m.n.*0]alkanes via the Schmidt Reaction: A Formal Synthesis of Gephyrotoxin

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The intramolecular capture of benzocyclobutyl, benzocyclopentyl, and benzocyclohexyl carbocations **7** by azides produces spirocyclic aminodiazonium ions **8**, which undergo 1,2-C-to-N rearrangement with loss of dinitrogen to produce benzo-fused iminium ions resulting from either aryl (**9**) or alkyl (**10**) migration to the electron-deficient nitrogen atom. Reduction of the iminium ions affords regioisomeric benzo-fused 1-azabicyclo[*m.n.*0]alkanes, e.g., benzopyrrolizidines, benzoindolizidines, benzoquinolizidines, or perhydrobenzo[*f*]pyrrolo[1,2-*a*]azepines in two regioisomeric versions, anilines (e.g., **11**−**14**) and benzylic amines (e.g., **15**−**18**), the result of aryl and alkyl migrations, respectively. Generally, aryl migration is preferred, despite modeling that shows that the lowest energy aminodiazonium ions are those where the departing dinitrogen is preferentially antiperiplanar to the migrating alkyl group rather than the aryl group. The utility of this methodology was illustrated by a formal synthesis of the alkaloid gephyrotoxin **4**. A dependence on the efficiency and regioselectivity of the Schmidt reaction upon subtle changes in the structure of the cation precursor was observed, necessitating the exploration of a variety of substrates. Fortunately, these materials were easily made. Ultimately, the azido-alkene **81** bearing a 2-bromoethyl side-chain was useful for the Schmidt reaction, producing the known benzo-fused indolizidine **49**, which had been transformed by Ito et al. into gephyrotoxin **4**. The synthesis of **49** required nine steps (five purifications) from commercially available 4-methoxy-1-indanone **60** and proceeded in 22% overall yield.

Introduction

The benzo-fused 1-azabicyclo[*m.n.*0]alkanes **1** and **2** and their oxidized or reduced forms are found in a variety of natural products and other pharmacologically important compounds (Figure 1 and Scheme 1). For example, the anticancer drug mitomycin C (**3**) is related to the benzo-fused pyrrolizidine **11**, gephyrotoxin (**4**) is a reduced form of the benzo-fused indolizidine **12**, the protoberberine alkaloid xylopinine (**5**) is an example of the benzo-fused quinolizidine **17**, and the perhydrobenzo[*f*]-pyrrolo[1,2-*a*]azepine **6**, an anxiolytic agent,[1] is a derivative of the benzo-fused pyrrolidinoazepane **14**.

On the basis of our earlier work on the intramolecular Schmidt reactions of azides with carbocations,[2,3] we expected that the benzylic carbocation **7** would cyclize to the spirocyclic aminodiazonium ion **8**, which would produce the iminium ions **9** and **10** by migration of an aryl or alkyl group, respectively (Scheme 1). Hydride reduction of **9** and **10** would then afford the tricyclic anilines **11**−**14** and the tricyclic benzylamines **15**−**18**. A key issue that arises is the regioselectivity of aryl vs alkyl migration. Herein we report the Schmidt reactions of the

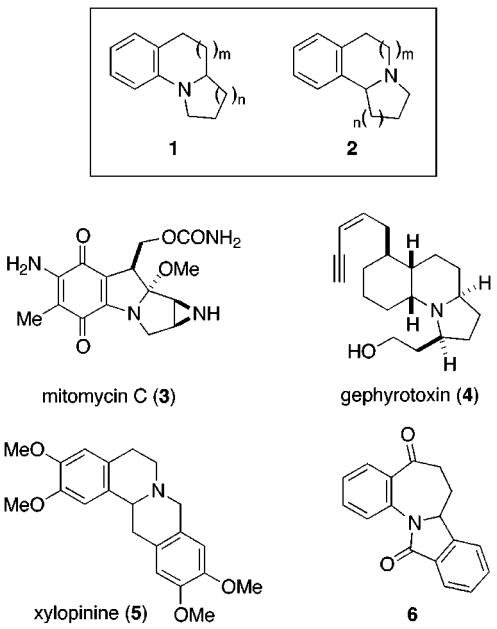

Figure 1. Benzo-fused 1-azabicyclo[*m.n.*0]alkanes and representative targets.

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(1) Ishihara, Y.; Kiyota, Y.; Goto, G. *Chem. Pharm. Bull.* **1990**, *38*, 3024−3030.

(2) (a) Pearson, W. H.; Schkeryantz, J. M. *Tetrahedron Lett.* **1992**, *33*, 5291−5294. (b) Pearson, W. H.; Walavalkar, R.; Schkeryantz, J. M.; Fang, W.-k.; Blickensdorf, J. D. *J. Am. Chem. Soc.* **1993**, *115*, 10183−10194. (c) Pearson, W. H.; Fang, W.-k.; Kampf, J. W. *J. Org. Chem.* **1994**, *59*, 2682−2684. (d) Pearson, W. H.; Fang, W.-k. *J. Org. Chem.* **1995**, *60*, 4960−4961. (e) Pearson, W. H. *J. Heterocycl. Chem.* **1996**, *33*, 1489−1496. (f) Pearson, W. H.; Fang, W.-k. *Isr. J. Chem.* **1997**, *37*, 39−46.

(3) Aubé has shown that aliphatic azides may participate in Schmidt reactions with ketones and related electrophiles. See: (a) Aubé, J.; Milligan, G. L. *J. Am. Chem. Soc.* **1991**, *113*, 8965−8966. (b) Aubé, J.; Milligan, G. L.; Mossman, C. J. *J. Org. Chem.* **1992**, *57*, 1635−1637. (c) Aubé, J.; Rafferty, P. S.; Milligan, G. L. *Heterocycles* **1993**, *35*, 1141−1147. (d) Milligan, G. L.; Mossman, C. J.; Aubé, J. *J. Am. Chem. Soc.* **1995**, *117*, 10449−10459. (e) Forsee, J. E.; Aubé, J. *J. Org. Chem.* **1999**, *64*, 4381−4385.

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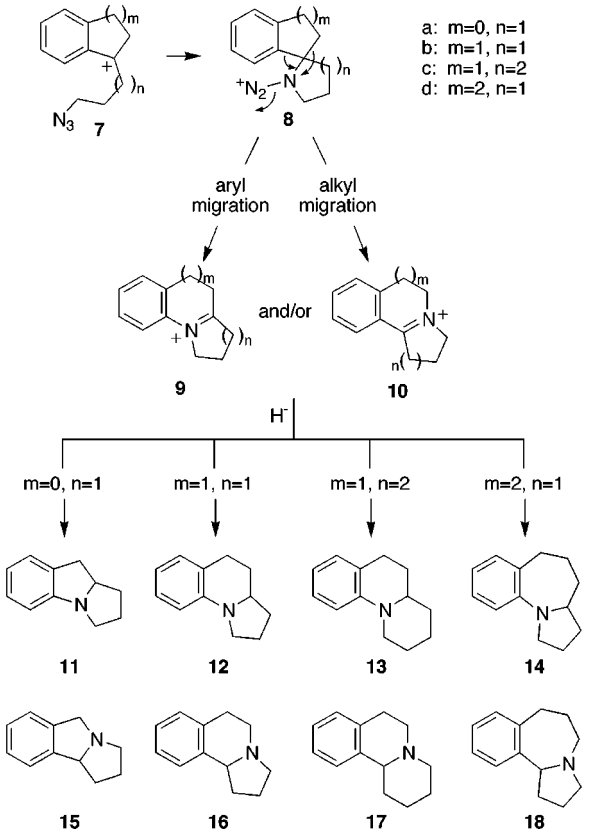
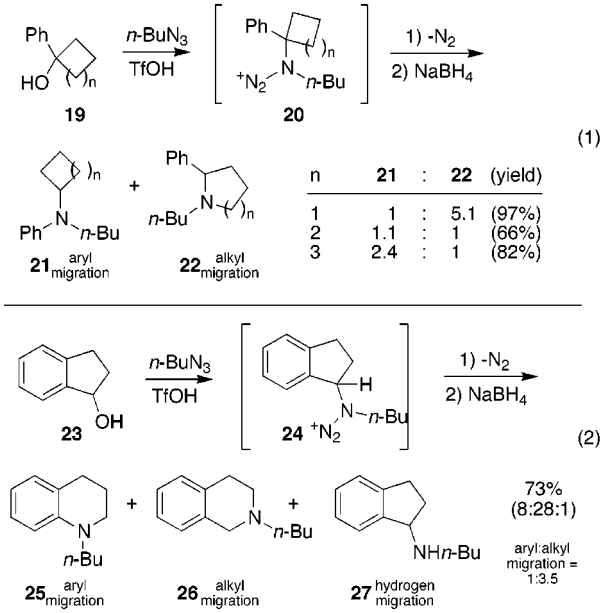
Scheme 1. Benzo-Fused 1-Azabicyclo[*m.n.*0]alkanes via Intramolecular Schmidt Reactions



cation systems **7a**−**d**, which produce the tricyclic amines **11**−**18** or their analogues. A formal synthesis of gephyrotoxin (**4**) using this method is described.

Regarding the regioselectivity of the rearrangement of the aminodiazonium ions **8** to the iminium ions **9** and **10**, we have previously encountered the aryl vs alkyl migration issue in *inter*molecular Schmidt reactions, as shown in eqs 1 and 2.[2d] Reaction of the cyclic tertiary benzylic alcohols **19** with *n*-butyl azide under acidic conditions produced the anilines **21** and the benzylic amines **22** as a result of aryl or alkyl migration, respectively, in the aminodiazonium ions **20**. The propensity for aryl migration was found to increase smoothly as a function of the size of the ring undergoing expansion. An explanation for this trend was proposed based on the conformation of the aminodiazonium ion about the benzylic C−N bond in **20**.[2d] As is often the case with 1,2-rearrangements to electron-deficient centers, the regioselectivity of the migration is difficult to predict because there are at least three factors that must be considered, namely the inherent migratory aptitude of the migrating group, the stability of the newly developing positive charge at the migration origin, and stereoelectronic factors (i.e., the migrating group and the leaving group prefer an antiperiplanar geometry).[2b,2d,4] Comparing **20** to **8** reveals that while both are secondary aminodiazonium ions attached to tertiary benzylic carbon atoms, there is a substantial difference in the conformational flexibility of these intermediates about their benzylic C−N bonds, making it difficult to extrapolate the regioselectivity of the rearrangement of **20** to that of **8**. The combination of 1-indanol **23** with *n*-butyl azide produces three Schmidt products from the aminodiazonium ion **24** (eq 2).[2d] The aniline **25** is a result of aryl migration, while the benzylic amines **26** and **27** are produced by alkyl and hydrogen migration, respectively. Neglecting hydrogen migration, which is not possible in the aminodiazonium ion **8**, alkyl migration in **24** is preferred over aryl migration by a margin of 3.5:1. While the structure of **24** is very close to that of **8**, once again the conformational mobility of **24** about the benzylic C−N bond makes it difficult to extrapolate the regioselectivity of its rearrangement to **8**.



Since our prior results (eqs 1 and 2) do not provide unequivocal guidance regarding the aryl vs alkyl migratory preference of the aminodiazonium ions **8** (Scheme 1), we carried out molecular modeling on these intermediates using a combination of molecular mechanics and semiempirical molecular orbital (AM1) methods in order to gain some insight into this regioselectivity question.[5] The aminodiazonium ions with the aryl group antiperiplanar to the departing dinitrogen group were consistently 2−4 kcal/mol higher in energy than the invertomers with the alkyl group antiperiplanar.[6] A representative result is shown in Figure 2. Thus, it might be expected that alkyl migration would be preferred, leading to the iminium ions **10** and thus the benzylic amines **15**−**18** as the major Schmidt products (Scheme 1). However, as stated above, such a stereoelectronic rationale is only one factor to consider; the ability of the migrating group and the migration origin to stabilize a positive charge are also important factors. For example, neglecting stereoelectronic issues, aryl groups have a higher migratory

(4) Hoffman, R. V.; Kumar, A. *J. Org. Chem.* **1985**, *50*, 1859−1863.

(5) For a discussion of the mechanism of the Schmidt reaction of azides with carbocations, including structural and theoretical work on aminodiazonium ions, see ref 2b. This paper also describes our procedure for using molecular mechanics and semiempirical MO methods to model aminodiazonium ions. See also: Fang, W.-k. Ph.D. Thesis, University of Michigan, 1997.

(6) With respect to the nitrogen-containing ring, the lowest energy aminodiazonium ions have the *endocyclic* alkyl group roughly antiperiplanar to the departing dinitrogen group. Since such a migration would result in ring contraction, often to a strained ring, we did not expect this pathway to dominate. Hence, we focused on the higher energy aminodiazonium ions where the exocyclic aryl or alkyl groups are considered.

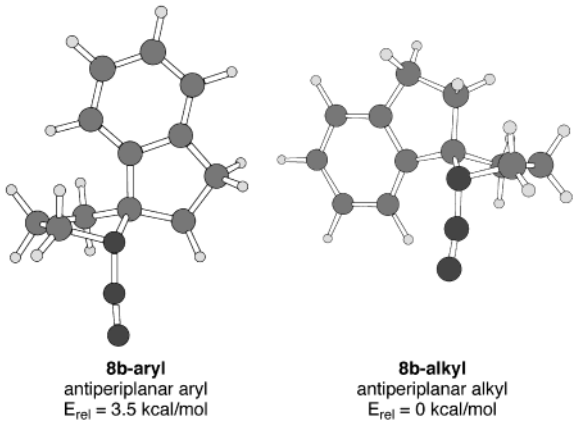


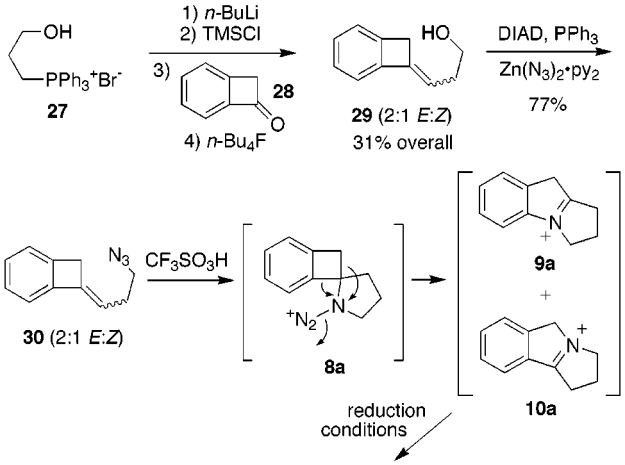
Figure 2. AM1 calculations on aminodiazonium ion **8b**: A representative result.

aptitude than alkyl groups in 1,2-rearrangements from C to N,[4,7] presumably due to their ability to bear positive charge in the rearrangement in the form of phenonium ion intermediates. Ideally, modeling of transition states and other intermediates encountered on the rearrangement pathway (e.g., phenonium ions) would be required for a more useful prediction. With these caveats in mind, we sought to explore the cyclizations of the cations **7** to the amines **11**−**18**.

Results and Discussion

Basic Cyclizations Leading to 1-Azabicyclo[*m.n.*0]-alkanes. For access the benzo-fused pyrrolizidines **11** and **15**, we required a benzocyclobutyl cation (see **7a** in Scheme 1), which should be accessible from the azido alkene **30** by protonation (Scheme 2). Formation and *O*-silylation of the dianion of the phosphonium salt **27** followed by the reaction of the resultant silyloxy ylide[8] with benzocyclobutenone **28**[9] gave the hydroxy alkene **29** as a mixture of geometrical isomers after desilylation with *n*-Bu_4NF. A Mitsunobu reaction[10] was then used to prepare the key azide **30**. Treatment of **30** with trifluoromethanesulfonic acid caused a Schmidt reaction via the aminodiazonium ion **8a**, producing the iminium ions **9a** and **10a** (not isolated or observed directly). Reduction of these ions with sodium borohydride gave the desired benzopyrrolizidines **11**[11,12] and **15**[13] accompanied by the indole **31**,[12,14,15] the result of deprotonation of **9a**. All three compounds are known; **11** and **31** were prepared in model studies for the synthesis of mitocenes and mitomycins. The ratio of aryl migration (**31** + **11**) to alkyl migration (**15**) was 3:1. Reduction of the iminium ions **9a** and **10a** under less basic conditions using borane gave only **11** and **15** in a 1.5:1 ratio, with none of the indole **31** detected. Hence, the simple aminodiazonium ion **8a** rearranged primarily by aryl migration, despite modeling studies that showed a preference for the aminodiazonium ion with the alkyl group roughly antiperiplanar to the departing dinitrogen group. This may be a reflection of the greater ability of a migrating aryl group to carry a positive charge in the transition state (i.e., as a phenonium ion), as discussed above.

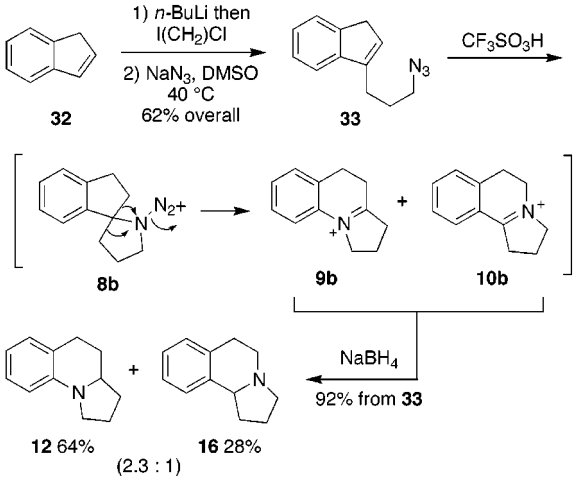
Scheme 2. Schmidt Route to Benzo-Fused Pyrrolizidines



Reduction conditions	Result
$NaBH_4$	27% of **31** + 21% of a 1:1.3 mixture of **11** and **15** [Ratio of (**31** + **11**) to **15** = 3:1]
BH_3·SMe_2	0% of **31** + 49% of a 1.5:1 mixture of **11** and **15**

A five-membered ring cation (see **7b** in Scheme 1) was then targeted in order to access the benzoindolizidines **12** and **16** (Scheme 3). Metalation of indene **32** with

Scheme 3. Schmidt Route to Benzo-Fused Indolizidines



n-butyllithium[16] followed by alkylation of the resultant indenyllithium with 1-chloro-3-iodopropane gave a mixture of alkenes, 1-(3-chloropropyl)indene and 3-(3-chlo-

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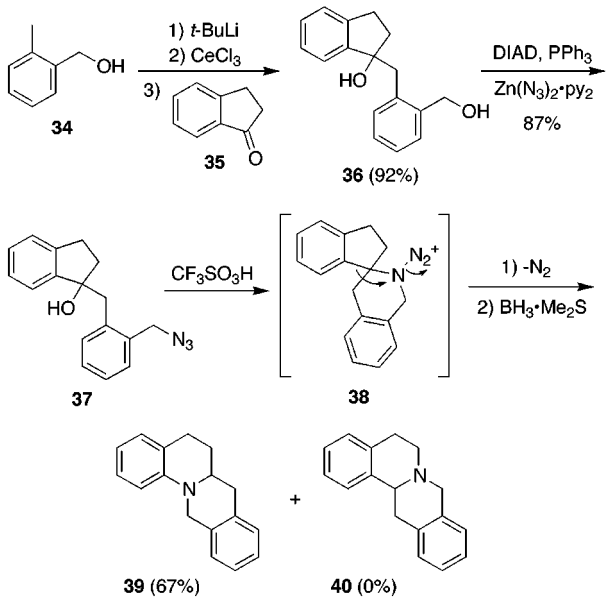
ropropyl)indene. Azide displacement of the chlorides followed by thermal isomerization of the indene double bond isomers afforded the azide **33** with the alkene in the most substituted position. This type of double bond isomerization is similar to those known for cyclopentadienes and has been well documented for indene systems.[17] Treatment of **33** with trifluoromethanesulfonic acid followed by in situ reduction of the presumed iminium ions **9b** and **10b** with sodium borohydride gave a 2.3:1 mixture of the two tricyclic compounds **12** and **16** in excellent (92%) combined yield. The regioisomer **12** was isolated in 64% yield and was easily separated from **16** (28% yield) due to its greater mobility on silica gel. The hexahydropyrroloquinoline **12**[15] and the hexahydropyrroloisoquinoline **16**[18,19] are both known compounds. Aryl migration rather than alkyl migration had occurred in the rearrangement of the intermediate aminodiazonium ion **8b** to an extent similar to that observed above for the rearrangement of **8a** (Scheme 2).

To access benzo-fused quinolizidines, we then studied a system that retained a five-membered ring cation but had a longer tether to the azide, resulting in a six-membered ring aminodiazonium ion (**38** in Scheme 4, cf.

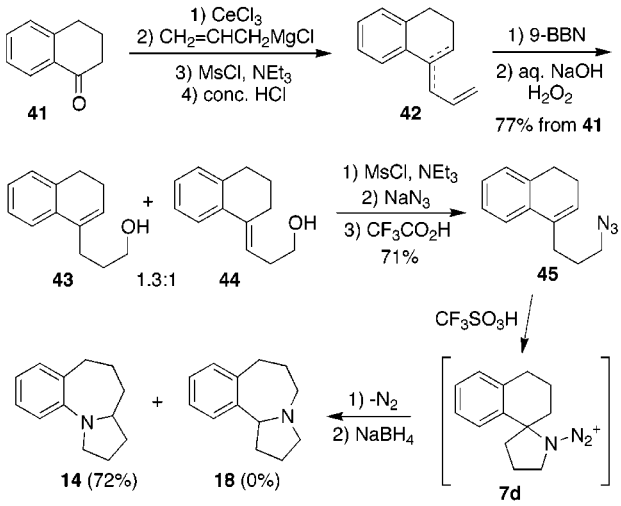
Scheme 4. Schmidt Route to Benzo-Fused Quinolizidines



8c in Scheme 1). Double metalation of 2-methylbenzyl alcohol **34** using the method of Braun[20] followed by transmetalation to the cerium(III) salt[21] and addition to 1-indanone **35** gave the diol **36**. A Mitsunobu reaction[10] was used to install an azido group selectively at the primary benzylic position, affording the desired azide **37**. Treatment of **37** with trifluoromethanesulfonic acid followed by reduction of the intermediate iminium ion with sodium borohydride afforded only the known quinolizidine **39**,[22] with none of the expected regioisomeric benzylic amine **40** being detected. Aryl migration had thus occurred exclusively in the aminodiazonium ion **38**.

In an attempt to access an azepane, we targeted a six-membered ring cation for the Schmidt reaction (see **7d** in Scheme 1), presumably accessible by protonation of the azido alkene **45** (Scheme 5). Thus, cerium-promoted

Scheme 5. Schmidt Route to Benzo-Fused Pyrrolidinoazepanes



addition[21] of allylmagnesium chloride to α-tetralone **41** followed by mesylation and elimination of the mesylate under acidic conditions gave the diene **42** as a mixture of regio- and stereoisomers. Hydroboration/oxidation of the terminal vinyl group of **42** gave an inseparable 1.3:1 mixture of the alcohols **43**[23] and **44**, which were converted to their azides using standard displacement methodology. The resultant mixture of alkene isomers was subjected to trifluoroacetic acid, which caused double bond isomerization, producing a 10:1 mixture of **45** and another alkene isomer (unidentified). Treatment of **45** with trifluoromethanesulfonic acid followed by reduction of the intermediate iminium ion gave the known benzo-fused pyrrolidinoazepane **14**,[24] with none of the regioisomeric amine **18** detected. Once again, aryl migration in the aminodiazonium ion intermediate (i.e., **7d**) had occurred preferentially.

The cyclizations in Schemes 2−5 clearly show that the intramolecular Schmidt reaction of azides with cyclic benzylic carbocations is an efficient process that affords benzo-fused 1-azabicyclo[*m*.*n*.0]alkanes. The substrates are easily prepared, and the regioselectivity of the rearrangment favors aryl migration, producing anilines as the major or exclusive products. The regioisomeric anilines and benzylic amines that are produced are easily separated by chromatography due to their substantially different basicities. The regioselectivity observed is contrary to predictions based on the energies of the various aminodiazonium ions encountered (e.g., Figure 2), where the lower energy ion consistently has the ring alkyl group antiperiplanar to the departing dinitrogen, indicating that alkyl migration would be preferred over aryl migration. A more complete study would require modeling of the transition states for rearrangement, i.e., alkyl migra-

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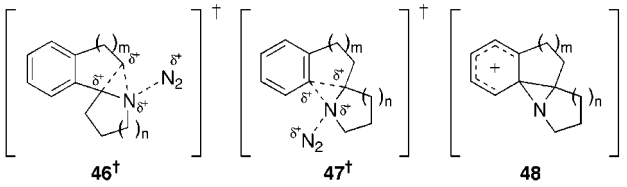
tion (**46**‡) vs aryl migration (**47**‡), as well as modeling of additional intermediates along the reaction coordinate, e.g., the phenonium ions **48**. Without such computations, we are left to conclude that aryl groups migrate selectively because of their increased ability to stabilize a positive charge during the migration, presumably via the phenonium ion intermediates **48**.



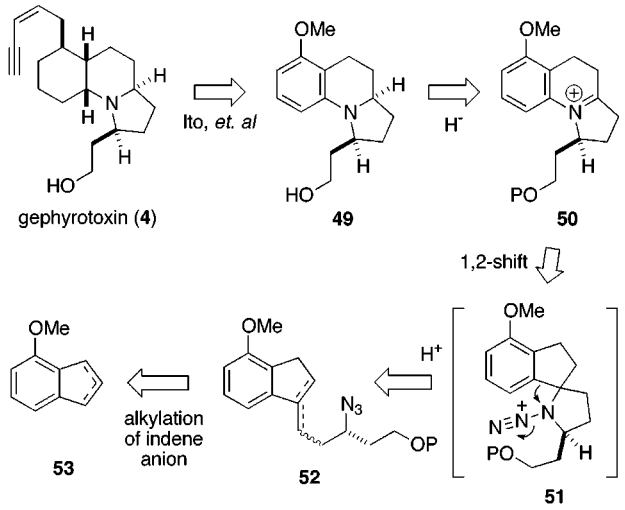
46† **47**† **48**

Application of the Methodology: A Formal Synthesis of Gephyrotoxin. Given that the Schmidt reactions outlined above produce anilines **1** rather than benzylic amines **2** (see Figure 1 above), we wished to determine whether this methodology would be useful for accessing more complex examples of this core structure. A formal synthesis of the alkaloid gephyrotoxin **4** is described below, a compound that has a similar skeleton to the benzo-fused indolizidine **12** synthesized in Scheme 3 above.[25]

Gephyrotoxin (**4**), originally isolated from *Dendrobates histrionicus*,[26] is a member of a class of alkaloids isolated from the skins of tropical frogs of the genus *Dendrobates*.[27] Its absolute configuration was determined to be as shown by X-ray analysis.[28] Gephyrotoxin is relatively nontoxic. Mild muscarinic activity was originally reported for this alkaloid,[29] however recent studies[30] have revealed a more complex and interesting array of neurological activities associated with gephyrotoxin. The low abundance of gephyrotoxin in amphibians and its unusual chemical and biological characteristics have led to synthetic interest in several laboratories.[31−39]

A retrosynthetic analysis of gephyrotoxin is shown in Scheme 6. Ito and co-workers have prepared **49** and converted it to gephyrotoxin **4**.[36] We planned to intercept Ito's intermediate by the stereoselective reduction of the iminium ion **50**, which would result from a Schmidt

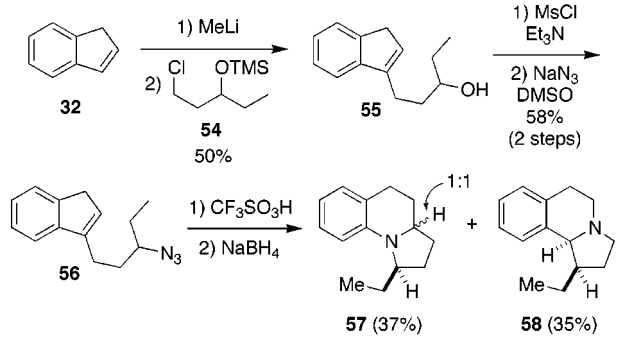
Scheme 6. Retrosynthetic Analysis of Gephyrotoxin (4)



reaction of the azido-alkene **52** proceeding through the aminodiazonium ion **51** by aryl migration in a fashion analogous to that shown above in Scheme 3, where the azido-alkene **33** was cyclized to the benzoindolizidines **12** and **16**, the former being the desired ring system for gephyrotoxin. The azido-alkene **52** should be available from the indene **53** by deprotonation and alkylation, as was done in Scheme 3. The stereoselectivity of the iminium ion reduction, the regioselectivity of the Schmidt reaction, and the regioselectivity of the indene alkylation are all interesting issues to be examined. Before disclosing the formal synthesis of racemic gephyrotoxin, model studies will be described that deal with the viability of the basic Schmidt reaction for the assembly of the three rings of this alkaloid.

The Use of a Secondary Azide in the Schmidt Reaction: Stereoselectivity of the Iminium Ion Reduction. While access to the basic ring skeleton gephyrotoxin was described above in Scheme 3 (i.e., compound **12**), a secondary rather than primary azide is desirable in the Schmidt precursor in order to install the 2-hydroxyethyl group of this alkaloid. Given the ease of assembly of the cyclization precursors using the indene alkylation method, a simple model study was conducted to ascertain whether a secondary azide can be used in the intramolecular Schmidt reaction (Scheme 7). This

Scheme 7. Model Cyclization of the Azide 56. Stereoselectivity of the Iminium Ion Reduction



study also addresses the stereoselectivity of the reduction of the resultant iminium ion. Metalation of indene **32** and alkylation with the chloride **54**[40] gave the alcohol **55** in

(25) For a preliminary communication, see: Pearson, W. H.; Fang, W.-k. *Electron. Conf. Heterocycl. Chem., 1998*, http://www.ch.ic.ac.uk/ectoc/echet98/pub/013/index.htm.

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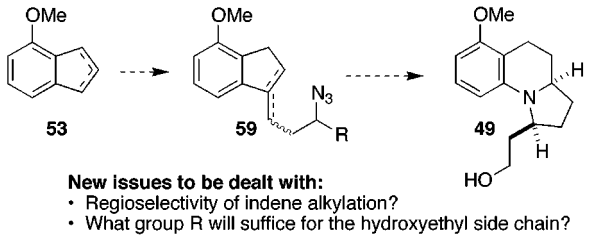


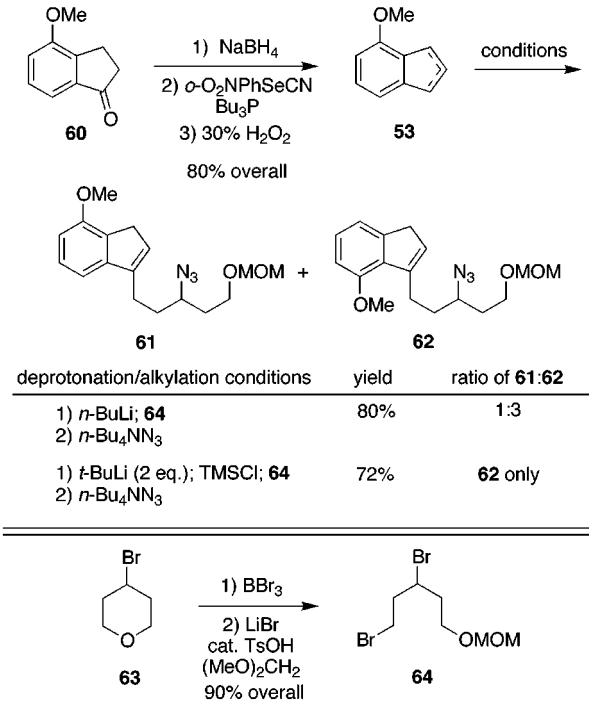
Figure 3. New questions.

good yield. Mesylation followed by azide displacement provided the desired azido-indene **56** in 58% yield. Treatment of **56** with trifluoromethanesulfonic acid in benzene afforded a mixture of iminium ions that were reduced with sodium borohydride to give the desired tricyclic aniline **57** (resulting from phenyl migration) and the benzylic amine regioisomer **58** (resulting from alkyl migration) in 72% combined yield. The iminium ion reduction had proceeded with poor stereoselectivity, producing **57** as a 1:1 mixture of diastereomers. However, we hoped that a bulkier hydride reagent in combination with a bulky alcohol protecting group on the 2-hydroxyethyl side chain required for gephyrotoxin would lead to an improvement in the stereoselectivity of the iminium ion reduction. An alternate side-chain in conjunction with the required methoxy-substituted indene might also alter the low regioselectivity of the Schmidt rearrangement.

Initial Efforts to Synthesize Gephyrotoxin: Regioselectivity of the Alkylation of Unsymmetrical Indene Anions. Moving from model systems to fully functionalized compounds that may lead to gephyrotoxin, two new issues arise (Figure 3). First, if we use the same indene alkylation approach that we developed in the model studies, methoxyindene (**53**) is needed as the starting material, and the regioselectivity of its alkylation becomes important. Second, we must choose a group R, a synthetic equivalent of a 2-hydroxyethyl group, that will survive the strongly acidic conditions of the Schmidt reaction and perhaps promote greater regioselectivity. Our initial efforts to address these issues are outlined below.

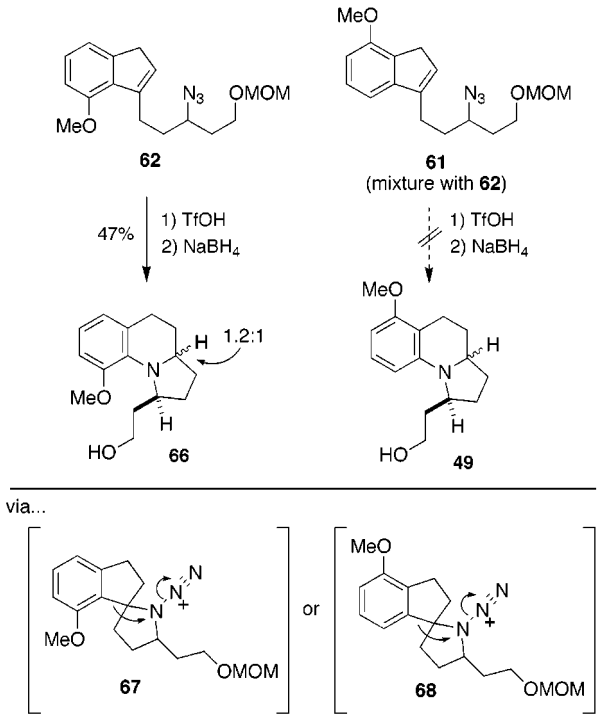
The desired methoxyindene **53** was prepared from commercially available 4-methoxy-1-indanone (**60**) by sodium borohydride reduction and dehydration according to Grieco's selenoxide method[41] (Scheme 8). We do not know the location of the double bond in **53**, although it appears to be a single regioisomer. Metalation of **53** with *n*-butyllithium followed by alkylation with **64**, easily prepared from commercially available 4-bromotetrahydropyran (**63**),[42,43] followed by azide displacement produced a 1:3 ratio of the desired indene **61** and the undesired regioisomeric indene **62**. Chelation of lithium to the methoxy group may explain this regioselectivity, which has been observed in other alkoxyindene metalation/alkylations.[17,44] Attempts to inhibit this internal chelation and thus alter the regioselectivity of the alkylation [e.g., KN(TMS); NaH; silyloxy rather than methoxy] were unsuccessful. Kelly's method for regioselective indene alkylation (*tert*-butyllithium/TMSCl) could be used to make the undesired indene **62** selectively.[17]

Scheme 8. Attempts at Regioselective Alkylation of Methoxyindene 53



Pure **62**, the "wrong" regioisomer, was subjected to the Schmidt reaction (Scheme 9), producing **66** in moderate yield as a single regioisomer, the result of only aryl migration in the intermediate aminodiazonium ion **67**. A sample of pure **61** could not be obtained by chromatography, so a mixture of **61** and **62** was subjected to the Schmidt reaction. Compound **66** (derived from **62**) was

Scheme 9. Schmidt Reaction of Azido-Indene Regioisomers 61 and 62



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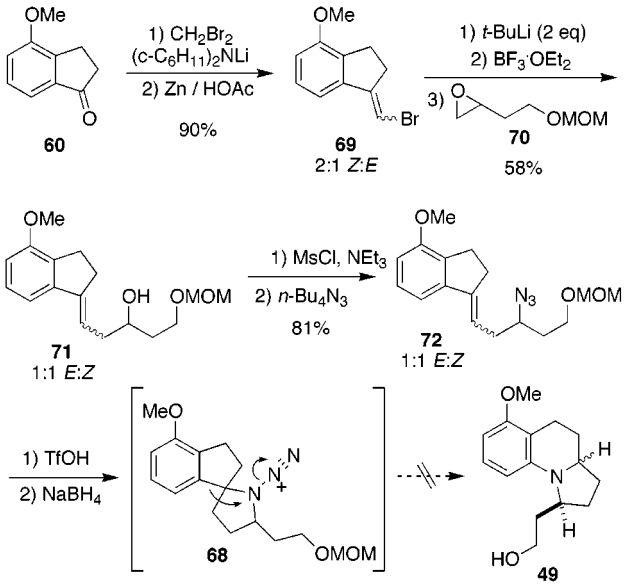
(43) Kulkarni, S. U.; Patil, V. D. *Heterocycles* **1982**, *18*, 163−167.
(44) Mazzocchi, P. H.; Stahly, B. C. *J. Med. Chem.* **1981**, *24*, 457−462.

the only product; no **49** was detected, perhaps indicating that **68** does not undergo rearrangement, although the use of a mixture of compounds made the study of this reaction more difficult. An alternate synthesis of the cyclization precursor was thus sought in order to avoid the lack of regiocontrol in the indene alkylation method.

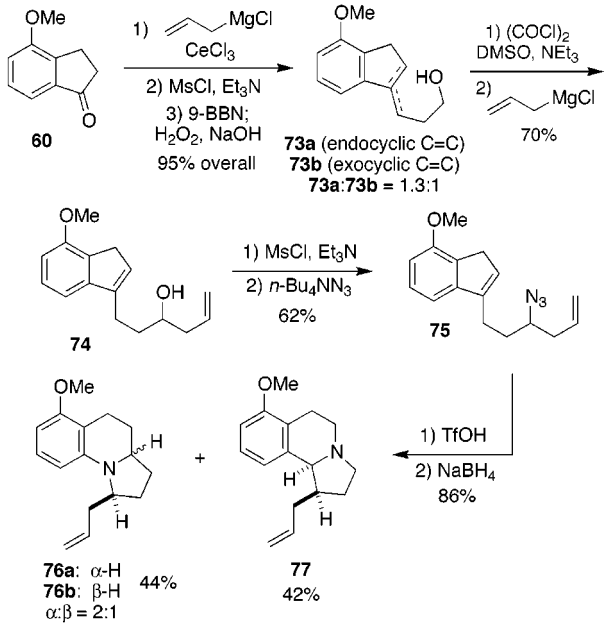
Regiocontrolled Routes to the Cyclization Precusors: Avoiding Indene Anion Alkylations. A single regioisomer of the related azido-alkene **72** was synthesized as shown in Scheme 10. Addition of dibromolithiomethane[45] to the indanone **60** followed by treatment of the resulting adduct with zinc dust[46] gave the vinyl bromide **69** as an inseparable 2:1 mixture of *Z* and *E* isomers. Metal halogen exchange on **69** followed by Lewis acid mediated opening[47] of the epoxide **70**[48] provided the alcohol **71** in good yield as a 1:1 mixture of *E* and *Z* isomers. Replacement of the alcohol with azide was accomplished by mesylation and azide displacement. When the azido-alkene **72** was subjected to the usual Schmidt reaction/iminium ion reduction sequence, no identifiable products were obtained, consistent with the observations in Scheme 9. Considering the data in Schemes 9 and 10 and the model studies already described (i.e., no methoxy on the ring, Schemes 3 and 7), we concluded that the electron density in the aromatic ring is an important influence in the success and regioselectivty of the Schmidt migration. Regarding rate, one might expect the most electron-rich aromatic ring to migrate fastest, i.e., the *o*-methoxyaryl group (**62**/**67**, Scheme 9), followed by a simple aryl group (**33**/**8b**, Scheme 3; **56**, Scheme 7), which should migrate faster than a *m*-methoxyaryl group (**61**/**68**, Scheme 9 and **72**/**68**, Scheme 10), thus explaining why there is no cyclization for **61** or **72**. The acid-sensitive MOM group may also be problematic in the more challenging cyclizations involving migration of a *m*-methoxyaryl group. Regarding regioselectivity, the more electron-rich aromatic ring will be better able to compete with alkyl migration. Thus one might expect the propensity for aryl migration (vs alkyl migration) to decrease in the order given above. Indeed, the *o*-methoxyaryl case is completely aryl selective, while the nonmethoxy cases gave significant amounts of alkyl migration. The lack of success in the *m*-methoxyaryl case does not allow us to discuss these data point, although it would be expected that a *m*-methoxyaryl group would be a poorer migrator than an *o*-methoxyaryl or simple aryl group.

Scheme 10. Regiocontrolled Alkene Synthesis and Attempted Schmidt Reaction



The failure of the Schmidt reactions of the azides **61** and **72** might also be due in part to the choice of side-chain; i.e., for the more difficult cyclizations involving *m*-methoxyaryl cations, a more robust and perhaps less electronegative side-chain than 2-(methoxymethoxy)ethyl might be desirable. Thus, we chose to examine an allyl group as the side-chain, since this group might be transformed later into the desired 2-(hydroxy)ethyl group of gephyrotoxin. The synthesis and cyclization of such a compound (**75**) is shown in Scheme 11. A cerium-mediated[21] addition of allylmagnesium chloride to methoxyindanone **60** gave an alcohol, that was mesylated and eliminated to furnish a diene (not shown). Selective hydroboration/oxidation of the terminal double bond of this alkene with 9-BBN[49] provided the alcohol **73** in excellent overall yield as a 1.3:1 mixture of endocyclic and exocyclic alkenes **73a** and **73b**, respectively. Isomer **73b** was a single alkene of undetermined geometry. A one-pot Swern oxidation/organometallic addition using Ireland's method[50] transformed **73** into **74**, which was isolated as a single isomer. The conversion of **74** to the azide **75** was accomplished with standard displacement chemistry. Schmidt reaction of **75** followed by hydride

Scheme 11. An Allyl Side-Chain Allows a Successful Schmidt Reaction



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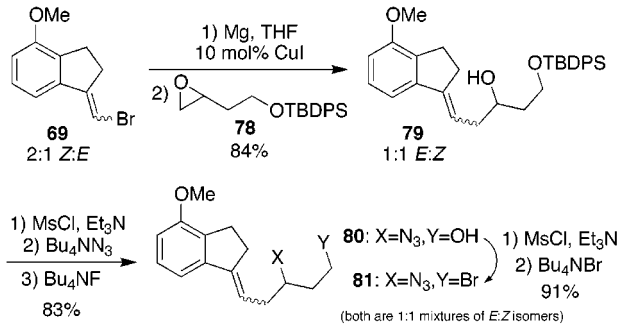
reduction of the resultant iminium ion proceeded in excellent yield to produce the easily separable amines **76** and **77** in 44% and 42% isolated yield, respectively. The desired benzoindolizidine **76** proved to be a 2:1 mixture of diastereomers, the major isomer having the desired cis configuration with respect to the pyrrolidine ring, i.e., **76a**. The undesired amine **77** was produced as a single diastereomer. Hence, the Schmidt reaction involving the migration of a *m*-methoxyaryl group can proceed efficiently if a more robust side-chain and a more nucleophilic azide are used (compare with Schemes 10 and 11), although the regioselectivity is poor, as predicted (vide supra). Nonetheless, oxidative cleavage of the alkene of **76** and reduction of the resultant aldehyde would complete a formal synthesis of gephyrotoxin by intercepting Ito's compound **49** (Scheme 6). However, all attempts at oxidative transformations of **76** were unsuccessful, perhaps due to interference by the highly electron-rich aromatic ring. Thus, we sought an alternative side-chain that would be stable to the strongly acidic Schmidt conditions and would be readily transformed into the 2-hydroxyethyl group of gephyrotoxin.

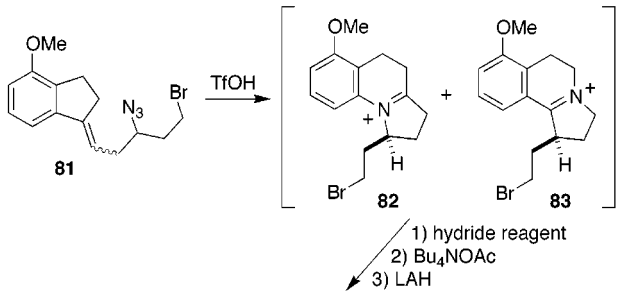
A Formal Synthesis of Gephyrotoxin. Our search for a useful 2-hydroxyethyl side-chain equivalent had so far led us to uncover several important aspects of the Schmidt reaction required for the synthesis of gephyrotoxin, but each strategy had a fatal flaw. Ultimately, we narrowed our search to a 2-bromoethyl group, which would survive the acidic conditions of the Schmidt reaction, but would be easily transformed into a 2-hydroxyethyl group without relying on an oxidative reaction. We were initially concerned that the 2-bromoethyl group might lead to complications arising from azetidinium ion formation after the Schmidt reaction, since γ-bromoamines are well-known to cyclize to such ions.[51] However, since the product of the rearrangement would produce an aniline-type nitrogen, this concern was diminished.

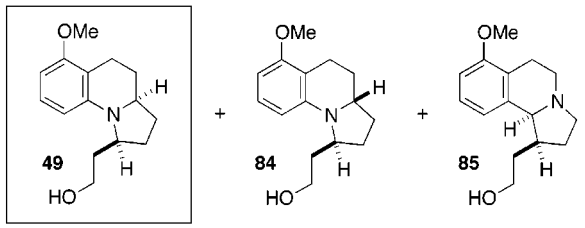
Scheme 12. Incorporation of a 2-Bromoethyl Side-Chain



The synthesis of the Schmidt reaction precursor **81** is presented in Scheme 12. Formation of the Grignard reagent derived from **69** (see Scheme 10) followed by a copper-catalyzed opening of the epoxide **78**[52] according to a procedure similar to that reported by Kocienski[53] gave the alcohol **79** in excellent yield. Mesylation of the alcohol and subsequent displacement with tetrabutylammonium azide and desilylation furnished the hydroxyazide **80** in high yield. Mesylation of the primary alcohol of **80** followed by bromide displacement afforded the desired bromo-azide **81**.

Scheme 13. Formal Synthesis of Gephyrotoxin





hydride reagent	result
$NaBH_4$	56% of a 1:1 mixture of **49** and **84**, plus 16% of **85**
DIBAL-H	47% of a 2:1 mixture of **49** and **84**, plus 13% of **85**
L-Selectride™	45% **49** (none of **84**), plus 10% of **85**

As shown in Scheme 13, treatment of **81** with trifluoromethanesulfonic acid in benzene followed by sodium borohydride reduction of the resultant iminium ions **82** and **83** generated a mixture of Schmidt products which were subjected, without purification, to displacement by acetate ion. Again without purification, the mixture of acetates was reduced with lithium aluminum hydride to produce a mixture of the desired alcohol **49**, its stereoisomer **84**, and the regioisomer **85** in good overall yield from **81**. As in earlier attempts, the stereoselectivity of the reduction of the desired iminium ion was poor. We were able to overcome the nonselective reduction by switching to bulkier reducing agents. L-Selectride proved to be the best choice, ultimately producing the desired compound **49** as a single diastereomer (i.e., none of **84** was detected) accompanied by a small amount of the regioisomer **85**. The overall yield of **49** from **81** using this procedure was 45%. Since the aromatic ring of **49** has been reduced by Ito et al.[36] to afford an advanced intermediate in Kishi's synthesis of gephyrotoxin,[31] our synthesis of **49** constitutes a formal total synthesis of gephyrotoxin **4**. The synthesis of **49** required nine steps (five purifications) from commercially available 4-methoxy-1-indanone **60** and proceeded in 22% overall yield.

Mechanistic Considerations. A summary of the results from the Schmidt reactions of the azides **33** (Scheme 3), **56** (Scheme 7), **61**/**62** (Scheme 9), **72** (Scheme 10), **75** (Scheme 11), and **81** (Scheme 13), represented by the generic azide **86**, to the benzoidolizidine iminium ions **90** and **93** are tabulated at the bottom of Scheme 14. No simple general explanation for the regioselectivity of the rearrangment is apparent, especially when one considers that the side-chain R in the cations **87** (where

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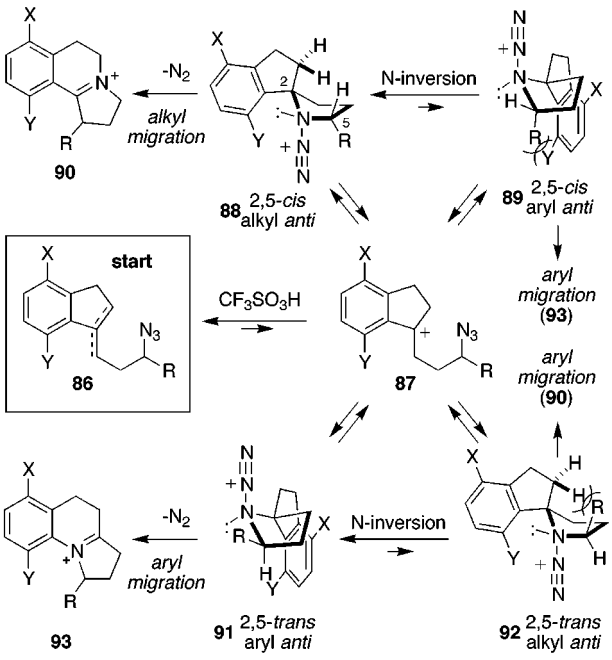
(53) Street, S. D. A.; Yeates, C.; Kocienski, P.; Campbell, S. F. *J. Chem. Soc. Chem. Commun.* **1985**, *20*, 1386-1388.

Scheme 14. Schmidt Pathways to Gephyrotoxin-type Compounds



Azide **86** (Scheme)	X	Y	R	ratio of **93** to **90**
33 (3)	H	H	H	2.3:1
56 (7)	H	H	Et	1:1
62 (9)	H	OMe	CH_2CH_2OMe	**93** only
61 & **72** (9, 10)	OMe	H	CH_2CH_2OMe	**90** only
75 (11)	OMe	H	$CH_2CH{=}CH_2$	1:1
81 (13)	OMe	H	CH_2CH_2Br	3.9:1 (avg.)

R ≠ H) renders the faces of the carbocation diastereotopic, resulting in two diastereomeric aminodiazonium ion manifolds represented by **88**/**89** (2,5-cis) and **91**/**92** (2,5-trans). Is the regioselectivity of the rearrangement related to the diastereoselectivity of the capture of the cation by the azide, or is that step a rapid preequilibrium, making the rearrangement step rate determining? Assuming such a preequilibrium, we are still left with a problem. Since it is known that pyramidal inversion in aminodiazonium ions is a low-barrier (ca. 1 kcal/mol) event,[54,2b] one can assume that N-inversion is rapid and reversible, leaving the rearrangement of the four ions **88**/**89** and **91**/**92** as the likely rate-determining steps. In the 2,5-cis manifold, models suggest that **88** would be preferred over **89** because of the steric interaction shown, but according to the Curtin−Hammett principle, this preference may be irrelevant, since the barrier to interconversion of **88** and **89** is so much lower than the expected barrier for the rearrangement to **90** and **93**, respectively. A similar analysis holds for **91** and **92** from the 2,5-trans manifold, where **91** seems more favorable than **92** according to models, but it may be irrelevant. Thus, we are left with a very complex picture, made more difficult by the lack of knowledge about the transition states for aryl vs alkyl migration, as discussed previously. At least one piece of data may be explained by the analysis shown in Scheme 14, i.e., that azide **62** (Scheme 9) leads to aryl migration as the sole product, i.e., yielding the iminium ion **93** in Scheme 14. The *o*-methoxy substituent Y on the aryl ring would lead to unfavorable steric interactions in **88**, **89**, and **92**, leaving **91** to account for the rearrangement, which would produce the aryl migration product **93**. The other rearrangements give lower regioselectivities, and a simple explanation for the trends shown at the bottom of Scheme 14 is not apparent. In particular, the higher selectivity for aryl migration when R = 2-bromoethyl (**81**; 3.9:1 aryl:alkyl migration) versus the nonselectivity when R = Et (**56**) or R = allyl (**75**) is intriguing. Nonetheless, this selectivity has proven useful for our application to the formal synthesis of gephyrotoxin.

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Conclusion

The intramolecular Schmidt reaction of azides with carbocations has proven to be an effective way to assemble a variety of benzo-fused 1-azabicyclo[*m*.*n*.0]-alkanes. In general, aryl migration in the intermediate aminodiazonium ion is preferred over alkyl migration, leading to anilines rather than benzylic amines, which are easily separated by column chromatography due to their diverse polarities. The ease of synthesis of the Schmidt cyclization precursors is another attractive feature of this chemistry. The methodology was shown to be useful for the synthesis of the tricyclic core of the alkaloid gephyrotoxin, resulting in a formal total synthesis of this compound. The aryl vs alkyl regioselectivity proved to be subject to small changes in the structure, but again, aryl migration was often preferred, producing aniline-like benzo-fused indolizidines.

Experimental Section[55]

(7*E*)- and (7*Z*)-7-(3-Hydroxypropylidene)bicyclo[4.2.0]-octa-1(6),2,4-triene (29). *n*-Butyllithium (10.5 mL of a 2.5 M solution in hexane, 26.3 mmol) was added to a suspension of (3-hydroxypropyl)triphenylphosphonium bromide (**27**)[8] (10.26 g, 25.59 mmol) in THF (80 mL) at 0 °C. After warming the mixture to room temperature over 10 min, it was recooled to 0 °C and treated with chlorotrimethylsilane (3.25 mL, 2.78 g, 25.6 mmol). After 10 min, benzocyclobutenone (**28**)[9] (3.02 g, 25.56 mmol) in THF (10 mL) was added. After refluxing for 20 min, the mixture was cooled to 0 °C and treated with tetra-*n*-butylammonium fluoride (30 mL of a 1.0 M solution in THF, 30 mmol). After 30 min at room temperature, the solution was concentrated and diluted with water (50 mL) and then extracted with ether (3×). The combined organic phases were washed with brine (3×), then dried ($MgSO_4$) and concentrated. Chromatography (2:1 hexane/ether) gave 1.26 g (31%) of the title compounds as an inseparable 2:1 mixture of *E* and *Z* isomers as judged by ^{1}H NMR, where the major isomer was assigned as the *E* configuration based on the larger $J_{\text{allylic},transoid}$ (1.4 Hz) coupling constant ($J_{\text{allylic},cisoid}$ ca. 0 Hz).[56] Characterized of the mixture: R_f = 0.25 (2:1 hexane/ether): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.27−7.19 (m, 6 H), 7.15−7.12 (m, 1 H), 5.74 (tt, J = 7.6, 1.4 Hz, 1 H), 5.34 (t, J = 7.6 Hz, 0.7 H), 3.80−3.69 (m, 3.5 H), 3.63 (s, 2H), 3.60 (s, 1.5 H), 2.65 (q, J = 6.5 Hz, 1.5 H), 2.43 (q, J = 6.5 Hz, 2 H), 2.13−2.06 (m, 1.7 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.9, 144.8, 144.5, 143.8, 139.6, 138.9, 128.1, 127.1, 122.6, 119.8, 117.6, 116.6, 114.8, 62.2, 38.0, 36.8, 33.5, 32.4; IR (neat) 3334 (br s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 161 ([M + H]$^+$, 100), 143 (21.7); HRMS (CI with NH_3) calcd for $C_{11}H_{12}OH$ ([M + H]$^+$) 161.0966, found 161.0961.

(7*E*)- and (7*Z*)-7-(3-Azidopropylidene)bicyclo[4.2.0]-octa-1(6),2,4-triene (30). Diisopropyl azodicarboxylate (3.25

(55) For general experimental issues, see: Pearson, W. H.; Hembre, E. J. *J. Org. Chem.* **1996**, *61*, 5537−5545.

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mL, 3.34 g, 16.52 mmol) was added to a mixture of the alcohols **29** (1.30 g, 8.11 mmol), triphenylphosphine (4.26 g, 16.23 mmol), and $Zn(N_3)_2$·(pyridine)$_2$ (2.00 g, 6.50 mmol) in toluene (40 mL) at room temperature over 10 min.[10] After 40 min, the mixture was concentrated, and the residue was chomatographed (2:1 hexane/ether) to give 1.16 g (77%) of the title compounds as an inseparable 2:1 mixture of *E* and *Z* isomers as judged by ^{1}H NMR, where the major isomer was assigned as the *E* configuration based on the larger $J_{\text{allylic},transoid}$ (1.4 Hz) coupling constant ($J_{\text{allylic},cisoid}$ ca. 0 Hz).[56] Characterized of the mixture: $R_f = 0.62$ (1:2 ether/hexane): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26−7.23 (m, 6.2 H), 7.18−7.15 (m, 1 H), 5.75 (t, J = 7.1 Hz, 1 H), 5.35 (t, J = 7.5 Hz, 0.8 H), 3.66 (s, 2 H), 3.62 (s, 1.6 H), 3.46−3.38 (m, 3.6 H), 2.70 (q, J = 7.1 Hz, 1.6 H), 2.49 (q, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.0, 144.7, 144.3, 143.8, 139.8, 139.1, 128.4, 127.2, 122.7, 119.8, 117.8, 116.0, 114.2, 51.2, 38.0, 36.7, 28.6; IR (neat) 2096 (s) cm^{-1}; MS (CI with NH_3) *m/z* (rel int) 203 ([M+NH_4]$^+$, 4.3), 158 (100); HRMS (CI with NH_3) calcd for $C_{11}H_{11}N_3NH_4$ ([M+NH_4]$^+$) 203.1297, found 203.1296.

2,3,8,8a-Tetrahydro-1*H*-3a-azacyclopenta[*a*]indene (11), 2,3,5,9b-Tetrahydro-1*H*-pyrrolo[2,1-*a*]isoindole (15), and 2,3-Dihydro-1*H*-3a-azacyclopenta[*a*]indene (31). Method A. Trifluoromethanesulfonic acid (254 mg, 1.68 mmol) was added to a solution of the azidoalkene **30** (300 mg, 1.62 mmol) in benzene (20 mL) at 0 °C. After 10 min, a solution of sodium borohydride (400 mg, 10.57 mmol) in methanol (10 mL) was added, and the mixture was warmed to room temperature for 14 h and treated with 15% aqueous sodium hydroxide (15 mL). The mixture was extracted with ether (3×), and the combined organic phases were washed with brine (3×), dried ($MgSO_4$) and concentrated. Chromatography (1:7 ether/hexane) gave 68 mg (27%) of the known indole **31**,[12,14,15] $R_f = 0.53$: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.65 (d, J = 7.7 Hz, 1 H), 7.33−7.29 (m, 1 H), 7.24−7.15 (m, 2 H), 6.26 (s, 1 H), 4.10 (t, J = 6.9 Hz, 2 H), 3.08 (t, J = 7.5 Hz, 2 H), 2.65 (qintet, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 144.5, 133.2, 132.4, 120.2, 120.0, 119.0, 109.3, 92.2, 43.5, 27.7, 24.2; IR (neat) 1616 (m), 1551 (m) cm^{-1}; MS (EI, 70 eV) *m/z* (rel int) 157 (M$^+$, 100), 129 (24.9); HRMS calcd for $C_{11}H_{11}N$ 157.0891, found 157.0886. These spectral data were consistent with those reported in the literature.[12,14]

Further elution gave 53 mg (21%) of an inseparable 1:1.3 mixture of **11**[11,12] and **15**.[13] The major isomer was assigned as **11** based on the doublet at δ 6.60 (J = 7.8 Hz) in the ^{1}H NMR spectrum, which should result from the coupling of the benzylic hydrogens with the bridgehead hydrogen in **11**. An AB quartet at δ 4.44 was assigned to the benzylic hydrogens in **15**. Characterization of the mixture of **11** and **15**: $R_f = 0.30$ (1:7 ether/hexane): ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.35−7.26 (m, 2 H), 7.20−7.12 (m, 3 H), 7.10−7.07 (m, 2 H), 6.75 (t, J = 7.4 Hz, 1.5 H), 6.60 (d, J = 7.8 Hz, 1.5 H), 4.90−4.88 (m, 1 H), 4.44 (ABq, $\Delta\nu_{AB}$ = 86.3 Hz, J_{AB} = 15.2 Hz, 2 H), 3.96−3.89 (m, 1.5 H), 3.47−3.39 (m, 3 H), 3.23−3.15 (m, 3 H), 3.00−2.93 (m, 3 H), 2.62−2.54 (m, 1 H), 2.29−2.22 (m, 1 H), 2.11−2.03 (m, 1 H), 1.94−1.75 (m, 5 H), 1.38−1.28 (m, 1 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 154.6 (−), 141.2 (−), 135.7 (−), 129.8 (−), 128.3 (+), 128.1 (+), 127.4 (+), 124.7 (+), 122.6 (+), 122.5 (+), 119.1 (+), 110.8 (+), 78.2 (+), 68.2 (−), 65.1 (+), 63.0 (−), 52.1 (−), 33.8 (−), 31.2 (−), 30.6 (−), 25.7 (−), 24.3); IR (neat) 2365 (s), 2317 (s), 2270 (s), 1603 (s) cm^{-1}; MS (EI, 70 eV) *m/z* (rel int) 159 (M$^+$, 100), 143 (5.3), 130 (77.3); HRMS calcd for $C_{11}H_{13}N$ 159.1048, found 159.1043.

The overall ratio of aryl migration products (**11**+**31**) to alkyl migration product (**15**) was thus 3:1.

Method B. Trifluoromethanesulfonic acid (475 mg, 3.17 mmol) was added to a solution of the azidoalkene **30** (594 mg, 3.21 mmol) in benzene (50 mL) at room temperature. After 10 min, the solution was cooled to 0 °C and treated with BH_3·SMe_2 (4.50 mL of a 2.0 M solution in THF, 9.00 mmol). After being warmed to room temperature for 14 h, the solution was treated with saturated aqueous sodium bicarbonate (20 mL), and the mixture was extracted with ether (3×). The combined organic phases were washed with brine (3×), dried ($MgSO_4$), and concentrated. Chromatography (1:7 ether/hexane) gave 249 mg (49%) of an inseparable 1.5:1 mixture of **11** and **15** as judged by ^{1}H NMR spectroscopy as outlined above.

3-(3-Azidopropyl)-1*H*-indene (33). *n*-Butyllithium (48.0 mL of a 2.5 M solution in hexane, 0.12 mol) was added to a solution of indene (**32**, 11.62 g, 0.10 mol) in THF (200 mL) at 0 °C. After 30 min, the solution was cooled to −78 °C, 1-chloro-3-iodopropane (16.1 mL, 30.7 g, 0.15 mol) was added, and the resulting mixture was allowed to warm to room temperature. After 14 h, saturated aqueous ammonium chloride was added, and the mixture was extracted with ether (3×). The combined organic phases were washed twice with brine, dried ($MgSO_4$), and concentrated to give the crude product, which was dissolved in DMSO (250 mL) and treated with NaN_3 (13.00 g, 0.20 mol). After 14 h at 40 °C, water was added, and the resulting mixture was extracted with ether (3×). The combined organic phases were washed with water (3×) and brine and then dried ($MgSO_4$) and concentrated. Chromatography (1:16 ether/hexane) gave 12.42 g (62%) of the title compound as a clear oil, $R_f = 0.60$ (1:7 ether/hexane): ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.51 (d, J = 7.3 Hz, 1 H), 7.42−7.34 (m, 2 H), 7.26 (dt, J = 7.3, 1.4 Hz, 1 H), 6.29−6.28 (m, 1 H), 3.45−3.39 (m, 4 H), 2.70 (tt, J = 5.2, 1.6 Hz, 2 H), 2.07−1.99 (m, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 145.0 (−), 144.5 (−), 143.0 (−), 128.5 (+), 126.1 (+), 124.7 (+), 123.8 (+), 118.8 (+), 51.0 (−), 37.7 (−), 27.2 (−), 24.7 (−); IR (neat) 2096 (s) cm^{-1}; MS (EI, 70 eV) *m/z* (rel int) 170 ([M − N_2 − H]$^+$, 100), 141 (14.1); HRMS calcd for $C_{12}H_{12}N$ ([M − N_2 − H]$^+$) 170.0970, found 170.0974.

1,2,3,3a,4,5-Hexahydropyrrolo[1,2-*a*]quinoline (12)[15] and 1,2,3,5,6,10b-Hexahydropyrrolo[2,1-*a*]isoquinoline (16).[18,19] Trifluoromethanesulfonic acid (1.15 g, 7.68 mmol) was added to a solution of the azido indene **33** (1.02 g, 5.13 mmol) in dry benzene (250 mL) at 15 °C via syringe. After 10 min, the mixture was cooled to 0 °C, and sodium borohydride (1164 mg, 30.77 mmol) in methanol (30 mL) was added. After 14 h at room temperature, 15% NaOH (80 mL) was added, and the resulting mixture was extracted with ether (3×). The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated. Chromatography (1:16 ether/hexane) gave 569 mg (64%) of **12**[15] as a clear oil, $R_f = 0.46$. Compound **12** was reported by Caddick and co-workers without spectral data, thus full characterization is provided here: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.05 (t, J = 7.7 Hz, 1 H), 6.96 (d, J = 7.1 Hz, 1 H), 6.53 (t, J = 7.3 Hz, 1 H), 6.38 (d, J = 8.0 Hz, 1 H), 3.44−3.35 (m, 1 H), 3.33−3.25 (m, 1 H), 3.23−3.15 (m, 1 H), 2.85−2.70 (m, 2 H), 2.14−1.99 (m, 3 H), 1.95−1.85 (m, 1 H), 1.52−1.34 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.9, 128.3, 127.0, 121.3, 114.9, 110.0, 58.1, 47.0, 33.2, 28.3, 27.7, 23.9; IR (neat) 2604 (w), 1873 (w), 1748 (w), 1604 (s), cm^{-1}; MS (CI with NH_3) *m/z* (rel int) 174 ([M + H]$^+$, 100), 158 (2.3), 145 (15.1); HRMS (CI with NH_3) calcd for $C_{12}H_{15}NH$ 174.1283, found 174.1270.

Further elution with 0.5:5:100 NH_3/MeOH/ether gave 245 mg (28%) of **16**[18,19] as a clear oil, $R_f = 0.46$ (0.5:5:100 NH_3/MeOH/ether): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.15−7.10 (m, 3 H), 7.08−7.05 (m, 1 H), 3.40 (t, J = 7.6 Hz, 1 H), 3.23−3.16 (m, 1 H), 3.13−3.06 (m, 2 H), 2.86−2.75 (m, 1 H), 2.67−2.58 (m, 1 H), 2.51 (q, J = 8.5 Hz, 1 H), 2.41−2.29 (m, 1 H), 2.00−1.82 (m, 2 H), 1.79−1.66 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.0, 134.2, 128.3, 125.9, 125.6, 125.5, 63.4, 53.4, 48.6, 30.3, 28.7, 22.3; IR (neat) 2783 (s), 2730 (s), 1605 (w), 1493 (s), 1452 (s) cm^{-1}; MS (CI with NH_3) *m/z* (rel int) 174 ([M + H]$^+$, 100), 157 (1.1), 145 (23.7), 130 (5.0), 117 (9.4), 103 (1.0), 91 (2.3); HRMS (CI with NH_3) calcd for $C_{12}H_{15}NH$ 174.1283, found 174.1275. The ^{1}H NMR and IR spectral data were consistent with those reported in the literature.[18,19] The overall yield (**12**+**16**) was 92%.

1-[(2-Hydroxymethyl)phenyl]methylindan-1-ol (36). Cerium chloride heptahydrate (22.40 g, 60.12 mmol) was heated to 140 °C in vacuo (<0.1 mmHg) for 3 h. Nitrogen was introduced, the flask was cooled to 0 °C, and cold (0 °C) THF (160 mL) was added. The resulting suspension was stirred at room temperature for 14 h.[21] In another flask, the dianion of 2-methylbenzyl alcohol (**34**) was prepared.[20] Thus, 2-methylbenzyl alcohol (3.66 g, 30.0 mmol) was dissolved in THF (8.0 mL) and cooled to −78 °C. *tert*-Butyllithium (39.0 mL of a 1.7 M solution in pentane, 66 mmol) was slowly added. After the

solution was allowed to warm to 0 °C over 30 min, an additional portion of THF (100 mL) was added, and the resultant red solution of the dianion was transferred via cannula to the $CeCl_3$ suspension prepared above, which had been cooled to −78 °C. After 1 h, a solution of 1-indanone (**35**, 2.64 g, 19.98 mmol) in THF (40 mL). After 1 h, the mixture was allowed to warm to room temperature over 2 h and then quenched by the addition of 10% aqueous acetic acid (150 mL). The mixture was extracted with ether (3×), and the combined organic phases were washed with saturated sodium bicarbonate (4×) and brine (2×) and then dried ($MgSO_4$) and concentrated. Chromatography (2:1 ether/hexane) gave 4.66 g (92%) of the title compound as a colorless oil, $R_f = 0.20$ (2:1 ether/hexane): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26−7.12 (m, 6 H), 7.00 (d, $J = 7.5$ Hz, 1 H), 6.90 (d, $J = 7.1$ Hz, 1 H), 4.48 (ABq, $\Delta\nu_{AB} = 27.9$ Hz, $J_{AB} = 11.8$ Hz, 2 H), 3.90 (br s, 2 H), 3.09 (ABq, $\Delta\nu_{AB} = 59.9$ Hz, $J_{AB} = 14.0$ Hz, 2 H), 2.92−2.88 (m, 2 H), 2.47−2.42 (m, 1 H), 1.93 (dd, $J = 12.7$, 9.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.2, 142.2, 140.1, 135.7, 132.1, 130.1, 128.1, 127.3, 126.8, 126.2, 124.7, 123.6, 83.2, 63.1, 42.0, 41.1, 29.2; IR (neat) 3285 (s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel int) 236 ([M − H_2O]$^+$, 12.6), 104 (100); HRMS calcd for $C_{17}H_{16}O$ ([M − H_2O]$^+$) 236.1201, found 236.1192.

1-[(2-Azidomethyl)phenyl]methylindan-ol (37). Diisopropyl azodicarboxylate (7.17 mL, 7.36 g, 36.4 mmol) was slowly added to a mixture of the diol **36** (4.56 g, 17.93 mmol), triphenylphosphine (9.41 g, 35.88 mmol), and $Zn(N_3)_2$·(pyridine)$_2$ (6.50 g, 21.13 mmol) in toluene (90 mL) at room temperature over 15 min.[10] After 1 h, the solution was concentrated, and the residue was chomatographed (2:1 hexane/ether) to give 4.35 g (87%) of the title compound, $R_f = 0.39$ (2:1 hexane/ether): ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.32−7.24 (m, 6 H), 7.14 (dt, $J = 7.6$, 2.1 Hz, 1 H), 6.85 (d, $J = 7.6$ Hz, 1 H), 4.08 (ABq, $\Delta\nu_{AB} = 14.8$ Hz, $J_{AB} = 13.8$ Hz, 2 H), 3.90 (br s, 2 H), 3.13 (ABq, $\Delta\nu_{AB} = 50.1$ Hz, $J_{AB} = 14.0$ Hz, 2 H), 2.95 (ddd, $J = 16.1$, 8.7, 5.8 Hz, 1 H), 2.88−2.81 (m, 1 H), 2.45−2.39 (m, 1 H), 2.08−1.99 (m, 1 H), 1.34−1.31 (m, 1 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 146.7 (−), 142.1 (−), 135.7 (−), 134.8 (−), 132.1 (+), 129.2 (+), 128.1 (+), 127.7 (+), 126.8 (+), 126.2 (+), 124.7 (+), 123.2 (+), 83.6 (−), 52.4 (−), 41.6 (−), 41.2 (−), 29.1 (−); IR (neat) 3431 (br s), 2098 (s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 262 ([M − H_2O + H]$^+$, 1.5), 234 (100); HRMS (CI with CH_4) calcd for $C_{17}H_{16}N$ ([M − N_2 − OH]$^+$) 234.1283, found 234.1284.

6,6a,7,12-Tetrahydro-5*H*-12a-azabenzo[*a*]anthacene (39). Trifluoromethanesulfonic acid (339 mg, 2.26 mmol) was added to a solution of the azide **37** in benzene (30 mL) at room temperature. After 10 min, the solution was cooled to 0 °C and treated with borane dimethyl sulfide complex (3.0 mL of a 2.0 M solution in THF, 6.0 mmol). After the mixture was warmed to room temperature for 14 h, 15% aqueous sodium hydroxide (15 mL) was added, and the resulting mixture was extracted with ether (3×). The combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated. Chromatography (1:7 ether/hexane) gave 307 mg (67%) of the known title compound **39**,[22] $R_f = 0.40$. Ochiai and Suzuki[22] reported only elemental analysis for this compound, thus full characterization is provided: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.21−7.12 (m, 5 H), 7.00 (d, $J = 7.3$ Hz, 1 H), 6.83 (d, $J = 8.2$ Hz, 1 H), 6.71−6.66 (m, 1 H), 4.76 (d, $J = 15.8$ Hz, 1 H), 4.22 (d, $J = 15.8$ Hz, 1 H), 3.38−3.30 (m, 1 H), 2.96−2.65 (m, 4 H), 2.11−2.01 (m, 1 H), 1.96−1.87 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.1, 134.8, 134.2, 128.3, 128.2, 127.1, 126.3, 126.1, 126.0, 125.2, 117.2, 112.1, 53.1, 50.3, 37.5, 29.7, 26.7; IR (neat) 1603 (s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel int) 235 (M$^+$, 100), 220 (11.1), 84 (95.8); HRMS (EI, 70 eV) calcd for $C_{17}H_{17}N$ 235.1361, found 235.1352.

1-(3-Hydroxypropyl)-3,4-dihydronaphthalene (43) and 1-(3-Hydroxypropylidene)-1,2,3,4-tetrahydronaphthalene (44). Cerium chloride heptahydrate (5.60 g, 15.00 mmol) was dried at 137 °C in vacuo (<0.1 mmHg) for 3 h. Nitrogen was introduced, the flask was cooled to 0 °C, and cold THF (40 mL, 0 °C) was added.[21] After the 14 h, a solution of α-tetralone (**41**, 1.46 g, 10.00 mmol) in dry THF (15 mL) was added, and the mixture was warmed to room temperature for 1 h. After this mixture was cooled to 0 °C, allylmagnesium chloride (10.0 mL of a 2.0 M solution in THF, 20 mmol) was added via syringe. After 30 min, triethylamine (10 mL, 7.3 g, 72 mmol) and methanesulfonyl chloride (1.55 mL, 2.29 g, 20.0 mmol) were added sequentially. After this mixture was warmed to room temperature over 1 h, concentrated hydrochloric acid (10 mL) and water (10 mL) were added. After 30 min, the mixture was extracted with ether (3×), and the combined organic phases were washed twice with saturated aqueous sodium bicarbonate and once with brine and then dried ($MgSO_4$) and concentrated to afford the crude dienes **42**. To this material was added 9-BBN (40 mL of a 0.5 M solution in THF, 20 mmol) at room temperature.[49] The resultant solution was kept at 80 °C for 1 h, cooled to room temperature, and carefully treated with 5 N sodium hydroxide (10 mL) and hydrogen peroxide (30% in water, 10 mL). The resultant mixture was heated to 60 °C for 1 h and then cooled to room temperature. The aqueous layer was saturated with solid potassium carbonate, and the organic phase was separated, dried ($MgSO_4$), and concentrated. Chromatography (1:2 ether/hexane) gave 1.44 g (77%) of the title compounds as a colorless oil, $R_f = 0.29$ (1:2 ether/hexane), which was found to be an inseparable 1.3:1 mixture of the endo- and exocyclic alkene regioisomers **43** and **44**, respectively, by ^{1}H NMR spectroscopy. The endocyclic alkene regioisomer **43** is known in the literature,[23] but no spectral data were reported. Data on the mixture of isomers: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.66−7.63 (m, 0.43 H), 7.33−7.12 (m, 3.57 H), 6.07 (t, $J = 7.3$ Hz, 0.43 H), 5.93 (t, $J = 4.5$ Hz, 0.57 H), 3.79−3.68 (m, 2 H), 2.84−2.76 (m, 3 H), 2.60−2.49 (m, 2 H), 2.33−2.26 (m, 1 H), 1.92−1.78 (m, 2 H), 1.75−1.52 (m,1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 137.1, 136.5, 135.8, 134.6, 128.6, 127.4, 126.4, 126.1, 125.8, 125.3, 124.8, 123.5, 122.4, 119.6, 62.3, 62.1, 31.7, 31.3, 30.4, 28.8, 28.4, 26.6, 23.2, 23.1; IR (neat) 3332 (br s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel int) 188 (M$^+$, 37.3), 157 (68.2), 144 (91.0), 129 (100); HRMS calcd for $C_{13}H_{16}O$ 188.1201, found 188.1198.

1-(3-Azidopropyl)-3,4-dihydronaphthalene (45). Methanesulfonyl chloride (2.9 mL, 4.3 g, 37 mmol) was added to a solution of the alcohols **43** and **44** (3.50 g, 18.59 mmol, a mixture of endocyclic and exocyclic double bond isomers), and triethylamine (7.8 mL, 5.6 g, 56 mmol) in CH_2Cl_2 (50 mL) at 0 °C. After 1.4 h, the mixture was diluted with ether and washed with brine, and then dried ($MgSO_4$) and concentrated to give the crude mesylate, which was dissolved in DMSO (80 mL) and treated with sodium azide (3.63 g, 55.84 mmol) at room temperature. After 14 h, the mixture was diluted with water and then extracted with ether (3×). The combined organic phases were washed twice with water and once with brine and then dried ($MgSO_4$) and concentrated. The crude azidoalkene was then dissolved in CH_2Cl_2 (30 mL) and treated with trifluoroacetic acid (1.43 mL, 2.12 g, 18.6 mmol) at room temperature to induce double bond isomerization. After 30 min, the solution was concentrated, and the residue was chromatographed (hexane) to give 2.82 g (71%) of the title compound as a clear oil, which was found to be a 10:1 ratio of **45** and another alkene isomer, presumably the exocyclic alkene, as judged by ^{1}H NMR spectroscopy, $R_f = 0.34$. The ^{1}H NMR signals from the minor isomer overlapped with those of the major isomer; therefore, only the resonances for the major isomer are provided here: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26−7.17 (m, 4 H), 5.93−5.90 (m, 1 H), 3.35 (t, $J = 6.8$ Hz, 12 H), 2.77 (dd, $J = 8.7$, 7.7 Hz, 2 H), 2.60−2.53 (m, 2 H), 2.32−2.25 (m, 2 H), 1.90−1.81 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.8, 135.2, 134.4, 127.7, 126.8, 126.4, 125.8, 122.5, 51.2, 29.9, 28.6, 27.8, 23.3; IR (neat) 2095 (s), cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel int) 213 (M$^+$, 2.2), 184 (100); HRMS calcd for $C_{13}H_{15}N_3$ 213.1266, found 213.1260.

2,3,3a,4,5,6-Hexahydro-1*H*-benzo[*f*]pyrrolo[1,2-*a*]azepine (14). Trifluoromethanesulfonic acid (950 mg, 6.33 mmol) was added to a solution of the azidoalkene **45** (894 mg, 4.19 mmol) in dry benzene (25 mL) at 15 °C. After 10 min, the mixture was cooled to 0 °C and treated with a solution of sodium borohydride (950 mg, 25.11 mmol) in methanol (15 mL). The resultant mixture was warmed to room temperature for 14 h and then treated with saturated aqueous sodium bicarbonate (20 mL). The mixture was extracted with ether

(3×), and the combined organic phases were washed twice with brine, dried (Na_2SO_4), and concentrated. Chromatography (1:7 ether/hexane) gave 563 mg (72%) of the known[24] title compound, $R_f = 0.58$, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25−7.16 (m, 2 H), 6.96−6.84 (m, 2 H), 3.40−3.22 (m, 3 H), 3.11−3.02 (m, 1 H), 2.77 (ddd, $J = 14.2, 10.1, 2.2$ Hz, 1 H), 2.32−2.19 (m, 1 H), 2.12−1.92 (m, 4 H), 1.82−1.78 (m, 2 H), 1.63−1.51 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.5 (−), 132.8 (−), 130.4 (+), 126.4 (+), 119.3 (+), 114.5 (+), 61.8 (+), 51.6 (−), 37.6 (−), 35.4 (−), 34.0 (−), 25.7 (−), 24.1 (−); IR (neat) 1597 (s) cm^{-1}; MS (EI, 70 eV) *m/z* (rel int) 187 (M^+, 100), 170 (9.3), 158 (74.1); HRMS calcd for $C_{13}H_{17}N$ 187.1361, found 187.1357. These data are consistent with those reported by Meyers.[24]

3-(3-Azidopentyl)-1*H*-indene (56). Methyllithium (21.3 mL of a 1.40 M solution in ether, 29.8 mmol) was added to a solution of indene (**32**, 2.89 g, 24.89 mmol) in THF (40 mL) at 0 °C. After 30 min, 3-chloro-3-(trimethylsilyloxy)pentane (**54**)[40] (2.89 g, 16.59 mmol) was added. After 14 h at room temperature, the mixture was treated with water (40 mL), and the organic phase was separated and washed with brine, dried ($MgSO_4$), and concentrated to give an oil, which was dissolved in THF (60 mL) and treated with tetra-*n*-butylammonium fluoride (20 mL, 1.0 M in THF, 20 mmol) at room temperature. After 10 min, the mixture was diluted with ether, and the organic phase was separated and washed twice with brine, dried ($MgSO_4$), and concentrated. Chromatography (1:1 ether/hexane) gave 1.68 g (50%) of 3-(3-hydroxypentyl)-1*H*-indene (**55**), which was dissolved in CH_2Cl_2 (15 mL), cooled to −50 °C, and treated with methanesulfonyl chloride (1.22 mL, 1.81 g, 16.6 mmol) and triethylamine (3.50 mL, 2.54 g, 25.1 mmol). After 2 h, the mixture was diluted with ether, and then the organic phase was separated and washed with brine, dried ($MgSO_4$), and concentrated to give the crude mesylate, which was dissolved in DMSO (30 mL) and treated with sodium azide (1.62 g, 24.93 mmol) at room temperature. After 14 h, the mixture was diluted with water and extracted with ether (3×). The combined organic phases were washed with water and brine and then dried ($MgSO_4$) and concentrated. Chromatography (1:2 ether/hexane) gave 1.10 g (58% based on the indenyl alcohol **55**) of the title compound, $R_f = 0.63$: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.50 (d, $J = 7.3$ Hz, 1 H), 7.41 (d, $J = 7.4$ Hz, 1 H), 7.34 (t, $J = 7.3$ Hz, 1 H), 7.25 (dt, $J = 7.3, 1.2$ Hz, 1 H), 6.27 (br s, 1 H), 3.37 (s, 2 H), 3.33−3.31 (m, 1 H), 2.77−2.66 (m, 2 H), 1.96−1.87 (m, 2 H), 1.71−1.62 (m, 2 H), 1.04 (t, $J = 7.4$ Hz, 3 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 145.0 (−), 144.4 (−), 143.3 (−), 128.3 (+), 126.0 (+), 124.6 (+), 123.8 (+), 64.1 (+), 37.7 (−), 32.4 (−), 27.5 (−), 24.3 (−), 10.5 (+); IR (neat) 2095 (s), 1610 (w) cm^{-1}; MS (EI, 70 eV) *m/z* (rel int) 198 ([M−N_2−H]$^+$, 100), 170 (12.0); HRMS (EI, 70 eV) calcd for $C_{14}H_{16}N$ ([M−N_2−H]$^+$) 198.1283, found 198.1282. Anal. Calcd for $C_{14}H_{17}N_3$: C, 73.98; H, 7.54; N, 18.49. Found: C, 73.61; H, 7.53; N, 18.18.

(1*R,3a*R**)- and (1*R**,3a*S**)-1-Ethyl-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline (57) and (1*R**,10b*S**)-1-Ethyl-1,2,3,5,6,10b-hexahydropyrrolo [2,1-*a*]isoquinoline (58).** Trifluoromethanesulfonic acid (390 mg, 2.58 mmol) was added to a solution of the azide **56** (477 mg, 2.10 mmol) in benzene (100 mL) at 5 °C. After 15 min, the solution was cooled to 0 °C, and sodium borohydride (477 mg, 12.61 mmol) in methanol (20 mL) was added. After 14 h at room temperature, saturated aqueous sodium bicarbonate (40 mL) was added, and the mixture was extracted with ether (3×). The combined organic phases were washed twice with brine, dried (Na_2SO_4), and concentrated to give the crude product. Chromatography (1:16 ether/hexanes) gave 157 mg (37%) of an inseparable 1:1 mixture of diastereomeric amines **57** as a clear oil. The ratio of diastereomers was judged by ^{1}H NMR based on the integration of the multiplet at 3.65−3.56 (m, 0.5 H). Data for the mixture of diastereomers of **57**: $R_f = 0.36$ (1:16 ether/hexanes); ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.06−6.90 (m, 2 H), 6.53−6.43 (m, 1 H), 6.36−6.31 (m, 1 H), 3.65−3.56 (m, 0.5 H), 3.55−3.48 (m, 1 H), 3.36−3.27 (m, 0.5 H), 2.95−2.82 (m, 0.5 H), 2.80−2.70 (m, 0.5 H), 2.66−2.61 (m, 0.5 H), 2.20−2.03 (m, 2 H), 1.98−1.85 (m, 2 H), 1.82−1.73 (m, 1 H), 1.66−1.29 (m, 3 H), 1.19−1.04 (m, 0.5 H), 0.95−0.85 (m, 3 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 144.0 (−), 143.8 (−), 129.1 (+), 128.3 (+), 127.0 (+), 126.6 (+), 121.7 (−), 114.7 (+), 114.1 (+), 110.8 (+), 109.4 (+), 59.8 (+), 58.6 (+), 58.2 (+), 32.3 (−), 30.6 (−), 30.3 (−), 30.0 (+), 28.6 (−), 28.5 (−), 28.4 (−), 28.0 (−), 27.4 (−), 26.1 (−), 25.3 (−), 10.8 (+), 9.8 (+); IR (neat) 1602 (s) cm^{-1}; MS (EI, 70 eV) *m/z* (rel int) 201 (M^+, 20.1), 172 (100); HRMS (EI, 70 eV) calcd for $C_{14}H_{19}N$ 201.1517, found 201.1526.

Further elution with 1:3 ether/hexanes gave 146 mg (35%) of the tricyclic compound **58** as a clear oil. Assignment of the relative configuration of **58** is based on the stereoelectronic model proposed for reduction of analogous iminium ions.[57−59] Data for **58**: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.13−7.09 (m, 3 H), 7.07−7.03 (m, 1 H), 3.33 (ddd, $J = 10.8, 7.2, 1.1$ Hz, 1 H), 3.25−3.09 (m, 2 H), 2.87 (dd, $J = 16.9, 4.7$ Hz, 1 H), 2.34 (dd, $J = 11.3, 5.0$ Hz, 1 H), 2.31−2.21 (m, 2 H), 2.12−2.01 (m, 1 H), 1.89−1.79 (m, 1 H), 1.73−1.62 (m, 1 H), 1.61−49 (m, 1 H), 1.36−1.26 (m, 1 H), 0.94 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 139.2 (−), 134.3 (−), 128.4 (+), 126.1 (+), 125.5 (+), 124.9 (+), 65.7 (+), 65.6 (+), 47.7 (−), 29.7 (−), 28.6 (−), 27.4 (−), 26.0 (−), 10.6 (+); IR (neat) 1493 (s), 1460 (s) cm^{-1}; MS (CI with NH_3) *m/z* (rel int) 202 ([M + H]$^+$, 100); HRMS (CI with CH_4) calcd for $C_{14}H_{19}NH$([M + H]$^+$) 202.1596, found 202.1590.

4- or 7-Methoxy-1*H*-indene (53). Sodium borohydride (2.33 g, 61.59 mmol) was added in small portions to a solution of commercially available 4-methoxyindanone (**60**, 10.00 g, 61.66 mmol) in methanol (50 mL) at 0 °C. After 10 min, water (50 mL) was added, and the mixture was concentrated and diluted with ether. The organic phase was washed twice with brine, dried ($MgSO_4$), and concentrated. The crude 4-methoxyindan-1-ol thus obtained was dissolved in THF (150 mL) and treated with *o*-nitrophenyl selenocyanate (18.12 g, 85.03 mmol) at room temperature,[41] followed by the slow addition of tri-*n*-butylphosphine (19.8 mL, 16.1 g, 79.6 mmol). After 1 h, the reaction mixture was cooled to 0 °C and treated with hydrogen peroxide (16 mL, 4.8 g, 141 mmol). The resulting mixture was slowly warmed to room temperature over 3 h and then diluted with ether. The organic layer was washed with brine (3×, and then dried ($MgSO_4$) and concentrated. Chromatography (1:7 ether/hexanes) yielded 6.62 g (80%) of the title compound as a light yellow oil, $R_f = 0.58$: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.29 (t, $J = 5.5$ Hz, 1 H), 7.09 (d, $J = 5.4$ Hz, 1 H), 6.90 (br s, 1 H), 6.78 (d, $J = 8.0$ Hz, 1 H), 6.60 (br s, 1 H), 3.94 (s, 3 H), 3.40 (br s, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 155.3, 146.6, 134.3, 131.8, 130.5, 127.9, 114.2, 107.0, 55.2, 36.5; IR (neat) 1596 (s) cm^{-1}; MS (EI, 70 eV) *m/z* (rel int) 146 (M^+, 100), 131 (50.4); HRMS calcd for $C_{10}H_{10}O$ 146.0732, found 146.0739. The spectral data of this compound support a single position of the indene double bond, but we have not assigned its position.

1,3-Dibromo-5-(methoxy)methoxypentane (64). Boron tribromide (45 mL of a 1.0 M solution in CH_2Cl_2, 45 mmol) was added to 4-bromotetrahydropyran[42] (**63**, 2.486 g, 15.06 mmol) at 0 °C, and then the solution was heated at reflux for 14 h. After being cooled to room temperature, the mixture was concentrated and slowly treated with methanol (50 mL). After heating at reflux for 30 min, the mixture was cooled and concentrated to yield the crude dibromo alcohol[43] which was dissolved in dimethoxymethane (30 mL) and treated with lithium bromide (1.95 g, 22.45 mmol) and *p*-toluenesulfonic acid monohydrate (280 mg, 1.47 mmol) at room temperature.[60] After 1 h, the mixture was diluted with brine and extracted twice with ether. The combined organic phases were washed with brine and then dried ($MgSO_4$) and concentrated to give 3.898 g (89%) of the title compound as a clear oil, which was shown by ^{1}H NMR to be pure enough for further use and thus carried on to the next reaction without further purification:

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(59) Polniaszek, R. P.; Belmont, S. E. *J. Org. Chem.* **1990**, *55*, 4688−4693.
(60) Gras, J.-L.; Chang, Y.-Y. K. W.; Guerin, A. *Synthesis* **1985**, 74−75.

^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.61 (s, 2 H), 4.37 (septet, J = 4.7 Hz, 1 H), 3.76−3.69 (m, 2 H), 3.61−3.54 (m, 2 H), 3.37 (s, 3 H), 2.34 (dd, J = 7.5, 1.4 Hz, 2 H), 2.17−2.02 (m, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 96.5, 65.0, 55.3, 51.7, 41.6, 38.8, 30.9; IR (neat) 1434 (s) cm^{-1}; MS (CI with CH_4) m/z (rel int) 291 ([M + H]$^+$, 3.2), 259 (23.1), 229 (100); HRMS (EI, 70 eV) calcd for $C_7H_{13}{}^{79}Br^{81}BrO_2$ ([M − H]$^+$) 288.9262, found 288.9273.

3-[3-Azido-5-(methoxy)methoxy]pentyl-4-methoxy-1*H*-indene (62) and 3-[3-Azido-5-(methoxy)methoxy]pentyl-7-methoxy-1*H*-indene (61). Method A: *n*-Butyllithium (8.0 mL of a 2.0 M solution in hexane, 16.0 mmol) was added to a solution of 7-methoxy-1*H*-indene (**53**, 1.98 g, 14.76 mmol) in THF (25 mL) at 0 °C. After 30 min, the solution was cooled to −78 °C and treated with a solution of the dibromide **64** in THF (10 mL). After 14 h at room temperature, saturated aqueous ammonium chloride was added, and the mixture was extracted with ether (3×). The combined organic phases were washed twice, dried ($MgSO_4$), and concentrated to give a crude mixture of 3-[3-bromo-5-(methoxymethoxy)]pentyl-4-methoxy-1*H*-indene and 3-[3-bromo-5-(methoxymethoxy)]pentyl-7-methoxy-1*H*-indene, which was dissolved in 10 mL of THF and treated with tetra-*n*-butylammonium azide (30 mL of a 1.0 M solution in THF, 30 mmol)[61] at room temperature. After 14 h, the mixture was diluted with ether, and the organic phases were washed with water and brine, dried ($MgSO_4$), and concentrated. Chromatography (1:7 ether/hexane) gave 2.54 g (80%) of a 3:1 mixture of the azido indenes **62** and **61** as a light yellow oil, R_f = 0.30. Compound **62** was assigned by comparison with the pure **62** prepared using method B below. The 3:1 ratio of **62** and **61** was determined by ^{1}H NMR based on integration of the olefinic hydrogens at δ 6.08 and 6.24 ppm in the mixture. Complete separation of the two isomers was not possible with conventional flash chromatography. Analytical samples of **62** and **61** were obtained by HPLC[62] (silica gel, 3% EtOAc/hexanes): Data for **62**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.16 (t, J = 7.6 Hz, 1 H), 7.07 (d, J = 7.4 Hz, 1 H), 6.79 (d, J = 8.1 Hz, 1 H), 6.08 (br s, 1 H), 4.63 (s, 2 H), 3.86 (s, 3 H), 3.69−3.64 (m, 2 H), 3.60−3.53 (m, 1 H), 3.31 (br s, 2 H), 3.05−2.86 (m, 2 H), 2.83−2.72 (m, 1 H), 1.98−1.88 (m, 2 H), 1.86−1.73 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 127.3, 125.9, 116.9, 108.8, 96.7, 64.6, 60.1, 55.3, 38.0, 34.8, 34.6, 27.3; IR (neat) 2099 (s) cm^{-1}; MS (CI with NH_3) m/z (rel int) 318 ([M + H]$^+$, 3.1), 304 (7.2), 290 (100); HRMS (CI with NH_3) calcd for $C_{17}H_{23}N_3O_3H$ 318.1818, found 318.1811. Data for **61**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (t, J = 7.9 Hz, 1 H), 7.02 (d, J = 7.5 Hz, 1 H), 6.77 (d, J = 8.1 Hz, 1 H), 6.24 (br s, 1 H), 4.62 (s, 2 H), 3.84 (s, 3 H), 3.70−3.63 (m, 2 H), 3.61−3.57 (m, 1 H), 3.35 (s, 3 H), 3.30 (d, J = 1.8 Hz, 2 H), 2.80−2.61 (m, 2 H), 1.96−1.78 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.2, 128.4, 127.8, 112.2, 107.6, 96.7, 64.4, 59.9, 55.4, 35.3, 34.9, 33.4, 24.5; IR (neat) 2100 (s) cm^{-1}; MS (CI with NH_3) m/z (rel int) 290 ([M − N_2 + H]$^+$, 75.3), 243 (30.9), 97 (100); HRMS (CI with NH_3) calcd for $C_{17}H_{23}NO_3H$ ([M − N_2 + H]+) 290.1756, found 290.1762.

Method B: *tert*-Butyllithium (4.70 mL of a 1.4 M solution in pentane, 6.58 mmol) was added to a solution of the indene **53** (4.3 mg, 3.00 mmol) in THF (3 mL) at −78 °C.[17] After 10 min, chlorotrimethylsilane (0.19 mL, 163 mg, 1.50 mmol) was added. After 30 min, a solution of dibromide **64** (435 mg, 1.50 mmol) in THF (5 mL) was added, and the mixture was allowed to warm to room temperature for 14 h. Saturated aqueous ammonium chloride was added and the mixture was extracted with ether (3×). The combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated to give crude 3-[3-bromo-5-(methoxymethoxy)]pentyl-7-methoxy-1*H*-indene, which was treated with tetra-*n*-butylammonium azide (5.0 mL of a1.0 M solution in THF, 5.0 mmol)[61] at room temperature for 14 h. After diluting the solution with ether and water, the organic phase was separated and washed with water and brine and then dried ($MgSO_4$) and concentrated. Chromatography (1:7 ether/hexanes) gave 343 mg (72%) of the single compound **62** as a light yellow oil whose spectral data matched those reported above.

(1*R,3a*R**)- and (1*R**,3a*S**)-1-(2-Hydroxyethyl)-9-methoxy-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline (66).** Trifluoromethanesulfonic acid (102 mg, 0.68 mmol) was added to a solution of the azide **62** (139 mg, 0.44 mmol) in benzene (25 mL) at 10 °C. After 5 min, sodium borohydride (100 mg, 2.64 mmol) in methanol (5 mL) was added, and the mixture was warmed to room temperature. After 14 h, saturated aqueous sodium bicarbonate was added, and the mixture was extracted with ether (3×). The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated to give the crude product. Chromatography (ether) gave 51 mg (47%) of an inseparable 1.2:1 mixture of diastereomeric amines **66** as a clear oil, as judged by integration of methyl singlets in the ^{1}H NMR spectrum. R_f = 0.65; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.72−6.66 (m, 5 H), 6.65−6.58 (m, 1 H), 4.52−4.41 (m, 1 H), 4.12−4.02 (m, 1 H), 3.96−3.85 (m, 1 H), 3.83 (s, 3 H), 3.78 (s, 3 H), 3.77−3.64 (m, 2 H), 3.62−3.52 (m, 3 H), 3.51−3.42 (m, 1 H), 2.88−2.75 (m, 2 H), 2.74−2.58 (m, 2 H), 2.26−2.12 (m, 2 H), 2.10−1.99 (m, 3 H), 1.98−1.87 (m, 2 H), 1.85−1.75 (m, 2 H), 1.74−1.62 (m, 4 H), 1.60−1.43 (m, 2 H), 1.42−1.32 (m, 1 H), 1.31−1.20 (m, 1 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 149.9, 149.7, 136.3, 133.9, 128.1, 126.8, 122.5, 121.8, 119.0, 118.3, 110.1, 110.0, 63.0, 62.0, 61.3, 58.1, 57.1, 55.8, 55.7, 55.5, 37.7, 36.0, 30.3, 29.7, 29.6, 28.9, 28.4, 26.6, 25.4; IR (neat) 3355 (br s) cm^{-1}; MS (EI, 70 eV) m/z (rel int) 247 (M$^+$, 24.0), 202 (100); HRMS calcd for $C_{15}H_{21}NO_2$ 247.1572, found 247.1560.

(*E*)- and (*Z*)-1-(Bromomethylene)-4-methoxyindan (69). Taguchi's method for the synthesis of polyhalomethyllithium carbonyl adducts was followed.[45] Thus, *n*-butyllithium (100 mL of a 2.0 M solution in hexane, 200 mmol) was added to a solution of dicyclohexylamine (36.20 g, 200 mmol) in THF (60 mL) at 0 °C. After 10 min, the lithium dicyclohexylamide thus generated was transferred via cannula to a solution of dibromomethane (60 mL) and 4-methoxyindanone (**60**, 16.20 g, 100 mmol) in THF (200 mL) at −78 °C. After 1 h, 6 N HCl (200 mL) was added. The solids formed were washed with ether (3×), and the combined organic materials were washed twice with brine, dried ($MgSO_4$) and concentrated to give the crude adduct, which was dissolved in CH_2Cl_2 (300 mL), and treated with acetic acid (24 mL) and zinc dust (10 g) according to Williams's protocol.[46] After refluxing for 1 h, the mixture was cooled to room temperature and diluted with ether. The organic phases were washed with saturated aqueous sodium bicarbonate (3×) and brine (2×) and then dried ($MgSO_4$) and concentrated. Chromatography (1:7 ether/hexane) gave 16.54 g (69% or 93% based on 4.10 g of 4-methoxyindanone recovered after further elution) of the title compound as an inseparable 2:1 ratio of geometric isomers. The major isomer was assigned as the *Z* isomer based on a larger allylic coupling (2.7 Hz) than in the *E* isomer (1.9 Hz) in the ^{1}H NMR spectrum.[56] The 2:1 ratio was determined by ^{1}H NMR based on integration of the olefinic hydrogens at δ 6.61 and 6.17 ppm. Characterization of the mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.02 (d, J = 7.8 Hz, 0.5 H), 7.31−7.26 (m, 0.5 H), 7.22−7.17 (m, 1 H), 7.00 (d, J = 7.8 Hz, 1 H), 6.83 (d, J = 8.0 Hz, 0.5 H), 6.74 (d, J = 8.0 Hz, 1 H), 6.61 (t, J = 2.7 Hz, 1 H), 6.17 (t, J = 1.9 Hz, 0.5 H), 3.87 (s, 3 H), 3.86 (s, 1.5 H), 2.99−2.91 (m, 3 H), 2.87−2.80 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.9, 148.8, 145.4, 141.0, 140.8, 135.5, 128.2, 127.6, 118.1, 112.7, 110.8, 109.9, 97.4, 94.8, 55.3, 34.0, 31.9, 27.1, 26.4; IR (neat) 1587 (s), 1481 (s) cm^{-1}; MS (EI, 70 eV) m/z (rel int) 238 (M$^+$, 93.2), 207 (4.7), 159 (100); HRMS calcd for $C_{11}H_{11}BrO$ 237.9993, found 237.9985.

(*E*)- and (*Z*)-1-[3-Hydroxy-5-(methoxy)methoxy]pentylidene-4-methoxyindan (71). *tert*-Butyllithium (12.4 mL of a 1.7 M solution in pentane, 21.1 mmol) was added to a solution of a mixture of *E* and *Z* isomers of the vinyl bromide **69** (2.52 g, 10.54 mmol) in THF (40 mL) at −78 °C. After 15 min, boron trifluoride etherate (1.34 mL, 1.50 g, 10.6 mmol)[47] was added, followed immediately by a solution of 4-(methoxy)-

(61) Brändström, A.; Lamm, B.; Palmertz, I. *Acta Chem. Scand. B* **1974**, *28*, 699−701.

(62) High performance liquid chromatography (HPLC) was performed on a Rainin Rabbit HP instrument equipped with an ISCO V^4 absorption detector (Wavelength: 254 nm) using a Dynamax-60 Å column composed of silica (SiO_2). General conditions were fixed solvent system, flow rate: 1.0 mL/min.

methoxy-1,2-epoxybutane[48] (**70**, 700 mg, 5.30 mmol) in THF (15 mL). This mixture was kept at −78 °C for 15 min before saturated aqueous sodium bicarbonate. The resulting mixture was extracted with ether (3×), and the combined organic phases were washed twice with brine and then dried ($MgSO_4$) and concentrated. Chromatography (2:1 ether/hexane) gave 894 mg (58%) of the title compound as an inseparable 1:1 mixture of geometric isomers as determined by integration of the olefinic hydrogens at δ 5.98−5.89 and 5.60−5.52 ppm in the ^{1}H NMR spectrum. Characterization of the mixture: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28−7.25 (m, 0.5 H), 7.16 (q, J = 7.9 Hz, 1 H), 7.06 (d, J = 7.6 Hz, 0.5 H), 6.69 (dd, J = 16.6, 8.0 Hz, 1 H), 5.98−5.89 (m, 0.5 H), 5.60−5.52 (m, 0.5 H), 4.64 (s, 2 H), 3.95 (br s, 1 H), 3.83 (s, 3 H), 3.81−3.64 (m, 2 H), 3.36 (s, 3 H), 2.96−2.80 (m, 2 H), 2.79−2.71 (m, 2 H), 2.70−2.60 (m, 1 H), 2.44−2.35 (m, 1 H), 1.92−1.73 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.5, 156.2, 145.1, 143.5, 143.1, 142.1, 136.0, 133.9, 127.8, 127.5, 118.0, 117.0, 114.7, 112.4, 109.1, 108.8, 96.5, 70.7, 70.3, 69.5, 66.0, 65.9, 64.9, 55.2, 39.2, 37.7, 36.5, 36.3, 34.8, 33.7, 28.1, 26.7, 26.6; IR (neat) 3442 (br s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 293 ([M + H]$^+$, 9.7), 278 (18.3), 261 (100); HRMS (CI with CH_4) calcd for $C_{17}H_{24}O_4H$ ([M + H]$^+$) 293.1753, found 293.1758.

***(E)*- and *(Z)*-1-[3-Azido-5-(methoxy)methoxy]pentylidene-4-methoxyindan (72).** Methanesulfonyl chloride (0.10 mL, 148 mg, 1.29 mmol) and triethylamine (0.30 mL, 218 mg, 2.15 mmol) were added to the alcohol **71** (178 mg, 0.61 mmol) in CH_2Cl_2 (50 mL) at −50 °C. After 2 h, ether was added, and the organic phase was collected and washed with saturated aqueous sodium bicarbonate and brine, and then dried ($MgSO_4$) and concentrated to give the crude mesylate, which was dissolved in THF (5 mL) and treated with tetra-*n*-butylammonium azide (2.0 mL of a 1.0 M solution in THF, 2.0 mmol)[61] at room temperature. After warming to 50 °C for 2 h, the solution was concentrated, and the residue was chromatographed (2:1 hexanes/ether) to give 158 mg (81%) of the title compound as an inseparable 1:1 mixture of geometric isomers as judged by integration of the olefinic hydrogens at δ 5.98−5.89 and 5.39−5.50 ppm in the ^{1}H NMR spectrum, R_f = 0.47. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26−7.20 (m, 1 H), 7.16 (d, J = 7.8 Hz, 0.4 H), 7.08 (d, J = 7.6 Hz, 0.6 H), 6.75 (d, J = 4.8 Hz, 0.4 H), 6.69 (d, J = 7.8 Hz, 0.6 H), 5.98−5.89 (m, 0.6 H), 5.58−5.50 (m, 0.4 H), 4.63 (s, 2 H), 3.85 (s, 3 H), 3.72−3.60 (m, 3 H), 3.37 (s, 3 H), 2.95 (t, J = 6.3 Hz, 1 H), 2.90−2.83 (m, 1 H), 2.81−2.73 (m, 3 H), 2.49 (t, J = 6.8 Hz, 1 H), 2.01−1.86 (m, 1 H), 1.84−1.70 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.5, 156.4, 145.6, 144.2, 142.9, 141.9, 134.1, 127.9, 127.7, 117.1, 116.9, 113.8, 112.5, 109.3, 109.0, 96.6, 64.4, 60.2, 60.0, 55.2, 34.9, 34.5, 34.4, 33.8, 33.7, 28.1, 26.8, 26.7; IR (neat) 2099 (s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 290 ([M − N_2 + H]$^+$, 17.1), 218 (100); HRMS (CI with CH_4) calcd for $C_{17}H_{23}NO_3H$ ([M − N_2 + H]$^+$) 290.1756, found 290.1764.

3-(3-Hydroxypropyl)-7-methoxy-1*H*-indene (73a) and 3-(3-Hydroxypropylidene)-7-methoxy-1*H*-indan (73b). Cerium chloride heptahydrate (11.20 g, 30.00 mmol) was dried at 137 °C in vacuo (<0.1 mmHg) for 3 h. Nitrogen was introduced, the flask was cooled to 0 °C, and cold THF (80 mL, 0 °C) was added.[21] After the suspension was stirred for 14 h, a solution of 4-methoxyindan-1-one (**60**, 3.24 g, 20.00 mmol) in dry THF (32 mL) was added, and the mixture was stirred for 1 h at room temperature and then recooled to 0 °C and treated with allylmagnesium chloride (20 mL of a 2.00 M solution in THF, 40 mmol) in a dropwise fashion. After 30 min at 0 °C, triethylamine (8.4 mL, 6.1 g, 60 mmol) and methanesulfonyl chloride (3.00 mL, 4.44 g, 38.8 mmol) were added sequentially. After 1 h, the mixture was warmed to room temperature over 30 min, quenched with saturated aqueous ammonium chloride, and extracted with ether (3×). The combined organic phases were washed twice with saturated aqueous ammonium bicarbonate and brine (3×) and then dried ($MgSO_4$) and concentrated. The crude diene was then treated with 9-BBN (80 mL of a 0.5 M solution in THF, 40 mmol).[49] After being warmed to 80 °C for 1 h, the solution was cooled to room temperature and treated carefully with aqueous sodium hydroxide (10 mL, 5 M) and hydrogen peroxide (30% in water, 10 mL). The mixture was then heated to 60 °C for 1 h. After being cooled to room temperature, the water layer was saturated with solid potassium carbonate, and the organic phase was separated, dried ($MgSO_4$), and concentrated. Chromatography (2:1 ether/hexane) gave 3.89 g (95%) of the title compounds as a light yellow oil, R_f = 0.41 (2:1 ether/hexane), which was found to be an inseparable 1.3:1 mixture of regioisomers **73a** and **73b** by integration of the olefinic hydrogens at δ 6.23 (0.6 H) and 5.95−5.86 (0.4 H) in the ^{1}H NMR spectrum. The major isomer was assigned as the indene derivative **73a** based on the appearance and chemical shift of the indenyl hydrogen at C2 (δ 6.23 ppm). The geometry of **73b** was not determined. Characterization of the mixture: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.31 (t, J = 7.6 Hz, 0.6 H), 7.18 (t, J = 7.8 Hz, 0.4 H), 7.10−7.04 (m, 1 H), 6.78)d, J = 8.1 Hz, 0.6 H), 6.69 (d, J = 7.9 Hz, 0.4 H), 6.23 (t, J = 1.6 Hz, 0.6 H), 5.95−5.86 (m, 0.4 H), 3.91 (s, 1.7 H), 3.85 (s, 1.3 H), 3.73 (q, J = 6.4 Hz, 2 H), 3.32 (q, J = 1.7 Hz, 1 H), 2.98−2.92 (m, 1 H), 2.80−2.73 (m, 1 H), 2.67−2.60 (m, 1 H), 2.47 (q, J = 6.6 Hz, 1 H), 2.38 (br s, 1 H), 2.00−1.92 (m, 1 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 156.5 (−), 155.3 (−), 147.2 (−), 145.3 (−), 143.8 (−), 143.1 (−), 134.0 (−), 131.2 (−), 128.0 (+), 127.9 (+), 127.8 (+), 115.0 (+), 112.4 (+), 112.3 (+), 108.7 (+), 107.2 (+), 62.4 (−), 62.2 (−), 55.2 (+), 55.1 (+), 35.1 (−), 33.0 (−), 31.0 (−), 27.9 (−), 26.7 (−), 24.1 (−); IR (neat) 3363 (br s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 205 ([M + H]$^+$, 100), 187 (4.7); HRMS (CI with NH_3) calcd for $C_{13}H_{16}O_2H$ ([M + H]$^+$) 205.1229, found 205.1232.

3-(3-Hydroxy-5-hexenyl)-7-methoxy-1*H*-indene (74). Dimethyl sulfoxide (2.13 mL, 2.35 g, 30.08 mmol) was added slowly to oxalyl chloride (2.63 mL, 3.83 g, 30.15 mmol) in THF (40 mL) at −78 °C.[63] After 20 min, the indenyl alcohol **73** in THF (25 mL) was added. The resultant mixture was warmed to −30 °C over 20 min and then treated with triethylamine (10.0 mL, 7.26 g, 71.8 mmol). After the solution was warmed to room temperature over 20 min and recooled to −78 °C, allylmagnesium chloride (40 mL of a 2.0 M solution in THF, 80 mmol) was added.[50] The mixture was stirred at −78 °C for 2 h and allowed to warm to room temperature over 30 min. Acetic acid (10% aqueous, 80 mL) was added, and the mixture was extracted with ether (3×). The combined organic phases were washed twice with saturated aqueous sodium bicarbonate and brine and then dried ($MgSO_4$) and concentrated. Chromatography (2:1 ether/hexane) gave 3.09 g (70%) of the title compound as a single isomer based on ^{1}H NMR, R_f = 0.41: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.32 (t, J = 8.0 Hz, 1 H), 7.07 (d, J = 7.5 Hz, 1 H), 6.79 (d, J = 8.1 Hz, 1 H), 6.25 (br s, 1 H), 5.94−5.79 (m, 1 H), 5.20−5.12 (m, 2 H), 3.91 (s, 3 H), 3.85 (br s, 1 H), 3.80−3.75 (m, 1 H), 3.33 (d, J = 1.8 Hz, 2 H), 2.81−2.58 (m, 2 H), 2.43−2.32 (m, 1 H), 2.30−2.18 (m, 1 H), 1.94−1.80 (m, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 155.4 (−),, 147.3 (−), 144.1 (−), 134.8 (+), 131.3 (−), 128.1 (+), 127.9 (+), 118.3 (−), 112.4 (+), 107.3 (+), 70.4 (+), 55.3 (+), 42.1 (−), 35.3 (−), 35.2 (−), 24.1 (−); IR (neat) 3421 (br s) cm^{-1}; MS (CI with CH_4) *m*/*z* (rel int) 245 ([M + H]$^+$, 86.3), 227 (100); HRMS (CI with CH_4) calcd for $C_{16}H_{20}O_2H$ 245.1542, found 245.1537.

3-(3-Azido-5-hexenyl)-7-methoxy-1*H*-indene (75). Methanesulfonyl chloride (1.51 mL, 2.23 g, 19.5 mmol) and triethylamine (4.09 mL, 2.97 g, 29.4 mmol) were added to the alcohol **74** (2.39 g, 9.77 mmol) in CH_2Cl_2 (40 mL) at −50 °C. After 2 h, ether was added, and the solution was washed with saturated aqueous sodium bicarbonate and brine and then dried ($MgSO_4$) and concentrated to give the crude mesylate, which was treated with tetra-*n*-butylammonium azide (30 mL of a 1.0 M solution in THF, 30 mmol)[61] at room temperature. After 14 h, the mixture was diluted with ether and washed twice with water and brine and then dried ($MgSO_4$) and concentrated. Chromatography (pentane) gave 1.62 g (62%) of the title compound as a light yellow oil, R_f = 0.41: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.32 (dd, J = 8.0, 7.6 Hz, 1 H), 7.04 (dd, J = 7.6, 0.6 Hz, 1 H), 6.79 (d, J = 8.1 Hz, 1 H), 6.25 (t, J = 1.5 Hz, 1 H), 5.88−5.81 (m, 1 H), 5.21−5.14 (m, 2 H), 3.89 (s, 3 H), 3.46−3.44 (m, 1 H), 3.32 (dd, J = 3.6, 1.8 Hz, 2 H), 2.78−

(63) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480−2482

2.66 (m, 1 H), 2.65−2.57 (m, 1 H), 2.41−2.31 (m, 2 H), 1.95−1.84 (m, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 155.3 (−), 147.0 (−), 143.1 (−), 133.7 (+), 131.2 (−), 128.5 (+), 127.8 (+), 118.3 (−), 112.2 (+), 107.3 (+), 61.8 (+), 55.2 (+), 38.8 (−), 35.1 (−), 32.5 (−), 24.3 (−); IR (neat) 2098 (s) cm $^{-1}$; MS (CI with NH_3) *m*/*z* (rel int) 270 ([M + H]$^+$, 3.8), 242 (100); HRMS (CI with NH_3) calcd for $C_{16}H_{19}N_3OH$ 270.1606, found 270.1593.

(1*R,3a*S**)-6-Methoxy-1-(2-propenyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline (76a), (1*R**,3a*R**)-6-Methoxy-1-(2-propenyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline (76b), and (1*R**,10b*R**)-7-Methoxy-1-(2-propenyl)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (77).** Trifluoromethanesulfonic acid (339 mg, 2.25 mmol) was added to a solution of the azide **75** (490 mg, 1.82 mmol) in benzene (30 mL) at room temperature. After 10 min, the solution was cooled to 0 °C, and sodium borohydride (413 mg, 10.92 mmol) in methanol (10 mL) was added. After to room temperature for 5 h, saturated aqueous sodium bicarbonate was added, and the mixture was extracted with ether (3×). The combined organic phases were washed twice with brine and then dried (Na_2SO_4) and concentrated to give the crude product. Chromatography (1:7 ether/hexanes) gave 194 mg (44%) of an inseparable 2:1 mixture of **76a** and **76b** as a clear oil, R_f = 0.61, as judged by integration of the hydrogens at δ 3.12−3.04 (m, 0.5 H) and 2.96 (dd, J = 17.3, 5.6 Hz, 1 H) in the ^{1}H NMR spectrum. The relative configuration of the major diastereomer was proposed to be as indicated for **76a** based on the stereoelectronic model proposed for the reduction of analogous iminium ions.[57−59] Further elution yielded 184 mg (42%) of the tricyclic compound **77** as a clear oil, R_f = 0.61, whose relative configuration was also proposed based on the same stereoelectronic model. Data for **76a/b**: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.08 (t, J = 8.2 Hz, 1 H), 6.27−6.22 (m, 2 H), 5.92−5.81 (m, 1 H), 5.19−5.11 (m, 2 H), 3.95−3.89 (m, 0.5 H), 3.88 (s, 2 H), 3.87 (s, 1 H), 3.77 (t, J = 7.2 Hz, 1 H), 3.55−3.48 (m, 0.5 H), 3.42−3.32 (m, 1 H), 3.12−3.04 (m, 0.5 H), 2.96 (dd, J = 17.3, 5.6 Hz, 1 H), 2.65−2.53 (m, 1 H), 2.52−2.40 (m, 0.5 H), 2.25−2.09 (m, 2 H), 2.06−1.89 (m, 2 H), 1.80−1.59 (m, 1 H), 1.57−1.32 (m, 1 H); ^{13}C NMR ($CDCl_3$, 90 MHz, JMOD) δ 158.0 (−), 157.4 (−), 144.9 (−), 144.7 (−), 136.1 (+), 135.5 (+), 127.0 (+), 126.9 (+), 117.1 (−), 116.8 (−), 109.9 (−), 109.5 (−), 1.4.7 (+), 104.2 (+), 98.0 (+), 58.5 (+), 58.3 (+), 57.1 (+), 56.9 (+), 55.5 (+), 55.3 (+), 37.8 (−), 37.6 (−), 31.8 (−), 30.6 (−), 29.2 (−), 28.6 (−), 28.5 (−), 27.4 (−), 22.1 (−), 21.2 (−); IR (neat) 1603 (s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel int) 243 (M$^+$, 21.5), 202 (100); HRMS calcd for $C_{16}H_{21}NO$ 243.1623, found 243.1634. Data for **77**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.12 (t, J = 8.0 Hz, 1 H), 6.70 (d, J = 8.0 Hz, 2 H), 5.93−5.79 (m, 1 H), 5.15−5.02 (m, 2 H), 3.81 (s, 3 H), 3.45−3.39 (m, 1 H), 3.24 (br t, J = 6.8 Hz, 1 H), 2.92−2.87 (m, 2 H), 2.60−2.52 (m, 1 H), 2.48−2.36 (m, 1 H), 2.35−2.22 (m, 2 H), 2.18−2.09 (m, 1 H), 2.06−1.98 (m, 1 H), 1.75−1.59 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz, JMOD) δ 157.1 (−), 140.4 (−), 135.7 (+), 126.0 (+), 123.4 (−), 117.1 (+), 115.9 (−), 107.8 (+), 65.3 (+), 63.4 (+), 55.2 (+), 47.4 (−), 37.9 (−), 28.8 (−), 27.8 (−), 24.6 (−); IR (neat) 1640 (m), 1585 (s) cm^{-1}; MS (CI with CH_4) *m*/*z* (rel int) 244 ([M + H]$^+$, 100), 202 (19.8); HRMS (CI with CH_4) calcd for $C_{16}H_{21}NOH$([M + H]$^+$) 244.1701, found 244.1694.

4-(*tert*-Butyldiphenylsilyl)oxy-1,2-epoxybutane (78).[52] 4-(*N*,*N*-Dimethylamino)pyridine (300 mg, 2.46 mmol) was added to a solution of but-3-en-1-ol (5.00 g, 69.34 mmol), *tert*-butyldiphenylsilyl chloride (15.88 g, 57.78 mmol), and imidazole (5.19 g, 76.23 mmol) in CH_2Cl_2 (300 mL) at room temperature. After 4 h, the mixture was diluted with ether and washed twice with water and brine. The organic phase was dried ($MgSO_4$) and concentrated to give the crude silylated alcohol, which was dissolved in CH_2Cl_2 (200 mL) and treated with *m*-chloroperbenzoic acid (17.60 g, 85% purity, 86.69 mmol). After 3 h at room temperature, the mixture was diluted with ether, washed with 20% aqueous NaOH (3×) and brine (2×), dried ($MgSO_4$), and concentrated to give 23.0 g (∼100%) of the title compound, which was found by ^{1}H NMR spectroscopy to be pure enough to use in the next step without purification. The ^{1}H NMR data for this material matched the literature values.[52]

(*E*)- and (*Z*)-1-[5-(*tert*-Butyldiphenylsilyl)oxy-3-hydroxy]-pentylidene-4-methoxyindan (79). A solution of (*E*)- and (*Z*)-1-(bromomethylene)-4-methoxyindan (**69**, 5.02 g, 21.0 mmol) in THF (10 mL) was added to a suspension of magnesium turnings (612 mg, 25.2 mmol) in THF (50 mL) at room temperature. After 14 h, this Grignard reagent was transferred by syringe to a solution of the epoxide **78** (3.27 g, 10.02 mmol) in THF (10 mL) at 0 °C, followed by addition of anhydrous cuprous iodide (400 mg, 2.10 mmol). After 30 min, the solution was warmed to room temperature and kept for 2 h before saturated aqueous ammonium chloride was added. The mixture was filtered though Celite, washing twice with ether. The water layer was separated from the filtrate and extracted twice with ether. The combined organic phases were washed twice with brine and then dried ($MgSO_4$) and concentrated. Chromatography (1:2 ether/hexane) gave 4.10 g (84%) of the title compounds as an inseparable 1:1 mixture of geometrical isomers as judged by integration of the olefinic hydrogens at δ 6.04−5.95 and 5.66−5.57 in the ^{1}H NMR spectrum. Data on the mixture of isomers: Yellow oil, R_f = 0.32; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.72 (dd, J = 7.3, 1.5 Hz, 4 H), 7.53−7.39 (m, 6 H), 7.33−7.10 (m, 2 H), 6.72 (dd, J = 17.9, 7.9 Hz, 1 H), 6.04−5.95 (m, 0.5 H), 5.66−5.57 (m, 0.5 H), 4.13−4.10 (m, 1 H), 3.98−3.86 (m, 2 H), 3.86 (s, 1.5 H), 3.85 (s, 1.5 H), 3.36 (br s, 1 H), 2.89−2.85 (m, 2 H), 2.83−2.63 (m, 3 H), 2.53−2.38 (m, 1 H), 1.84−1.76 (m, 2 H), 1.10 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.6, 156.3, 144.9, 143.3, 142.3, 136.0, 135.5, 133.3, 129.7, 127.7, 118.3, 117.2, 115.0, 112.5, 109.2, 108.8, 71.5, 71.1, 63.2, 63.0, 55.3, 38.5, 37.7, 36.6, 33.7, 28.2, 27.0, 26,8, 26.7, 19.2; IR (neat) 3461 (br s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 469 ([M−H_2O+H]$^+$, 22.4), 409 (91.7), 163 (100); HRMS (CI with NH_3) calcd for $C_{31}H_{36}O_2SiH$ ([M − H_2O + H]$^+$) 469.2563, found 469.2544.

(*E*)- and (*Z*)-1-(3-Azido-5-hydroxy)pentylidene-4-methoxyindan (80). Methanesulfonyl chloride (0.31 mL, 459 mg, 4.01 mmol) and triethylamine (0.90 mL, 653 mg, 6.46 mmol) were added to the alcohol **79** (974 mg, 2.00 mmol) in CH_2Cl_2 (10 mL) at 0 °C. After 1 h, ether was added, and the solution was washed with water and brine and then dried ($MgSO_4$) and concentrated. The crude mesylate was then treated with tetra-*n*-butylammonium azide (8 mL of a 1.0 M solution in THF, 8 mmol)[61] at room temperature. After 14 h, ether was added, and the solution was washed with water and brine and then concentrated. The crude silyl ether was then treated with tetra-*n*-butylammonium fluoride (8 mL of a1.0 M in THF, 8 mmol) at room temperature. After 6 h, ether was added, and the mixture was washed with water and brine and then dried ($MgSO_4$) and concentrated. Chromatography (1:2 ether/hexane) gave 454 mg (83%) of the title compounds as an inseparable 1:1 mixture of geometrical isomers as judged by integration of the olefinic hydrogens at δ 5.98−5.86 and 5.57−5.52 in the ^{1}H NMR spectrum. Data on the mixture of isomers: Yellow oil, R_f = 0.35; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.23−7.21 (m, 1 H), 7.17 (d, J = 7.8 Hz, 0.5 H), 7.09 (d, J = 7.6 Hz, 0.5 H), 6.76 (t, J = 4.2 Hz, 1 H), 6.70 (d, J = 7.8 Hz, 0.5 H), 5.98−5.86 (m, 0.5 H), 5.57−5.52 (m, 0.5 H), 3.85 (s, 1.5 H), 3.84 (s, 1.5 H), 3.80−3.76 (m, 2 H), 3.72−3.69 (m, 1 H), 2.98−2.93 (m, 1 H), 2.90−2.86 (m, 1 H), 2.81−2.73 (m, 3 H), 2.55−2.46 (m, 1 H), 2.21 (s, 1 H), 1.95−1.83 (m, 1 H), 1.81−1.68 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.4, 156.28, 145.6, 144.2, 142.8, 141.7, 136.2, 134.0, 127.8, 127.6, 116.8, 113.6, 112.4, 109.3, 109.0, 60.2, 60.0, 59.6, 55.1, 36.6, 34.7, 33.6, 28.0, 26.7, 26.6; IR (neat) 3362 (br s), 2102 (s) cm^{-1}; MS (CI with CH_4) *m*/*z* (rel int) 274 ([M + H]$^+$, 7.3), 246 ([M − N_2 + H]$^+$, 47.7), 231 (38.5), 173 (100),; HRMS (CI with NH_3) calcd for $C_{15}H_{19}NO_2H$ ([M − N_2 + H]$^+$) 246.1494, found 246.1487.

(*E*)- and (*Z*)-1-(3-Azido-5-bromo)pentylidene-4-methoxyindan (81). Methanesulfonyl chloride (1.40 mL, 2.07 g, 18.1 mmol) and triethylamine (3.70 mL, 2.69 g, 26.6 mmol) were added to the azido alcohol **80** (2.41 g, 8.82 mmol) in CH_2Cl_2 (50 mL) at 0 °C. After 1 h, ether was added, and the mixture was washed with water and brine and then dried ($MgSO_4$) and concentrated. The crude mesylate was then treated with tetra-*n*-butylammonium bromide (8.53 g, 26.46 mmol) and THF (40 mL) at room temperature. After 14 h,

ether was added, and the mixture was washed with water and brine and then dried ($MgSO_4$) and concentrated. Chromatography (1:7 ether/hexane) gave 2.69 g (91%) of the title compounds as an inseparable 1:1 mixture of geometrical isomers as judged by integration of the olefinic hydrogens at δ 5.95−5.87 and 5.58−5.49 in the ^{1}H NMR spectrum. Data on the mixture of isomers: Yellow oil, $R_f = 0.51$; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.26−7.17 (m, 1.5 H), 7.09 (d, J = 7.6 Hz, 0.5 H), 6.76 (dd, J = 7.0, 1.7 Hz, 0.5 H), 6.71 (d, J = 9.5 Hz, 0.5 H), 5.95−5.87 (m, 0.5 H), 5.58−5.49 (m, 0.5 H), 3.86 (s, 1.5 H), 3.85 (s, 1.5 H), 3.80−3.73 (m, 1 H), 3.54−3.50 (m, 2 H), 2.96 (t, J = 6.3 Hz, 1 H), 2.89−2.86 (m, 1.5 H), 2.81−2.74 (m, 3 H), 2.55−2.46 (m, 0.5 H), 2.11−2.02 (m, 2 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 156.4, 146.1, 144.7, 141.7, 136.3, 134.1, 128.0, 127.8, 116.8, 116.3, 113.1, 112.5, 109.3, 109.0, 61.0, 60.8, 55.2, 37.0, 36.9, 34.4, 33.7, 33.3, 29.9, 28.1, 26.7, 26.6; IR (neat) 2100 (s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 336 ([M + H]$^+$, 3.7), 308 (25.7), 173 (100); HRMS (CI with NH_3) calcd for $C_{15}H_{18}N_3BrOH$ ([M + H]$^+$) 336.0711, found 336.0699.

(1*R,3a*R**)-1-(2-Hydroxyethyl)-6-methoxy-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline (49), (1*R**,3a*S**)-1-(2-Hydroxyethyl)-6-methoxy-1,2,3,3a,4,5-hexahydropyrrolo-[1,2-*a*]quinoline (84), and (1*R**,10b*R**)-1-(2-Hydroxyethyl)-7-methoxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (85). Method A.** Trifluoromethanesulfonic acid (356 mg, 2.37 mmol) was added to a solution of the bromo azide **81** (490 mg, 1.82 mmol) in benzene (40 mL) at 10 °C. After 10 min, the mixture was cooled to 0 °C and treated with sodium borohydride (359 mg, 9.49 mmol) in methanol (10 mL). After warming to room temperature for 14 h, saturated aqueous sodium bicarbonate was added, and the mixture was extracted with ether (3×). The combined organic phases were washed twice with brine and then dried (Na_2SO_4) and concentrated to give a mixture of (1*R**,3a*R**)-1-(2-bromoethyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline, (1*R**,3a*S**)-1-(2-bromoethyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline, and (1*R**,10b*R**)-1-(2-bromoethyl)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline, which was dissolved in THF (10 mL), and treated with tetra-*n*-butylammonium acetate (1.43 g, 4.74 mmol) in THF (5 mL) at room temperature. After 4 h, ether was added, and the solution was washed with water and brine and then dried (Na_2SO_4) and concentrated. The crude acetates were dissolved in THF (10 mL) and transferred to a suspension of lithium aluminum hydride (100 mg, 2.64 mmol) in THF (5 mL) at 0 °C. After warming to room temperature for 1 h, 15% aqueous sodium hydroxide (0.2 mL) was carefully added, followed by water (0.5 mL). The mixture was filtered, washing the solids with ether (3×). The filtrate was dried (Na_2SO_4) and concentrated. Chromatography of the residue (2:1 ether/hexanes) gave 218 mg (56%) of an inseparable mixture of **49** and **84** as a clear oil, $R_f = 0.43$, that was shown by ^{1}H NMR spectroscopy to be a 1:1 mixture of diastereomers as judged by integration of hydrogens at δ 4.02−3.96 and 3.94−3.86. The ^{13}C NMR spectral data for the mixture of **49** and **84** was consistent with that reported for a mixture of the same two compounds by Ito and co-workers.[36] Data for the mixture of **49** and **84**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.06 (t, J = 8.2 Hz, 1 H), 6.32−6.23 (m, 2 H), 4.02−3.96 (m, 0.5 H), 3.94−3.86 (m, 0.5 H), 3.79 (s, 1.5 H), 3.78 (s, 1.5 H), 3.77−3.63 (m, 2 H), 3.56−3.45 (m, 0.5 H), 3.30 (tdd, J = 10.8, 4.7, 2.1 Hz, 0.5 H), 3.05 (ddd, J = 16.5, 4.3, 2.6 Hz, 0.5 H), 2.93 (dd, J = 17.4, 5.1 Hz, 0.5 H), 2.50 (ddd, J = 19.3, 12.7, 6.7 Hz, 0.5 H), 2.42 (ddd, J = 17.5, 13.3, 5.0 Hz, 0.5 H), 2.25−2.12 (m, 3 H), 2.11−1.95 (m, 2 H), 1.89−1.78 (m, 0.5 H), 1.72−1.41 (m, 3 H), 1.39−1.28 (m, 0.5 H); ^{13}C NMR ($CDCl_3$, 75 MHz, JMOD) δ 157.7 (−), 157.0 (−), 144.9 (−), 144.7 (−), 126.8 (+), 126.6 (+), 110.1 (−), 109.6 (−), 104.7 (+), 104.3 (+), 98.3 (+), 98.1 (+), 60.6 (−), 60.3 (−), 58.3 (+), 56.7 (+), 55.3 (+), 55.2 (+), 54.7 (+), 36.2 (−), 36.0 (−), 31.6 (−), 30.7 (−), 29.9 (−), 29.5 (−), 28.5 (−), 27.1 (−), 21.9 (−), 20.9 (−); IR (neat) 3356 (br s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 2482 ([M + H]$^+$, 42.4), 202 (100); HRMS (CI with NH_3) calcd for $C_{15}H_{21}NO_2H$ 248.1651, found 248.1642.

Eluting further with 1:10:200 NH_3/MeOH/ether gave 63 mg (16%) of the amine **85** as a clear oil, $R_f = 0.42$ (1:10:200 NH_3/MeOH/ether). The relative configuration is based on the stereoelectronic model proposed for the reduction of analogous iminium ions.[57−59] Data for **85**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13 (t, J = 7.8 Hz, 1 H), 6.72−6.65 (m, 2 H), 4.79 (br s, 1 H), 4.00 (dt, J = 11.0, 2.9 Hz, 1 H), 3.82 (s, 3 H), 3.78−3.75 (m, 1 H), 3.65 (tt, J = 11.0, 4.2 Hz, 1 H), 3.56 (ddd, J = 14.6, 6.0, 2.6 Hz, 1 H), 3.24 (dd, J = 10.6, 6.1 Hz, 1 H), 2.86−2.75 (m, 2 H), 2.35−2.25 (m, 2 H), 2.17−1.96 (m, 2 H), 1.94−1.80 (m, 1 H), 1.78−1.66 (m, 1 H), 1.63−1.52 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz, JMOD) δ 157.1 (−), 139.7 (−), 126.3 (+), 123.2 (−), 117.0 (+), 108.0 (+), 65.6 (+), 62.4 (+), 59.6 (−), 55.3 (+), 47.4 (−), 31.6 (−), 28.4 (−), 26.6 (−), 24.6 (−); IR (neat) 3336 (br s) cm^{-1}; MS (CI with NH_3) *m*/*z* (rel int) 248 ([M + H]$^+$, 100), 202 (86.3); HRMS (CI with NH_3) calcd for $C_{15}H_{21}NO_2H$([M + H]$^+$) 248.1651, found 248.1652.

Method B. Trifluoromethanesulfonic acid (102 mg, 0.68 mmol) was added to a solution of the azide **81** (162 mg, 0.48 mmol) in benzene (10 mL) at 10 °C. After for 10 min, the solution was cooled to 0 °C and treated with diisobutylaluminum hydride (DIBAL-H, 2.0 mL of a 1.5 M solution in toluene, 3.0 mmol). After the mixture was warmed to room temperature for 30 min, 15% aqueous NaOH (0.1 mL) and water (0.3 mL) were carefully added, and the resulting mixture was filtered though a pad of Celite, washing the solids twice with ether. The filtrate was concentrated to give a mixture of (1*R**,3a*R**)-1-(2-bromoethyl)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline, (1*R**,3a*S**)-1-(2-bromoethyl)-1,2,3,3a,4,5-hexahydropyrrolo-[1,2-*a*]quinoline, and (1*R**,10b*R**)-1-(2-bromoethyl)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline, which was dissolved in THF (10 mL), and treated with tetra-*n*-butylammonium acetate (434 mg, 1.44 mmol) at room temperature. After 14 h, ether was added, and the solution was washed with water and brine and then dried (Na_2SO_4) and concentrated. The resultant oil was dissolved in THF (10 mL) and transferred to a suspension of lithium aluminum hydride (50 mg, 1.32 mmol) in THF (5 mL) at 0 °C. After the mixture was warmed to room temperature for 1 h, 15% aqueous sodium hydroxide (0.2 mL) and water (0.5 mL) were slowly added in a sequential fashion. The mixture was filtered, washing the solids with ether (3×). The filtrate was dried (Na_2SO_4) and concentrated. Chromatography (2:1 ether/hexanes) of the residue gave 56 mg (47%) of an inseparable mixture of **49** and **84** as a clear oil, R_f = 0.43, that was shown by ^{1}H NMR spectroscopy to be a 2:1 mixture of diastereomers as judged by integration of hydrogens at δ 4.02−3.96 and 3.94−3.86. Comparison of the ^{13}C NMR data with the literature data[36] showed that the major diastereomer was **49**, i.e., the (1*R**,3a*R**) isomer. Further elution as above gave 15.4 mg (13%) of the isomeric amine **85**, whose spectral data matched those reported above.

Method C. Trifluoromethanesulfonic acid (339 mg, 2.26 mmol) was added to a solution of azide **81** (500 mg, 1.49 mmol) in benzene (25 mL) at 10 °C. After 10 min, the solution was cooled to 0 °C and treated with L-Selectride (6.0 mL of a 1.0 M solution in THF, 6.0 mmol) was added. The mixture was warmed to reflux for 1 h and then cooled to room temperature and treated carefully with 15% aqueous sodium hydroxide (5 mL). Potassium carbonate was added until the aqueous layer was saturated, and then the organic phase was separated, dried (Na_2SO_4), and concentrated. The crude bromide was dissolved in THF (5 mL) and treated with tetra-*n*-butylammonium acetate (1.80 g, 5.97 mmol) at room temperature. After 14 h, the solution was diluted with ether, washed with water and brine, dried (Na_2SO_4), and concentrated. The resulting acetate was dissolved in THF (5 mL) and added to a suspension of lithium aluminum hydride (113 mg, 2.98 mmol) in THF (5 mL) at 0 °C. After warming to room temperature for 1 h, 15% aqueous sodium hydroxide (0.5 mL) and water (0.5 mL) were carefully added in a sequential fashion. The mixture was filtered, washing the solids twice with ether. The filtrate was concentrated, and the residue was chromatographed (2:1 ether/hexane) to give 166 mg (45%) of **49**, which was found to be a single compound as judged by ^{1}H NMR spectroscopy, The ^{13}C NMR spectrum of this material was consistent with the partial data reported by Ito and co-workers.[36] The ^{1}H NMR spectral data for this compound was consistent with data on similar compounds reported by Hart

and co-workers.[34] Data for **49**: $R_f = 0.43$ (2:1 ether/hexanes), ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.03 (t, $J = 8.2$ Hz, 1 H, Ar-*H*), 6.25 (t, $J = 5.2$, 2 H, Ar-*H*), 3.95−3.83 (m, 1 H), 3.79 (s, 3 H, Ar-OCH_3), 3.77−3.65 (m, 2 H, HOCH_2-), 3.35−3.23 (m, 1 H, benzylic H), 2.89 (dd, $J = 16.9$, 5.2 Hz, 1 H, benzylic H), 2.54 (ddd, $J = 19.3$, 12.4, 6.7 Hz, 1 H, *H*(1)), 2.25−2.14 (m, 1 H, bridgehead H), 2.07−1.95 (m, 2 H), 1.90−1.80 (m, 1 H), 1.73−1.51 (m, 3 H), 1.49−1.38 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.8, 145.0, 126.8, 110.1, 105.0, 98.7, 60.8, 58.5, 55.3, 55.1, 36.3, 30.8, 29.7, 28.6, 22.0; IR (neat) 3362 (br s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel int) 247 (M^+, 19.5), 229 (3.2), 202 (100); HRMS calcd for $C_{15}H_{21}NO_2$ 247.1572, found 247.1582. Further elution with (1:10:200 NH_3:MeOH:ether) gave 37 mg (10%) of tricyclic amine **85**, whose spectral data matched those reported above.

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Supporting Information Available: ^{1}H NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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