Cycloaddition−Rearrangement Sequence of 2-Amido Substituted Furans as a Method of Synthesizing Hexahydroindolinones

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A convenient synthesis of various substituted hexahydroindolinones has been achieved by an intramolecular Diels−Alder cycloaddition (IMDAF) reaction of 2-amido substituted furans. The initially formed [4 + 2] cycloadduct undergoes nitrogen-assisted ring opening followed by deprotonation of the resulting zwitterion to give the rearranged ketone. The stereochemical outcome of the IMDAF cycloaddition has the sidearm of the tethered alkenyl group oriented syn with respect to the oxygen bridge. The reaction rate and product yield were found to be markedly dependent upon the electronic properties of the alkenyl π-bond. 2-[2-(*tert*-Butoxycarbonylfuran-2-yl-amino)-ethyl]acrylic acid methyl ester was synthesized from 3-chlorocarbonyl-but-3-enoic acid methyl ester. Thermolysis of the carbomethoxy activated furanamide occurred at 80 °C to produce a rearranged hexahydroindolinone. When Me_3Al or $(MeO)_3Al$ was used as a Lewis acid to promote the cycloaddition, a rearranged alcohol was obtained. The initially formed [4 + 2] cycloadduct undergoes ring opening in the presence of the Lewis acid, and the resulting aluminum intermediate delivers the substituent group from the same face as the neighboring oxygen to ultimately furnish a rearranged *cis*-alcohol. In contrast to this result, a mixture of diastereomeric methoxy alcohols was isolated when the IMDAF cycloaddition was carried out in methanol. The major isomer corresponds to the *trans*-diastereomer that results from trapping of the iminium ion from the less crowded face of the π-bond.

The hexahydroindolinone nucleus is a structural feature found in a wide variety of alkaloids,[1] including the strychnos,[2] amaryllidaceae,[3] and aspidosperma[4] families. These alkaloids possess diverse physiological properties[5] as well as structural complexity and have attracted the interest of many synthetic chemists.[6] Strategies to prepare the hexahydroindolinone skeleton include [4 + 2] cycloadditions,[7] sigmatropic rearrangements,[8] Pummerer-induced cyclizations,[9] intramolecular condensation of amines onto carbonyl compounds,[10] 1,3-dipolar cycloadditions,[11] reaction of isocyanates with isocyanides,[12] and transition metal mediated cyclization reactions.[13] Despite the availability of many synthetic methods, there still exists a need to develop more efficient procedures than those currently in existence.

In our approach to the hexahydroindolinone core unit, we chose to explore the ring opening reaction of an aza-substituted oxabicyclo[2.2.1]heptene derivative.[14] Oxabi-

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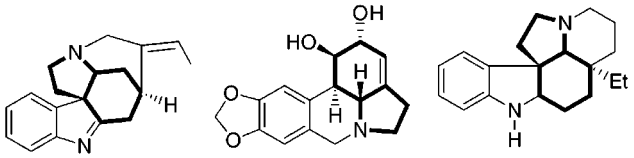
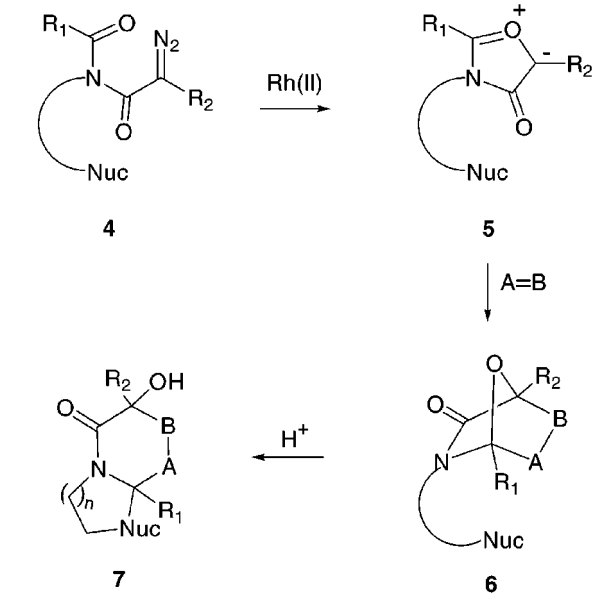


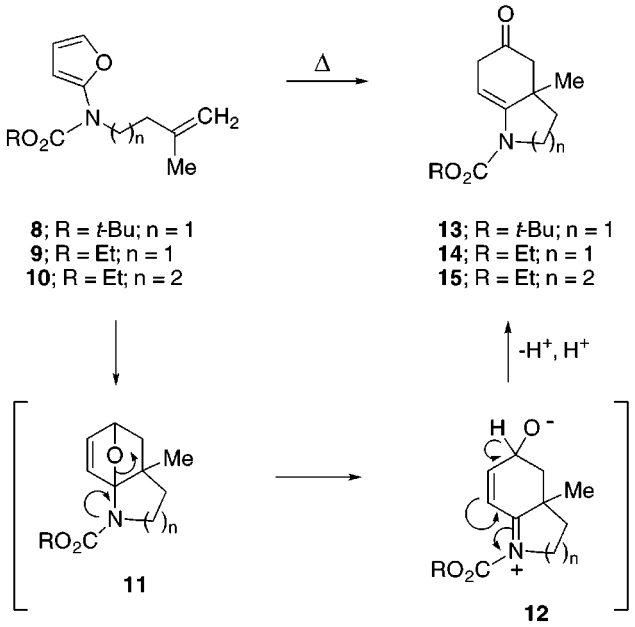
1; dehydrotubifoline **2**; lycorine **3**; aspidospermidine

cyclic compounds are known to be valuable intermediates[15] for the synthesis of a variety of molecules of biological interest.[16] A crucial transformation in many syntheses, employing oxabicyclic intermediates, has been the cleavage of the oxygen bridge to produce functionalized cyclohexane or cycloheptane derivatives.[17] To this end, many groups have developed different solutions, including β-eliminations of suitable derivatives,[18] treatment with strong acids,[19] reductive elimination of *endo* functionalities, such as Cl or SO_2Ph,[20] fragmentation,[21] and hydrolytic conditions.[22] Our interest in the ring opening of these oxabicyclic compounds was stimulated by earlier studies in our laboratory dealing with the Rh(II)-catalyzed reaction of diazoimides (e.g., **4**).[23] We found that this reaction induces formation of an isomünchnone dipole (i.e., **5**) by intramolecular cyclization of the rhodium carbenoid onto the neighboring carbonyl oxygen (Scheme 1). The resultant mesoionic ylide is trapped by various alkenyl π-bonds to give cycloadducts of type **6** in high yield.[24] These uniquely functionalized oxabicyclic cycloadducts contain a "*masked*" *N*-acyliminium ion which can be released by treatment with a Lewis acid. With an internal nucleophile incorporated on the tether, annulation of the original cycloadduct **6** allows for the construction of complex azapolycyclic ring systems, such as **7**.[25]

Scheme 1



Scheme 2



As an extension of this work, we undertook a study dealing with the intramolecular Diels–Alder reaction (IMDAF)[26] of the related 2-amidofuran system (i.e., **8**). The initially formed [4 + 2] oxabicyclic adduct **11** was found to undergo a related nitrogen-assisted ring opening, and this was followed by a subsequent hydrogen shift of the resulting zwitterion **12** to give the hexahydroindolinone ring system (Scheme 2).[14] To better understand the scope and stereoselectivity of this novel reaction, we chose to explore the *cycloaddition–ring opening*

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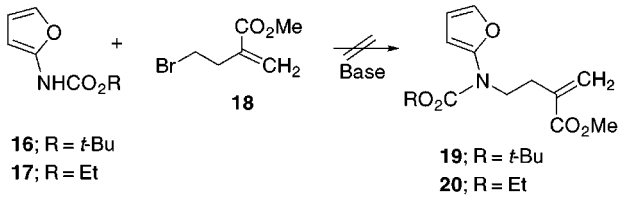
sequence in greater detail. In this paper, we report the results of our model studies that demonstrate that the IMDAF cycloaddition of 2-amidofurans represents a convenient method to synthesize hexahydroindolinones.

Results and Discussion

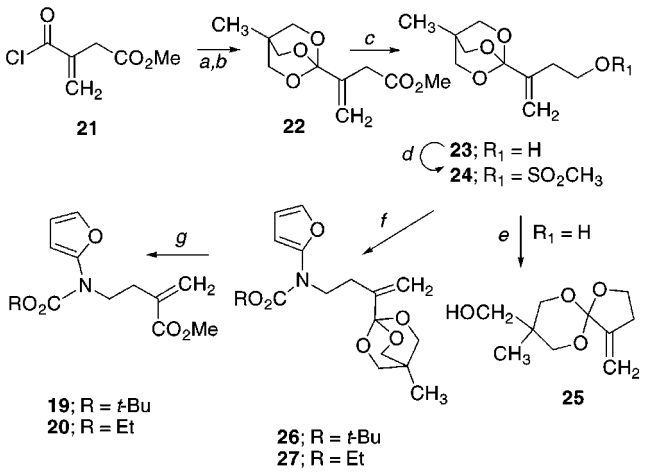
We began our investigation of the intramolecular [4 + 2] aminofuran cycloaddition reaction by studying the thermal behavior of *N*-alkenyl furanyl carbamates **8**−**10** that contain an unactivated π-bond on the tether. Attachment of the alkenyl group was accomplished by treating the appropriate NH-carbamate with base followed by the addition of either 4-bromo-2-methyl-1-butene or 5-bromo-2-methyl-1-pentene. The IMDAF cycloaddition was performed by heating a solution of the carbamate in benzene in a sealed tube at 165−200 °C for 14−36 h. In all three cases, the only products isolated corresponded to the rearranged ketones **13**−**15** in 71, 90, and 68% yield, respectively. The isolation of the hexahydroindolinone ring system from this reaction is in full agreement with the proposed *cycloaddition/ring opening/rearrangement* sequence outlined in Scheme 2.

Our previous studies dealing with the bimolecular [4 + 2] cycloadditions of 2-amino substituted furans have shown that the reaction rates and product yields are markedly dependent upon the electronic properties of the alkenyl group.[27] Because electron-withdrawing substituents on the π-bond exhibit a powerful influence on the rate of HOMO-dienyl [4+2] cycloadditions,[28] the synthesis of a 2-carbomethoxy substituted olefinic carbamate, such as **19** or **20**, appeared to us to be a worthwhile goal. In addition to facilitating the IMDAF cycloaddition by modulation of the electronic properties of the π-bond, the carbomethoxy group also provides a handle by which a number of hexahydroindolinone derivatives may be prepared and studied. As was pointed out earlier, the general procedure used for the synthesis of *N*-alkenyl substituted furanyl carbamates involves alkylation using a primary bromide. Unfortunately, the alkylation method utilized for the methyl-substituted alkenyl bromides was not successful when applied to 4-bromo-2-carbomethoxy-1-butene (**18**). Under a variety of conditions, the reaction of the anion of carbamate **16** (or **17**) with bromide **18** failed to produce the desired furan **19** (or **20**). Apparently, problems associated with both conjugate addition and halide elimination became major drawbacks with this approach.



Of the alternate methods considered for the synthesis of carbamate **19** or **20**, the Corey method for carboxylic acid protection seemed best suited for our purposes.[29]

Scheme 3



Conditions: (a) 3-methyloxetane-3-methanol, pyridine, CH_2Cl_2, 77%; (b) BF_3•OEt_2, CH_2Cl_2, -10 °C, 91%; (c) LAH, ether, 0 °C, 90%; (d) MsCl, NEt_3, CH_2Cl_2, 0 °C, 93%;(e) $CDCl_3$, H^+, 40%; (f) carbamate **16** or **17**, K_2CO_3, NaOH, TBAHS, benzene, 80 °C, 84%; (g) MeOH/H_2O, PPTS, K_2CO_3, 85%.

Protection of the carboxylic acid group as an ortho ester has proven to have advantages in a variety of syntheses.[30−32] Thus, we felt that mesylate **24** would be an excellent synthetic equivalent to bromide **18**, especially since this substrate would not undergo conjugate addition and/or elimination to carbomethoxy-1,3-butadiene. After the typical Corey procedure was used,[29] the known acid chloride **21**[33] was converted into trioxabicyclooctane (OBO) ortho ester **22** by esterification with 3-methyloxetane-3-methanol followed by rearrangement using boron trifluoride etherate (Scheme 3). LAH reduction of **22** gave alcohol **23**, which was somewhat sensitive toward acid and furnished ortho ester **25** when allowed to stand under acidic conditions. More than likely, alcohol **23** reacts with the available acid to produce a ring-opened tertiary allylic cation that is trapped by the neighboring homoallylic alcohol to afford **25**. In the absence of acid, however, **23** was readily transformed into mesylate **24** in 93% yield. Treatment of **24** with the anion derived from the NH-carbamate **16** or **17** furnished the OBO-protected furans **26** and **27** in excellent yield. Methanolysis of the ortho ester group was carried out in methanol with 0.1 equiv of pyridinium *p*-toluenesulfonate (PPTS) followed by the addition of 1.1 equiv of potassium carbonate.[34] After these conditions were used, the desired furanyl carbamates **19** and **20** were isolated in high yield. In the case of the *tert*-butyl carbamate **26**, addition of potassium carbonate to the methanolic solution is necessary, otherwise the intermediate 2,2-bis(hydroxymethyl)-propyl ester was isolated from the reaction.[30]

To test the importance of dienophile activation, we compared the rate of the IMDAF cycloadditions of

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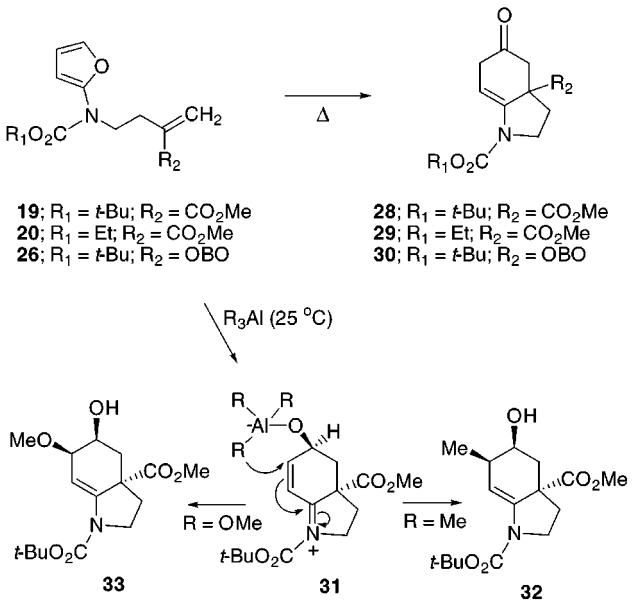
Scheme 4



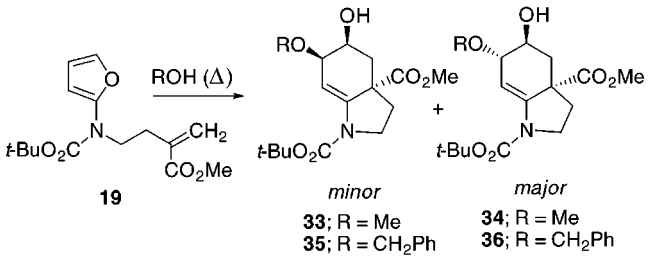
19; R_1 = *t*-Bu; R_2 = CO_2Me
20; R_1 = Et; R_2 = CO_2Me
26; R_1 = *t*-Bu; R_2 = OBO

28; R_1 = *t*-Bu; R_2 = CO_2Me
29; R_1 = Et; R_2 = CO_2Me
30; R_1 = *t*-Bu; R_2 = OBO

33 **31** **32**

furanamides **8**, **26**, and **19**. The temperature and time required for the reaction of **26** (165 °C) and yield of the resulting hexahydroindolinone **30** were similar to that encountered with the methyl-substituted systems (i.e., **13**). Incorporation of the carbomethoxy substituent on the alkenyl π-bond, on the other hand, greatly facilitated the cycloaddition (80 °C, 6 h) that afforded ketones **28** and **29** in 87% and 80% yield, respectively. This result is to be expected since placement of an electron-withdrawing substituent on the π-bond lowers the LUMO energy of the dienophile and enhances the rate of the [4 + 2] cycloaddition.[28] Most interestingly, when a Lewis acid such as Me_2AlCl was used to promote the cycloaddition,[35] it was possible to carry out the reaction at temperatures as low as 25 °C. In this case, the only product isolated (40%) corresponded to the rearranged alcohol **32**. The yield of **32** was significantly increased (82%) when a trimethylaluminum/toluene solution was used to promote the cycloaddition. We suspect that the initially formed [4 + 2] cycloadduct undergoes a Lewis acid assisted ring opening, and the resulting intermediate **31** delivers a methyl group from the same face as the neighboring oxygen to ultimately furnish the *cis*-alcohol **32** (Scheme 4).[36]

For comparison purposes, we have also carried out the IMDAF cycloaddition of furanamide **19**, using 2 equiv of $(MeO)_3Al$ in benzene at 65 °C. Under these conditions, *cis*-methoxy alcohol **33** was obtained as the major product (80%) together with lesser quantities of ketone **28** (10%) (Scheme 4). The structure and stereochemistry of **33** was unequivocally established by a single-crystal X-ray analysis of its 3,5-dibromo benzoate ester.[37] Interestingly, when the thermolysis of **19** was carried out in MeOH at 65 °C, a 1:3 mixture of the *cis*- and *trans*-methoxy alcohols **33** and **34** was obtained in 85% yield. The structure of the trans alcohol **34** was based in part on the large coupling constant (J = 7.2 Hz) between the C_4 and C_5 hydrogens. Further support for its assignment was obtained from a single-crystal X-ray analysis of the 3,5-dibromo benzoate ester.[37] A similar distribution of alcohols was also observed when benzyl alcohol was used as the solvent. In this case, compounds **35** and **36** were produced as a 1:3



19

33; R = Me
35; R = CH_2Ph

34; R = Me
36; R = CH_2Ph

mixture in 80% overall yield. Control experiments demonstrated that the two diastereomeric alcohols were not interconverted on extended heating. Mechanistically, these results can be explained in terms of a ring-opening reaction of the [4 + 2] oxabicyclic adduct and subsequent trapping of the zwitterionic intermediate (e.g., **12**) with the solvent from either the α- or β-face. The preferred mode of attack takes place on the side opposite the alcohol functionality that corresponds to the less-congested face of the π-bond.

Intramolecular Diels−Alder reactions where the tether connecting the diene and dienophile consists of three carbon atoms have been extensively studied.[38,39] However, this internal cycloaddition reaction is not as simple as it might appear.[40] In many cases, it is neither purely kinetically controlled nor thermodynamically controlled. Indeed, with certain systems, the reaction can be reversible and is capable of giving a mixture of *endo* and *exo* products.[41] To account for the stereochemical results, it becomes necessary to consider not only the relative stabilities of the *endo* and *exo* products and the stabilizing effect of FMO overlap on the transition state[42] but also the ability of the connecting chain to fold into the required conformation necessary for the cycloaddition to proceed. The stereochemical results that we have encountered with the IMDAF cycloaddition of 2-amidofuran **19** is consistent with that reported by others for related furanyl systems possessing short tethers.[43,44] The ring-opened alcohols (i.e., **32**−**36**) are derived from an IMDAF

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(36) The trans relationship between the carbomethoxy and hydroxyl groups of **32** was assigned by comparison of its NMR properties with those of related compounds whose structures were established by X-ray crystallography.

(37) The authors have deposited atomic coordinates for the 3,5-dibromobenzoate esters of alcohols **33** and **34** as well as compound **40** with the Cambridge Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, U.K.

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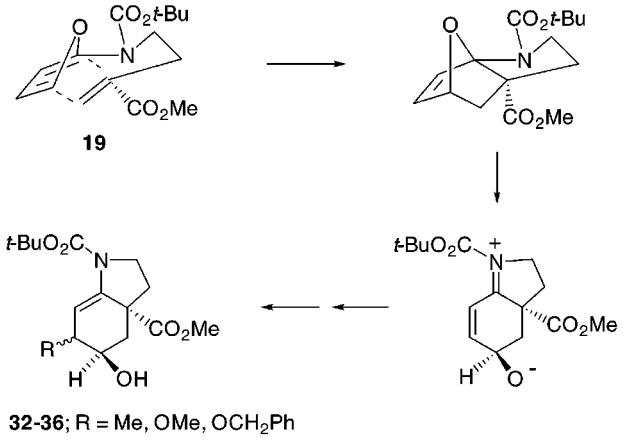
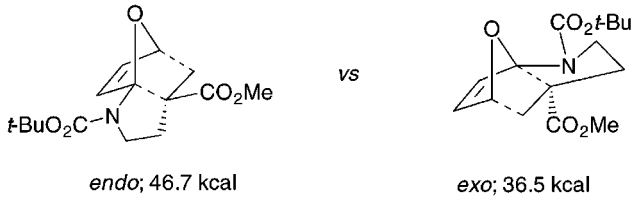


Figure 1. *Exo* transition state for IMDAF cycloaddition of 2-amidofuran **19**.

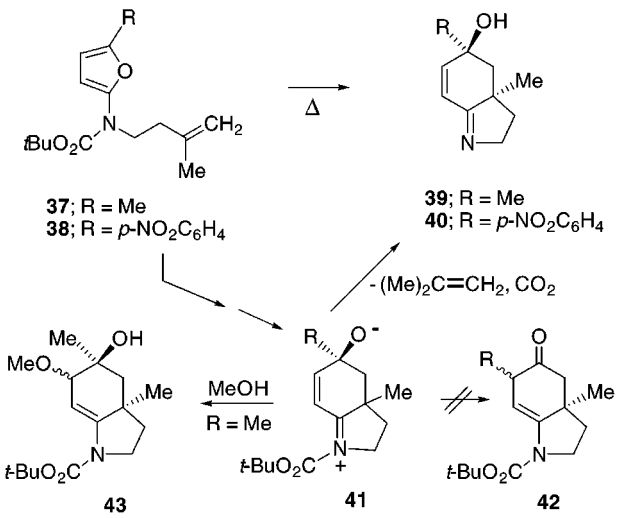
cycloaddition where the sidearm of the tethered alkenyl group is oriented syn (*exo*) with respect to the oxygen bridge (Figure 1). Products resulting from an *endo* sidearm transition state were neither detected nor isolated. This result is not so surprising since, in these mobile cycloaddition equilibria, the *exo* adducts are expected to be thermodynamically more favored. We have used the Still−Steliou model program to model energy differences in the transition state for the IMDAF cycloaddition of 2-amidofuran **19**. The transition-state geometry was approximated by fixing the distance between



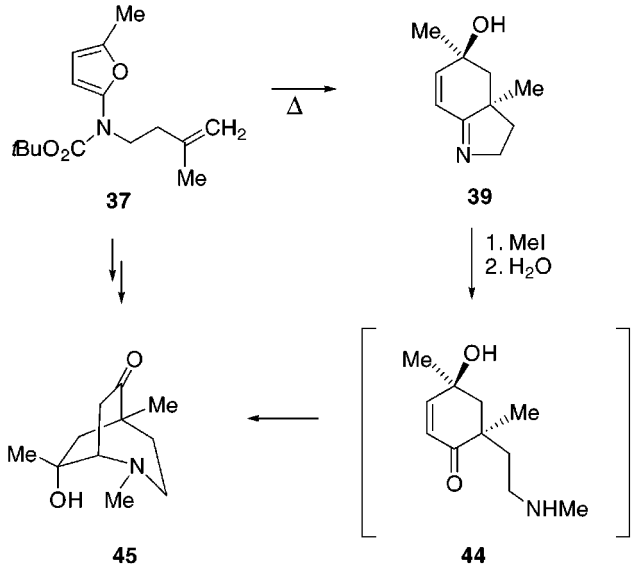
the reacting centers of the furan and alkene to be 3.0 ± 1.0 Å. A Boltzmann distribution of the various conformers of the fixed transition state was obtained from the Bakmdl output. We assume that the relative energy conformation of the starting furan and "*approximated*" cycloadduct will parallel the activation energy of the reaction. The calculations show that the energy difference is ca. 10 kcal lower for the *exo* adduct, which is in accord with the experimental findings.

In all of the above examples, products were derived from an oxabicyclic intermediate that either undergoes deprotonation or reacts with an external nucleophile. In the next phase of our study, we investigated the effect of placing an alkyl or aryl group at the 5-position of the furan ring since it was not at all clear what would happen on blocking the deprotonation reaction. One possibility would involve a [1,2]-alkyl or aryl shift proceeding from the zwitterionic intermediate **41** (Scheme 5). We found, however, that the reaction pathway changed quite dramatically by replacing the hydrogen atom with a substituent group in the 5-position of the furan ring. Thus, when furans **37** and **38** were subjected to the IMDAF cycloaddition in benzene, tetrahydro-2*H*-indoles **39** and

Scheme 5



Scheme 6



40 were isolated in 89% and 82% yield, respectively. No signs of a rearranged hexahydroindolinone (i.e., **42**) could be detected in the crude reaction mixture by NMR analysis. In the case of **40**, its stereochemistry was established from a single-crystal X-ray analysis that clearly fixes the syn relationship of the methyl and aryl groups. The isolation of a single diastereomer from this reaction is consistent with the *exo*-mode of cycloaddition. In contrast to this result, when the IMDAF cycloaddition of **37** was carried out in methanol, the expected ring-opened methoxy alcohol **43** was isolated as a 2:1 mixture of diastereomers in 76% yield. Formation of the tetrahydro-2*H*-indole ring system from the benzene thermolysis suggests that fragmentation of the *t*-Boc group to give isobutylene and CO_2 proceeds at a faster rate than either an alkyl or aryl group shift. Interestingly, when **39** was treated with methyl iodide followed by an aqueous workup, azabicyclo[3.2.2]nonanone **45** was obtained in 90% yield. This novel sequence of reactions, whereby furan **37** is transformed into **45** in 81% overall yield, can be rationalized by the hydrolysis of the iminium ion derived from the methylation step followed by an intramolecular Michael addition across the resulting cyclohexenone intermediate **44** (Scheme 6).

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In conclusion, this paper describes a versatile new approach toward hexahydroindolinones that contain various substitution patterns. The synthetic procedure described herein involves an intramolecular Diels−Alder reaction of 2-amidofurans containing a tethered alkenyl group on the nitrogen atom. The initially formed [4 + 2] cycloadduct undergoes a nitrogen-assisted ring opening followed by a subsequent deprotonation of the resulting zwitterionic intermediate to give the rearranged ketone. The ability to carry out the domino cascade with Lewis acid catalysts at room temperature makes this reaction even more useful for the synthesis of complex nitrogen-containing natural products. Further applications of this cycloaddition approach toward several alkaloids are in progress and will be reported in due course.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of dry argon. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate/hexane mixture as the eluent unless, specified otherwise. All solids were recrystallized from ethyl acetate/hexane for analytical data.

***tert*-Butyl *N*-(3-Methyl-3-butenyl)-*N*-(2-furyl)carbamate (8).** A 2.3 g (13 mmol) sample of furan-2-ylcarbamic acid *tert*-butyl ester (**16**),[27] 4.0 g (13 mmol) of tetrabutylammonium bromide, and 4.0 g (28 mmol) of 4-bromo-2-methyl-1-butene[45] in 100 mL of CH_2Cl_2 at 0 °C was treated dropwise with a 50% aqueous NaOH solution. The mixture was heated at reflux for 15 h, cooled to room temperature, and diluted with water, and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with 3 N HCl, water, and brine and was dried over sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 2.5 g (79%) of **8** as a colorless oil: IR (neat) 3403, 2975, 2925, and 1716 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.45 (s, 9H), 1.74 (s, 3H), 2.27 (t, 2H, J = 7.2 Hz), 3.67 (dd, 2H, J = 9.2 and 6.0 Hz), 4.71 (s, 1H), 4.76 (s, 1H), 6.33 (brs, 1H), 7.14 (t, 1H, J = 1.2 Hz), and 7.18 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.2, 28.0, 36.6, 46.9, 80.7, 100.9, 110.7, 111.8, 137.8, 142.3, 148.3, and 153.5. Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.93; H, 8.38; N, 5.60.

***tert*-Butyl 3*a*-Methyl-5-oxo-2,3,3*a*,4,5,6-hexahydroindol-1-carboxylate (13).** A 2.2 g (8.7 mmol) sample of carbamate **8** in 10 mL of benzene in a sealed tube was heated at 165 °C for 14 h. The solution was concentrated under reduced pressure after cooling to room temperature, and the residue was purified by flash silica gel chromatography to give 1.5 g (71%) of ketone **13** as a white solid: mp 112−113 °C; IR (KBr) 3402, 2961, 1709, and 1388 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 0.94 (s, 3H), 1.42 (s, 9H), 1.72 (m, 2H), 2.35 (d, 1H, J = 14.6 Hz), 2.49 (d, 1H, J = 14.6 Hz), 2.63 (dd, 1H, J = 14.6 and 2.8 Hz), 2.89 (dd, 1H, J = 14.6 and 4.8 Hz), 3.51 (m, 1H), 3.66 (m, 1H), and 5.78 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 22.8, 27.7, 35.2, 36.7, 42.5, 46.1, 51.6, 79.6, 96.4, 143.7, 151.5, and 208.3. Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.99; H, 8.38; N, 5.49.

Ethyl *N*-(3-Methyl-3-butenyl)-*N*-(2-furyl)carbamate (9). A solution containing 19.0 g (142 mmol) of 2-furyl azide in 250 mL of ethanol was heated at reflux for 12 h. The solution was concentrated under reduced pressure, and the residue was purified by flash silica gel chromatography to give 17.6 g (80%) of furan-2-ylcarbamic acid ethyl ester (**17**) as a white solid: mp 27−28 °C; IR (neat) 3288, 1723, 1531, and 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.28 (t, 3H, J = 7.2 Hz), 4.21 (q, 2H, J = 7.2 Hz), 6.06 (s, 1H), 6.33 (dd, 1H, J = 3.2 and 2.0 Hz), 7.06 (s, 1H), and 7.14 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 62.0, 95.4, 111.5, 136.4, 145.2, and 153.1. HRMS Calcd for $C_7H_9NO_3$: 155.0582. Found: 155.0577.

To solution containing containing 2.3 g (15 mmol) of carbamate **17**, 2.1 g (53 mmol) of powdered sodium hydroxide, 4.2 g (30 mmol) of potassium carbonate, 1.0 g (3.0 mmol) of tetrabutylammonium hydrogen sulfate in 250 mL of benzene was heated at reflux for 30 min, and then 4.5 g (30.2 mmol) of 4-bromo-2-methyl-1-butene in 10 mL of benzene was added dropwise to the solution. The mixture was heated for an additional 5 h, quenched with 200 mL of H_2O, and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 2.4 g (71%) of **9** as a colorless oil: IR (neat) 2982, 1723, 1652, 1616, and 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22 (t, 3H, J = 6.8 Hz), 1.72 (s, 3H), 2.26 (t, 2H, J = 6.8 Hz), 3.70 (t, 2H, J = 6.8 Hz), 4.16 (q, 2H, J = 6.8 Hz), 4.69 (d, 1H, J = 0.8 Hz), 4.76 (s, 1H), 6.03 (brs, 1H), 6.35 (dd, 1H, J = 3.2 and 2.4 Hz), and 7.19 (d, 1H, J = 0.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 22.6, 36.7, 47.6, 62.3, 102.6, 111.1, 112.1, 138.7, 142.6, 148.0, and 155.0. Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.71; H, 7.73; N, 6.12.

Ethyl 3*a*-Methyl-5-oxo-2,3,3*a*,4,5,6-hexahydroindol-1-carboxylate (14). A 0.8 g (3.4 mmol) sample of carbamate **9** in 10 mL benzene in a sealed tube was heated at 165 °C for 14 h. The solution was concentrated under reduced pressure after cooling to room temperature, and the residue was purified by flash silica gel chromatography to give 0.7 g (90%) of ketone **14** as a white solid: mp 48−49 °C; IR (KBr) 2974, 1716, 1665, and 1464 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.06 (s, 3H), 1.30 (t, 3H, J = 6.8 Hz), 1.79−1.83 (m, 2H), 2.45 (d, 1H, J = 14.2 Hz), 2.54 (d, 1H, J = 14.2 Hz), 2.94 (s, 1H), 2.95 (d, 1H, J = 1.2 Hz), 3.61 (q, 1H, J = 9.6 Hz), 3.83 (m, 1H), 4.19 (q, 2H, J = 6.8 Hz), and 5.99 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.8, 23.7, 36.7, 37.6, 43.1, 46.6, 52.8, 61.6, 97.9, 144.4, 153.4, and 210.1. Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.44; H, 7.68; N, 6.18.

Ethyl *N*-(4-Methyl-pent-4-enyl)-*N*-(2-furyl)carbamate (10). To a solution containing 5.0 g (32 mmol) of carbamate **17** and 300 mL of a 4:1 DMF/THF mixture at room temperature was added 21 g (64 mmol) of cesium carbonate. The reaction mixture was stirred at room temperature for 45 min and then charged with 10.5 g (64 mmol) of 5-bromo-2-methylpent-1-ene.[46] The mixture was heated at 70 °C for 6 h, quenched with 50 mL of H_2O, and extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 7.0 g (91%) of **10** as a clear oil: IR (neat) 2980, 1731, 1616, and 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.23 (t, 3H, J = 6.8 Hz), 1.69 (s, 3H), 1.71−1.75 (m, 2H), 2.01 (t, 2H, J = 7.6 Hz), 3.57 (t, 2H, J = 7.6 Hz), 4.16 (q, 2H, J = 6.8 Hz), 4.65−4.69 (m, 2H), 6.03 (brs, 1H), 6.34−6.35 (m, 1H), and 7.18−7.19 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 22.5, 26.5, 34.8, 49.0, 62.3, 102.1, 110.4, 111.1, 138.7, 145.0, 148.2, and 155.2. Anal. Calcd for $C_{13}H_{19}O_3N$: C, 65.80; H, 8.07; N, 5.90. Found: C, 66.05; H, 8.04; N, 5.67.

Ethyl 4*a*-Methyl-6-oxo-3,4,4*a*,5,6,7-hexahydro-(2*H*)-quinoline-1-carboxy-late (15). A solution of 1.2 g (5 mmol) of furan **10** in 13 mL of benzene was heated in a sealed tube at 200 °C for 36 h. The solution was concentrated under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.8 g (68%) of **15** as a clear oil: IR (KBr) 2932, 1716, 1467, 1410, and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.05 (s, 3H), 1.20 (t, 3H, J = 7.2 Hz), 1.52−1.59 (m, 1H), 1.61−1.67 (m, 2H), 1.71−1.79 (m, 1H), 2.31 (dd, 1H, J = 13.6 and 1.6 Hz), 2.56 (d, 1H, J = 13.6 Hz), 2.85−2.89 (m, 1H), 2.91 (d, 1H, J = 3.2 Hz), 3.05 (dd, 1H, J = 21.8 and 3.6

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Hz), 4.10 (dq, 2H, J = 7.2 and 0.8 Hz), 4.22−4.27 (m, 1H), and 5.50 (t, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 21.5, 24.2, 39.3, 39.5, 39.6, 46.6, 54.0, 61.7, 116.9, 140.5, 155.7, and 208.3. HRMS Calcd for $C_{13}H_{19}NO_3$: 237.1365. Found: 237.1365.

2-Methylenesuccinic Acid 4-Methyl Ester 1-(2-Methyloxetan-2-yl-methyl) Ester. To a solution containing 48 g (470 mmol) of 3-methyl-3-oxetanemethanol and 500 mL of CH_2Cl_2 at 0 °C was added 41 g (517 mmol) of pyridine. The mixture was allowed to stir at 0 °C for 20 min, and then 70 g (430 mmol) of 3-chlorocarbonyl-but-3-enoic acid methyl ester (**21**)[33] was added over a 30 min period. The reaction mixture was allowed to stir at 0 °C for 4 h and was then quenched with 300 mL of H_2O and extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by flash silica gel chromatography to give 71 g (77%) of the above ester as a colorless oil: IR (neat) 2954, 1737, 1637, 1324, and 969 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.31 (s, 3H), 3.32 (s, 2H), 3.66 (s, 3H), 4.21 (s, 2H), 4.35 (d, 2H, J = 6 Hz), 4.49 (d, 2H, J = 6 Hz), 5.71 (s, 1H), and 6.34 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.2, 21.3, 37.7, 39.3, 52.2, 69.4, 79.5, 129.3, 133.6, 166.1, and 171.2. Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.70; H, 6.99.

3-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-but-3-enoic Acid Methyl Ester (22). To a solution containing 32 g (138 mmol) of the above oxetane in 500 mL of CH_2Cl_2 at −10 °C was added 4.9 g (105 mmol) of boron trifluoride diethyl etherate. The reaction mixture was allowed to stir at −10 °C for 15 h and was quenched at 0 °C with 14 g (138 mmol) of triethylamine. The solution was concentrated under reduced pressure, and the crude residue was purified by flash silica gel chromatography to give 29 g (91%) of **22** as a white solid: mp 80−81 °C; IR (neat) 2961, 2868, 1751, 1445, and 1189 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (s, 3H), 3.15 (s, 2H), 3.68 (s, 3H), 3.94 (s, 6H), 5.20 (s, 1H), and 5.65 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 30.6, 37.3, 52.5, 68.9, 73.2, 106.8, 118.0, 137.8, and 171.9. Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.82; H, 7.02.

3-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-but-3-en-1-ol (23). To a suspension of 9.7 g (256 mmol) of lithium aluminum hydride in ether at 0 °C was slowly added 39 g (170 mmol) of ester **22**. The reaction mixture was allowed to stir at 0 °C for 4 h and was slowly quenched at 0 °C with 5 mL of H_2O. The aluminum complex was broken up by the addition of 5 mL of a 50% NaOH solution followed by 2.5 mL of H_2O. The organic layer was dried over sodium sulfate, and the mixture was filtered and concentrated under reduced pressure to provide 31 g (90%) of **23** as a colorless oil: IR (neat) 3487, 2876, 1652, 1467, and 1147 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.82 (s, 3H), 2.37 (brs, 1H), 2.44 (t, 2H, J = 5.6 Hz), 3.72 (t, 2H, J = 5.2 Hz), 3.95 (s, 6H), 5.10 (d, 1H, J = 1.2 Hz), and 5.55 (d, 1H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 30.5, 35.3, 62.1, 73.0, 107.1, 117.3, 141.7. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.84; H, 7.94.

If alcohol **23** was allowed to stand for a period of time in $CDCl_3$ that contained a trace of DCl, it was slowly converted into 8-methyl-4-methylene-1,6,10-trioxaspiro[4.5]-dec-8-yl-methanol (**25**) in 85% yield: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.73 (s, 3H), 2.63−2.65 (m, 2H), 3.30 (s, 1H), 3.62−3.65 (m, 2H), 3.77 (s, 2H), 3.98−3.94 (m, 4H), 5.13 (m, 1H), and 5.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.1, 29.9, 34.4, 64.6, 64.8, 66.9, 67.9, 109.9, 115.3, and 145.7.

Methanesulfonic Acid 3-(4-Methyl-2,6,7-trioxabicyclo-[2.2.2]oct-1-yl)-but-3-enyl Ester (24). To a 6.0 g (30 mmol) sample of alcohol **23** in 100 mL of CH_2Cl_2 was added a mixture of 3.3 g (33 mmol) of triethylamine in 200 mL of CH_2Cl_2 at 0 °C. To this solution was added 3.8 g (33 mmol) of methanesulfonyl chloride dropwise over a 10 min period. The reaction mixture was allowed to stir at 0 °C for 6 h and was then quenched at 0 °C with 150 mL of H_2O and extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to give 7.72 g (93%) of mesylate **24** as a white solid: mp 50−51 °C; IR (neat) 2947, 2876, 1716, 1628, and 1474 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.83 (s, 3H), 2.62 (t, 2H, J = 7.2 Hz), 2.98 (s, 3H), 3.95 (s, 6H), 4.36 (t, 2H, J = 6.8 Hz), 5.14 (s, 1H), and 5.58 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 30.6, 31.7, 37.7, 69.1, 73.0, 107.0, 117.7, and 139.4. HRMS Calcd for $C_{10}H_{16}SO_5$ (M − CH_2O): 248.0718. Found: 248.0725.

***tert*-Butyl *N*-[3-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-butenyl]-*N*-(2-furyl)carbamate (26).** A solution containing 1.0 g (5.5 mmol) of carbamate **16**, 0.8 g (19 mmol) of sodium hydroxide, 1.5 g (11 mmol) of potassium carbonate, and 0.4 g (1.3 mmol) of tetrabutylammonium hydrogen sulfate in 60 mL of benzene was heated at reflux for 20 min, and then 1.5 g (5.5 mmol) of mesylate **24** in 10 mL of benzene was added dropwise to the solution. The mixture was heated for 2 h, quenched with 100 mL of H_2O, and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 1.7 g (84%) of **26** as a white solid: mp 68−69 °C; IR (neat) 2975, 1702, 1616, 1403, 1360, and 1154 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.80 (s, 3H), 1.44 (s, 9H), 2.44 (t, 2H, J = 7.6 Hz), 3.66−3.71 (m, 2H), 3.92 (s, 6H), 5.02 (s, 1H), 5.49 (s, 1H), 6.01 (brs, 1H), 6.31 (t, 1H, J = 2.0 Hz), and 7.16 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 28.4, 30.5, 30.7, 48.6, 73.0, 81.1, 100.9, 111.0, 115.3, 138.1, 142.1, 148.8, 153.9, and 161.3. Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.18; H, 7.61; N, 3.73.

2-[2-(*tert*-Butoxycarbonyl-furan-2-yl-amino)ethyl]acrylic Acid Methyl Ester (19). To a solution containing 1.5 g (4.1 mmol) of carbamate **26**, 35 mL of methanol, and 0.5 mL of H_2O at room temperature was added 0.1 g (0.4 mmol) of pyridinium *p*-toluenesulfonate. The mixture was stirred at room temperature for 2 h, and to this solution was added 0.15 g (1.1 mmol) of potassium carbonate and the mixture was stirred for an additional 2 h at room temperature. The solution was quenched with H_2O, extracted with ethyl acetate, dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was purified by flash silica gel chromatography to give 0.98 g (85%) of **19** as a colorless oil: IR (neat) 2975, 1716, 1609, 1531, 1445, and 1303 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.42 (s, 9H), 2.56 (t, 2H, J = 6.8 Hz), 3.73 (s, 3H), 3.72 (t, 2H, J = 6.8 Hz), 5.60 (d, 1H, J = 1.2 Hz), 5.99 (brs, 1H), 6.19 (s, 1H), 6.32 (d, 1H, J = 2.0 Hz), and 7.15 (d, 1H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.3, 31.8, 47.7, 52.0, 81.4, 101.2, 111.1, 127.3, 137.4, 138.1, 148.6, 153.9, and 167.3. HRMS Calcd for $C_{15}H_{21}NO_5$: 295.1420. Found: 295.1419.

When the above reaction was carried out without the addition of potassium carbonate, the only product isolated (100%) corresponded to 2-[2-(*tert*-butoxy-carbonyl-furan-2-yl-amino)ethyl]acrylic acid 3-hydroxy-2-hydroxymethyl propyl ester, which was obtained as a clear oil: IR (neat) 3490, 2967, 1725, 1613, and 1502 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.84 (s, 3H), 1.38 (s, 9H), 2.54 (t, 2H, J = 6.8 Hz), 3.46 (bs, 2H), 3.52 (m, 4H), 3.70 (t, 2H, J = 6.8 Hz), 4.19 (s, 2H), 5.61 (s, 1H), 5.95 (brs, 1H), 6.19 (s, 1H), 6.31 (s, 1H), and 7.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.1, 28.2, 32.0, 40.9, 47.6, 66.9, 67.2, 77.5, 81.6, 101.6, 111.1, 127.9, 137.2, 138.3, 148.3, 154.1, and 167.3. Further treatment of this ester under the above conditions gave furanyl carbamate **19**.

5-Oxo-2,3,5,6-tetrahydro-4*H*-indole-1,3*a*-dicarboxylic Acid *N*-*tert*-Butyl Ester 3*a*-Methyl Ester (28). A solution of 0.1 g (0.3 mmol) of furan **19** in 10 mL of benzene was heated at 80 °C for 6 h in a sealed tube. The solution was concentrated under reduced pressure, and the residue was subjected to to flash silica gel chromatography to give 0.09 g (87%) of **28** as a yellow solid: mp 78−79 °C; IR (KBr) 2982, 1729, 1705, 1665, and 1474 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.49 (s, 9H), 1.74−1.83 (m, 1H), 2.30 (d, 1H, J = 16.0 Hz), 2.46−2.50 (m, 1H), 2.88 (d, 1H, J = 15.6 Hz), 2.91 (dd, 1H, J = 20.0 and 5.6 Hz), 3.06 (dd, 1H, J = 20.0 and 2.0 Hz), 3.67 (s, 3H), 3.75−3.85 (m, 2H), and 5.57−6.21 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.5, 29.9, 32.8, 36.9, 48.2, 52.9, 70.8, 81.2, 101.8, 138.5, 152.7, 172.8, and 207.3. Anal. Calcd for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74. Found: C, 60.73; H, 7.24; N, 4.35.

***tert*-Butyl 3*a*-(4-Methyl-2,6,7-trioxabicyclic[2.2.2]oct-1-yl)-5-oxo-2,3,3*a*,-4,5,6-hexahydroindol-1-carboxylate (30).**

A 0.3 g (0.7 mmol) sample of carbamate **26** in 10 mL of benzene in a sealed tube was heated at 165 °C for 14 h. The solution was concentrated under reduced pressure after cooling to room temperature, and the residue was purified by flash silica gel chromatography to give 0.17 g (70%) of ketone **30** as a white solid: mp 217−218 °C; IR (KBr) 1726, 1694, 1664, 1392, and 1176 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.74 (s, 3H), 1.50 (s, 9H), 1.54−1.63 (m, 1H), 2.03 (d, 1H, J = 16.0 Hz), 2.41 (dd, 1H, J = 12.8 and 7.2 Hz), 2.73 (dd, 1H, J = 22.4 and 5.6 Hz), 2.94 (d, 1H, J = 16.0 Hz), 3.09 (d, 1H, J = 22.4 Hz), 3.53−3.58 (m, 1H), 3.62−3.67 (m, 1H), 3.81 (s, 6H), and 6.27 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 28.7, 30.6, 31.9, 37.8, 48.1, 48.2, 52.5, 72.8, 80.3, 102.8, 112.0, 139.4, 152.9, and 209.8. Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.22; H, 7.40; N, 3.83.

Ethyl-*N*-[3-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-butenyl]-*N*-(2-furyl)carbamate (27). To a solution containing 2.5 g (16 mmol) of carbamate **17** and 250 mL of a 4:1 DMF/THF mixture at room temperature was added 5.3 g (16.4 mmol) of cesium carbonate. The reaction mixture was stirred at room temperature for 45 min and was then allowed to react with 7.7 g (27 mmol) of mesylate **24**. The mixture was heated at 70 °C for 8 h and quenched with 100 mL of H_2O and extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was subjected to flash silica gel chromatography to give 3.2 g (70%) of **27** as a colorless oil: IR (neat) 2954, 1716, 1616, 1502, 1296, and 1196 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.81 (s, 3H), 1.24 (t, 3H, J = 7.2 Hz), 2.46 (t, 2H, J = 8.0 Hz), 3.72−3.76 (m, 2H), 3.94 (s, 6H), 4.17 (q, 2H, J = 7.2 Hz), 5.03 (d, 1H, J = 0.8 Hz), 5.50 (s, 1H), 6.05 (brs, 1H), 6.34−6.35 (m, 1H), and 7.19 (d, 1H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.5, 31.1, 31.3, 49.5, 63.0, 73.5, 73.8, 103.2, 108.1, 111.9, 116.1, 139.4, 142.9, 149.5, 155.9. Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.40; H, 6.80; N, 4.09.

2-[2-Ethoxycarbonyl-furan-2-yl-amino)ethyl]acrylic Acid Ethyl Ester (20). To a solution containing 2.7 g (8 mmol) of the above carbamate **27**, 35 mL of methanol, and 5 mL of H_2O at room temperature was added 0.2 g (0.8 mmol) of pyridinium *p*-toluenesulfonate. The reaction mixture was stirred at room temperature for 1 h and was concentrated under reduced pressure. The residue was diluted with ethyl acetate and washed with water, and the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude oil was taken up in 35 mL of methanol. To this solution was added 0.3 g (1.8 mmol) of potassium carbonate, and the mixture was allowed to stir at room temperature for 3 h. The solution was quenched with H_2O and extracted with ethyl acetate, and the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by flash silica gel chromatography to give 1.5 g (71%) of **20** as a colorless oil: IR (neat) 2947, 1730, 1616, 1445, 1410, and 1139 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.21−1.25 (m, 3H), 2.59 (t, 2H, J = 6.8 Hz), 3.74 (s, 3H), 3.77 (t, 2H, J = 6.8 Hz), 4.15 (q, 2H, J = 6.8 Hz), 5.60 (s, 1H), 6.03 (brs, 1H), 6.20 (d, 1H, J = 0.8 Hz), 6.34−6.36 (m, 1H), and 7.19 (d, 1H, J = 0.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 31.7, 48.1, 52.1, 62.4, 102.5, 111.2, 127.4, 137.3, 138.8, 148.1, 155.2, and 167.3. HRMS Calcd for $C_{13}H_{17}NO_5$: 267.1107. Found: 267.1099.

5-Oxo-2,3,5,6-tetrahydro-4*H*-indole-1,3*a*-dicarboxylic Acid 1-Ethyl Ester 3*a*-Methyl Ester (29). A solution of 0.15 g (0.6 mmol) of furan **20** in 12 mL of benzene was heated in a sealed tube. The solution was concentrated under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.11 g (80%) of **29** as a clear oil: IR (neat) 2975, 1723, 1666, 1403, and 1324 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.28 (t, 3H, J = 6.8 Hz), 1.74−1.84 (m, 1H), 2.29 (d, 1H, J = 16.0 Hz), 2.50 (dd, 1H, J = 12.6 and 5.8 Hz), 2.89 (d, 1H, J = 16 Hz), 2.93 (d, 1H, J = 5.6 Hz), 3.05 (dd, 1H, J = 20.0 and 2.8 Hz), 3.65 (s, 3H), 3.78−3.83 (m, 2H), 4.18 (q, 2H, J = 6.8 Hz), and 5.79−6.23 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 32.9, 36.8, 47.9, 48.1, 52.7, 53.0, 61.7, 102.2, 138.4, 153.3, 172.7, and 207.1. HRMS Calcd for $C_{13}H_{17}NO_5$: 267.1107. Found: 267.1104.

5-Hydroxy-6-methyl-2,3,5,6-tetrahydro-4*H*-indole-1,3*a*-dicarboxylic Acid *N*-*tert*-Butyl Ester 3*a*-Methyl Ester (32). To a solution of 0.25 g (0.9 mmol) of furan **19** in 20 mL of benzene was added 1.7 mL (1.7 mmol) of a 1.0 M solution of dimethylaluminum chloride in hexane dropwise over a 5 min period. The reaction mixture was allowed to stir for 30 min at room temperature and was then quenched with 2 mL of H_2O and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.1 g (40%) of **32** as a colorless oil: IR (neat) 2975, 1716, 1374, and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (d, 3H, J = 6.8 Hz), 1.23−1.34 (m, 1H), 1.49 (s, 9H), 1.58 (t, 1H, J = 12.0 Hz), 1.71−1.79 (m, 1H), 2.25 (dd, 1H, J = 12.6 and 6.2 Hz), 2.39 (dd, 1H, J = 12.4 and 3.6 Hz), 2.64 (brs, 1H), 3.42 (dt, 1H, J = 11.0 and 6.0 Hz), 3.58−3.63 (m, 1H), 3.69 (s, 3H), 3.96−4.01 (m, 1H), and 5.99 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.3, 28.3, 28.6, 34.5, 36.6, 46.6, 52.9, 68.0, 80.5, 81.6, 111.4, 137.0, 152.6, and 174.8. HRMS Calcd for $C_{16}H_{25}NO_5$: 311.1733. Found: 311.1732.

To a solution of 0.2 g (0.5 mmol) of furan **19** in 10 mL of benzene was added 0.3 mL (0.6 mmol) of a 2.0 M solution of trimethylaluminum in toluene dropwise over a 5 min period. The reaction mixture was allowed to stir for 2 h at room temperature and was concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.1 g (82%) of **32**.

5-Hydroxy-6-methoxy-2,3,5,6-tetrahydro-4*H*-indole-1,3*a*-dicarboxylic Acid *N*-*tert*-Butyl Ester 3*a*-Methyl Ester (33 and 34). A solution of 0.2 g (0.7 mmol) of furan **19** in 10 mL of MeOH was heated to reflux for 4 h. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.05 g (22%) of *cis*-alcohol **33** and 0.14 g (64%) of *trans*-alcohol **34**. The minor *cis*-isomer **33** was isolated as a colorless oil: IR (KBr) 3499, 2974, 1730, 1478, and 1392 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50 (s, 9H), 1.59 (t, 1H, J = 12.4 Hz), 1.75−1.83 (m, 1H), 2.27 (dd, 1H, J = 12.4 and 5.2 Hz), 2.43 (dd, 1H, J = 12.0 and 3.6 Hz), 2.84 (d, 1H, J = 9.6 Hz), 3.36−3.45 (m, 1H), 3.46 (s, 3H), 3.63−3.67 (m, 1H), 3.69 (s, 3H), 3.71−3.76 (m, 1H), 3.83 (t, 1H, J = 4.6 Hz), and 6.40 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.5, 34.1, 38.9, 46.9, 52.9, 53.3, 56.6, 68.9, 80.8, 83.5, 103.1, 141.0, 152.2, and 174.0. Anal. Calcd for $C_{16}H_{25}NO_6$: C, 58.70; H, 7.70; N, 4.28. Found: C, 58.65; H, 7.81; N, 4.22.

The major *trans*-isomer **34** was obtained as a colorless oil: IR (KBr) 3449, 2974, 1716, 1471, and 1385 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.48 (s, 9H), 1.61 (t, 1H, J = 12.4 Hz), 1.69−1.78 (m, 1H), 2.21 (dd, 1H, J = 12.2 and 5.6 Hz), 2.55 (dd, 1H, J = 12.4 and 4.0 Hz), 2.81 (s, 1H), 3.37 (s, 3H), 3.42 (dt, 1H, J = 11.6 and 6.0 Hz), 3.64 (dd, 1H, J = 11.2 and 8.8 Hz), 3.68 (s, 3H), 3.75−3.81 (m, 1H), 3.91 (dd, 1H, J = 7.0 and 3.4 Hz), and 6.19 (brs,1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.5, 34.1, 38.9, 46.9, 52.9, 53.3, 56.0, 68.9, 80.8, 83.5, 103.1, 141.0, 152.2, and 174.0. HRMS Calcd for $C_{16}H_{25}NO_6$: 327.1682. Found: 327.1679.

The *cis*-isomer **33** was obtained as the exclusive stereoisomer by carrying out the reaction of furan **19** in the presence of aluminum methoxide in benzene. To a solution of 0.15 g (0.5 mmol) of **19** in 10 mL of benzene was added 0.32 g (2.0 mmol) of aluminum methoxide. The mixture was heated at 65 °C for 6 h under an argon atmoshere, and the solvent was removed under reduced pressure. The residue was subjected to flash silica gel chromatography to give **33** in 80% yield together with lesser quantities of ketone **28** (10%).

***cis*-5-(3,5-Dibromobenzoyloxy)-6-methoxy-2,3,5,6-tetrahydro-4*H*-indole-1,3*a*-dicarboxylic Acid *N*-*tert*-Butyl Ester 3*a*-Methyl Ester.** To a solution of 0.6 g (1.8 mmol) of *cis*-alcohol **33** in 40 mL of CH_2Cl_2 at room temperature was added 0.5 g (2.0 mmol) of 1,3-dicyclohexylcarbodiimide, 0.7 g (2.4 mmol) of 3,5-dibromobenzoic acid, and 0.05 g (0.5 mmol) of 4-(dimethylamino)pyridine. The reaction mixture was allowed to stir at room temperature for 4 h, and then the suspension was taken up in ether and filtered. The solvent

was then removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.9 g (83%) of the 3,5-dibromobenzoate ester of **33** as a white solid suitable for an X-ray crystal analysis: mp 153−154 °C; IR (KBr) 1725, 1558, 1390, and 1269 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50 (s, 9H), 1.81−1.90 (m, 1H), 2.07 (t, 1H, J = 12.4 Hz), 2.31 (dd, 1H, J = 12.4 and 6.0 Hz), 2.51 (dd, 1H, J = 12.0 and 3.2 Hz), 3.40 (s, 3H), 3.46 (dt, 1H, J = 11.2 and 6.0 Hz), 3.68 (dd, 1H, J = 10.0 and 9.2 Hz), 3.80 (s, 3H), 4.17 (t, 1H, J = 11.2 Hz), 5.12 (dt, 1H, J = 12.8 and 3.6 Hz), 6.35 (brs, 1H), 7.84 (t, 1H, J = 1.6 Hz), and 8.08 (d, 2H, J = 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.5, 33.9, 46.7, 53.2, 53.6, 58.6, 60.5, 72.0, 73.1, 81.0, 103.7, 123.2, 131.6, 133.4, 138.6, 141.4, 152.3, 163.7, and 173.6. Anal. Calcd for $C_{23}H_{27}NO_7Br_2$: C, 46.88; H, 4.62; N, 2.38. Found: C, 46.96; H, 4.65; N, 2.35.

***trans*-5-(3,5-Dibromobenzoyloxy)-6-methoxy-2,3,5,6-tetrahydro-4*H*-indole-1,3*a*-dicarboxylic Acid *N*-*tert*-Butyl Ester 3*a*-Methyl Ester.** To a solution of 0.3 g (1.0 mmol) of *trans*-alcohol **34** in 10 mL of CH_2Cl_2 at room temperature was added 0.2 g (1.1 mmol) of 1,3-dicyclohexylcarbodiimide, 0.3 g (1.1 mmol) of 3,5-dibromobenzoic acid, and 0.02 g (0.1 mmol) of 4-(dimethylamino)pyridine. The reaction mixture was allowed to stir at room temperature for 45 min, and the suspension was taken up in ether and filtered. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.5 g (84%) of the 3,5-dibromobenzoate ester of **34** as a white solid suitable for an X-ray crystal analysis: mp 146−147 °C; IR (KBr) 1726, 1710, 1665, 1560, and 1480 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.52 (s, 9H), 1.71−1.80 (m, 2H), 2.31 (dd, 1H, J = 12.2 and 5.6 Hz), 2.74 (dd, 1H, J = 12.2 and 4.4 Hz), 3.34 (s, 3H), 3.53 (dt, 1H, J = 11.4 and 5.6 Hz), 3.71 (t, 1H, J = 10.4 Hz), 3.80 (s, 3H), 4.36 (dd, 1H, J = 7.0 and 3.6 Hz), 4.35 (ddd, 1H, J = 12.0, 6.8 and 4.8 Hz), 6.24 (brs, 1H), 7.84 (t, 1H, J = 1.6 Hz), and 8.08 (d, 2H, J = 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.6, 34.1, 37.1, 47.2, 53.2, 54.8, 60.8, 72.2, 79.0, 81.5, 103.7, 123.2, 126.2, 131.6, 138.5, 141.8, 152.3, 163.5, and 173.2. Anal. Calcd for $C_{23}H_{27}NO_7Br_2$: C, 46.88; H, 4.62; N, 2.38. Found: C, 47.16; H, 4.73; N, 2.17.

6-Benzyloxy 5-Hydroxy-2,3,5,6-tetrahydro-4*H*-indole-1,3*a*-dicarboxylic Acid *N*-*tert*-Butyl Ester 3*a*-Methyl Ester (35 and 36). A solution of 1.0 g (3.4 mmol) of furan **19** in 20 mL of benzyl alcohol was heated at 70 °C for 4 h. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.3 g (20%) of *cis*-alcohol **35** and 0.8 g (60%) of *trans*-alcohol **36**. The *cis*-isomer **35** was obtained as a colorless oil: IR (neat) 3530, 1730, 1709, 1666, and 1388 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50 (s, 9H), 1.67 (t, 1H, J = 12.4 Hz), 1.76−1.84 (m, 1H), 2.27 (dd, 1H, J = 12.4 and 6.0 Hz), 2.43 (dd, 1H, J = 12.0 and 3.6 Hz), 2.82 (brs, 1H), 3.41 (dt, 1H, J = 11.4 and 6.0 Hz), 3.66−3.67 (m, 1H), 3.69 (s, 3H), 3.74−3.80 (m, 1H), 4.12 (m, 1H), 4.48−4.54 (m, 1H), 4.70−4.79 (m, 1H), 6.44 (brs, 1H), and 7.27−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.5, 33.8, 36.9, 46.6, 52.9, 66.7, 71.6, 73.0, 77.5, 81.1, 103.4, 128.1, 128.2, 128.7, 138.3, 142.4, 152.5, and 174.0. HRMS Calcd for $C_{22}H_{29}NO_6$: 403.1995. Found: 403.2003.

The *trans*-isomer **36** was isolated as a colorless oil: IR (neat) 3480, 1730, 1709, 1666, and 1388 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.51 (s, 9H), 1.62 (t, 1H, J = 12.4 Hz), 1.71−1.81 (m, 1H), 2.23 (dd, 1H, J = 12.6 and 6.0 Hz), 2.42 (brs, 1H), 2.58 (dd, 1H, J = 12.4 and 4.0 Hz), 3.46 (dt, 1H, J = 11.6 and 6.0 Hz), 3.65−3.69 (m, 1H), 3.70 (s, 3H), 3.85−3.90 (m, 1H), 4.12 (dd, 1H, J = 7.4 and 3.2 Hz), 4.51 (d, 1H, J = 11.2 Hz), 4.73 (m, 1H), 6.31 (brs, 1H), and 7.31−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.5, 34.2, 38.9, 47.0, 52.9, 69.3, 69.9, 77.4, 80.9, 81.9, 103.5, 127.8, 128.1, 128.6, 138.8, 141.1, 152.3, and 174.0. HRMS Calcd for $C_{22}H_{29}NO_6$: 403.1995. Found: 403.1988.

***tert*-Butyl *N*-[2-(5-Methylfuryl)]carbamate.** A solution of 2.3 g (18 mmol) of 5-methylfuran-2-carboxylic acid, 5.8 g (21 mmol) of diphenylphosphoryl azide, and 2.2 g (22 mmol) of triethylamine in 25 mL of *tert*-butyl alcohol was heated at reflux for 15 h. The reaction mixture was cooled to room temperature and poured into 250 mL of a saturated sodium bicarbonate solution at 0 °C. The resultant percipitate was collected by filtration, washed with 50 mL of H_2O, and dried under reduced pressure to give 3.1 g (87%) of *tert*-butyl *N*-[2-(5-methylfuryl)]carbamate as a white solid: mp 76−77 °C; IR (KBr) 3331, 1550, and 1709 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.49 (s, 9H), 2.21 (s, 3H), 5.90 (brs, 2H), and 6.42 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.3, 28.2, 81.0, 97.4, 106.7, 143.1, 146.2, and 152.4. HRMS Calcd for $C_{10}H_{15}NO_3$: 197.1052. Found 197.1056.

***tert*-Butyl *N*-[3-(2-Methylbutenyl)]-*N*-[2-(5-methylfuryl)]carbamate (37).** A solution containing 3.7 g (19 mmol) of the above furanyl carbamate, 2.6 g (65 mmol) of powdered sodium hydroxide, 5.2 g (38 mmol) of potassium carbonate, and 0.6 g (1.8 mmol) of tetrabutylammonium hydrogen sulfate in 50 mL of benzene was heated at reflux for 30 min, and then 4.2 g (28 mmol) of 2-methyl-4-bromobutene in 25 mL of benzene was added dropwise to the solution. The mixture was heated for an additional 4 h, quenched with 50 mL of H_2O, and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 3.5 g (70%) of **37** as a colorless oil: IR (neat) 3075, 1709, 1623, and 1573 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.44 (s, 9H), 1.73 (s, 3H), 2.24 (s, 3H), 2.26 (t, 2H, J = 7.2 Hz), 3.62 (t, 2H, J = 7.2 Hz), 4.70 (s, 1H), 4.75 (s, 1H), 5.86 (brs, 1H), and 5.90 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.6, 22.4, 28.1, 36.6, 47.4, 80.7, 102.6, 106.4, 111.7, 142.7, 146.5, 147.7, and 154.1. HRMS Calcd for $C_{15}H_{23}NO_3$: 265.1678. Found: 265.1686.

3*a*,5-Dimethyl-5-hydroxy-3,3*a*,4,5-tetrahydro-2*H*-indole (39). A solution of 0.3 g (1.2 mmol) of furan **37** in 12 mL of benzene was heated in a sealed tube at 190 °C for 12 h. The solution was concentrated under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.18 g (89%) of **39** as a colorless solid: mp 82−83 °C; IR (KBr) 3300, 2961, 1795, and 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.06 (s, 3H), 1.42 (s, 3H), 1.56 (m, 1H), 1.78 (m, 1H), 1.82 (d, 1H, J = 13.2 Hz), 2.22 (d, 1H, J = 13.2 Hz), 3.69 (m, 1H), 3.88 (m, 2H), 6.10 (d, 1H, J = 4.0 Hz), and 6.15 (d, 1H, J = 4.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.8, 29.0, 40.3, 47.9, 51.7, 57.5, 69.6, 120.8, 146.9, and 177.3. HRMS Calcd for $C_{10}H_{15}NO$: 165.1154. Found: 165.1160.

***tert*-Butyl *N*-[2-(5-*p*-Nitrophenylfuryl)]carbamate.** A solution of 3.0 g (13 mmol) of 5-(*p*-nitrophenyl)furan-2-carboxylic acid, 3.9 g (14 mol) of diphenylphosphoryl azide, and 1.5 g (15 mmol) of triethylamine in 50 mL of *tert*-butyl alcohol was heated at reflux for 16 h. The reaction mixture was cooled to room temperature and poured into 300 mL of saturated sodium bicarbonate. The resulting mixture was extracted with ether and washed with brine, and the combined organic layers were dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 3.4 g (86%) of *tert*-butyl *N*-[2-(5-*p*-nitrophenylfuryl)]carbamate as a yellow solid: mp 147−148 °C; IR (KBr) 3409, 1706, 1557, 1331, and 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.53 (s, 9H), 6.22 (brs, 1H), 6.84 (d, 1H, J = 3.6 Hz), 7.10 (brs, 1H), 7.59 (d, 2H, J = 9.2 Hz), and 8.17 (d, 2H, J = 9.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.1, 82.0, 96.1, 111.6, 122.6, 124.3, 136.1, 144.3, 145.5, 147.7, and 150.9. Anal. Calcd for $C_{15}H_{16}N_2O_5$: C, 59.21; H, 5.30; N, 9.21. Found: C, 59.01; H, 5.31; N, 9.00.

***tert*-Butyl *N*-[3-(2-Methylbutenyl)]-*N*-[2-(5-*p*-nitrophenylfuryl)] Carbamate (38).** A solution containing 0.9 g (2.5 mmol) of the above furanyl carbamate, 0.5 g (13 mmol) of powered sodium hydroxide, 2.0 g (15 mmol) of potassium carbonate, and 0.1 g (0.3 mmol) of tetrabutylammonium hydrogen sulfate in 30 mL of benzene was heated at reflux for 30 min, and then 0.7 g (5 mmol) of 2-methyl-4-bromobutene in 10 mL of benzene was added dropwise to the solution. The mixture was heated for an additional 12 h, quenched with 50 mL of H_2O, and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.7 g (57%) of **38** as an orange solid: mp 74−75 °C; IR (KBr) 2976, 1709, 1559, 1337, and 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50 (s, 9H), 1.78 (s, 3H), 2.36 (t,

2H, J = 8.0 Hz), 3.84 (t, 2H, J = 8.0 Hz), 4.74 (s, 1H), 4.81 (s, 1H), 6.05 (brs, 1H), 6.86 (d, 1H, J = 3.6 Hz), 7.68 (d, 2H, J = 8.0 Hz), and 8.22 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.4, 28.2, 36.9, 46.5, 81.9, 102.1, 111.0, 112.4, 122.9, 124.4, 136.3, 142.3, 145.8, 146.0, 150.3, and 152.7. Anal. Calcd for $C_{20}H_{24}N_2O_5$: C, 64.50; H, 6.50; N, 7.52. Found: C, 64.54; H, 6.55; N, 7.39.

5-Hydroxy-3*a*-methyl-5-*p*-nitrophenyl-3,3*a*,4,5-tetrahydro-2*H*-indole (40). A solution of 0.3 g (0.8 mmol) of furan **38** in 15 mL of benzene was heated in a sealed tube at 180 °C for 16 h. The solution was concentrated under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.18 g (82%) of **40** as a colorless solid: mp 209−210 °C; IR (KBr) 3197, 1640, 1517, and 1342 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.61 (s, 3H), 1.70 (m, 1H), 1.75 (brs, 1H), 1.76 (m, 1H), 2.25 (d, 1H, J = 13.6 Hz), 2.76 (d, 1H, J = 13.6 Hz), 3.73 (m, 1H), 3.95 (m, 1H), 6.50 (d, 1H, J = 10.4 Hz), 7.63 (d, 1H, J = 10.4 Hz), 7.74 (d, 2H, J = 6.8 Hz), and 8.23 (d, 2H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.0, 40.5, 47.6, 52.5, 57.9, 73.3, 123.6, 125.0, 127.7, 142.3, 147.4, 153.2, and 176.3. HRMS (M + H) Calcd for $C_{15}H_{17}N_2O_3$: 273.1239. Found: 273.1235.

5-Hydroxy-6-methoxy-3*a*,5-dimethyl-2,3,3*a*,4,5,6-hexahydroindole-1-carboxylic Acid *tert*-Butyl Ester (43). A solution of 0.2 g (0.6 mmol) of furan **37** in 5 mL of methyl alcohol was heated to 140 °C for 17 h. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give a 2:1 diastereomeric mixture of **43** in 76% yield. Extensive shaving of the front and tail fractions eventually gave samples of each diastereomer. The major isomer was obtained as a colorless oil: IR (neat) 3420, 2975, 2819, 1709, and 1545 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.04 (s, 3H), 1.35 (s, 3H), 1.37 (d, 1H, J = 12 Hz), 1.46 (bs, 10H), 1.58 (m, 1H), 1.66 (d, 1H, J = 12.0 Hz), 1.98 (dd, 1H, J = 12.0 and 6.8 Hz), 2.16 (dd, 1H, J = 12.8 and 3.6 Hz), 3.34 (s, 3H), 3.48 (m, 1H), 3.62−3.69 (m, 1H), and 6.30 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.4, 21.0, 28.4, 31.5, 36.9, 44.8, 48.5, 58.1, 79.9, 83.3, 85.0, 103.1, 140.8, and 153.9. HRMS Calcd for $C_{16}H_{27}NO_4$: 298.2018. Found: 298.2026.

The minor diastereomer was isolated as a colorless oil: IR (neat) 3446, 2969, and 1702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.11 (s, 3H), 1.38 (s, 3H), 1.46 (bs, 10H), 1.49 (d, 1H, J = 12.0 Hz), 1.58 (dd, 1H, J = 12.0 and 6.0 Hz), 1.67 (dd, 1H, J = 12.0 and 3.0 Hz), 1.95 (dd, 1H, J = 12.0 and 6.0 Hz), 2.06 (d, 1H, J = 12.0 Hz), 3.34 (s, 3H), 3.40−3.60 (m, 2H), and 6.40 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 21.8, 28.4, 33.9, 36.1, 49.5, 50.8, 55.8, 80.7, 83.9, 84.9, 102.0, 141.0, and 154.1. HRMS Calcd for $C_{16}H_{27}NO_4$: 298.2018. Found: 298.2012.

8-Hydroxy-2,5,8-trimethyl-2-azabicyclo[3.2.2]nonan-6-one (45). To a solution of 0.02 g (0.14 mmol) of tetrahydro-2*H*-indole **39** in 10 mL of CH_2Cl_2 was added 0.02 g (0.15 mmol) of iodomethane, and the reaction was stirred for 12 h. The solution was concentrated under reduced pressure, and to the residue was added 1 mL of H_2O and 0.5 g (3.1 mmol) of K_2CO_3. The aqueous layer was extracted with ether, and the combined organic layers were dried over $MgSO_4$ and subjected to flash silica gel chromatography to give 0.02 g (90%) of **45** as a white solid: mp 110−111^{o}C; IR (KBr) 3281, 2925, and 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97 (s, 3H), 1.27 (s, 3H), 1.47 (dq, 1H, J = 13.6 and 2.0 Hz), 1.61 (dd, 1H, J = 14.0 Hz), 1.96 (d, 1H, J = 14.0 Hz), 2.14 (td, 1H, J = 14.0 (t) and 4.8 (d) Hz), 2.31 (t, 1H, J = 4.8 Hz), 2.38 (d, 1H, J = 4.8 Hz), 2.42 (s, 3H), 2.61 (dd, 1H, J = 17.0 and 2.5 Hz), 2.72−2.78 (m, 2H), and 3.46 (s, 1H, exchanged with D_2O); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.4, 30.1, 33.3, 36.7, 45.8, 46.8, 49.8, 50.3, 66.9, 67.3, and 213.4. HRMS Calcd for $C_{11}H_{19}NO_2$: 197.1416. Found: 197.1416.

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for new compounds lacking analyses together with ORTEP drawings for the 3,5-dibromo-benzoate esters of alcohols **33** and **34** as well as compound **40**. This material is available free of charge via the Internet at http://pubs.acs.org.

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