IMDAF Cycloaddition as a Method for the Preparation of Pyrrolophenanthridine Alkaloids

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Acylation of 5-amino-2-furancarboxylic acid methyl ester with alkenoyl acid chlorides gives 2-amidofurans that undergo intramolecular Diels−Alder cycloadditions. The reactions occur at 165 °C in toluene or at 100 °C when 4 M ethereal $LiClO_4$ was used as the solvent. The resultant dihydroindoles are formed by the nitrogen lone pair assisted ring opening of the initial oxa-bridged cycloadducts, followed by loss of water. Under certain conditions, alternative cationic cyclization routes become important pathways. Several members of the pyrrolophenanthridine class of alkaloids were obtained by a short, efficient method based on the intramolecular Diels−Alder furan cycloaddition of 2-amidofurans containing a tethered alkenyl group. The resulting dihydroindoles were elaborated in one step to the 1*H*-pyrrolo[3,2,1-*de*]phenanthridine ring system by a free radical induced cyclization using bis(tributyltin).

The importance and versatility of the Diels−Alder reaction for the construction of unsaturated six-membered ring systems is well documented in the literature.[1] An area which is gaining prominence in Diels−Alder chemistry involves the use of heteroaromatic compounds as either the diene or dienophile component.[2−4] By far the most extensively studied five-membered heteroaromatic system for Diels−Alder cycloaddition is furan and its substituted derivatives.[5−7] The resultant 7-oxabicyclo-[2.2.1]heptanes are valuable synthetic intermediates which have been further elaborated to substituted arenes, carbohydrate derivatives, and various natural products.[8−17] A crucial synthetic transformation employing these intermediates involves cleavage of the oxygen bridge to produce functionalized cyclohexene derivatives.[18−23] In many cases, however, the Diels−Alder strategy is not feasible because of the low reactivity of furan toward monoactivated dienophiles.

The intramolecular Diels−Alder reaction of furans, often designated as IMDAF, helps to overcome the sluggishness of this heteroaromatic ring system toward [4 + 2]-cycloaddition. Not only do IMDAF reactions allow for the preparation of complex oxygenated polycyclic compounds, they often proceed at lower temperatures than their intermolecular counterparts.[24] Even more significantly, unactivated π-bonds are often suitable dienophiles for the internal cycloaddition.[7] While the carbocyclic IMDAF reaction has been the subject of many reports in the literature,[7] much less is known regarding the cycloaddition behavior of furan Diels−Alder systems that contain heteroatoms attached directly to the furan ring.[25−27]

In this regard, we have recently demonstrated that simple 2-aminofurans such as **1** react with various dienophiles in an intermolecular fashion with high regioselectivity. The resultant ring-opened cycloadducts **3** are readily dehydrated using $BF_3{\cdot}OEt_2$ to give polysubsti-

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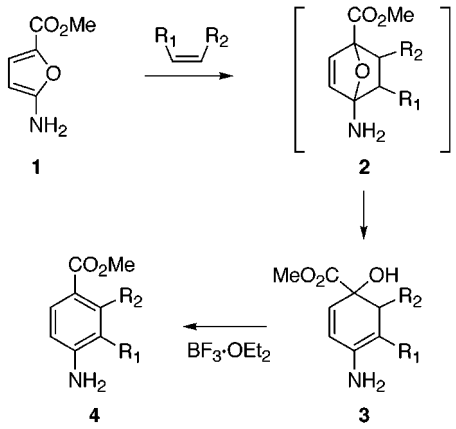
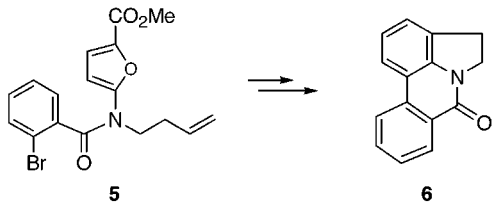
Scheme 1



tuted anilines **4** (Scheme 1).[25] This reaction sequence is one of only a handful of reports that describe the [4 + 2]-cycloaddition of furans substituted with an amino group at the 2-position of the heteroaromatic ring.[26] The paucity of examples of this type of reaction is undoubtedly due to the unavailability of the highly unstable parent 2-aminofuran system.[28] However, the presence of the electron-withdrawing carbomethoxy group stabilizes the furan ring[29] and allows for the preparation of various polysubstituted anilines.[25] Having established the feasibility of 5-substituted 2-aminofurans to undergo bimolecular Diels−Alder reactions, we initiated a study of the intramolecular reaction. Amidofurans containing olefinic tethers were prepared to determine their ability to undergo the IMDAF reaction, thus providing access to various polyheterocyclic ring systems. In conjunction with these studies, we now report the application of this methodology to a general synthesis of the pyrrolophenanthridine class of alkaloids (i.e., **6**).[30]



Results and Discussion

The IMDAF reaction has been extensively studied since its initial report in the literature over three decades ago.[31] These research efforts have culminated in a broad outline of both the scope and limitations of the reaction. The effect of a number of variables[32,33] including (i) tether length,[34] (ii) heteroatom substitution in the tether,[35] (iii) substitution on both the tether and furan ring,[36] and (iv) the use of high pressures,[37] aqueous conditions,[38] Lewis acids,[39] cyclodextrin catalysts,[40] and high temperatures[41] was probed. These studies were carried out as a consequence of either the reluctance of the furan of interest to undergo the desired IMDAF reaction or the ease of cycloreversion. In our laboratory, these problems have been overcome by the placement of an amino nitrogen atom adjacent to the furan oxygen, as exemplified by the transformations outlined in Scheme 1. In an effort to further investigate the scope of IMDAF cycloadditions, a number of new furan substrates have been prepared and tested for cyclization. Tethered amidofurans **7** and **8** were easily synthesized starting from aminofuran **1** and 4-pentenoyl chloride. Gratifyingly, the thermal reaction of **7** at 200 °C for 24 h afforded tetrahydroquinolinone **9** in 66% yield. Heating a sample of the N-methylated analogue **8** at 160 °C furnished a 6:1 mixture of cyclohexadienol **10** (77%) and tetrahydroquinolinone **11** (13%), the former being easily converted to **11** by treatment with BF_3·OEt_2. In both cases, the initial cycloadducts were not isolated, as they readily underwent ring opening, assisted by the lone pair of electrons on the adjacent nitrogen atom (Scheme 2).

For comparison purposes, we have also investigated the IMDAF chemistry of the closely related amidofurans **12** and **13** where the carbonyl group has been switched from "inside" the tether to the "outside" position (Scheme 3). Heating a sample of furan **12** afforded a 2:1 mixture of cyclohexadienol **14** (52%) and dihydroindole **15** (25%). As before, cyclohexadienol **14** was converted to **15** (74%) on treatment with BF_3·OEt_2. Similar results were obtained when the tether was lengthened by one methylene unit as illustrated in Scheme 3 for the conversion of furan **13** into a 2:1 mixture of **16** and **17** (94%). Tetrahydroquinoline **17** was formed in 84% yield when **16** was heated with BF_3·OEt_2 at 80 °C.

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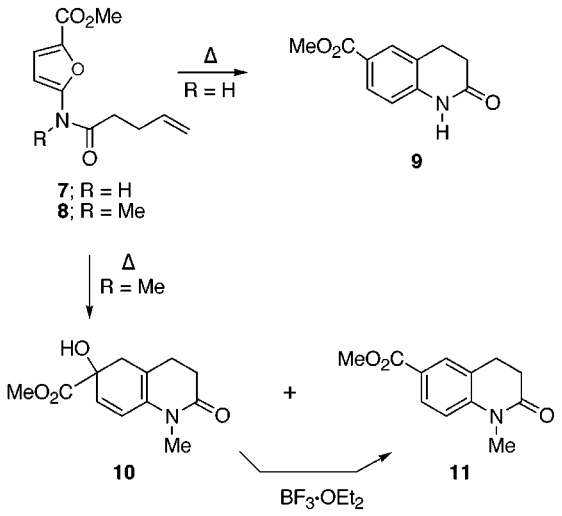
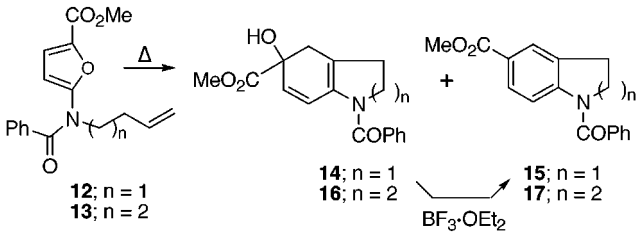
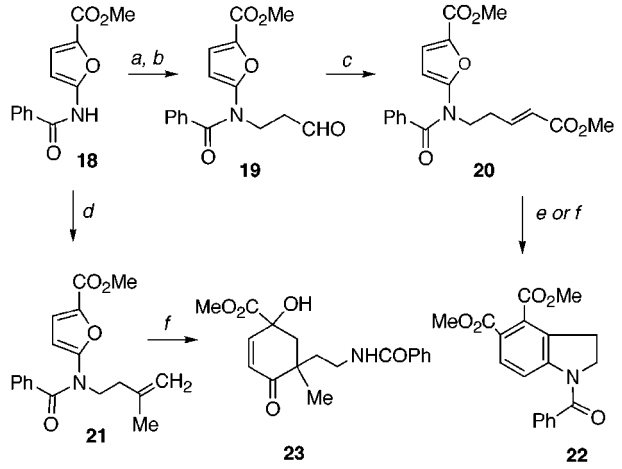
Scheme 2



Scheme 3



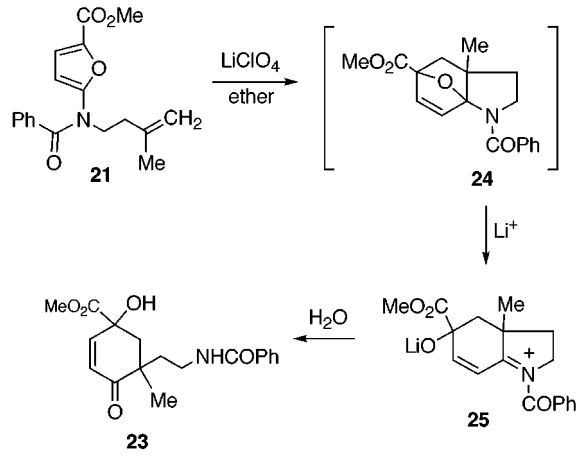
Scheme 4



Conditions: (*a*) 2-(2-bromoethyl)-1,3-dioxolane, Cs_2CO_3, THF/DMF, 75 °C, 84%; (*b*) oxalic acid, MeOH/H_2O, 50 °C, 77%; (*c*) $Ph_3P{=}CHCO_2Me$, rt, 79%; (*d*) 4-bromo-2-methyl-1-butene, Cs_2CO_3, THF/DMF, 80 °C, 74%; (*e*) toluene, sealed tube, 160 °C, 24h; (*f*) $LiClO_4$, 100 °C, 24 h.

To test the importance of dienophile activation, amidofurans **20** and **21** were prepared according to the sequence of reactions outlined in Scheme 4. Ester activation of the π-bond had little effect on the efficiency of the IMDAF cycloadditions. The temperature required for the reaction (190 °C) and yield of the resulting dihydroindole **22** were similar to that encountered with the unactivated *N*-butenyl amidofuran **12** (77%). Incorporation of a methyl substituent on the alkenyl π-bond, however, completely suppressed the thermal IMDAF cycloaddition even at temperatures as high as 240 °C in toluene (sealed tube). The failure of **21** to undergo the Diels−Alder reaction is consistent with FMO theory.[42] Placement of an alkyl substituent on the π-bond raises the LUMO energy of the dienophile and significantly diminishes the rate of the [4 + 2]-cycloaddition reaction.

Scheme 5



Lithium perchlorate in diethyl ether has become recognized as an excellent medium in which Diels−Alder reactions can be performed.[43] Some reactions, which usually take place only under vigorous conditions, can occur smoothly under mild conditions when ethereal lithium perchlorate is used as the solvent. In certain cases, it also allows for the synthesis of previously inaccessible cycloadducts. Because many of these sluggish reactions were accelerated under high pressure, the effect of $LiClO_4$/ether on the Diels−Alder reaction was attributed by Grieco and co-workers to a better aggregation between the reaction partners owing to a hydrophobic effect or "internal pressure" on the reactants encapsulated in solvent cavities.[44] This correlation is in line with similar effects observed using water, a solvent with a very large cohesive pressure.[45] More recent work indicates that these accelerations are not only due to a solvent effect but also to catalysis by the lithium ion.[46]

During the course of our studies we have found that the IMDAF cycloadditions of furanamides such as **21** can be performed by using 4 M ethereal $LiClO_4$ as solvent. Thus, the use of $LiClO_4$/ether as solvent allowed the activated furanamide **21** to undergo cycloaddition whereas no reaction occurred under strictly thermal conditions. The Grieco conditions were also successfully employed using the unactivated four-carbon tethered furanamide **12** which gave dihydroindole **15** in 73% isolated yield. In the case of furan **21**, the IMDAF cycloaddition now occurred to produce cyclohexenone **23** as the major product in 68% yield. This reaction presumably involved an initial [4 + 2]-cycloaddition to give **24** followed by rapid ring opening to afford iminium ion **25** which was subsequently converted to **23** upon reaction with water.

When the IMDAF reaction of carbamate **26** was carried out in 4 M ethereal $LiClO_4$, efficient [4 + 2]-cycloaddition occurred at 100 °C to give dihydroindole **27** as the exclusive product in 66% yield. Interestingly, the five-

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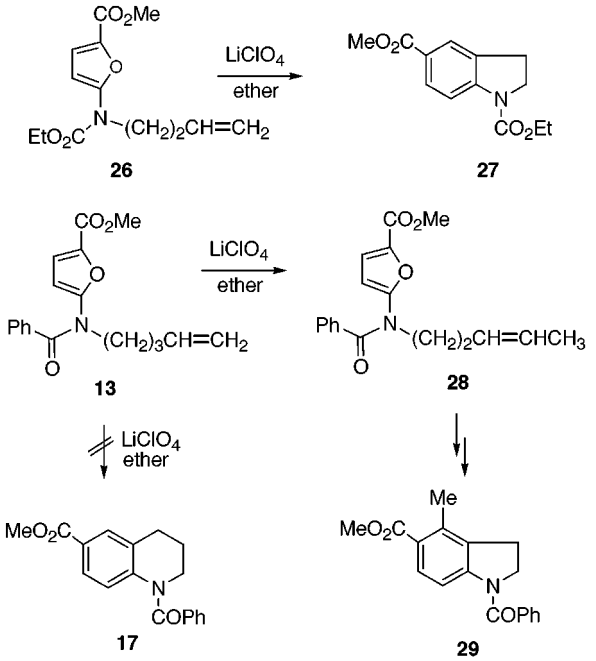
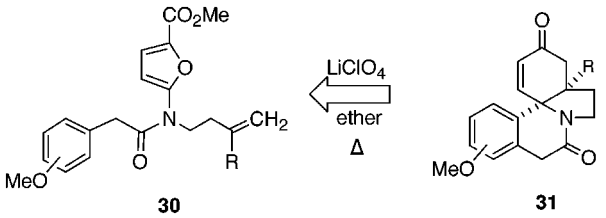
Scheme 6



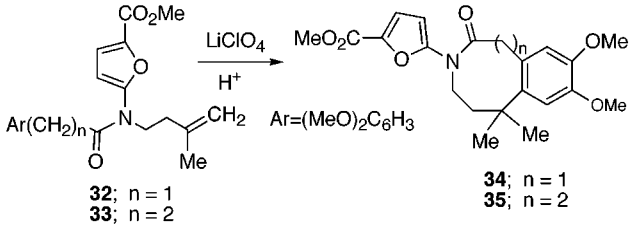
carbon tethered furanamide **13** was unreactive when $LiClO_4$/ether was used as the solvent. More forcing conditions resulted in the isolation of dihydroindole **29** (73%) which can be attributed to a 1,3-hydrogen shift to internalize the double bond (i.e., **28**), followed by [4 + 2]-cycloaddition and subsequent elimination of water.

Our attention was next directed toward the synthesis and cycloaddition behavior of aromatic furanamides such as **30** under typical Grieco conditions. 2-Amidofurans of this type are of interest to our group because of their potential to undergo tandem Diels−Alder/*N*-acyliminium ion cyclization and eventually lead to the erythrinane (**31**) skeleton of alkaloids.[47] It was found, however, that

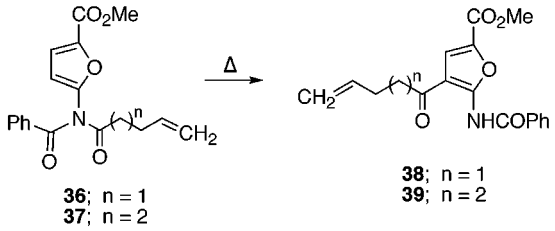


furanamides **32** and **33** did not undergo the desired cyclization. Instead, reaction of **32** (or **33**) in $LiClO_4$/ether with a trace of camphorsulfonic acid provided a new compound whose ^{1}H NMR indicated that the furan ring was still intact. Moreover, the ^{1}H NMR showed the presence of two equivalent methyl groups at δ 1.17 (s, 6H). Further spectroscopic analysis (^{13}C NMR, infrared, and mass spectroscopy) indicated that lactam **34** (or **35**) was the sole product formed from this reaction (Scheme 7). A reasonable mechanism to rationalize this transformation involves alkene protonation to generate a tertiary carbocation followed by an internal Friedel−Crafts alkylation. The propensity of activated aromatic rings to undergo cationic cyclization is well-documented in the literature,[48] thereby providing good analogy for this reaction.

Scheme 7



Scheme 8



We next turned our attention to the thermal behavior of the closely related imido-substituted furans **36** and **37** which were easily prepared from aminofuran **1** by standard acylation conditions. Surprisingly, both compounds afforded no products derived from an IMDAF process. Instead they underwent a Fries-type rearrangement to give the 3-acylated furans **38** (42%) and **39** (51%) in modest yield. Although the Fries rearrangement is generally carried out using Lewis acids as promoters,[49] there are some examples where the reaction occurs when *N*-acyl derivatives of arylamines are heated at 160−250 °C.[50] As far as we can tell, there are no examples of this type of Fries rearrangement using *N*-acyl-substituted furans.

As was noted earlier, the presence of the electron-withdrawing carbomethoxy substituent on the furan stabilizes the highly reactive 2-amino-substituted furanyl ring system. In addition to the carbomethoxy group, the nitro functionality may also serve in this capacity. 2,5-Dinitrofuran (**40**) is readily available from 2-nitrofuran by treatment with concentrated nitric acid.[51] Substitution of one of the nitro groups occurs upon reaction of **40** with various heteronucleophiles, presumably by an addition−elimination mechanism.[52] Using this protocol, we synthesized *N*-tosylamino furans **40** and **41** in 94% and 92% yields, respectively. Heating a sample of **40** in toluene at reflux resulted in a mixture of phenols **44** (25%) and **48** (7%). Similar results were obtained when the dienophile tether was lengthened by one methylene unit as illustrated in Scheme 9 for the conversion of nitrofuran **41** into **45** (55%) and **49** (7%). From these results it is evident that nitro-substituted aminofurans display some interesting cycloaddition chemistry. Two

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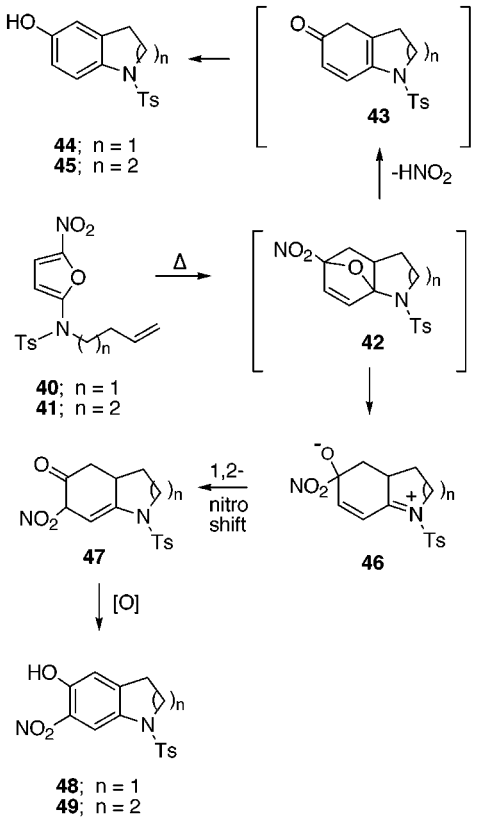
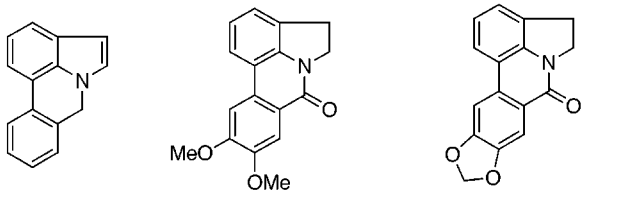
Scheme 9



distinct reaction pathways are observed: (1) cycloaddition followed by loss of the nitro group to give phenols (i.e., **44** and **45**) and (2) cycloaddition followed by 1,2-nitro migration to eventually afford the corresponding *o*-nitrophenols **48** and **49**. We had previously observed 1,2-nitro migrations in intermolecular cycloaddition reactions of related nitrofurans,[25] and similar 1,2-shifts have been reported in cycloadditions involving silyl-substituted furans,[53] thereby providing good precedence for this rearrangement pathway.

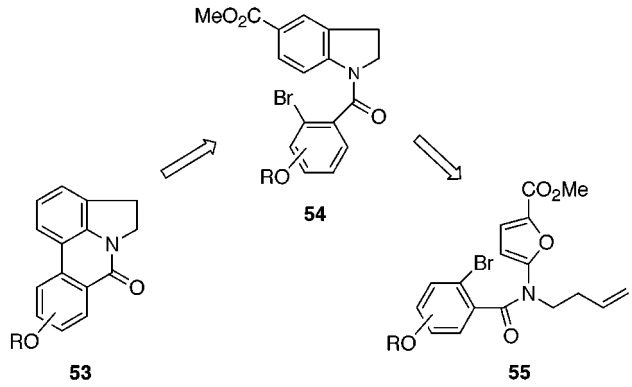
Having established the suitability of 2-amidofurans to generate dihydroindoles, we turned our attention to the application of the method toward the synthesis of oxoassoanine (**51**)[54,55] and anhydrolycorin-7-one (**52**).[56] These



50 **51**; oxoassoanine **52**; anhydrolycorin-7-one

compounds are members of the pyrrolophenanthridine class of alkaloids which have been isolated from various species of *Amaryllidaceae*.[57] The 1*H*-pyrrolo[3,2,1-*de*]-

Scheme 10



phenanthridine ring system (**50**) constitutes the core structural framework of the pyrrolophenanthridine alkaloids. Although a number of synthetic routes are available for this ring system, many of these suffer from low yields and a lack of generality.[58] Our approach to this skeleton is shown in retrosynthetic format in Scheme 10. This approach is centered on the construction of the key dihydroindole **54**. We reasoned that **54**, formed by an IMDAF cycloaddition of amidofuran **55**, should undergo a metal-mediated coupling to form the biaryl carbon−carbon bond of **53**.

A short synthesis of oxoassoanine (**51**) and anhydrolycorin-7-one (**52**) was carried out as depicted in Scheme 11. Acylation of aminofuran **1** with the appropriate acyl chloride proceeded in 85−90% yield. It was crucial to the success of the reaction that the acid chloride be added slowly to the reaction mixture using a syringe pump. Alkylation of amides **56** and **57** was carried out as described earlier to give the advanced intermediates **58** and **59**. The IMDAF cycloadditions of these substrates were successful both thermally (165 °C) or using the Grieco conditions (80% yield). The next step in the sequence required the introduction of a new carbon−carbon bond between the two aromatic rings. Aryl−aryl bond formation is often the key step in many natural product syntheses. As such, a variety of methods have been developed to carry out this coupling reaction.[59] Due to literature precedence,[60] we felt that a radical cyclization would be a particularly attractive method for the required biaryl coupling. After some experimentation, it was found that the use of bis(tributyltin) under photochemical conditions[61] afforded the aryl-coupled products **62** and **63** in 71% and 79% yields, respectively. Final elaboration to oxoassoanine (**51**) and anhydrolycorin-7-one (**52**) was accomplished in 80% yield by a two-step sequence composed of ester hydrolysis followed by

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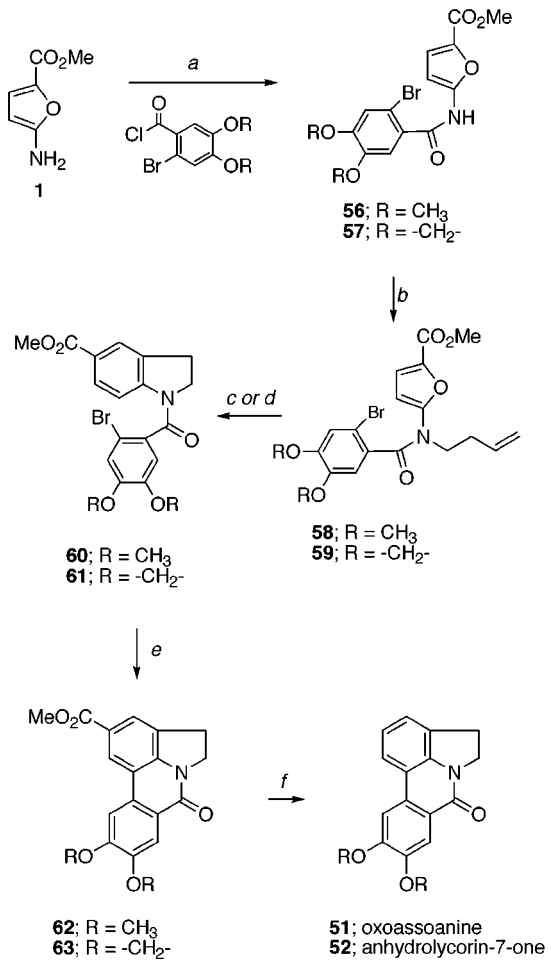
Scheme 11



Conditions: (*a*) acid chloride, pyridine, benzene, reflux, 12 h; (*b*) 4-bromo-1-butene, Cs_2CO_3, DMF/THF, 70-80 °C, 3h; (*c*) toluene, sealed tube, 165 °C, 20 h; (*d*) 5M $LiClO_4$, ether, 100 °C, 36-42 h; (*e*) $Bu_3SnSnBu_3$, hν; (*f*) (*i*) KOH/MeOH, reflux, 2 h; (*ii*) Cu bronze, quinoline, 225 °C, 2.5 h.

heating the resultant acid in quinoline (220 °C) in the presence of copper bronze.[62]

In conclusion, this paper describes a versatile new approach to dihydroindoles with various substitution patterns that can be applied to the synthesis of several pyrrolophenanthridine alkaloids. The synthetic procedure described here involves an intramolecular Diels–Alder reaction of a 2-amidofuran containing a tethered alkenyl group on the nitrogen atom. The resultant dihydroindoles are formed by a subsequent nitrogen atom lone pair assisted ring opening of the initially formed oxa-bridged cycloadduct followed by loss of water. Further studies of the IMDAF cycloaddition of 2-amidofurans 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 under an atmosphere of dry argon in flame-dried glassware. 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. *A cautionary note*: heating an ether solution in a sealed tube can generate considerable pressure and researchers are advised to utilize a safety shield when carrying out sealed tube reactions. Also, researchers should handle the resulting products derived from the $LiClO_4$/ether promoted cycloadditions with care since contact between organic compounds and perchlorates are known to result in occasional explosions.[63]

5-(Pent-4-enoylamino)furan-2-carboxylic Acid Methyl Ester (7). A solution containing 0.2 mL (2.0 mmol) of 4-pentenoic acid in 15 mL of CH_2Cl_2 was treated dropwise with 0.5 mL (5.8 mmol) of oxalyl chloride. The mixture was stirred at 25 °C for 12 h, and the solvent was removed under reduced pressure. The resulting 4-pentenoyl chloride was dissolved in 5 mL of CH_2Cl_2 and was used without further purification. To a mixture containing 0.15 g (1.1 mmol) of furan **1**[29] and 0.18 mL (2.2 mmol) of pyridine in 10 mL of CH_2Cl_2 was added dropwise a solution of the above 4-pentenoyl chloride, and the mixture was stirred at 0 °C for 3 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.24 g (96%) of **7** as a white solid: mp 83–84 °C; IR (KBr) 3284, 1696, and 1537 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.44–2.51 (m, 2H), 2.54–2.60 (m, 2H), 3.86 (s, 3H), 5.02–5.13 (m, 2H), 5.79–5.92 (m, 1H), 6.54 (d, 1H, J = 3.6 Hz), 7.20 (d, 1H, J = 3.6 Hz), and 8.89 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.0, 35.8, 51.8, 96.4, 116.1, 121.4, 135.9, 136.3, 149.6, 159.2, and 169.1. Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.21; H, 5.92; N, 6.26.

2-Oxo-1,2,3,4-tetrahydroquinoline-6-carboxylic Acid Methyl Ester (9). A 0.21 g (0.94 mmol) sample of furan **7** in 10 mL of toluene was heated in a sealed tube at 200 °C for 24 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.13 g (66%) of **9** as a white solid: mp 186–187 °C; IR (KBr) 3197, 3125, 1716, and 1675 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.66–2.71 (m, 2H), 3.03 (t, 2H, J = 7.6 Hz), 3.90 (s, 3H), 6.88 (d, 1H, J = 8.7 Hz), 7.87–7.89 (m, 2H), and 9.33 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.1, 30.4, 52.0, 115.2, 123.3, 124.8, 129.5, 129.5, 141.3, 166.6, and 172.1. Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.46; H, 5.43; N, 6.77.

5-(Methylpent-4-enoylamino)furan-2-carboxylic Acid Methyl Ester (8). A mixture containing 0.12 g (0.54 mmol) of furan **7**, 0.12 g (2.1 mmol) of powdered KOH, 0.08 g (0.5 mmol) of anhydrous K_2CO_3, and 0.1 g (0.3 mmol) of Bu_4NHSO_4 in 5 mL of benzene was stirred at room temperature for 1 h. To the above mixture was added 0.034 mL (0.7 mmol) of methyl iodide. After being stirred at room temperature for 1 h, the reaction mixture was filtered through a pad of Celite. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.11 g (86%) of **8** as a colorless oil: IR (neat) 2954, 1729, and 1689 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.36 (m, 4H), 3.26 (brs, 3H), 3.90 (s, 3H), 4.95–5.04 (m, 2H), 5.77–5.80 (m, 1H), 6.26 (brs, 1H), and 7.20 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.7, 33.2, 35.6, 51.7, 104.5, 115.4, 119.3, 136.9, 140.8, 152.4, 158.6, and 172.5; HRMS calcd for $C_{12}H_{15}NO_4$ (M^+ + Li) 244.1161, found 244.1161.

1-Methyl-2-oxo-1,2,3,4-tetrahydroquinoline-6-carboxylic Acid Methyl Ester (11). A 0.13 g (0.5 mmol) sample of furan **8** in 10 mL of toluene was heated in a sealed tube at 160 °C for 24 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.10 g (77%) of 6-hydroxy-1-methyl-2-oxo-1,2,3,4,5,6-hexahydroquinoline-6-carboxylic acid methyl ester (**10**) and 0.015 g (13%) of 1-methyl-2-oxo-1,2,3,4-tetrahydroquinoline-6-carboxylic acid methyl ester (**11**).

Amide **10** exhibited the following spectral properties: IR (neat) 3371, 1736, and 1653 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.20–2.60 (m, 4H), 2.99 (m, 1H), 3.06 (m, 1H), 3.15 (s, 1H), 3.68 (s, 3H), 3.83 (s, 3H), 5.85 (d, 1H, J = 9.9 Hz), and 6.35 (d, 1H, J = 9.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.7, 29.1, 30.9, 38.1, 53.2, 70.8, 112.0, 122.4, 125.3, 130.0, 169.7, and 175.3; HRMS calcd for $C_{12}H_{15}NO_4$ 237.1001, found 237.1001.

(62) Wiley: R. H.; Smith, N. R. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. 4, p 732.

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To a solution containing 0.09 g (0.4 mmol) of **10** in 10 mL of benzene was added 0.07 mL (0.6 mmol) of $BF_3{\cdot}OEt_2$. The mixture was heated at reflux for 1 h, quenched with a saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.076 g (91%) of **11** as a white solid: mp 147−148 °C; IR (KBr) 3395, 1725, 1669, and 1603 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.66−2.71 (m, 2H), 2.96 (t, 2H, J = 7.4 Hz), 3.39 (s, 3H), 3.91 (s, 3H), 7.02 (d, 1H, J = 8.6 Hz), 7.86 (s, 1H), and 7.95 (dd, 1H, J = 8.6 and 2.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 29.7, 31.4, 52.0, 114.3, 124.3, 125.9, 129.0, 129.4, 144.5, 166.5, and 170.3. Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.81; H, 6.01; N, 6.35.

5-(Benzoylamino)furan-2-carboxylic Acid Methyl Ester (18). To a mixture containing 0.74 g (5.2 mmol) of furan **1** and 0.85 mL (10.4 mmol) of pyridine in 40 mL of CH_2Cl_2 was added dropwise a solution containing 0.67 mL (5.7 mmol) of benzoyl chloride in 5 mL of CH_2Cl_2 at 0 °C, and the mixture was stirred at this temperature for 3 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 1.17 g (91%) of **18** as a yellow solid: mp 128−129 °C; IR (KBr) 3309, 3287, 1693, 1679, and 1601 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.82 (s, 3H), 6.68 (d, 1H, J = 3.6 Hz), 7.21 (d, 1H, J = 3.6 Hz), 7.44−7.58 (m, 3H), 7.89−7.92 (m, 2H), and 9.21 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.7, 96.8, 121.2, 127.3, 128.8, 132.5, 132.6, 136.5, 149.6, 159.0, and 163.6. Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.56; H, 4.59; N, 5.67.

5-(Benzoylbut-3-enylamino)furan-2-carboxylic Acid Methyl Ester (12). To a mixture containing 0.17 g (0.69 mmol) of furan **18** and 0.6 g (2.1 mmol) of cesium carbonate in 10 mL of a 1:4 mixture of THF/DMF was added 0.2 mL (2.1 mmol) of 4-bromo-1-butene. The mixture was heated at 75 °C for 5 h, cooled, and washed with water. The aqueous phase was extracted with ether, and the combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.14 g (67%) of **12** as a yellow oil: IR (neat) 2952, 1730, and 1678 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.45 (q, 2H, J = 7.2 Hz), 3.87 (s, 3H), 3.96 (t, 2H, J = 7.2 Hz), 5.05−5.14 (m, 2H), 5.75 (d, 1H, J = 3.5 Hz), 5.77−5.89 (m, 1H), 6.95 (d, 1H, J = 3.5 Hz), and 7.22−7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 32.3, 47.4, 51.8, 106.6, 117.1, 119.1, 127.4, 127.9, 130.4, 134.4, 134.9, 140.2, 151.8, 158.5, and 169.9; HRMS calcd for $C_{17}H_{17}NO_4$ 299.1158, found 299.1156.

1-Benzoyl-2,3-dihydro-1*H*-indole-5-carboxylic Acid Methyl Ester (15). A 0.14 g (0.60 mmol) sample of furan **12** in 10 mL of toluene was heated in a sealed tube at 190 °C for 19 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography afforded 0.03 g (25%) of **15**, as well as 0.07 g (52%) of 1-benzoyl-5-hydroxy-2,3,4,5-tetrahydro-1*H*-indole-5-carboxylic acid methyl ester (**14**) as a yellow oil. Dihydroindole **15** exhibited the following properties: mp 142−143 °C; IR (KBr) 1710, 1652, and 1379 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.15 (t, 2H, J = 8.4 Hz), 3.89 (s, 3H), 4.13 (t, 2H, J = 8.4 Hz), 7.45−7.57 (m, 6H), and 7.88 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.6, 50.9, 52.0, 116.1, 125.5, 126.3, 127.1, 128.7, 129.8, 130.7, 132.6, 136.4, 146.7, 166.7, and 169.3. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N 4.98. Found: C, 72.47; H, 5.46; N, 4.92.

Cyclohexadienol **14** exhibited the following spectral properties: ^1H NMR ($CDCl_3$, 300 MHz) δ 2.65 (m, 4H), 3.10 (d, 1H, J = 15 Hz), 3.34 (s, 1H), 3.83 (s, 3H), 3.90 (brs, 1H), 5.30 (brs, 1H), 5.75 (brs, 1H), and 7.30−7.49 (m, 5H). This compound was not purified but rather was converted directly to dihydroindole **15**. To a solution containing 0.07 g (0.24 mmol) of **14** in 10 mL of benzene was added 0.07 mL (0.6 mmol) of $BF_3{\cdot}OEt_2$, and the mixture was heated at reflux for 3 h, quenched with a saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 0.05 g (74%) of **15**.

5-(Benzoylpent-4-enylamino)furan-2-carboxylic Acid Methyl Ester (13). To a mixture containing 0.16 g (0.6 mmol) of furan **18** and 0.6 g (2.0 mmol) of cesium carbonate in 10 mL of a 1:4 mixture of THF/DMF was added 0.23 mL (2.0 mmol) of 5-bromo-1-pentene. The mixture was heated at 75 °C for 5 h, cooled to room temperature, and washed with water. The aqueous phase was extracted with ether, and the combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.16 g (85%) of **13** as a yellow oil: IR (neat) 2950, 1731, and 1670 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.78 (m, 2H), 2.15 (q, 2H, J = 7.2 Hz), 3.87 (s, 3H), 3.86−3.91 (m, 2H), 4.96−5.07 (m, 2H), 5.74−5.87 (m, 2H), 6.95 (d, 1H, J = 3.3 Hz), and 7.23−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.0, 30.6, 47.9, 51.7, 106.3, 115.1, 119.1, 127.5, 127.9, 130.4, 135.0, 137.2, 140.2, 151.9, 158.5, and 169.9; HRMS calcd for $C_{18}H_{19}NO_4$ 313.1314, found 313.1312.

1-Benzoyl-1,2,3,4-tetrahydroquinoline-6-carboxylic Acid Methyl Ester (17). A 0.13 g (0.42 mmol) sample of furan **13** in 10 mL of toluene was heated in a sealed tube at 190 °C for 20 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography afforded 0.04 g (33%) of **17** and 0.08 g (61%) of 1-benzoyl-6-hydroxy-1,2,3,4,5,6-hexahydroquinoline-6-carboxylic acid methyl ester (**16**). The latter compound exhibited the following spectral properties: IR (neat) 3354, 1738, 1634, and 1267 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.95 (brs, 2H), 2.27 (t, 2H, J = 6.6 Hz), 2.50 (d, 1H, J = 18.3 Hz), 2.91 (d, 1H, J = 18.3 Hz), 3.44 (brs, 1H), 3.58 (m, 1H), 3.80 (s, 3H), 3.89 (m, 1H), 5.49 (d, 1H, J = 3.0 Hz), 5.90 (brs, 1H), and 7.34−7.58 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.5, 27.7, 38.8, 52.9, 71.3, 119.9, 121.8, 127.8, 128.1, 128.4, 128.5, 129.1, 130.5, 135.9, and 175.0; HRMS calcd for $C_{18}H_{19}NO_4$ 313.1314, found 313.1311.

To a solution containing 0.07 g (0.2 mmol) **16** in 5 mL of dry benzene was added 0.05 mL (0.4 mmol) of $BF_3{\cdot}OEt_2$. The mixture was heated at reflux for 3 h, quenched with a saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.062 g (84%) of **17** as a white solid: mp 134−135 °C; IR (KBr) 2948, 1705, and 1637 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.07 (m, 2H), 2.90 (t, 2H, J = 6.6 Hz), 3.87 (s, 3H), 3.92 (t, 2H, J = 6.6 Hz), 6.79 (d, 1H, J = 8.4 Hz), 7.30−7.41 (m, 5H), 7.53 (dd, 1H, J = 8.4 and 1.5 Hz), and 7.85 (d, 1H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 27.0, 44.8, 51.9, 124.8, 125.6, 126.9, 128.2, 128.5, 130.0, 130.5, 130.7, 135.7, 143.4, 166.5, and 170.5. Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N 4.74. Found: C, 73.23; H, 5.84; N, 4.79.

5-[Benzoyl(4-(methoxycarbonyl)but-3-enyl)amino]furan-2-carboxylic Acid Methyl Ester (20). To a mixture containing 0.2 g (0.8 mmol) of furan **18** and 0.8 g (2.5 mmol) of cesium carbonate in 15 mL of a 1:4 THF/DMF mixture was added 0.25 mL (2.0 mmol) of 2-(2-bromoethyl)-1,3-dioxolane. The mixture was heated at 75 °C for 18 h, cooled to room temperature, and washed with water. The aqueous phase was extracted with ether, and the combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.24 g (84%) of 5-[benzoyl(2-[1,3]dioxolan-2-ylethyl)amino]furan-2-carboxylic acid methyl ester as a colorless oil: IR (neat) 1726, 1669, 1534, and 1306 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.05−2.11 (m, 2H), 3.85 (m, 2H), 3.88 (s, 3H), 3.95−4.05 (m, 4H), 5.01 (t, 1H, J = 4.5 Hz), 5.77 (d, 1H, J = 3.6 Hz), 6.94 (d, 1H, J = 3.6 Hz), and 7.23−7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 32.1, 43.8, 51.8, 64.8, 102.4, 106.7, 119.1, 127.5, 127.9, 130.4, 135.0, 140.4, 151.9, 158.5, and 170.0; HRMS calcd for $C_{18}H_{19}NO_6$ 345.1212, found 345.1210.

A solution containing 0.2 g (0.58 mmol) of the above methyl ester and 0.04 g (0.31 mmol) of oxalic acid dihydrate in 10 mL of a 1:1 MeOH/H_2O mixture was heated at 50 °C for 24 h. The mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was subjected to

flash silica gel chromatography to give 0.14 g (77%) of 5-[(benzoyl-3-oxopropyl)amino]furan-2-carboxylic acid methyl ester (**19**) as a colorless oil: IR (neat) 1726, 1669, and 1533 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.90 (dt, 2H, J = 6.8 and 1.2 Hz), 3.88 (s, 3H), 4.21 (t, 2H, J = 6.8 Hz), 5.77 (d, 1H, J = 3.6 Hz), 6.94 (d, 1H, J = 3.6 Hz), 7.23−7.39 (m, 5H), and 9.83 (d, 1H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 42.3, 42.6, 51.9, 107.0, 119.1, 127.7, 128.0, 130.9, 134.3, 140.7, 151.3, 158.5, 170.2, and 199.6; HRMS calcd for $C_{16}H_{15}NO_5$ 301.0950, found 301.0948.

A mixture containing 0.13 g (0.4 mmol) of **19** and 0.17 g (0.5 mmol) of methyl (triphenylphosphoranylidene)acetate in 10 mL of CH_2Cl_2 was stirred at room temperature for 3 h. Filtration through a pad of silica gel followed by removal of the solvent under reduced pressure left a residue which was subjected to silica gel chromatography to give 0.13 g (79%) of the *E*-isomer of **20** as a colorless oil: IR (neat) 2952, 1725, 1671, and 1534 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.63 (q, 2H, J = 7.2 Hz), 3.73 (s, 3H), 3.89 (s, 3H), 4.02 (t, 2H, J = 7.2 Hz), 5.74 (d, 1H, J = 3.6 Hz), 5.90 (d, 1H, J = 15.6 Hz), 6.88−6.95 (m, 2H), and 7.23−7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.8, 46.8, 51.4, 51.9, 106.8, 119.1, 123.0, 127.5, 128.0, 130.7, 134.6, 140.5, 144.5, 151.5, 158.4, 166.3, and 169.9; HRMS calcd for $C_{19}H_{19}NO_6$ 357.1212, found 357.1216.

1-Benzoyl-2,3-dihydro-1*H*-indole-4,5-dicarboxylic Acid Dimethyl Ester (22). A 0.12 g (0.3 mmol) sample of furan **20** in 6 mL of toluene was heated in a sealed tube at 160 °C for 65 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.08 g (70%) of **22** as a white solid: mp 119−120 °C; IR (KBr) 1720, 1649, and 1377 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.17 (t, 2H, J = 8.4 Hz), 3.87 (s, 3H), 3.92 (s, 3H), 4.13 (t, 2H, J = 8.4 Hz), 7.44−7.57 (m, 6H), and 7.78 (d, 1H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.6, 50.9, 52.4, 52.6, 117.2, 123.8, 127.0, 128.7, 129.8, 130.3, 130.8, 131.5, 131.6, 136.1, 146.4, 166.1, 168.3, and 169.4. Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N 4.13. Found: C, 67.33; H, 5.07; N, 4.14.

5-[Benzoyl(3-methylbut-3-enyl)amino]furan-2-carboxylic Acid Methyl Ester (21). To a mixture containing 0.45 g (1.8 mmol) of furan **18** and 1.8 g (5.5 mmol) of cesium carbonate in 25 mL of a 1:4 mixture of THF/DMF was added 0.8 g (5.4 mmol) of 4-bromo-2-methyl-1-butene. The mixture was heated at 80 °C for 24 h, cooled to room temperature, and washed with water. The aqueous phase was extracted with ether, and the combined organic phases were washed with brine and dried with $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.38 g (74%) of furan **21** as a yellow oil: IR (neat) 1731, 1671, and 1533 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.77 (s, 3H), 2.39 (t, 2H, J = 7.5 Hz), 3.88 (s, 3H), 4.01 (t, 2H, J = 7.5 Hz), 4.75 (s, 1H), 4.81 (s, 1H), 5.74 (d, 1H, J = 3.6 Hz), 6.95 (d, 1H, J = 3.6 Hz), and 7.23−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.0, 35.8, 46.4, 51.6, 106.4, 112.1, 119.0, 127.3, 127.8, 130.2, 134.9, 140.1, 141.9, 151.8, 158.3, and 169.7; HRMS calcd for $C_{18}H_{19}NO_4$ 313.1314, found 313.1312.

5-(2-(Benzoylamino)ethyl)-1-hydroxy-5-methyl-4-oxocyclohex-2-enecarboxylic Acid Methyl Ester (23). A 0.12 g (0.4 mmol) sample of furan **21** in 5 mL (4.0 M) of lithium perchlorate/ether was heated in a sealed tube at 95 °C for 24 h. The mixture was cooled, diluted wth ether, washed with water, and dried over $MgSO_4$ to afford 42 mg (68%) of cyclohexenone **23** as a yellow oil: IR (KBr) 3338, 1739, 1679, and 1638 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.19 (s, 3H), 1.97 (m, 1H), 2.12 (m, 1H), 2.28 (d, 1H, J = 14.8 Hz), 2.36 (d, 1H, J = 14.8 Hz), 3.39 (m, 1H), 3.67 (m, 1H), 3.82 (s, 3H), 4.25 (s, 1H), 6.05 (d, 1H, J = 10.0 Hz), 6.63 (d, 1H, J = 10.0 Hz), 6.68 (brs, 1H), 7.39−7.50 (m, 3H), and 7.75 (d, 2H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.3, 35.9, 37.1, 42.5, 43.6, 53.6, 71.3, 126.8, 128.5, 128.9, 131.4, 134.3, 143.7, 167.4, 174.6, and 203.0; HRMS calcd for $C_{18}H_{21}NO_5$ 331.1420, found 331.1418.

5-[(Ethoxycarbonyl)amino]furan-2-carboxylic Acid Methyl Ester. To a mixture containing 0.33 g (2.3 mmol) of furan **1** and 0.28 mL (3.5 mmol) of pyridine in 30 mL of CH_2Cl_2 was added dropwise 0.25 mL (2.5 mmol) of ethyl chloroformate at 0 °C. The mixture was stirred at room temperature for 2 h followed by removal of the solvent under reduced pressure and flash silica gel chromatography to give 0.15 g (30%) of 5-[(ethoxycarbonyl)amino]furan-2-carboxylic acid methyl ester as a white solid: mp 102−103 °C; IR (KBr) 3280, 1730, 1701, and 1579 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, J = 7.2 Hz), 3.86 (s, 3H), 4.28 (q, 2H, J = 7.2 Hz), 6.31 (brs, 1H), 7.20 (d, 1H, J = 3.6 Hz), and 8.40 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 51.5, 62.1, 94.5, 121.2, 136.3, 149.9, 152.0, and 158.9; HRMS calcd for $C_9H_{11}NO_5$ 213.0637, found 213.0635.

5-(But-3-enyl(ethoxycarbonyl)amino)furan-2-carboxylic Acid Methyl Ester (26). To a mixture containing 0.16 g (0.8 mmol) of the above furan carbamate and 0.8 g (2.3 mmol) of cesium carbonate in 10 mL of a 1:4 mixture of THF/DMF was added 0.24 mL (2.3 mmol) of 4-bromo-1-butene. The mixture was heated at 50 °C for 1 h, cooled to room temperature, and washed with water. The aqueous phase was extracted with ether, and the combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography afforded 0.18 g (86%) of **26** as a yellow oil: IR (neat) 2980, 1735, 1718, and 1534 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.29 (t, 3H, J = 7.2 Hz), 2.38 (q, 2H, J = 7.2 Hz), 3.83−3.89 (m, 2H), 3.87 (s, 3H), 4.24 (q, 2H, J = 7.2 Hz), 5.01−5.11 (m, 2H), 5.71−5.85 (m, 1H), 6.25 (brs, 1H), and 7.17 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 33.0, 46.7, 51.5, 62.5, 101.3, 117.1, 120.1, 134.3, 138.3, 151.1, 153.5, and 158.7; HRMS calcd for $C_{13}H_{17}NO_5$ 267.1107, found 267.1108.

2,3-Dihydroindole-1,5-dicarboxylic Acid 1-Ethyl Ester 5-Methyl Ester (27). A 0.16 g (0.6 mmol) sample of furan **26** in 4 mL (4.0 M) of lithium perchlorate/ether was heated in a sealed tube at 100 °C for 26 h. The mixture was cooled, diluted with ether, washed with water, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.097 g (66%) of dihydroindole **27** as a white solid: mp 96−97 °C; IR (KBr) 3389, 1712, and 1607 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.37 (t, 3H, J = 6.8 Hz), 3.15 (t, 2H, J = 8.9 Hz), 3.89 (s, 3H), 4.07 (t, 2H, J = 8.9 Hz), 4.31 (q, 2H, J = 6.8 Hz), and 7.83−7.92 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 26.7, 47.8, 51.7, 61.7, 113.8, 124.0, 125.9, 130.0, 130.9, 147.0, 153.0, and 166.7. Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.55; H, 6.09; N, 5.55.

1-Benzoyl-4-methyl-2,3-dihydro-1*H*-indole-5-carboxylic Acid Methyl Ester (29). A solution containing 0.25 g (0.6 mmol) of furan **13** and 10 mg of camphorsulfonic acid in 5 mL (4.0 M) of lithium perchlorate/ether was heated in a sealed tube at 100 °C for 48 h. The mixture was cooled, diluted with ether, washed with water, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.12 g (73%) of dihydroindole **29** as a white solid: mp 171−172 °C; IR (KBr) 1712, 1638, and 1378 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.48 (s, 3H), 3.05 (t, 2H, J = 8.4 Hz), 3.84 (s, 3H), 4.10 (t, 2H, J = 8.4 Hz), 7.40−7.55 (m, 6H), and 7.76 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.1, 27.0, 50.4, 51.5, 113.4, 124.7, 126.9, 128.5, 130.4, 131.0, 132.4, 136.4, 136.8, 145.2, 167.4, and 169.2. Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.06; H, 5.83; N, 4.81.

5-[2-(2,3-Dimethoxyphenyl)acetylamino]furan-2-carboxylic Acid Methyl Ester. To a mixture containing 0.3 g (2.0 mmol) of furan **1** and 0.3 mL (4.0 mmol) of pyridine in 15 mL of CH_2Cl_2 was added 0.48 g (2.2 mmol) of 3,4-dimethoxyphenylacetyl chloride at 0 °C. The mixture was stirred at this temperature for 3 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.62 g (96%) of 5-[2-(2,3-dimethoxyphenyl)acetylamino]furan-2-carboxylic acid methyl ester as a white solid: mp 126−127 °C; IR (KBr) 3272, 1695, 1536, and 1514 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.72 (s, 2H), 3.84 (s, 3H), 3.89 (s, 3H), 3.91 (s, 3H), 6.54 (d, 1H, J = 3.6 Hz), 6.78−6.91 (m, 3H), 7.16 (d, 1H, J = 3.6 Hz), and 8.01 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 43.6, 51.8, 55.9, 56.0, 96.4, 112.0, 112.4, 121.1, 121.8, 125.3, 136.3, 149.0, 149.1, 149.7, 158.9, and 167.7. Anal. Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.07; H, 5.42; N, 4.30.

5-[[(3,4-Dimethoxyphenyl)acetyl](3-methylbut-3-enyl)-amino]furan-2-carboxylic Acid Methyl Ester (32). To a mixture containing 0.51 g (1.6 mmol) of the above furan and 1.6 g (4.8 mmol) of cesium carbonate in 30 mL of a 1:4 mixture of THF/DMF was added 0.71 g (4.8 mmol) of 4-bromo-2-methyl-1-butene. The mixture was heated at 75 °C for 72 h, cooled to room temperature, and washed with water. The aqueous phase was extracted with ether, and the combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.35 g (72%) of furan **32** as a yellow oil: IR (neat) 1731, 1683, and 1519 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.71 (s, 3H), 2.25 (t, 2H, J = 7.2 Hz), 3.50 (brs, 2H), 3.80 (t, 2H, J = 7.2 Hz), 3.84 (s, 6H), 3.91 (s, 3H), 4.68 (s, 1H), 4.76 (s, 1H), 6.17 (brs, 1H), 6.61 (d, 1H, J = 8.8 Hz), 6.68 (s, 1H), 6.76 (d, 1H, J = 8.8 Hz), and 7.18 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.0, 35.7, 40.6, 51.8, 55.4, 55.5, 107.0, 110.8, 111.8, 112.0, 118.9, 120.8, 126.5, 141.1, 141.8, 147.7, 148.5, 151.0, 158.3, and 171.0; HRMS calcd for $C_{21}H_{25}NO_6$ 387.1682, found 387.1680.

5-(8,9-Dimethoxy-6,6-dimethyl-2-oxo-1,4,5,6-tetrahydro-2*H*-benzo[*d*]azocin-3-yl)furan-2-carboxylic Acid Methyl Ester (34). A 0.14 g (0.36 mmol) sample of furan **32** and 10 mg of camphorsulfonic acid in 5 mL (4.0 M) of lithium perchlorate/ether was heated in a sealed tube at 100 °C for 20 h. The mixture was cooled, diluted with ether, washed with water, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.11 g (79%) of lactam **34** as a yellow oil: IR (neat) 1722, 1678, and 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.17 (s, 6H), 1.66 (m, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 3.88 (s, 3H), 3.90 (m, 2H), 4.15 (s, 2H), 6.79 (d, 1H, J = 8.0 Hz), 6.91 (m, 2H), and 7.11 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.3, 30.1, 37.4, 40.8, 42.2, 51.6, 55.7, 55.8, 110.9, 112.5, 115.0, 118.0, 121.3, 126.8, 137.7, 146.2, 147.8, 148.7, 158.7, and 169.3; HRMS calcd for $C_{21}H_{25}NO_6$ 387.1682, found 387.1679.

5-[[3-(3,4-Dimethyoxyphenyl)propionyl]amino]furan-2-carboxylic Acid Methyl Ester. A solution containing 1.2 g (5.7 mmol) of 3-(3,4-dimethoxyphenyl)propionic acid in 20 mL of CH_2Cl_2 was treated dropwise with 0.6 mL (6.9 mmol) of oxalyl chloride. The mixture was stirred at room temperature for 12 h, and the solvent was removed under reduced pressure. The residue was diluted with 15 mL of CH_2Cl_2 and was used in the next step without further purification. To a mixture containing 0.73 g (5.2 mmol) of furan **1** and 0.84 mL (10.4 mmol) of pyridine in 45 mL of CH_2Cl_2 was added the above acid chloride solution at 0 °C. The mixture was stirred at 0 °C for 3 h, poured over 1 N HCl and ice, extracted with CH_2Cl_2, and dried over Na_2SO_4. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 1.56 g (90%) of 5-[[3-(3,4-dimethyoxyphenyl)propionyl]-amino]furan-2-carboxylic acid methyl ester as a yellow solid: mp 113−114 °C; IR (KBr) 3297, 1713, and 1698 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.67 (t, 2H, J = 7.5 Hz), 2.99 (t, 2H, J = 7.5 Hz), 3.82 (s, 3H), 3.84 (s, 3H), 3.86 (s, 3H), 6.52 (d, 1H, J = 3.6 Hz), 6.72−6.81 (m, 3H), 7.17 (d, 1H, J = 3.6 Hz), and 7.99 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.8, 38.6, 51.8, 55.8, 55.9, 96.4, 111.3, 111.5, 120.0, 121.3, 132.7, 136.0, 147,6, 148.9, 149.3, 159.1, and 168.9. Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.75; N, 4.20. Found: C, 61.15; H, 5.74; N, 4.12.

5-[[3-(3,4-Dimethoxyphenyl)propionyl](3-methylbut-3-enyl)amino]furan-2-carboxylic Acid Methyl Ester (33). To a mixture containing 0.34 g (1.0 mmol) of the above furan and 1.0 g (3.0 mmol) of cesium carbonate in 25 mL of a 1:4 mixture of THF/DMF was added 0.46 g (3.0 mmol) of 4-bromo-2-methyl-1-butene. The mixture was heated at 70 °C for 24 h, cooled to room temperature, and washed with water. The aqueous phase was extracted with ether, and the combined organic phase was washed with brine and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.24 g (69%) of furan **33** as a colorless oil: IR (neat) 1732, 1684, and 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.72 (s, 3H), 2.23 (t, 2H, J = 7.4 Hz), 2.44 (t, 2H, J = 7.4 Hz), 2.88 (t, 2H, J = 7.6 Hz), 3.78 (t, 2H, J = 7.6 Hz), 3.84 (s, 3H), 3.86 (s, 3H), 3.89 (s, 3H), 4.68 (s, 1H), 4.76 (s, 1H), 6.06 (brs, 1H), 6.66−6.77 (m, 3H), and 7.14 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.3, 30.9, 36.0, 36.3, 46.4, 52.0, 55.7, 55.8, 107.0, 111.1, 111.7, 112.1, 119.0, 120.1, 133.3, 141.4, 142.4, 147.3, 148.7, 151.3, 158.5, and 172.2; HRMS calcd for $C_{22}H_{27}NO_6$ 401.1838, found 401.1836.

5-(9,10-Dimethoxy-1,1-dimethyl-5-oxo-1,2,3,5,6,7-hexahydrobenzo[*e*]azonin-4-yl)furan-2-carboxylic Acid Methyl Ester (35). A 0.15 g (0.37 mmol) sample of furan **33** and 10 mg of camphorsulfonic acid in 5 mL (4.0 M) of lithium perchlorate/ether was heated in a sealed tube at 100 °C for 24 h. The mixture was cooled, diluted with ether, washed with water, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.091 g (61%) of **35** as a colorless oil: IR (neat) 1723, 1676, and 1611 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.20 (s, 6H), 1.66 (m, 2H), 3.00 (t, 2H, J = 7.8 Hz), 3.18 (t, 2H, J = 7.8 Hz), 3.84 (s, 3H), 3.85 (s, 3H), 3.89 (m, 5H), 6.77−6.86 (m, 3H), and 7.13 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.2, 30.0, 30.9, 37.3, 40.3, 51.4, 55.6, 110.9, 111.7, 114.5, 117.7, 120.1, 133.2, 137.6, 146.2, 147.1, 148.5, 158.4, and 170.1; HRMS calcd for $C_{22}H_{27}NO_6$ 401.1838, found 401.1837.

5-(Benzoylamino)-4-pent-4-enoylfuran-2-carboxylic Acid Methyl Ester (38). A mixture containing 0.15 g (0.67 mmol) of furan **7**, 0.19 mL (1.4 mmol) of triethylamine, and 0.086 mL (0.74 mmol) of benzoyl chloride in 10 mL of benzene was heated at reflux for 50 h. After being cooled to room temperature, the mixture was washed with water and dried over Na_2SO_4. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.16 g (73%) of 5-(benzoylpent-4-enoylamino)furan-2-carboxylic acid methyl ester (**36**) as a yellow oil: IR (neat) 1709, 1517, and 1304 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.46 (q, 2H, J = 7.2 Hz), 2.85 (t, 2H, J = 7.5 Hz), 3.86 (s, 3H), 5.01−5.12 (m, 2H), 5.77−5.91 (m, 1H), 6.23 (d, 1H, J = 3.6 Hz), 7.07 (d, 1H, J = 3.6 Hz), and 7.33−7.66 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.5, 36.1, 51.9, 110.0, 115.8, 119.1, 128.3, 128.5, 132.6, 133.5, 136.2, 142.3, 146.8, 158.3, 170.3, and 174.5. This material was used in the next step without further purification.

A mixture containing 0.12 g (0.37 mmol) of furan **36** in 5 mL of toluene was heated at 200 °C in a sealed tube for 24 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 15 mg (17%) of furan **18** and 50 mg (42%) of furan **38** as a white solid: mp 114−115 °C; IR (KBr) 1719, 1650, and 1567 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.49 (m, 2H), 2.89 (t, 2H, J = 7.2 Hz), 3.93 (s, 3H), 5.03−5.13 (m, 2H), 5.83−5.93 (m, 1H), 7.50−7.66 (m, 4H), 8.02 (d, 2H, J = 7.5 Hz), and 11.48 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.7, 39.2, 52.2, 106.3, 115.8, 116.6, 127.7, 129.0, 132.0, 133.2, 136.4, 137.6, 155.0, 158.3, 162.6, and 196.9. Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 65.92; H, 5.27; N, 4.19.

5-(Benzoylhex-5-enoylamino)furan-2-carboxylic Acid Methyl Ester (37). A solution containing 5-hexenoyl chloride (3.2 mmol) in 5 mL of CH_2Cl_2 was added to a mixture containing 0.22 g (1.6 mmol) of furan **1** and 0.26 mL (3.2 mmol) of pyridine in 15 mL of CH_2Cl_2 at 0 °C. The solution was stirred at 0 °C for 1 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography afforded 0.36 g (98%) of 5-(hex-5-enoylamino)furan-2-carboxylic acid methyl ester as a white solid: mp 71−72 °C; IR (KBr) 3288, 3065, and 1699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.75 (m, 2H), 2.04 (q, 2H, J = 7.2 Hz), 2.45 (t, 2H, J = 7.5 Hz), 3.77 (s, 3H), 4.86−4.96 (m, 2H), 5.61−5.75 (m, 1H), 6.48 (d, 1H, J = 3.5 Hz), 7.13 (d, 1H, J = 3.5 Hz), and 8.76 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.0, 32.8, 35.3, 51.5, 96.2, 115.1, 121.4, 135.5, 137.3, 150.0, 159.1, and 170.4. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.65; H, 6.44; N, 5.82.

A solution containing 0.12 g (0.5 mmol) of the above methyl ester, 0.14 mL (1.0 mmol) of triethylamine, and 0.07 mL (0.6 mmol) of benzoyl chloride in 10 mL of benzene was heated at reflux for 36 h. The mixture was washed with water and dried over Na_2SO_4. Removal of the solvent under reduced pressure followed by flash silica gel chromatography provided 0.12 g (70%) of **37** as a yellow oil: IR (neat) 1723, 1517, and 1303

cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.84 (m, 2H), 2.14 (q, 2H, J = 7.2 Hz), 2.76 (t, 2H, J = 7.2 Hz), 3.88 (s, 3H), 4.98−5.08 (m, 2H), 5.71−5.84 (m, 1H), 6.21 (d, 1H, J = 3.6 Hz), 7.07 (d, 1H, J = 3.6 Hz), and 7.33−7.65 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.8, 32.8, 36.2, 52.0, 109.8, 115.5, 119.2, 128.4, 128.6, 132.7, 133.8, 137.5, 142.4, 147.1, 158.4, 170.5, and 175.2; HRMS calcd for $C_{19}H_{19}NO_5$ 341.1263, found 341.1263.

5-(Benzoylamino)-4-hex-5-enoylfuran-2-carboxylic Acid Methyl Ester (39). A 0.12 g (0.35 mmol) sample of furan **37** in 5 mL of toluene was heated at 200 °C in a sealed tube for 24 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.010 g (12%) of furan **18** and 0.061 g (51%) of furan **39** as a white solid: mp 111−112 °C; IR (KBr) 1714, 1592, and 1570 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.84 (m, 2H), 2.16 (q, 2H, J = 7.2 Hz), 2.79 (t, 2H, J = 7.2 Hz), 3.94 (s, 3H), 5.01−5.09 (m, 2H), 5.74−5.88 (m, 1H), 7.48−7.67 (m, 4H), 8.01−8.04 (m, 2H), and 11.51 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.0, 33.0, 39.3, 52.2, 106.4, 115.7, 116.7, 127.8, 129.1, 132.1, 133.2, 137.5, 137.6, 155.0, 158.4, 162.6, and 197.7. Anal. Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.79; H, 5.63; N, 4.08.

***N*-But-3-enyl-4-methyl-*N*-(5-nitrofuran-2-yl)benzenesulfonamide (40).** To a stirred solution containing 4.73 g (17.4 mmol) of freshly prepared *N*-(*tert*-butylcarbamate)sulfonamide[64] in 20 mL of THF was added 9.1 g (35 mmol) of triphenylphosphine followed by the addition of 0.84 g (11.6 mmol) of 3-buten-1-ol. The mixture was cooled to 0 °C, and 4.6 mL (29 mmol) of diethyl acetylenedicarboxylate was added dropwise. The mixture was allowed to stir at room temperature for 3 h, and the solvent was removed under reduced pressure. The resulting oil was subjected to silica gel chromatography to give 3.5 g (93%) of *N*-(*tert*-butylcarbamate)-*N*-but-3-enyl-4-methylbenzenesulfonamide as a colorless oil: IR (neat) 2978, 1729, 1642, and 1595 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.52 (s, 9H), 2.33 (s, 3H), 2.42 (q, 2H, J = 7.5 Hz), 3.80 (t, 2H, J = 7.5 Hz), 5.00−5.20 (m, 2H), 5.70−5.80 (m, 1H), 7.21 (d, 2H, J = 8.1 Hz), and 7.71 (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 27.8, 34.5, 46.3, 84.0, 117.3, 127.8, 129.2, 134.4, 137.4, 144.1, and 150.8; HRMS calcd for $C_{16}H_{23}NO_4S$ 325.1348, found 325.1354.

To a stirred solution containing 3.5 g (11 mmol) of the above sulfonamide in 50 mL of CH_2Cl_2 was added 2.5 mL (0.3 mol) trifluoroacetic acid. The solution was allowed to stir at room temperature for 12 h and was quenched with an aqueous K_2CO_3 solution. The organic layer was separated, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel chromatography of the residue afforded 2.14 g (88%) of *N*-but-3-enyl-4-methylbenzenesulfonamide[65] as a colorless oil: IR (neat) 3278, 2934, 1641, 1430, and 1325 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.20 (q, 2H, J = 6.9 Hz), 2.42 (s, 3H), 2.99 (q, 2H, J = 6.9 Hz), 5.00−5.10 (m, 2H), 5.17 (brs, 1H), 5.6−5.75 (m, 1H), 7.30 (d, 2H, J = 8.2 Hz), and 7.77 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 33.6, 42.3, 117.8, 127.1, 129.7, 134.3, 136.9, and 143.4; HRMS calcd for $C_{11}H_{15}NO_2S$ 225.0823, found 225.0825.

To a stirred solution containing 1.4 g (6.3 mmol) of the above sulfonamide in 30 mL of THF at 0 °C was added 0.33 g (8.8 mmol) of 60% NaH in mineral oil. The mixture was stirred for 30 min at room temperature and cooled to 0 °C; then a solution of 1.0 g (6.3 mmol) of 2,5-dinitrofuran[51] in 5 mL of THF was added. The mixture was allowed to warm to room temperature, stirred at this temperature for 3.5 h, and then quenched with water. The solvent was removed under reduced pressure, and the residue was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel chromatography afforded 2.0 g (94%) of **40** as a clear oil: IR (neat) 3133, 2920, 1600, 1493, and 1347 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.35 (q, 2H, J = 7.2 Hz), 2.43 (s, 3H), 3.72 (t, 2H, J = 7.2 Hz), 5.06 (m, 2H), 5.71 (m, 1H), 6.49 (d, 1H, J = 3.6 Hz), 7.32 (d, 3H, J = 7.2 Hz), and 7.57 (d, 2H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 33.1, 48.8, 107.2, 113.8, 117.9, 127.4, 130.1, 133.4, 134.9, 145.1, and 148.1; HRMS calcd for $C_{15}H_{16}N_2O_5S$ 336.0780, found 336.0774.

1-(Toluene-4-sulfonyl)-2,3-dihydro-1*H*-indol-5-ol (44). A 1.0 g (3.1 mmol) sample of furan **40** in 30 mL of toluene was heated at reflux for 12 h. The solution was allowed to cool to room temperature, and 10 mL of a saturated NH_4Cl solution was added. The mixture was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to silica gel chromatography. The first fraction contained 0.071 g (7%) of 6-nitro-1-(toluene-4-sulfonyl)-2,3-dihydro-1*H*-indol-5-ol (**48**): mp 219−221 °C; IR ($CHCl_3$) 3324, 2919, 1736, 1642, and 1593 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.40 (s, 3H), 2.94 (t, 2H, J = 8.3 Hz), 3.96 (t, 2H, J = 8.3 Hz), 6.88 (s, 1H), 7.28 (d, 2H, J = 8.2 Hz), 7.69 (d, 2H, J = 8.2 Hz), 8.24 (s, 1H), and 10.69 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.8, 28.5, 50.1, 109.4, 116.3, 127.6, 130.2, 133.5, 135.5, 144.1, 145.0, 153.0, and 158.6. Anal. Calcd for $C_{15}H_{14}N_2O_5S$: C, 53.89; H, 4.22; N, 8.38. Found: C, 53.95; H, 4.28; N, 8.32.

The second fraction contained 0.226 g (25%) of 1-(toluene-4-sulfonyl)-2,3-dihydro-1*H*-indol-5-ol (**44**): mp 196−197 °C; IR (neat) 3369, 2909, 1606, 1459, and 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.37 (s, 3H), 2.71 (t, 2H, J = 8.2 Hz), 3.90 (t, 2H, J = 8.2 Hz), 4.60 (s, 1H), 6.57 (d, 1H, J = 2.0 Hz), 6.68 (dd, 1H, J = 8.6 and 2.3 Hz), 7.21 (d, 2H, J = 8.0 Hz), 7.51 (d, 1H, J = 8.6 Hz), and 7.60 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.8, 28.5, 50.6, 112.4, 114.5, 177.1, 127.6, 129.8, 134.1, 134.5, 135.8, 144.1, 152.8, and 152.8. Anal. Calcd for $C_{15}H_{15}NO_3S$: C, 62.26; H, 5.23; N, 4.84. Found: C, 62.24; H, 5.27; N, 4.79.

***N*-Pent-4-enyl-4-methyl-*N*-(5-nitrofuran-2-yl)benzenesulfonamide (41).** To a stirred solution containing 4.2 g (15.6 mmol) of freshly prepared *N*-(*tert*-butylcarbamate)sulfonamide[64] in 20 mL of THF was added 8.1 g (23.4 mmol) of triphenylphosphine followed by 0.9 g (10.4 mmol) of 4-penten-1-ol. The mixture was cooled to 0 °C, and 4.9 mL (29 mmol) of diethyl acetylenedicarboxylate was added dropwise. The reaction mixture was allowed to stir at room temperature for 3 h. The solvent was removed under reduced pressure, and the resulting oil was subjected to silica gel chromatography to give 3.35 g (95%) of *N*-(*tert*-butylcarbamate)-*N*-pent-4-enyl-4-methylbenzenesulfonamide as a colorless oil: IR (neat) 3073, 2973, 1727, 1347, and 1154 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33 (s, 9H), 1.87 (m, 2H), 2.13 (q, 2H, J = 7.8 Hz), 2.44 (s, 3H), 3.83 (t, 2H, J = 7.8 Hz), 5.85 (m, 1H), 5.10 (m, 2H), 7.32 (d, 2H, J = 10.5 Hz), and 7.79 (d, 2H, J = 10.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 27.9, 29.2, 30.9, 32.9, 46.8, 115.2, 127.8, 128.5, 129.2, 133.8, 137.5, and 150.9; HRMS calcd for $C_{17}H_{25}NO_4S$ 339.1504, found 339.1508.

To a stirred solution containing 3.4 g (9.9 mmol) of the above sulfonamide in 50 mL of CH_2Cl_2 was added 2.8 mL (0.3 mol) of trifluoroacetic acid. The solution was allowed to stir at room temperature for 12 h and was then quenched with an aqueous K_2CO_3 solution. The organic layer was separated, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel chromatography afforded 2.3 g (96%) of *N*-pent-4-enyl-4-methylbenzenesulfonamide[65] as a colorless oil: IR (neat) 3289, 2930, 1636, 1330, and 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.49 (m, 2H), 1.97 (q, 2H, J = 7.0 Hz), 2.35 (s, 3H), 2.86 (q, 2H, J = 6.5 Hz), 4.88 (m, 2H), 5.30 (s, 1H), 5.63 (m, 1H), 7.24 (d, 2H, J = 8.1 Hz), and 7.72 (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 28.7, 30.6, 42.6, 115.5, 127.1, 129.7, 137.0, 137.2, and 143.4; HRMS calcd for $C_{12}H_{17}NO_2S$ 239.0979, found 239.0936.

To a stirred solution containing 1.5 g (6.3 mmol) of the above sulfonamide in 30 mL of THF at 0 °C was added 0.34 g (8.8 mmol) of 60% NaH in mineral oil. The ice bath was removed, and the mixture was stirred for 30 min at room temperature. The solution was cooled to 0 °C, and 1.0 g (6.3 mmol) of 2,5-dinitrofuran in 5 mL of THF was added. The mixture was allowed to warm to room temperature, stirred at room temperature for 3.5 h, and then quenched with water. The solvent was removed under reduced pressure, and the residue was

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extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel chromatography afforded 2.04 g (92%) of **41** as a clear oil: IR (neat) 3136, 2923, 1636, 1489, and 1343 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.71 (q, 2H, J = 7.2 Hz), 2.10 (q, 2H, J = 7.2 Hz), 2.43 (s, 3H), 3.66 (t, 2H, J = 7.2 Hz), 5.00 (m, 2H), 5.75 (m, 1H), 6.51 (d, 1H, J = 3.9 Hz), 7.32 (m, 3H), and 7.64 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 27.8, 30.3, 48.9, 106.9, 113.8, 115.7, 127.4, 130.1, 134.8, 136.8, 145.1, 148.1, and 148.3; HRMS calcd for $C_{16}H_{18}N_2O_5S$ 350.0936, found 350.0941.

1-(Toluene-4-sulfonyl)-1,2,3,4-tetrahydroquinolin-6-ol (45). A 1.1 g (3.1 mmol) sample of furan **41** in 30 mL of toluene was heated at reflux for 12 h. The solution was allowed to cool to room temperature, and 10 mL of a saturated NH_4Cl solution was added. The mixture was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to silica gel chromatography. The first fraction contained 0.077 g (7%) of 6-nitro-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydroquinolin-6-ol (**49**): mp 174−175 °C; IR ($CHCl_3$) 3419, 3119, 1632, 1592, and 1535 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.66 (m, 2H), 2.40 (s, 3H), 2.46 (t, 2H, J = 6.5 Hz), 3.79 (t, 2H, J = 6.5 Hz), 6.81 (s, 1H), 7.24 (d, 2H, J = 8.2 Hz), 7.52 (d, 2H, J = 8.2 Hz), 8.52 (s, 1H), and 10.41 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 21.8, 27.4, 46.1, 119.2, 120.9, 127.4, 130.1, 130.1, 132.1, 136.2, 142.8, 144.4, and 151.8. Anal. Calcd for $C_{16}H_{16}N_2O_5S$: C, 55.16; H, 4.63; N, 8.04. Found: C, 55.22; H, 4.70; N, 8.08.

The second fraction contained 0.52 g (55%) of 1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydroquinolin-6-ol (**45**): mp 155−156 °C; IR ($CHCl_3$) 3414, 2919, 1611, 1504, and 1155 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.54 (m, 2H), 2.28 (t, 2H, J = 6.7 Hz), 2.38 (s, 3H), 3.74 (t, 2H, J = 6.7 Hz), 5.29 (s, 1H), 6.49 (d, 1H, J = 2.8 Hz), 6.68 (dd, 1H, J = 8.8 and 2.8 Hz), 7.18 (d, 2H, J = 8.1 Hz), 7.43 (d, 2H, J = 8.1 Hz), and 7.62 (d, 1H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 21.5, 26.3, 46.4, 113.7, 115.1, 127.1, 127.2, 129.5, 129.7, 133.0, 136.5, 143.5, and 153.2. Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.35; H, 5.65; N, 4.62. Found: C, 63.28; H, 5.65; N, 4.54.

5-[(2-Bromo-4,5-dimethyoxybenzoyl)amino]furan-2-carboxylic Acid Methyl Ester (56). To a suspension of 0.76 g (2.9 mmol) of 2-bromo-4,5-dimethoxybenzoic acid in 10 mL of CH_2Cl_2 at room temperature was added 0.6 mL (6.9 mmol) of oxalyl chloride. The solution was stirred at room temperature for 12 h, and the solvent was removed under reduced pressure. The residue was rinsed with 20 mL of CH_2Cl_2 and concentrated under reduced pressure. The resulting acid chloride was used without further purification. To a refluxing solution containing 0.4 g (2.8 mmol) of furan **1** and 0.5 mL (5.6 mmol) of pyridine in 75 mL of benzene was added a solution of the above acid chloride in 50 mL of benzene by syringe pump over a period of 6 h. After the addition was complete, the mixture was heated at reflux for 12 h. Removal of the solvent under reduced pressure was followed by flash silica gel chromatography to give 0.96 g (88%) of 5-[(2-bromo-4,5-dimethyoxybenzoyl)amino]furan-2-carboxylic acid methyl ester (**56**) as a pale yellow oil: IR (neat) 3253, 3022, 1716, and 1531 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.81 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 6.70 (d, 1H, J = 3.6 Hz), 6.97 (s, 1H), 7.19 (s, 1H), 7.21 (d, 1H, J = 3.6 Hz), and 9.58 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.6, 55.9, 56.1, 96.9, 110.5, 112.5, 115.7, 121.1, 126.8, 136.4, 148.0, 149.0, 151.1, 158.8, and 162.9; HRMS calcd for $C_{15}H_{14}NO_6Br$ 383.0005, found 383.0004.

5-[(2-Bromo-4,5-dimethoxybenzoyl)but-3-enylamino]-furan-2-carboxylic Acid Methyl Ester (58). To a mixture containing 0.32 g (0.8 mmol) of amidofuran **56** and 0.9 g (2.6 mmol) of cesium carbonate in 25 mL of 1:4 THF/DMF was added 0.26 mL (2.6 mmol) of 4-bromo-1-butene. The mixture was heated at 80 °C for 3 h to give 0.31 g (85%) of **58** as a yellow oil: IR (neat) 3075, 1723, and 1680 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.46 (brs, 2H), 3.78 (s, 3H), 3.83 (s, 3H), 3.85 (s, 3H), 3.95 (m, 2H), 5.07−5.17 (m, 2H), 5.84 (m, 1H), 5.96 (brs, 1H), 6.72 (s, 1H), and 6.89 (brs, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.2, 46.6, 51.7, 55.9, 56.0, 106.5, 109.9, 110.5, 114.8, 117.2, 118.9, 129.3, 134.3, 140.7, 147.8, 149.8, 150.6, 158.3, and 168.1; HRMS calcd for $C_{19}H_{20}NO_6Br$ 437.0474, found 437.0476.

1-(2-Bromo-4,5-dimethoxybenzoyl)-2,3-dihydro-1*H*-5-carboxylic Acid Methyl Ester (60). A mixture containing 0.21 g (0.48 mmol) of amidofuran **58** in 5 mL of a 4 M $LiClO_4$/etherate solution was heated at 100 °C in a sealed tube for 42 h. After being cooled to room temperature, the solution was diluted with ether, washed with water, and dried over Na_2SO_4. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.16 g (79%) of **60** as a white solid: mp 134−135 °C; IR (KBr) 1715, 1656, and 1398 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 3.15 (t, 2H, J = 8.4 Hz), 3.80 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 3.90 (brs, 2H), 7.14 (s, 1H), 7.23 (s, 1H), 7.84 (s, 2H), and 8.10 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 26.5, 49.0, 51.4, 55.9, 108.1, 111.2, 115.7, 124.8, 125.6, 128.9, 130.2, 133.0, 148.7, 150.1, and 165.5. Anal. Calcd for $C_{19}H_{18}NO_5Br$: C, 54.30; H, 4.32; N, 3.33. Found: C, 54.24; H, 4.28; N, 3.27.

9,10-Dimethoxy-7-oxo-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]-phenanthridine-2-carboxylic Acid Methyl Ester (62). A solution containing 0.32 g (0.76 mmol) of bromide **60** and 0.8 mL (1.5 mmol) of bis(tributyltin) in 250 mL of benzene was irradiated with a 250 W sunlamp for 24 h at 80 °C. The solvent was removed under reduced pressure, and the residue was subjected to silica gel chromatography to give 0.18 g (71%) of **62** as a white solid: mp 238−239 °C; IR (KBr) 1719, 1702, and 1641 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.44 (t, 2H, J = 8.4 Hz), 3.99 (s, 3H), 4.06 (s, 3H), 4.13 (s, 3H), 4.54 (t, 2H, J = 8.4 Hz), 7.62 (s, 1H), 7.94 (s, 1H), 7.97 (d, 1H, J = 1.2 Hz), and 8.59 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.0, 46.9, 52.2, 56.3, 56.4, 103.0, 108.7, 115.9, 121.2, 122.3, 124.4, 125.1, 128.0, 131.1, 142.7, 149.9, 153.1, 159.8, and 167.1. Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.01; H, 5.16; N, 3.96.

Oxoassoanine (51). A mixture containing 0.13 g (0.38 mmol) of ester **62** in 20 mL of a 10% methanolic KOH solution was heated at reflux for 2 h. The solvent was removed under reduced pressure, and the residue was suspended in 15 mL of a cold 10% HCl solution and stirred at 25 °C for 1 h. The solution was filtered, and the resulting solid was suspended in 10 mL of freshly distilled quinoline. After the addition of 180 mg of copper bronze, the mixture was heated at 220−225 °C for 2.5 h. The mixture was cooled to room temperature and filtered through a pad of Celite. The resulting solution was washed with a 10% HCl solution and dried over Na_2SO_4. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.088 g (81%) of oxoassoanine (**51**) as a pale yellow solid: mp 266−267 °C (lit.[58] mp 266−269 °C); IR (KBr) 1644, and 1607 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.45 (t, 2H, J = 8.4 Hz), 4.05 (s, 3H), 4.09 (s, 3H), 4.50 (t, 2H, J = 8.4 Hz), 7.22 (t, 1H, J = 7.2 Hz), 7.29 (dd, 1H, J = 7.2 and 1.2 Hz), 7.54 (s, 1H), 7.82 (d, 1H, J = 7.6 Hz), and 7.95 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.4, 46.5, 56.1, 56.2, 102.9, 108.7, 116.7, 119.2, 121.3, 123.1, 123.6, 128.5, 130.9, 139.4, 149.6, 152.8, and 159.6; HRMS calcd for $C_{17}H_{15}NO_3$ 281.1052, found 281.1056.

5-[(6-Bromobenzo[1,4]dioxole-5-carbonyl)amino]furan-2-carboxylic Acid Methyl Ester (57). To a solution containing 4.9 g (0.02 mol) of 6-bromo-1,3-benzodioxole-5-carboxaldehyde and 3 drops of a 1 M H_3PO_4 solution in 200 mL of acetone at 10 °C was added a solution containing 3.0 g (0.026 mol) of $NaClO_2$ in 100 mL of water. The yellow solution was warmed to room temperature, and a 35% H_2O_2 solution was added dropwise until the mixture became colorless. The solution was acidified to pH 1 at 0 °C, and the resulting solid was filtered, washed with cold water, and dried to give 4.9 g (94%) of 6-bromo-1,3-benzodioxole-5-carboxylic acid as a white solid: ^1H NMR ($CDCl_3$, 300 MHz) δ 6.08 (s, 2H), 7.14 (s, 1H), 7.50 (s, 1H), and 10.50 (brs, 1H). To a suspension of 0.9 g (3.7 mmol) of the above acid in 15 mL of CH_2Cl_2 at room temperature was added 1.0 mL (11 mmol) of oxalyl chloride. The mixture was stirred at room temperature for 12 h, and the solvent was removed under reduced pressure. The resulting acid chloride was used without further purification. To a refluxing solution containing 0.5 g (3.5 mmol) of furan **1** and

0.6 mL (7.0 mmol) of pyridine in 75 mL of benzene was added the above acid chloride in 50 mL of benzene over a period of 6 h. The mixture was heated at reflux for 12 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column to give 1.11 g (85%) of **57** as a pale yellow solid: mp 172−173 °C; IR (KBr) 3187, 1725, and 1672 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.85 (s, 3H), 6.07 (s, 2H), 6.68 (d, 1H, J = 3.6 Hz), 7.04 (s, 1H), 7.17 (s, 1H); 7.23 (d, 1H, J = 3.6 Hz), and 8.84 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.8, 97.0, 102.6, 110.1, 111.3, 113.5, 121.1, 128.5, 136.8, 147.7, 148.6, 150.7, 158.9, and 162.5. Anal. Calcd for $C_{14}H_{10}NO_6Br$: C, 45.68; H, 2.74; N, 3.80. Found: C, 45.74; H, 2.81; N, 3.70.

5-[(6-Bromobenzo[1,3]dioxole-5-carbonyl)but-3-enylamino]furan-2-carboxylic Acid Methyl Ester (59). To a mixture containing 0.42 g (1.1 mmol) of amidofuran **57** and 1.1 g (3.4 mmol) of cesium carbonate in 30 mL of 1:4 THF/DMF was added 0.34 mL (3.3 mmol) of 4-bromo-1-butene. The mixture was heated at 80 °C for 5 h to give 0.4 g (84%) of **59** as a yellow oil: IR (neat) 1731, 1678, and 1533 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.44 (m, 2H), 3.87 (s, 3H), 3.95 (brs, 2H), 5.06−5.15 (m, 2H), 5.82 (m, 1H), 5.96 (brs, 3H), 6.65 (brs, 1H), 6.88 (brs, 1H), and 6.95 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.2, 46.6, 51.8, 102.1, 106.3, 107.7, 110.7, 112.6, 117.3, 119.0, 130.5, 134.3, 140.8, 147.0, 149.0, 150.5, 158.4, and 167.7; HRMS calcd for $C_{18}H_{16}NO_6Br$: 421.0161, found 421.0159.

1-(6-Bromobenzo[1,3]dioxole-5-carbonyl)-2,3-dihydro-1*H*-indole-5-carboxylic Acid Methyl Ester (61). A mixture containing 0.14 g (0.33 mmol) of amidofuran **59** in 5 mL of a 5 M $LiClO_4$/etherate solution was heated at 100 °C in a sealed tube for 36 h. After cooling, the solution was diluted with ether, washed with water, and dried over Na_2SO_4. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 0.11 g (80%) of **61** as a white solid: mp 139−140 °C; IR (KBr), 1719, 1707, 1658, and 1482 cm^{-1}; ^1H NMR (DMSO-d_6, 80 °C, 400 MHz) δ 3.17 (t, 2H, J = 8.6 Hz), 3.84 (s, 3H), 3.90 (brs, 2H), 6.14 (s, 2H), 7.13 (s, 1H), 7.28 (s, 1H), 7.84 (s, 2H) and 8.20 (brs, 1H); ^{13}C NMR (DMSO-d_6, 80 °C, 100 MHz) δ 26.5, 49.1, 51.4, 102.1, 107.4, 108.9, 112.2, 116.6, 125.6, 128.9, 131.3, 132.2, 133.1, 146.1, 147.3, 148.8, 149.2, and 165.5. Anal. Calcd for $C_{18}H_{14}NO_5Br$: C, 53.49; H, 3.49; N, 3.47. Found: C, 53.57; H, 3.44; N, 3.47.

7-Oxo-4,5-dihydro-7*H*-[1,3]dioxole[4,5-*j*]pyrrolo[3,2,1-*de*]phenanthridine-2-carboxylic Acid Methyl Ester (63). A solution containing 0.34 g (0.84 mmol) of bromodihyroindole **61** and 0.85 mL (1.7 mmol) of bis(tributyltin) in 250 mL of benzene at 80 °C was irradiated using a 250 W sunlamp for 24 h. The solvent was removed under reduced pressure, and the resulting solid was dissolved in 250 mL of CH_3CN and washed with hexane. Removal of the solvent followed by flash silica gel chromatography gave 0.08 g of recovered starting material and 0.22 g (79%) of **63** as a pale yellow solid: mp 280−281 °C; IR (KBr) 1702, 1651, and 1607 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.45 (t, 2H, J = 8.4 Hz), 3.97 (s, 3H), 4.51 (t, 2H, J = 8.4 Hz), 6.16 (s, 2H), 7.61 (s, 1H), 7.88 (s, 1H), 7.95 (d, 1H, J = 1.2 Hz), and 8.50 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.0, 46.9, 52.2, 101.0, 102.2, 106.7, 115.9, 122.6, 123.0, 124.6, 125.2, 130.2, 131.0, 142.6, 148.8, 152.1, 159.6, and 166.9. Anal. Calcd for $C_{18}H_{13}NO_5$: C, 66.87; H, 4.05; N, 4.33. Found: C, 66.60; H, 4.10; N, 4.23.

Anhydrolycorin-7-one (52). A mixture containing 0.090 g (0.28 mmol) of ester **63** in 15 mL of a 10% methanolic KOH solution was heated at reflux for 2 h. The solvent was removed under reduced pressure, and the residue was suspended in 15 mL of a cold 10% HCl solution and stirred for 1 h. The solution was filtered and concentrated under reduced pressure, and the residue was suspended in 10 mL of freshly distilled quinoline. To this solution was added 135 mg of copper bronze, and the mixture was heated at 220−225 °C for 2.5 h. After being cooled to room temperature, the mixture was filtered through a pad of Celite, washed with 10% HCl, and dried over Na_2SO_4. Removal of the solvent under reduced pressure followed by flash silica gel chromatography gave 60 mg (80%) of anhydrolycorin-7-one (**52**) as a tan solid: mp 231−232 °C (lit.[56] mp 230−231 °C); IR (KBr) 1644, 1618, and 1468 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.44 (t, 2H, J = 8.4 Hz), 4.49 (t, 2H, J = 8.4 Hz), 6.14 (s, 2H), 7.20 (t, 1H, J = 7.9 Hz), 7.30 (dd, 1H, J = 7.2 and 1.2 Hz), 7.56 (s, 1H), 7.76 (d, 1H, J = 7.9 Hz), and 7.93 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.3, 46.4, 100.7, 102.0, 106.5, 116.5, 119.2, 122.8, 123.0, 123.6, 130.7, 139.1, 148.2, 151.6, and 159.2; HRMS calcd for $C_{16}H_{11}NO_3$ 265.0739, found 265.0740.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra for new compounds lacking analyses (28 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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