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Diels−Alder Reactions of *N*-Acyl-2-alkyl(aryl)-5-vinyl-2,3-dihydro-4-pyridones

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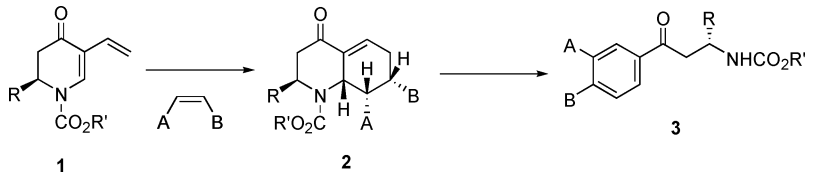

Readily available *N*-acyl-5-vinyl-2,3-dihydro-4-pyridones undergo Diels−Alder cyclization with various dienophiles to afford novel octahydroquinolines containing synthetically useful functionality. With dihydropyridone **5** and cis-disubstituted dienophiles, the resulting cycloadducts were obtained as single diastereomers in good to excellent yield. The corresponding reaction of **5** with methyl acrylate, acrylonitrile, and phenyl vinyl sulfone showed modest preference for the endo adducts. The effect of the dihydropyridone C-2 and C-4 substituents on the degree of diastereofacial control was examined. By using this methodology, the core decahydroquinoline skeleton of gephyrotoxin was prepared in a stereocontrolled fashion. Interesting reactivity was observed with certain dienophiles leading to ring-opening of the initially formed cycloadducts. This tandem reaction provides a route to uniquely substituted β-aminoketones, alcohols, and unnatural amino acids.

Introduction

The Diels−Alder reaction provides an efficient and rapid means of constructing highly functionalized six-membered heterocyclic ring systems with excellent control of the regio-, diastereo-, and enantioselectivity.[1] The heteroatom-assisted Diels−Alder reaction has emerged as an extremely powerful method for the preparation of complex heterocycles. In particular, the increased reactivity of amino-substituted dienes allows for the facile preparation of functional arrays which would otherwise be difficult to obtain.[2] Bimolecular and intramolecular Diels−Alder reactions of 1-*N*-acylamino-1,3-dienes[3] and *N*,*N*-dialkylamino-1,3-dienes[3g,4] have been well-studied and typically proceed with a high degree of regioselectivity and facial selectivity. In addition, the Diels−Alder reactions of 2-*N*-acylamino-1,3-dienes[5] and *N*-tosylamino-1,3-dienes[6] have been reported. Due to this success, it is not surprising that heteroatom-assisted Diels−Alder reactions continue to see a number of advances and synthetic applications in target oriented synthesis.

The deca-, octa-, and hexahydroquinoline ring systems are present as a key structural feature in several major classes of alkaloids (Figure 1). Representative members include, but are not limited to, gephyrotoxin and lycopo-

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(1) For leading references, see: (a) Corey, E. J. *Angew. Chem.*, *Int. Ed.* **2002**, *41*, 1650. (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem.*, *Int. Ed.* **2002**, *41*, 1668. (c) Tietze, L. F.; Kettschau, G. In *Topic in Current Chemistry*; Metz, P., Ed.; Springer-Verlag: Berlin, 1997; Vol. 189, pp 1−120 and references therein. (d) Waldmann, H. *Synthesis* **1994**, 535.

(2) For reviews on the Diels−Alder reaction of amino-substituted dienes, see: (a) Enders, D.; Meyer, O. *Liebigs Ann.* **1996**, 1023. (b) Barluenga, J.; Suarez-Sobrino, A.; Lopez, L. A. *Aldrichim. Acta* **1999**, *32*, 4.

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(4) (a) Aelterman, W.; De Kimpe, N. *Tetrahedron* **1998**, *54*, 2563. (b) Jiang, J.; DeVita, R. J.; Doss, G. A.; Goulet, M. T.; Wyvratt, M. J. *J. Am. Chem. Soc.* **1999**, *121*, 593. (c) Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdés, C. *Tetrahedron Lett.* **2002**, *43*, 8159 and references therein.

(5) (a) Ha, J. D.; Kang, C. H.; Belmore, K. A.; Cha, J. K. *J. Org. Chem.* **1998**, *63*, 3810 and references therein. (b) Occhiato, E. G.; Trabocchi, A.; Guarna, A. *Org. Lett.* **2000**, *2*, 1241. (c) Galbo, F. L.; Occhiato, E. G.; Guarna, A.; Faggi, C. *J. Org. Chem.* **2003**, *68*, 6360.

(6) (a) Luker, T.; Hiemstra, H.; Speckamp, W. N. *J. Org. Chem.* **1997**, *62*, 8131. (b) Harrison, T. J.; Dake, G. R. *Org. Lett.* **2004**, *6*, 5023.

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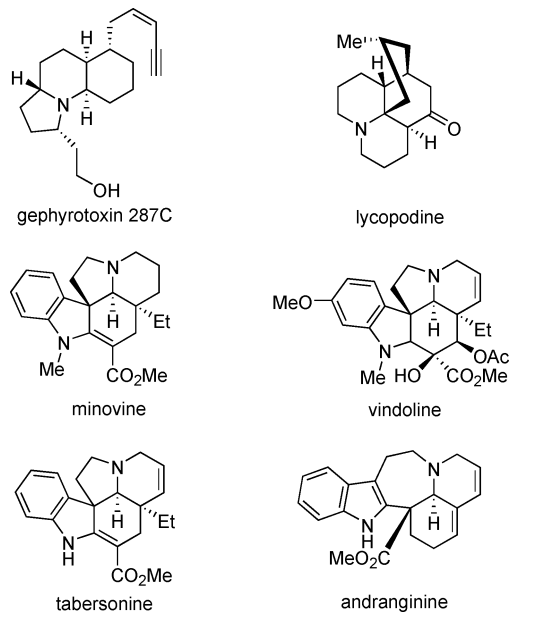
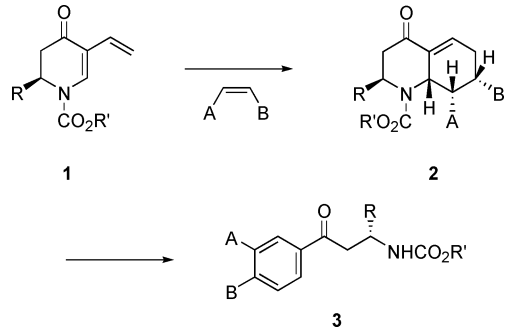


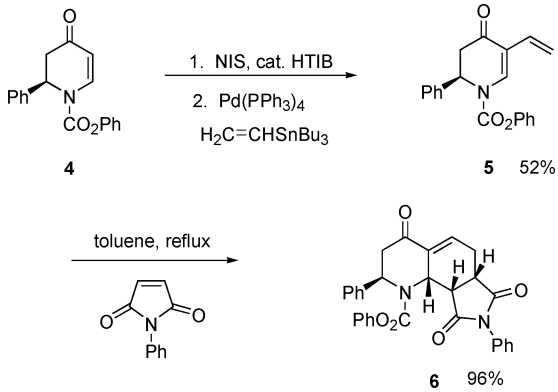
FIGURE 1. Representative deca-, octa-, and hexahydroquinoline alkaloids.

dine (decahydro-), minovine and vindoline (octahydro-), and tabersonine and andranginine (hexahydro-).[7–11] Many of these natural products, as well as related synthetic unnatural products, exert diverse biological activities

SCHEME 1



SCHEME 2



depending upon the type and degree of substitution and relative ring fusion. The ability to construct both multiple functional arrays and subsequently the ring systems found in these and other natural and unnatural products with complete control of both regio- and stereocontrol is effectively useful in synthesis. As part of a program to develop and expand the synthetic versatility of *N*-acyl-2,3-dihydro-4-pyridones for alkaloid synthesis,[12] we recently reported the Diels–Alder reactions of substituted *N*-acyl-5-vinyl-2,3-dihydro-4-pyridones of type **1** with various dienophiles as an effective method for the construction of novel octahydroquinoline derivatives of general type **2**.[13] In addition, we also reported interesting reactivity of diene **1** with certain dienophiles leading to ring-opening of the initially formed cycloadduct **2** giving rise to β-amino ketones, alcohols, and amino acids of type **3**.[14] Herein we present a complete account of these investigations.

Results and Discussion

Preparation of Octahydroquinolines. Our initial study began with the preparation of *N*-acyl-2-phenyl-5-vinyl-2,3-dihydro-4-pyridone (**5**; Scheme 2). Iodination of readily available 2,3-dihydropyridone (**4**) with NIS/cat. [hydroxyl(tosyloxy)iodo]benzene (HTIB) followed by Stille coupling with vinyltributyltin afforded the desired Diels–

(7) For approaches to gephyrotoxin, see: (a) Pearson, W. H.; Fang, W.-K. *J. Org. Chem.* **2000**, *65*, 7158. (b) Holmes, A. B.; Hughes, A. B.; Smith, A. L. *J. Chem. Soc., Perkin Trans. 1* **1993**, *5*, 633. (c) Holmes, A. B.; Hughes, A. B.; Smith, A. L.; Williams, S. F. *J. Chem. Soc., Perkin Trans. 1* **1992**, *9*, 1089. (d) Pearson, W. H.; Poon, Y.-F. *Tetrahedron Lett.* **1989**, *30*, 6661. (e) Ito, Y.; Nakajo, E.; Nakatsuka, M.; Saegusa, T. *Tetrahedron Lett.* **1983**, *24*, 2881. (f) Overman, L. E.; Lesuisse, D.; Hashimoto, M. *J. Am. Chem. Soc.* **1983**, *105*, 5373. (g) Hart, D. J.; Kanai, K. *J. Am. Chem. Soc.* **1983**, *105*, 1255. (h) Fujimoto, R.; Kishi, Y. *Tetrahedron Lett.* **1981**, *22*, 4197. (i) Overman, L. E.; Fukaya, C. *J. Am. Chem. Soc.* **1980**, *102*, 1454. (j) Fujimoto, R.; Kishi, Y.; Blount, J. F. *J. Am. Chem. Soc.* **1980**, *102*, 7154.

(8) For reviews on the *Lycopodium* alkaloids, see: (a) Ayer, W. A.; Trifonov, L. S. In *The Alkaloids*; Cordell, G. A., Brossi, A., Eds.; Academic Press: New York, 1994; Vol. 45, p 233. (b) Ayer, W. A. *Nat. Prod. Rep.* **1991**, *8*, 455. (c) MacLean, D. B. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1985; Vol. 26, p 241. (d) MacLean, D. B. In *The Alkaloids*; Manske, R. H. F., Ed.; Academic Press: New York, 1973; Vol. 14, p 348. (e) MacLean, D. B. In *The Alkaloids*; Manske, R. H. F., Ed.; Academic Press: New York, 1968; Vol. 10, p 305.

(9) For leading references to Minovine, see: (a) Yuan, Z. Q.; Ishikawa, H.; Boger, D. L. *Org Lett.* **2005**, *7*, 741. (b) Kalaus, G.; Kiss, M.; Kajtar-Peredy, M.; Brlik, J.; Szabo, L.; Szantay, C. *Heterocycles* **1985**, *23*, 2783. (c) Kuehne, M. E.; Huebner, J. A.; Matsko, T. H. *J. Org. Chem.* **1979**, *44*, 2477. (d) Kutney, J. P.; Chan, K. K.; Failli, A.; Fromson, J. M.; Gletsos, C.; Leutwiler, A.; Nelson, V. R.; de Souza, J. P. *Helv. Chim. Acta* **1975**, *58*, 1648. (e) Ziegler, F. E.; Spitzner, E. B. *J. Am. Chem. Soc.* **1973**, *95*, 7146. (f) Kutney, J. P.; Chan, K. K.; Failli, A.; Fromson, J. M.; Gletsos, C.; Leutwiler, A.; Nelson, V. R. *J. Am. Chem. Soc.* **1968,** *90*, 3891.

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(11) For a leading reference to Andranginine, see: Danieli, B.; Martinelli, L. M.; Passarella, D.; Silvani, A. *J. Org. Chem.* **1997**, *62*, 6519 and references therein.

(12) For leading references, see: (a) Comins, D. L.; Al-awar, R. S.; Foti, C. J. *J. Org. Chem.* **1999**, *64*, 2184. (b) Comins, D. L.; Brooks, C. A.; Al-awar, R. S.; Goehring, R. R. *Org Lett.* **1999**, *1*, 229. (c) Comins, D. L.; Fulp, A. B. *Org. Lett.* **1999**, *1*, 1941. (d) Kuethe, J. T.; Comins, D. L. *Org. Lett.* **2000**, *2*, 855. (e) Huang, S.; Comins, D. L. *Chem. Commun.* **2000**, *7*, 569.

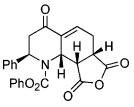
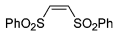
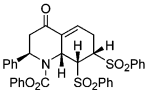
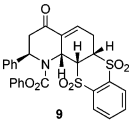
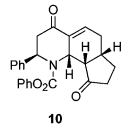
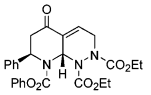
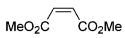
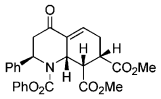
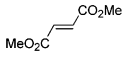
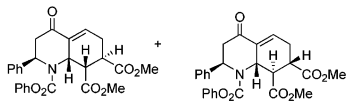
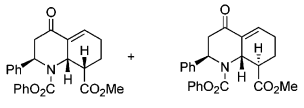
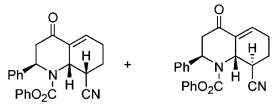
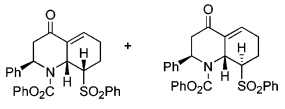
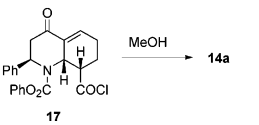
(13) Kuethe, J. T.; Brooks, C. A.; Comins, D. L. *Org. Lett.* **2003**, *5*, 321.

(14) Kuethe, J. T.; Comins, D. L. *Tetrahedron Lett.* **2003**, *44*, 4179.

Alder precursor **5** in good overall yield.[15] The Diels–Alder reaction of **5** with *N*-phenylmaleimide in refluxing toluene gave cycloadduct **6** as a single diastereomer in 96% isolated yield. The relative stereochemistry of **6** was unequivocally established by single-crystal X-ray analysis, which showed the exclusive preference for endo approach of the dienophile.[13] Since the C-2 phenyl group of diene **5** occupies a pseudoaxial orientation,[16] excellent diastereofacial control was observed due to addition of the dienophile exclusively anti to the phenyl substituent, thus setting the three new contiguous chiral centers with complete stereocontrol. The Diels–Alder reactions of **5** with various dienophiles are summarized in Table 1. When cis-disubstituted dienophiles were employed (entries 1–6), the corresponding cycloadducts were obtained as single diastereomers in good to excellent yield. The structures were determined by ^{1}H NMR analysis by comparison of coupling constants with those observed for cycloadduct **6**. On the other hand, when dimethyl fumarate served as the dienophile (entry 7), no endo/exo selectivity was observed and cycloadducts **13a** and **13b** were obtained as a 1:1 mixture of diastereomers. Interestingly, reaction of **5** with methyl acrylate, acrylonitrile, and phenyl vinyl sulfone (entries 8–10) only showed modest preference for the endo adducts. In contrast, the Diels–Alder reaction of **5** and acryloyl chloride (entry 11) proceeded at room temperature to afford the labile adduct **17** as one diastereomer. Treatment of the crude product with anhydrous methanol provided the methyl ester **14a** in moderate yield. In each case the products were in full accord with that predicted by HOMO diene–LUMO dienophile interactions. In addition, in all cases there was no detectable amount of double bond isomerization of the cycloadducts.[5a]

Having established that the presence of a C-2 phenyl group provided excellent diastereofacial control, we next probed the diastereoselectivity of the reaction by varying the C-2 substituent (Scheme 3). While the C-2 phenyl group exerted a significant steric influence causing the dienophile to approach exclusively anti, unbranched alkyl substitutents resulted in erosion of diastereoselectivity. For example, reaction of diene **18**[15] with *N*-phenylmaleimide under the identical reaction conditions as described for diene **5** provided a 95% combined yield of a 7:1 mixture of diastereomers (**19**:**20**) which were easily separated by chromatography. In like fashion, reaction of diene **21** with either *N*-phenylmaleimide or benzodithiin tetraoxide[17] provided mixtures of diastereomers **22**:**23** (14:1, 87%) and **24**:**25** (3:1, 80%), respectively. While the spectroscopic and physical data for major cycloadducts **19**, **22** (X-ray),[18] and **24** for each of these reactions were in full agreement with the C-2 substituent providing bias for the anti approach of the dieneophile, the stereochemical assignment of the minor adducts **20**, **23**, and **25** was not immediately straightforward.

TABLE 1. Diels–Alder Reactions of 5 with Various Dienophiles

entry	dienophile	conditions	cycloadduct	yield, %
1		toluene reflux, 12 h	 **7**	90
2		toluene reflux, 12 h	 **8**	76
3		toluene reflux, 24 h	 **9**	44
4		toluene 200 °C, 12 h	 **10**	74
5	$EtO_2CN{=}NCO_2Et$	benzene reflux, 10 min	 **11**	93
6		toluene 200 °C, 12 h	 **12**	82
7		toluene reflux, 12 h	 **13a** + **13b** **13a:13b** = 1:1	78
8		toluene reflux, 12 h	 **14a** + **14b** **14a:14b** = 2.5:1	86
9		toluene reflux, 12h	 **15a** + **15b** **15a:15b** = 2:1	91
10		toluene 200 °C, 12 h	 **16a** + **16b** **16a:16b** = 2:1	66
11		$CDCl_3$ rt, 10 h	 **17**	51

In theory, there are four possible isomers from each of these reactions (Scheme 4). Endo approach of the dienophile from the α-face via transition structure **26** leads to the observed major diatereomer **19** when *N*-phenylmaleimide serves as the dienophile. Exo approach via transition structure **28** would lead to **29**. However, if the

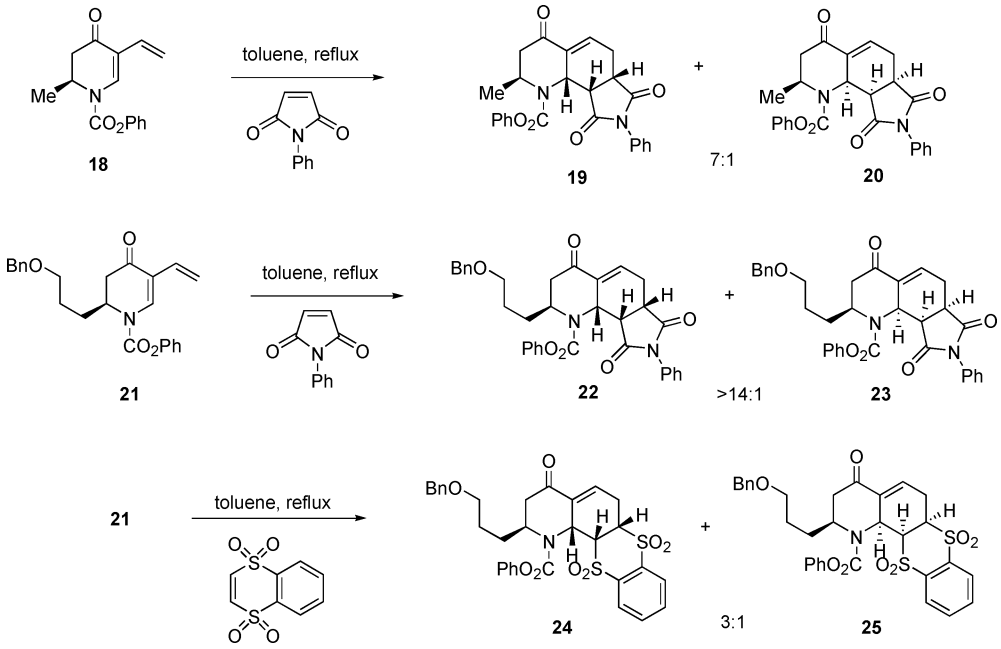
(15) (a) Comins, D. L.; Joseph, S. P.; Chen, X. *Tetrahedron Lett.* **1995**, *36*, 9141. (b) For a more convenient procedure with ICl, see: Comins, D. L.; Hiebel, A.; Huang, S. *Org. Lett*. **2001**, *3*, 769.

(16) Comins, D. L.; Joseph, S. P. In *Advances in Nitrogen Heterecycles*; Moody, C. J., Ed.; JAI Press: Greenwich, CT, 1996; Vol. 2, pp 251–294 and references therein.

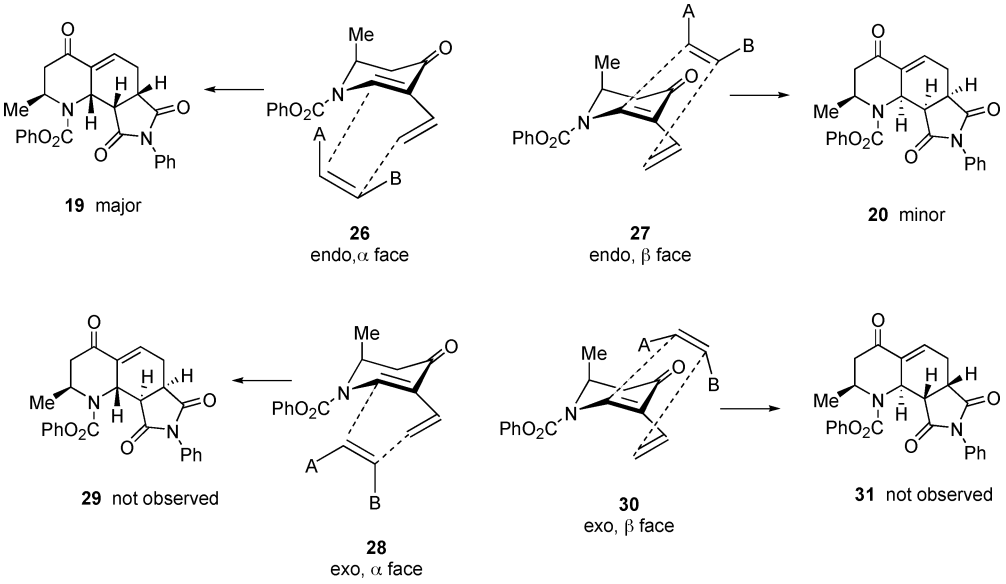
(17) Nakayama, J.; Nakamura, Y.; Hoshino, M. *Heterocycles* **1985**, 1119.

(18) See Supporting Information for details.

SCHEME 3

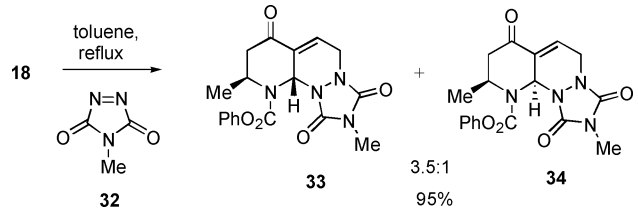


SCHEME 4



C-2 substituent does not provide a sufficient steric influence, endo approach from the β-face would lead to **20** and exo approach from the same face would lead to **31**. Due to the propensity of maleimides, and cyclic dienophiles in general, to preferentially approach dienes in an endo fashion due to secondary orbital interactions,[19] the formation of **29** and **31** seemed unlikely. The stereochemistry of the minor cycloadduct **20** was unequivocally established by both low-temperature and high-temperature NMR experiments. A series of nOe experiments clearly established the all-cis configuration of the maleimide and octahydroquinoline ring junction.[18] In addition, the reaction of **18** with 4-methyl-1,2,4-triazole-3,5-dione (**32**) provided a 3.5:1 mixture of diastereomers

SCHEME 5

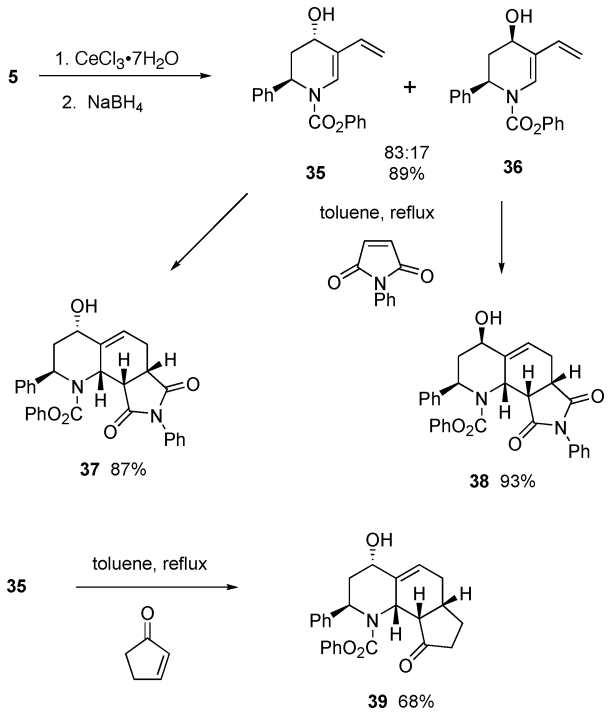


33 and **34** in 95% combined yield (Scheme 5). In this case only approach of the dienophile from both the α and β face would furnish the diastereomeric mixture that further reinforced our stereochemical assignment of **20**, **23**, and **25** (Scheme 3).

To further explore the synthetic utility of the process, reduction of the C-4 carbonyl group of dihydropyridone **5** was studied (Scheme 6). While the C-2 substitutent

(19) Fleming, I. *Frontier Orbital and Organic Chemical Reactions*; Wiley-Interscience: New York, 1990; pp 1−249.

SCHEME 6

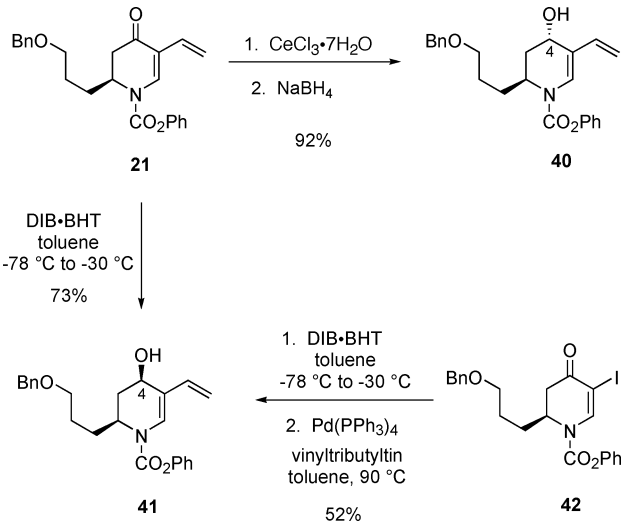


plays a critical role in controlling the diastereoselectivity of the Diels−Alder reaction, what role the C-4 hydroxyl group would play invited investigation. Luche reduction of **5** provided diastereomers **35** and **36** as a 83:17 mixture in a combined yield of 89%. The isomers were easily separated by silca gel chromatography. Individual reaction of **35** and **36** with *N*-phenylmaleimide in refluxing toluene for 30 min gave cycloadducts **37** and **38** as single diastereomers in 87% and 93% yield, respectively. In similar fashion, reaction of **35** with cyclopentenone provided **39** in 68% isolated yield. The stereochemistry of each of these cycloadducts was established by NMR analysis, and the results demonstrated that the C-4 hydroxyl group did not provide any significant amount of influence over the approach of the dienophile.

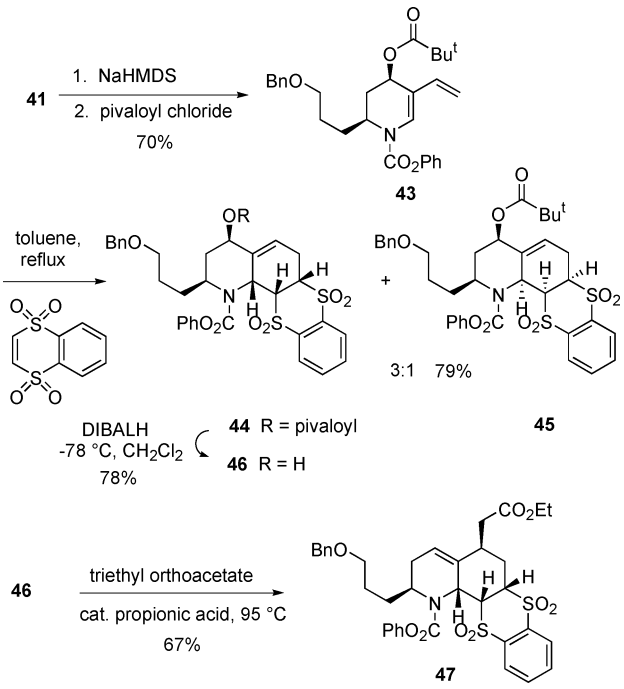
In an approach to the ring system of gephyrotoxin, we examined the Diels−Alder reaction of diene **41** (Scheme 7). The axial hydroxyl group of diene **41** was required to effect a stereoselective ortho ester Claisen rearrangement later in the synthesis to establish the C-6 stereocenter of the gephyrotoxin ring system (vida infra). It was envisioned that the use of benzodithiin tetraoxide as the dienophile, which is an ethylene equivalent via subsequent desulfonylation, would provide an attractive extension of this work and provide the core decahydroquinoline skeleton of gephyrotoxin in a limited number of steps. Reduction of **21** under Luche conditions provided **40** in 92% yield with the expected, but undesired, C-4 stereochemistry, and only a minor amount of the desired diastereomer **41** (4%) was formed. After extensive experimentation, it was discovered that reduction of **21** with diisobutylaluminum 2,6-di-*tert*-butylphenoxide (DIB·BHT)[20] provided the needed diastereomer **41** in 67% yield as a 30:1 (**41**:**40**) mixture that was easily separated by

(20) Iguchi, S.; Nakai, H.; Hayashi, M.; Yamamoto, H.; Moruoda, K. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3033.

SCHEME 7



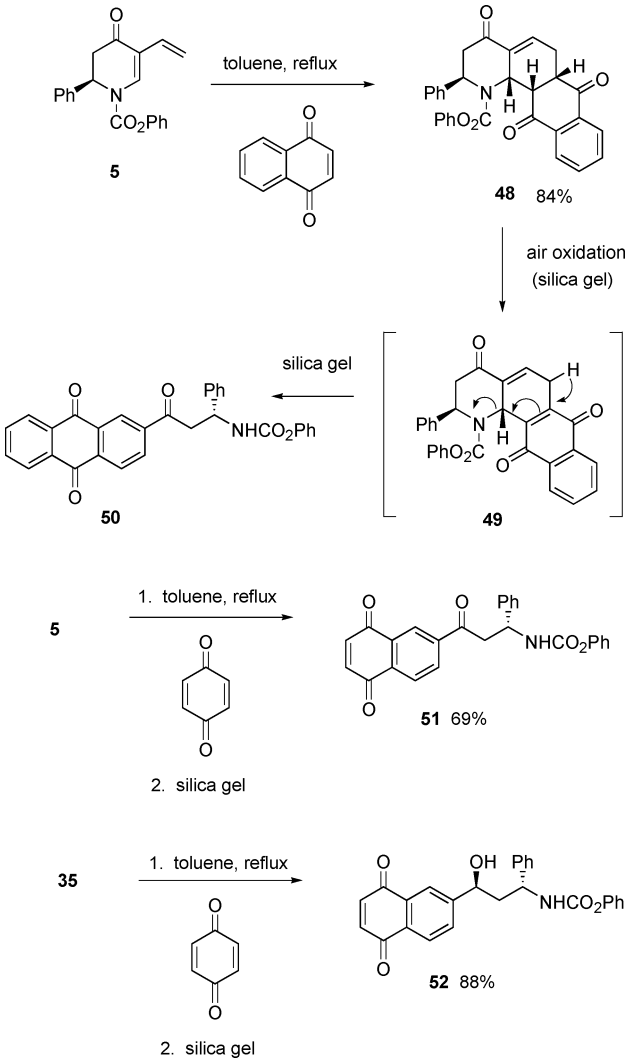
SCHEME 8



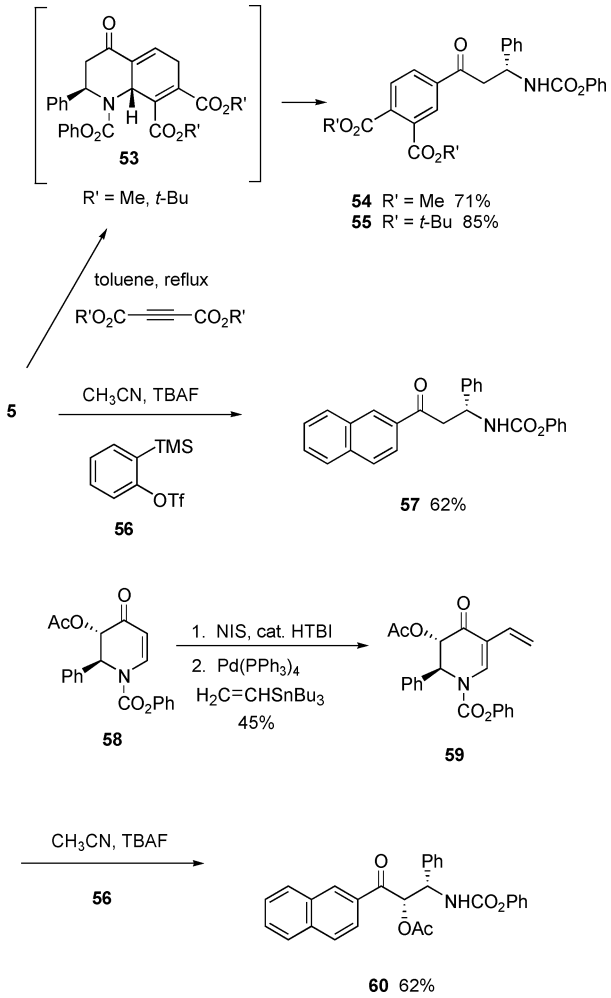
chromatography. Alternatively, **41** could be prepared by DIB·BHT reduction of iodide **42** followed by Stille cross coupling of the major isomer to give **41** in 41% overall yield from **42**.

The reaction of **41** with benzodithiin tetraoxide gave an extremely complex mixture of diastereomers that were difficult to separate by conventional chromatography. On the other hand, protection of **41** as pivaloyl ester **43** (70%) prior to cyclization proved fruitful (Scheme 8). The Diels−Alder reaction of **43** with benzodithiin tetraoxide gave a 3:1 mixture of **44** and **45** in 79% combined yield. The pivaloyl group could be easily removed by treatment of **44** with DIBAL in CH_2Cl_2 to give **46** in 78% yield. Reaction of **46** with triethyl orthoacetate in the presence of a catalytic amount of propionic acid furnished **47** in 67% yield where the relative stereochemistry of all five chiral centers was unequivocally established by single-crystal X-ray analysis.[18] The synthesis of **47** represents

SCHEME 9



SCHEME 10



a potential route to gephyrotoxin as three of the five stereocenters of the target ring system have been set with complete regio- and stereocontrol.

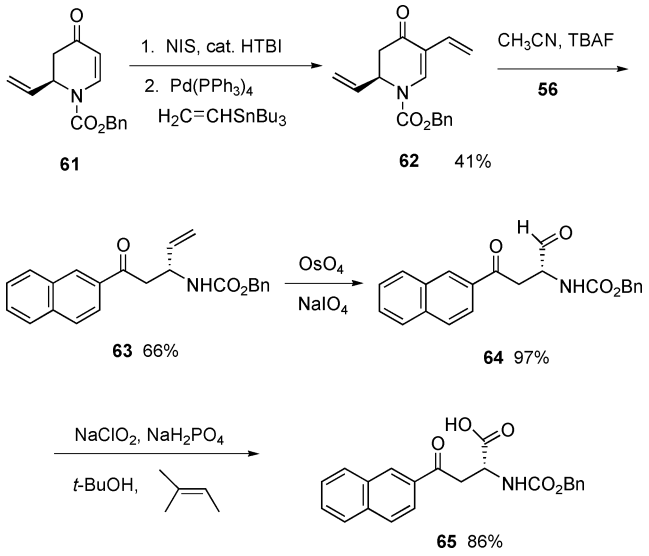
Tandem Diels–Alder Cyclization/Aromatization Reactions. During the course of the Diels–Alder studies of diene **5**, interesting reactivity was observed with certain dienophiles leading to ring-opening of the initially formed cycloadducts of type **2**. This methodology provides a route to uniquely substituted β-aminoketones, alcohols, and amino acids. For example, the Diels–Alder reaction of **5** with 1,4-naphthoquinone in refluxing toluene afforded the expected cycloadduct **48** in 84% isolated yield as a single diastereomer (Scheme 9). Analysis of the NMR spectrum of the crude product showed that **48** was the only isomer present, and the stereochemistry was in complete agreement with that observed for adducts listed in Table 1. However, attempted purification of **48** on silica gel resulted in the isolation of a new product that was identified as the anthraquinone derivative **50** on the basis of its spectral properties and high-resolution mass spectra. We suspect that **50** arises from air oxidation of **48** to **49**, which is followed by silica gel promoted aromatization of the quinone moiety via ejection of the carbamate functionality leading to **50**. The formation of **50** could be effected in a one-pot procedure by adding silica gel to the Diels–Alder adduct **48** in toluene and stirring overnight at room temperature to give **50** in 88% yield from **5**. Reaction of **5** with 1,4-benzoquinone also occurred in refluxing toluene to give the initially formed cycloadduct as an unstable single diastereomer. When subjected to silica gel-promoted oxidative rearrangement, naphthoquinone derivative **51** was isolated in 69% yield from **5**. In similar fashion, reaction of **35** with 1,4-benzoquinone followed by the direct addition of silica gel and stirring overnight gave β-amino alcohol **52** in 88% yield as a single product.

When diene **5** was allowed to react with DMAD or di-*tert*-butylacetylene dicarboxylate in refluxing toluene, the initially formed cycloadducts **53** could not be isolated (Scheme 10). Instead, intermediate **53** rapidly aromatized via ejection of the phenyl carbamate to give the substituted benzene derivatives **54** and **55** in 71% and 85% yields, respectively. There was no detectable amount of **53** in the crude reaction mixture even when the reaction was stopped prior to complete conversion of starting materials.

We also investigated the reaction of **5** with benzyne (Scheme 10). Treatment of a mixture of **5** and triflate **56** in acetonitrile with TBAF[21] resulted in the rapid forma-

(21) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211.

SCHEME 11



tion of ring-opened naphthalene derivative **57** as the sole product in 62% isolated yield. Once again, the initially formed cycloadduct could not be isolated and underwent rapid aromatization via ejection of the phenyl carbamate. To investigate the possibility of synthesizing more highly functionalized systems, we prepared diene **59** from the known dihydropyridone **58**.[22] Iodination of **58** with NIS/cat. [hydroxyl(tosyloxy)iodo]benzene (HTIB) followed by Stille coupling with tributyl(vinyl)tin gave **59** in 45% overall yield.[10] Reaction of **59** with benzyne under the conditions described above afforded compound **60** as a single diastereomer in 62% yield with the stereochemistry as shown.

Finally, we investigated an approach to α-amino acids by taking advantage of the vinyl substituent at the C-2 position of diene **62** for further elaboration to a carboxylic acid group (Scheme 11). Diene **62** was prepared from dihydropyridone **61**[23] via the iodination/Stille coupling procedure as previously described. Reaction of **62** with benzyne in acetonitrile yielded the expected naphthalene product **63** arising from the tandem Diels−Alder cyclization/aromatization protocol in 66% yield. Treatment of **63** with sodium periodate in the presence of osmium tetroxide gave aldehyde **64** in near quantitative yield. Oxidation of **64** to amino acid **65** was accomplished with sodium chlorite/sodium phosphate solution in a 2:1 mixture of *t*-BuOH:2-methyl-2-butene in 86% yield.

In conclusion, the Diels−Alder reaction of 2-substituted *N*-acyl-5-vinyl-2,3-dihydro-4-pyridones provides a highly efficient means of preparing octahydroquinolines, *β*-amino ketones, alcohols, and amino acids containing various functionalities. By taking advantage of the C-2 axial substituent, three contiguous centers can be set in a single synthetic operation. Although this study used racemic starting materials, the methodology can lead to enantiopure products of either antipode by starting with readily available nonracemic dihydropyridones.[24] In addition, this synthetic protocol may be useful for the preparation of advanced intermediates for alkaloid synthesis, as well as preparation of stereodefined hydroxy amino alcohols and hydroxy amino acids, functional arrays which are well recognized as important components for various protease inhibitors and other potential pharmaceuticals.[25]

Experimental Section

(2*R,6a*S**,9a*S**,9b*R**)-4,7,9-Trioxo-2,8-diphenyl-1-((phenoxy)carbonyl)-2,3,4,6,6a,7,8,9,9a,9b-decahydropyrrolo-[3,4-*h*]quinoline (6).** To a solution of 68 mg (0.213 mmol) of **5** in 7 mL of toluene was added 47 mg (0.271 mmol) of *N*-phenylmaleimide. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 100 mg (96%) of **6** as a white solid: mp 199−200 °C (EtOAc/hexanes); IR (thin film) 3034, 2929, 1707, 1613, 1493, 1383, 1190, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.41 (m, 1H), 2.84 (dd, 1H, J = 15.6 and 2.3 Hz), 3.17 (dd, 1H, J = 15.6 and 7.9 Hz), 3.31 (dd, 1H, J = 15.6 and 6.3 Hz), 3.44 (t, 1H, J = 8.2 Hz), 4.71 (m, 1H), 5.01 (m, 1H), 5.94 (m, 1H), 6.86 (m, 1H), 7.07−7.50 (m, 15H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.6, 39.9, 42.5, 44.3, 55.9, 58.4, 121.9, 125.6, 126.0, 126.6, 128.1, 129.2, 129.5, 129.6, 131.6, 135.8, 141.7, 151.1, 155.0, 176.2, 177.5, 191.7.

(2*R,6a*S**,9a*S**,9b*R**)-4,7,9-Trioxo-1-((phenoxy)carbonyl)-2-phenyl-3,4,6,6a,7,9,9a,9b-octahydro-2*H*-furo[3,4-*h*]-quinoline (7).** To a solution of 29 mg (0.091 mmol) of **5** in 5 mL of toluene was added 12 mg (0.122 mmol) of maleic anhydride. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The residue was recrystalized from EtOAc/hexanes to give 34 mg (90%) of **7** as a colorless solid: mp 228 °C dec; IR (thin film) 1766, 1701, 1360, 1331, 1258, 1211, 1180, 1079, 977 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.39 (m, 1H), 2.89 (d, 1H, J = 15.6 Hz), 3.11 (dd, 1H, J = 15.6 and 7.7 Hz), 3.28 (dd, 1H, J = 15.6 and 6.1 Hz), 3.59 (t, 1H, J = 8.6 Hz), 4.87 (m, 1H), 5.97 (m, 1H), 6.84 (d, 1H, J = 7.1 Hz), 7.25 (m, 11H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 40.3, 43.6, 44.1, 55.2, 58.4, 121.7, 125.6, 126.2, 128.2, 129.6, 129.7, 135.7, 135.9, 141.3, 150.9, 170.9, 172.6, 190.8. Anal. Calcd for $C_{24}H_{19}NO_6$: C, 69.06; H, 4.59; N, 3.36. Found: C, 69.19; H, 4.70; N, 3.33.

(2*R,7*S**,8*R**,8a*R**)-7,8-Bis(benzenesulfonyl)-4-oxo-1-((phenoxy)carbonyl)-3,4,6,7,8,8a-hexahydro-2*H*-quinoline (8).** To a solution of 35 mg (0.110 mmol) of **5** in 7 mL of toluene was added 40 mg (0.130 mmol) of *cis*-1,2-bis(phenylsulfonyl)ethylene. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 52 mg (76%) of **8** as a white solid: mp 200 °C dec; IR (thin film) 3060, 1713, 1642, 1448, 1385, 1310, 1267, 1197, 1149, 1083 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.13 (m, 1H), 2.96 (m, 1H), 3.15 (dd, 1H, J = 17.9 and 4.8 Hz), 3.31 (m, 2H), 5.12 (s, 1H), 5.44 (s, 1H), 5.82 (s, 1H), 6.54 (m, 1H), 6.90 (m, 4H), 7.04 (m, 2H), 7.33 (m, 6H), 7.60 (m, 2H), 7.77 (m, 4H), 8.03 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.7, 42.6, 53.0, 54.2, 59.5, 62.2, 121.9, 126.0, 126.5, 127.6, 128.3, 128.8, 129.0, 129.2, 129.4, 129.6, 132.6, 133.9, 134.1, 138.3, 140.1, 140.3, 150.5, 155.7, 196.9. Anal. Calcd for $C_{34}H_{29}NO_7S_2$: C, 65.05; H, 4.66; N, 2.23. Found: C, 64.78; H, 4.67; N, 2.17.

(2*R,6a*S**,12a*R**,12b*R**)-4,7,7,12,12-Pentaoxo-2-phenyl-3,4,6,6a,7,12,12a,12b-octahydro-2*H*-7λ^6,12λ^6-dithia-1-aza-benzo[*a*]anthracene-1-carboxylic Acid Phenyl Ester (9).**

(22) Comins, D. L.; Stolze, D. A.; Thakker, P.; McArdle, C. L. *Tetrahedron Lett.* **1998**, *39*, 5693.

(23) Brooks, C. A.; Comins, D. L. *Tetrahedron Lett.* **2000**, *41*, 3551.

(24) (a) Comins, D. L.; Joseph, S. P.; Goehring, R. R. *J. Am. Chem. Soc.* **1994**, *116*, 4719. (b) Comins, D. L.; LaMunyon, D. H. *Tetrahedron Lett.* **1994**, *35*, 7343. (c) Comins, D. L.; Guerra-Weltzien, L. *Tetrahedron Lett.* **1996**, *37*, 3807.

(25) Goodman, M.; Ro, S. In *Burger's Medicinal Chemistry and Drug Discovery*, 5th ed.; Wolff, M., Ed.; Wiley and Sons: New York, 1995; pp 803−861.

To a solution of 20 mg (0.063 mmol) of **5** in 2 mL of toluene was added 15 mg (0.063 mmol) of benzodithiin tetraoxide.[18] The mixture was degassed with argon for 15 min and then refluxed for 24 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, EtOAc/hexanes) to afford 15 mg (44%) of **9** as a yellow oil: IR (NaCl) 3029, 2961, 2924, 1705, 1630, 1328, 1263, 1198, 1151, 1128 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14−8.11 (m, 1H), 8.08−8.05 (m, 1H), 8.00−7.80 (m, 3H), 7.40−7.28 (m, 7H), 7.10−7.07 (m, 1H), 6.81−6.77 (m, 2H), 6.11−6.09 (m, 1H), 5.93−5.90 (m, 1H), 5.39 (br s, 1H), 4.07−4.04 (m, 1H), 3.52 (dd, 1H, J = 16.0 and 4.8 Hz), 3.08−2.98 (m, 2H), 2.88−2.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$), δ 194.9, 150.7, 139.4, 138.5, 135.3, 134.2, 134.1, 133.1, 133.0, 129.6, 129.3, 128.3, 126.6, 126.1, 125.7, 125.5, 125.3, 121.6, 59.0, 58.2, 58.1, 57.8, 43.9, 29.9, 24.1; HRMS calcd for $C_{28}H_{23}NO_7S_2$ ($[M + H]^+$) 550.0994, found 550.1023.

(3a*S,8*R**,9a*R**,9b*S**)-1,6-Dioxo-9-((phenoxy)carbonyl)-8-phenyl-1,2,3,3a,4,6,7,8,9a,9b-decahydro-9-azacyclopenta[*a*]naphthalene (10).** To a solution of 30 mg (0.094 mmol) of **5** in 5 mL of toluene was added 10 mg (0.122 mmol) of 2-cyclopentenone. The mixture was heated at 200 °C in a sealed tube for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 27 mg (74%) of **10** as a colorless foam: IR (thin film) 3060, 2931, 1731, 1689, 1614, 1493, 1300, 1260, 1197 cm^{-1}; ^{1} H NMR ($CDCl_3$, 300 MHz) δ 1.65 (m, 1H), 1.91 (m, 1H), 2.11−2.46 (m, 3H), 2.81 (dd, 1H, J = 15.4 and 3.0 Hz), 2.95 (dd, 1H, J = 16.5 and 10.4 Hz), 3.08 (m, 1H), 3.28 (m, 1H), 3.44 (dd, 1H, J = 15.4 and 6.0 Hz), 3.85 (m, 1H), 4.85 (m, 1H), 5.91 (m, 1H), 6.83 (m, 1H), 7.24 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.4, 30.1, 34.5, 39.0, 44.2, 50.9, 56.3, 58.2, 121.9, 125.8, 127.8, 128.5, 128.7, 129.3, 129.4, 136.2, 137.8, 144.9, 151.1, 154.9, 193.2, 224.0; HRMS calcd for $C_{25}H_{23}NO_4$ ($[M + H]^+$) 402.1705, found 402.1727.

(7*R,8a*R**)-1,2-((Diethoxy)carbonyl)-5-oxo-8-((phenoxy)carbonyl)-7-phenyl-3,6,7,8a-tetrahydro-5*H*-pyrido[2,3-*c*]-pyridazine (11).** To a solution of 38 mg (0.119 mmol) of **5** in 10 mL of benzene was added 27 mg (0.155 mmol) of diethyl azodicarboxylate. The mixture was heated at reflux for 10 min, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 55 mg (93%) of **11** as a colorless oil: IR (neat) 2977, 1711, 1649, 1405, 1311, 1233, 1205 cm^{-1}; ^1H NMR (C_2D_6SO, 300 MHz, 130 °C) δ 1.17 (m, 6H), 3.22 (dt, 1H, J = 17.4 and 2.8 Hz), 3.62 (m, 1H), 3.69 (m, 1H), 4.00 (m, 1H), 4.17 (m, 4H), 5.48 and 5.71 (m, due to rotamers, 1H), 6.39 and 6.44 (m, due to rotamers, 1H), 6.77 and 6.95 (m, due to rotamers, 1H), 7.16−7.50 (m, 10H); ^{13}C NMR (C_2D_6SO, 75 MHz, 130 °C) δ 13.4 and 13.5 (due to rotamers), 13.7, 41.4 and 42.5 (due to rotamers), 52.3 and 53.6 (due to rotamers), 61.2, 62.0, 61.9 and 62.5 (due to rotamers), 63.3, 120.4 and 120.8 (due to rotamers), 124.4, 125.0 and 125.1 (due to rotamers), 127.4 and 127.7 (due to rotamers), 128.4, 128.8, 131.9, 133.2, 137.2 and 139.1 (due to rotamers), 139.6 and 140.1 (due to rotamers), 150.9, 153.6 and 154.2 (due to rotamers), 195.0; HMRS calcd for $C_{26}H_{27}N_3O_7$ ($[M]^+$) 493.1849, found 493.1844.

(2*R,7*S**,8*S**,8a*R**)-4-Oxo-1-((phenoxy)carbonyl)-2-phenyl-3,4,6,7,8,8a-hexahydro-2*H*-quinoline-7,8-dicarboxylic Acid 7,8-Dimethyl Ester (12).** To a solution of 31 mg (0.971 mmol) of **5** in 6 mL of toluene was added 18 mg (0.126 mmol) of dimethyl maleate. The mixture was heated at 200 °C in a sealed tube for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 36 mg (82%) of **12** as a colorless solid: mp 206−207 °C (ethyl acetate/hexane); IR (thin film) 3055, 2954, 1725, 1691, 1626, 1450, 1430, 1351, 1315, 1271, 1239, 1204, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.60 (m, 1H), 2.82−3.10 (m, 3H), 3.18 (dd, 1H, J = 16.3 and 4.9 Hz), 3.71 (s, 6H), 4.47 (m, 1H), 4.99 (m, 1H), 5.58 (m, 1H), 6.77 (d, 1H, J = 7.8 Hz), 6.87 (m, 1H), 7.29 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 41.0, 43.3, 52.2, 52.5, 57.1, 57.2, 121.7, 125.8, 126.4, 128.0, 129.2, 133.5, 137.6, 140.2, 150.8, 155.0, 171.3, 172.5, 195.7. Anal. Calcd for $C_{26}H_{25}NO_7$: C, 67.38; H, 5.44; N, 3.02. Found: C, 67.41; H, 5.52; N, 3.00.

Diels−Alder Reaction of 5 with Dimethyl fumarate. To a solution of 63 mg (0.197 mmol) of **5** in 8 mL of toluene was added 34 mg (0.257 mmol) of dimethyl fumarate. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 70 mg (78%) of an inseparable 1:1 mixture of diastereomers **13a**,**b** as a colorless foam: IR (thin film) 3027, 2953, 1734, 1627, 1483, 1434, 1397, 1317, 1269, 1205, 1023, 811, 735 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) (diastereomer **13a**) δ 1.96 (m, 1H), 2.45−3.32 (m, 4H), 3.69 (s, 3H), 3.74 (s, 3H), 4.86 (m, 1H), 5.15 (m, 1H), 6.12 (d, 1H, J = 5.1 Hz), 6.83 (m, 1H), 7.36 (m, 10H); ^1H NMR ($CDCl_3$, 300 MHz) (diastereomer **13b**) δ 2.16 (t, 1H, J = 11.0 Hz), 2.45−3.32 (m, 4H), 3.59 (s, 6H), 3.70 (m, 1H), 4.34 (t, 1H, J = 5.2 Hz), 5.74 (t, 1H, J = 5.1 Hz), 6.70 (m, 1H), 7.00 (m, 1H), 7.36 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.9, 28.6, 40.9, 42.0, 43.6, 45.0, 47.1, 52.3, 52.4, 52.5, 52.7, 54.1, 54.3, 55.1, 56.0, 57.7, 121.4, 121.7, 126.0, 126.8, 127.9, 128.2, 128.4, 128.6, 128.8, 129.2, 129.4, 129.5, 134.0, 134.3, 135.7, 136.5, 137.4, 141.0, 150.8, 151.3, 154.5, 154.8, 172.2, 172.4, 173.5, 173.9, 193.7; HRMS calcd for $C_{26}H_{25}NO_7$ ($[M + H]^+$) 464.1709, found 464.1733.

Diels−Alder Reaction of 5 with Methyl Acrylate. To a solution of 50 mg (0.157 mmol) of **5** in 7 mL of toluene was added 67 mg (0.783 mmol) of methyl acrylate. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexane) to give 54 mg (86%) of an inseparable 2.5:1 mixture of diastereomers **14a**,**b** as a colorless foam: IR (thin film) 2953, 1729, 1699, 1617, 1495, 1529, 1399, 1318, 1266, 1202, 1164 cm^{-1}; (major diastereomer **14a**) ^1H NMR ($CDCl_3$, 300 MHz) δ 1.89−2.46 (m, 4H), 2.94 (dd, 1H, J = 16.1 and 5.9 Hz), 3.26 (d, 1H, J = 16.1 Hz), 3.71 (s, 3H), 3.89 (m, 1H), 4.84 (m, 1H), 5.73 (t, 1H, J = 5.9 Hz), 6.76 (m, 2H), 7.35 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.5, 23.9, 42.2, 43.6, 51.9, 55.8, 57.3, 121.7, 125.6, 126.2, 127.7, 128.5, 129.1, 129.4, 134.4, 138.1, 140.1, 150.9, 173.1, 195.5; (minor disatereomer **14b**) ^1H NMR ($CDCl_3$, 300 MHz) δ 1.89−2.46 (m, 4H), 2.98 (dd, 1H, J = 16.1 and 5.9 Hz), 3.27 (d, 1H, J = 16.1 Hz), 3.58 (s, 3H), 3.68 (m, 1H), 5.07 (m, 1H), 6.08 (m, 1H), 6.91 (m, 2H), 7.35 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.7, 24.7, 42.0, 45.7, 52.2, 54.5, 57.3, 121.6, 125.7, 126.2, 127.8, 128.1, 128.2, 128.5, 134.0, 138.1, 141.1, 154.6, 173.5, 195.5; HRMS calcd for $C_{24}H_{23}NO_5$ ($[M + H]^+$) 406.1654, found 406.1665.

Diels−Alder Reaction of 5 with Acrylonitrile. To a solution of 60 mg (0.188 mmol) of **5** in 8 mL of toluene was added 50 mg (0.939 mmol) of acrylonitrile. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 63 mg (91%) of an inseparable 2:1 mixture of diastereomers **15a**,**b** as a colorless foam: IR (thin film) 3050, 2943, 2247, 1728, 1700, 1627, 1493, 1278 cm^{-1}; (major diastereomer **15a**) ^1H NMR ($CDCl_3$, 300 MHz) δ 1.76−2.48 (m, 3H), 2.69 (m, 1H), 3.14 (m, 2H), 4.12 (m, 1H), 4.89 (m, 1H), 5.65 (m, 1H), 6.73 (d, 1H, J = 7.7 Hz), 6.94 (m, 1H), 7.33 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 23.9, 30.5, 43.6, 56.4, 57.3, 121.5, 126.0, 126.8, 127.7, 128.1, 129.1, 129.5, 133.8, 139.2, 150.5, 155.2, 195.6; (minor disatereomer **15b**) ^1H NMR ($CDCl_3$, 300 MHz) δ 1.76−2.48 (m, 4H), 2.69 (m, 1H), 3.14 (m, 2H), 5.24 (m, 1H), 6.13 (d, 1H, J = 5.8 Hz), 6.79 (m, 1H), 7.33 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.7, 25.6, 33.4, 41.4, 51.7, 53.9, 119.8, 122.0, 126.1, 126.8, 127.7, 128.1, 129.5, 129.5, 133.6, 138.4, 139.5, 151.4, 195.6; HRMS calcd for $C_{23}H_{20}N_2O_3$ ($[M + H]^+$) 373.1552, found 373.1571.

Diels−Alder Reaction of 5 with Phenyl Vinyl Sulfone. To a solution of 50 mg (0.157 mmol) of **5** in 8 mL of toluene was added 34 mg (0.201 mmol) of phenyl vinyl sulfone. The mixture was heated at 200 °C in a sealed tube for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 49 mg (65%) of a mixture of diastereomers **16a**,**b**. Fractional cyrstallization from $CHCl_3$/hexane afforded the minor diastereomer (**16b**) as a white solid: mp 240 °C dec; IR (thin film) 1714, 1697, 1629, 1401, 1316, 1278, 1202, 1142 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.42 (m, 1H), 1.85 (m, 2H), 2.26 (m, 1H), 2.38 (br s, 1H), 3.10 (dd, 1H, J = 19.0 and 6.5 Hz), 3.23 (d, 1H, J = 19.0 Hz), 5.75 (br s, 1H), 6.23 (d, 1H, J = 6.5 Hz), 6.74 (m, 1H), 7.20 (m, 1H), 7.29−7.56 (m, 10H), 7.58 (m, 3H), 7.72 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.3, 24.7, 41.6, 51.2, 52.9, 61.0, 122.2, 125.7, 128.3, 128.4, 128.6, 128.8, 129.0, 129.1, 129.2, 129.5, 133.8, 134.9, 138.7, 139.1, 152.0, 197.7. Anal. Calcd for $C_{28}H_{25}NO_5S$: C, 68.98; H, 5.17; N, 2.87. Found: C, 68.68; H, 4.86; N, 2.56.

The major diastereomer (**16a**) was obtained from the mother liquor as a colorless oil: IR (thin film) 1714, 1699, 1625, 1400, 1317, 1278, 1200, 1145 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.16 (m, 1H), 2.27 (m, 2H), 2.76 (m, 1H), 2.82 (d, 1H, J = 15.1 Hz), 3.85 (dd, 1H, J = 15.1 and 6.3 Hz), 5.02 (m, 1H), 5.23 (s, 1H), 5.69 (m, 1H), 6.45 (d, 1H, J = 7.4 Hz), 7.26 (m, 12H), 7.64 (m, 2H), 7.96 (d, 1H, J = 7.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.8, 44.1, 57.5, 59.1, 59.4, 121.6, 125.8, 125.8, 128.0, 128.1, 129.4, 129.6, 132.8, 133.8, 138.4, 141.4, 142.5, 150.8, 155.4, 193.8; HRMS calcd for $C_{28}H_{24}NO_5S$ ($[M + H]^+$) 488.1532, found 488.1537.

Diels−Alder Reaction of 5 with Acryloyl Chloride To Give 14a. In an NMR tube, acryloyl chloride (4 μL, 0.052 mmol, 1.05 equiv) was added to a solution of the dihydropyridone **5** (16 mg, 0.050 mmol, 1.0 equiv) in $CDCl_3$, and the mixture was kept at room temperature for 10 h to afford **17**: ^1H NMR (400 Hz, $CDCl_3$) δ 7.42−7.15 (m, 10H), 6.92 (m, 1H), 6.85 (d, J = 7.6 Hz, 1H), 5.91 (t, J = 5.2 Hz, 1H), 4.72 (t, J = 4.0 Hz, 1H), 4.54 (d, J = 4.0 Hz, 1H), 3.36−3.29 (m, 1H), 2.99 (dd, J = 16.4 Hz, J = 4.0 Hz, 1H), 2.48−2.38 (m, 1H), 2.18−2.11 (m, 1H), 1.37−1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 173.6, 150.8, 140.3, 138.0, 136.9, 133.3, 129.9, 129.3, 128.2, 126.5, 126.0, 121.8, 57.2, 56.1, 53.7, 43.3, 24.7, 23.0. The NMR tube was placed in a ice cold bath and MeOH (1 mL) at 0 °C was added. The mixture was kept at 0 °C for 30 min. The solvent was removed by evaporation. The product was purified by radial PLC (silica gel, 50% EtOAc/hexanes) to give 10.3 mg (51%) of **14a** as an off-white foam. IR ($CDCl_3$) 2963, 1730, 1699, 1621, 1275, 1202, 1165, 742 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 7.35 (m, 9H), 6.76 (m, 2H), 5.73 (t, 1H J = 5.9 Hz), 4.84 (m, 1H), 3.89 (m, 1H), 3.71 (m, 3H), 3.26 (d, 1H, J = 16.1 Hz), 2.94 (dd, 1H, J = 16.1 Hz, J = 5.9 Hz), 2.46−1.89 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 173.1, 150.9, 140.1, 138.1, 134.4, 129.4, 129.1, 128.5, 127.7, 126.2, 125.6, 121.7, 57.3, 55.8, 51.9, 43.6, 42.2, 23.9, 23.5; HRMS calcd for $C_{24}H_{23}NO_5$ ($[M + H]^+$) 406.1654, found 406.1655.

Diels−Alder Reaction of 18 with *N*-Phenylmaleimide. To a stirred solution of 500 mg (1.94 mmol) of **18**[15] in 8 mL of toluene was added 370 mg (2.14 mmol) of *N*-phenylmaleimide. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (EtOAc/hexanes). The first product to elute from the column (100 mg, 12%) was identified as (2*S**,6a*R**,9a*R**,9b*R**)-2-methyl-4,7,9-trioxo-8-phenyl-2,3,4,6,6a,7,8,9,9a,9b-decahydropyrrolo[3,4-*h*]quinoline-1-carboxylic acid phenyl ester (**20**) and was obtained as a colorless solid: mp 209−210 °C; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.00 (d, 3H, J = 6.7 Hz), 2.35 (m, 1H), 2.43 (dd, 1H, J = 16.3 and 2.5 Hz), 2.89 (m, 1H), 3.07 (m, 1H), 3.43 (m, 1H), 4.38 (br m, 1H), 4.89 (br m, 1H), 5.11 (br m, 1H), 7.21 (m, 6H), 7.43 (m, 5H); ^{13}C NMR (CD_2Cl_2, 100 MHz, −20 °C) δ 20.3 and 20.9 (due to rotamers), 23.0 and 23.4 (due to rotomers), 38.7 and 39.0 (due to rotamers), 40.4 and 42.6 (due to rotamers), 45.6, 46.7 and 47.5 (due to rotamers), 51.0 and 51.5 (due to rotamers), 122.1 and 122.2 (due to rotamers), 125.9 and 126.0 (due to rotamers), 126.1 and 126.6 (due to rotamers), 126.9, 129.1 and 129.5 (due to rotamers), 129.5 and 129.7 (due to rotamers), 129.7 and 129.8 (due to rotamers), 131.9 and 132.1 (due to rotamers), 139.5 and 139.6 (due to rotamers), 151.5 and 151.6 (due to rotamers), 154.0 and 154.1 (due to rotamers), 174.7 and 174.9 (due to rotamers), 177.8 and 178.0 (due to rotamers), 192.7 and 193.0 (due to rotamers). Anal. Calcd for $C_{25}H_{22}N_2O_5$: C, 69.76; H, 5.15; N, 6.51. Found: C, 69.43; H, 4.99; H, 6.35.

The second product to elute from the column (700 mg, 83%) was identified as (2*S**,6a*S**,9a*S**,9b*S**)-2-methyl-4,7,9-trioxo-8-phenyl-2,3,4,6,6a,7,8,9,9a,9b-decahydropyrrolo[3,4-*h*]quinoline-1-carboxylic acid phenyl ester (**19**) and was obtained as a colorless solid: mp 179−180 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.35 (d, 3H, J = 6.7 Hz), 2.33 (m, 1H), 2.44 (d, 1H, J = 15.5 Hz), 3.02 (m, 1H), 3.12 (m, 1H), 3.37 (m, 1H), 4.67 (m, 2H), 4.97 (m, 1H), 7.09 (m, 2H), 7.17 (m, 3H), 7.27 (m, 1H), 7.41 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.6, 25.3, 39.4, 42.1, 43.8, 49.9, 53.9, 121.7, 125.8, 126.4, 128.9, 129.3, 129.5, 131.5, 135.1, 135.8, 151.1, 154.5, 175.9, 177.4, 192.4. Anal. Calcd for $C_{25}H_{22}N_2O_5$: C, 69.76; H, 5.15; N, 6.51. Found: C, 69.69; H, 5.11; N, 6.49.

2-(3-Benzyloxypropyl)-1-(phenoxycarbonyl)-5-vinyl-2,3-dihydro-4-pyridone (21). Magnesium turnings (1.06 g, 43.6 mmol) were mechanically activated by stirring under argon overnight. To the activated Mg was added 13 mL of THF, two drops of dibromoethane, and 5.00 g (21.8 mmol) of benzyl 3-bromopropyl ether. The formation of the Grignard was complete after 1.5 h. The Grignard was transferred via double tipped needle to a stirred solution of 1.11 g (10.9 mmol) of 4-methoxypyridine in 26 mL of THF at −42 °C. Phenyl chloroformate (1.517 mL, 10.9 mmol) was quickly added, and the resulting solution was stirred at −42 °C for 30 min. The reaction mixture was quenched with 10% HCl, stirred at room temperature for 1 h, and extracted with diethyl ether (3 × 2 mL). The combined extracts were washed with brine (2 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by radial PLC (silica gel, 5−10% EtOAc/hexanes) to give 3.74 g (94%) of 2-(3-benzyloxypropyl)-1-(phenoxycarbonyl)-2,3-dihydro-4-pyridone as a clear oil: IR (neat) 3456, 3324, 3064, 2944, 2862, 1738, 1672, 1604, 1494, 1423, 1333, 1270, 1192, 1099, 991, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.64−1.92 (m, 4H), 2.53 (d, 1H, J = 17.2 Hz), 2.92 (dd, 1H, J = 16.4 and 6.4 Hz), 3.48 (t, 2H, J = 5.6 Hz), 4.47 (s, 2H), 4.78 (s, 1H), 5.43 (d, 1H, J = 7.6 Hz), 7.14−7.43 (m, 10H), 7.87 (d, 1H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.2, 27.9, 40.2, 53.8, 69.7, 73.2, 121.4, 126.6, 127.8, 128.5, 129.7, 138.4, 141.1, 150.6, 193.1; HRMS calcd for $C_{22}H_{23}NO_4$ ($[M + H]^+$) 366.1705, found 366.1722.

To a stirred solution of 3.70 g (10.1 mmol) of the above dihydropyridone in 100 mL of CH_2Cl_2 at 0 °C was added 15.1 mL (15.1 mmol) of 1.0 M ICl in CH_2Cl_2. The solution was stirred at 0 °C for 2 h in the dark and then neutralized with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with saturated aqueous Na_2SO_3 and brine (1 × 10 mL each) and then dried over K_2CO_3. The solvent was removed under reduced pressure and the residue was purified by radial PLC (silica gel, 5% EtOAc/hexanes) to afford 4.71 g (95%) of (2*S**)-2-(3-benzyloxypropyl)-5-iodo-1-(phenoxycarbonyl)-2,3-dihydro-4-pyridone (**42**) as a yellow oil: IR (neat) 3063, 2927, 2860, 1738, 1878, 1582, 1494, 1388, 1312, 1260, 1199, 1144, 1103, 1026, 998, 914, 838, 751, 691 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.61−1.89 (m, 5H), 2.82 (d, 1H, J = 16.4), 2.95 (dd, 1H, J = 16.4 and 6.4 Hz), 3.46 (t, 2H, J = 6.0), 4.45 (s, 2H), 4.80 (d, 1H, J = 6.0), 7.15 (d, 1H, J = 8.0), 7.24−7.42 (m, 9H), 8.39 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.0, 27.9, 38.8, 54.1, 69.4, 73.0, 121.2, 126.6, 127.6, 127.7, 128.4, 129.7,

138.2, 146.4, 150.2, 186.6; HRMS calcd for $C_{22}H_{22}INO_4$ ([M + H]$^+$) 492.0672, found 492.0661.

To a solution of 2.00 g (4.07 mmol) of the above iodide in 20 mL of toluene was added 249 mg (0.l84 mmol) of $AsPh_3$ and 93 mg (0.10 mmol) of Pd_2dba_3. The resulting solution was degassed with argon for 15 min. Tributylvinyltin (1.54 mL, 5.29 mmol) was added, and the mixture was heated to 50 °C for 2 h and then cooled to room temperature. A solution of 1:1 EtOAc:H_2O (5 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by radial PLC (silica gel, 5% EtOAc/hexanes) to give 1.29 g (81%) of **21** as a clear oil: IR (neat) 3064, 2945, 2859, 1737, 1673, 1590, 1320, 1264, 1198, 1104 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.55−1.90 (m, 4H), 2.58 (dd, 1H, J = 16.1 and 1.5 Hz), 2.95 (dd, 1H, J = 16.5 and 6.2 Hz), 3.48 (t, 2H, J = 5.9 Hz), 4.46 (s, 2H), 4.79 (d, 1H, J = 5.9 Hz), 5.16 (d, 1H, J = 7.0 Hz), 5.79 (dd, 1H, J = 17.6, 1.5 Hz), 6.41 (dd, 1H, J = 17.6, 11.7), 7.16 (d, 1H, J = 22.0 Hz), 7.15−7.44 (m, 9H), 7.97 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 28.0, 40.5, 53.6, 69.6, 73.0, 114.7, 121.4, 126.5, 127.7, 127.8, 128.5, 129.1, 129.7, 138.3, 150.5, 191.7; HRMS calcd for $C_{24}H_{25}NO_4$ ([M + H]$^+$) 392.1862, found 392.1859.

Diels−Alder Reaction of 21 with *N*-Phenylmaleimide. To a stirred solution of 35 mg (0.09 mmol) of **21** in 2 mL of toluene was added 30 mg (0.18 mmol) of *N*-phenylmaleimide. The mixture was refluxed for 17 h and then the solvent was removed under reduced pressure. The residue was purified by radial PLC (silica gel, 10% EtOAc/hexanes) to afford 44 mg (87%) of **22** as a colorless solid: mp 193 °C; IR (NaCl) 2919, 2867, 1701, 1614, 1494, 1380, 1271 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.06 (m, 16H), 4.87−4.83 (m, 2H), 4.63 (br s, 1H), 4.45 (s, 2H), 3.51−3.46 (m, 2H), 3.36 (t, 1H, J = 8.0 Hz), 3.12 (dd, 1H, J = 8.0 Hz), 2.99 (dd, 1H, J = 15.6 and 4.8 Hz), 2.57 (dd, 1H, J = 16.0 and 2.4 Hz), 2.34−2.27 (m, 1H), 1.90−1.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$), δ 192.4, 177.7, 176.0, 154.8, 151.2, 138.5, 136.2, 135.3, 131.6, 129.7, 129.5, 129.1, 128.6, 127.9, 126.6, 126.1, 122.0, 73.2, 69.7, 54.0, 53.8, 41.9, 39.6, 31.7, 26.5, 25.5; HRMS calcd for $C_{34}H_{32}N_2O_6$ ([M + H]$^+$) 565.2339, found 565.2333.

Diels−Alder Reaction of 21 with Benzodithiin Tetraoxide. To a solution of 1.17 g (2.30 mmol) of **21** in 21 mL of toluene was added 655 mg (2.85 mmol) of benzodithiin tetraoxide.[17] The mixture was degassed for 10 min by bubbling nitrogen through the solution and then was heated to 90 °C for 18 h. The reaction was cooled to room temperature and concentrated under reduced pressure. The major isomer was obtained by recrystalization of the crude reaction mixture from hot toluene to give 1.06 g (60%) of (2*R**,6a*R**,12a*S**,12b*S**)-2-(3-benzyloxypropyl)-1-(phenoxycarbonyl)-4,7,7,12,12-pentaoxo-3,4,6,6a,7,12,12a,12b-octahydro-2*H*-7λ^6, 12λ^6-dithia-1-azabenzo-[α]anthracene (**24**) as a white solid: mp 156−157 °C; IR (thin film) 2850, 2359, 1702, 1628, 1432, 1329, 1198, 1129, 912, 735, 702 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz) δ 1.50−1.85 (m, 2H), 2.60−2.80 (m, 3H), 2.80−3.20 (m, 3H), 3.51 (t, 2H, J = 6.0 Hz), 4.46 (s, 2H), 4.64 (t, 1H, J = 5.1 Hz), 4.99−5.06 (m, 1H), 5.42 (br s, 1H), 5.89 (t, 1H, J = 4.5 Hz), 6.70 (d, 1H, J = 2.7 Hz), 7.18−7.44 (m, 10H), 7.96−8.08 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.0, 26.9, 30.7, 55.2, 56.6, 58.0, 58.5, 69.8, 73.1, 77.6, 121.9, 125.2, 125.5, 126.2, 127.8, 128.6, 129.7, 132.9, 133.1, 133.6, 134.0, 135.2, 138.6, 139.4, 150.8, 196.0; HRMS calcd for $C_{32}H_{31}NO_8S_2$ ([M + H]$^+$) 622.1569, found 622.1572.

The minor isomer (354 mg, 20%) was isolated as clear oil from the mother liquers and identified as (2*S**,6a*R**,12a*S**,-12b*S**)-2-(3-(benzyloxy)propyl)-4,7,7,12,12-pentaoxo-3,4,6,6a,7,-12,12a,12b-octahydro-2*H*-7λ^6,12λ^6-dithia-1-azabenzo[*a*]anthracene-1-carboxylic acid phenyl ester (**25**) as a clear oil: IR (neat) 3064, 3026, 2926, 2872, 1721, 1706, 1631, 1593, 1407, 1323, 1205, 1150, 1131, 751 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz) δ 1.50−2.01 (m, 4H), 2.49 (s, 2H), 2.94−3.17 (m, 2H), 3.46−3.58 (m, 2H), 4.49 (s, 3H), 4.61−4.81 (m, 3H), 5.91 (d, 1H, J = 5.7 Hz), 6.83 (d, 1H, J = 3.6 Hz), 6.97 (d, 2H, J = 7.2 Hz), 7.14−7.34 (m, 7H), 7.66 (t, 1 H, J = 6.6 Hz), 7.82−7.87 (m, 2H), 8.03 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.7, 24.0, 25.9, 30.0, 45.0, 48.6, 58.5, 62.3, 69.8, 73.1, 73.9, 76.9, 121.9, 125.2, 126.2, 127.9, 128.4, 129.2, 132.6, 138.4; HRMS calcd for $C_{32}H_{31}NO_8S_2$ ([M + H]$^+$) 622.1569, found 622.1575.

Diels−Alder Reaction of 18 with 4-Methyl-1,2,4-triazole-3,5-dione. To a stirred solution of 280 mg (1.09 mmol) of **18**[15] in 8 mL of toluene was added 147 mg (1.30 mmol) of 4-methyl-1,2,4-triazole-3,5-dione. The resulting mixture was heated at reflux for 30 min, cooled to room temperature, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (EtOAc/hexanes). The first product to elute from the column (88 mg, 22%) was identified as (8*S**,9a*R**)-2,8-dimethyl-1,3,6-trioxo-2,3,4,7,8,9a-hexahydro-1*H*-6*H*-2,3a,9,9b-tetraazacyclopenta[*a*]naphthalene-9-carboxylic acid phenyl ester (**34**) and was obtained as a white solid: mp 160−161 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.46 (d, 3H, J = 7.3 Hz), 2.54 (dd, 1H, J = 18.5 and 1.0 Hz), 2.86 (m, 1H), 3.07 (s, 3H), 4.19 (dt, 1H, J = 19.8 and 3.0 Hz), 4.56 (dt, 1H, J = 19.8 and 3.0 Hz), 5.06 (m, 1H), 6.47 (s, 1H), 6.93 (t, 1H, J = 3.0 Hz), 7.23 (m, 3H), 7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.5, 25.2, 44.7, 44.9, 45.1, 67.4, 121.8, 126.0,129.5, 132.7, 133.2, 151.0, 151.1, 153.5, 153.6, 193.2. Anal. Calcd for $C_{18}H_{18}N_4O_5$: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.27; H, 4.91; N, 14.92.

The second product to elute from the column (292 mg, 73%) was identified as (8*S**,9a*S**)-2,8-dimethyl-1,3,6-trioxo-2,3,4,7,8,-9a-hexahydro-1*H*,6*H*-2,3a,9,9b-tetraazacyclopenta[*a*]naphthalene-9-carboxylic acid phenyl ester (**33**) and was obtained as a white solid: mp 142−143 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.56 (d, 3H, J = 6.5 Hz), 2.63 (dd, 1H, J = 16.8 and 9.2 Hz), 2.84 (dd, 1H, J = 16.8 and 6.8 Hz), 2.92 (s, 3H), 4.06 (d, 1H, J = 18.8 Hz), 4.50 (m, 2H), 6.07 (s, 1H), 6.99 (m, 3H), 7.17 (m, 1H), 7.31 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.2, 25.1, 43.4, 44.7, 48.1, 60.6, 121.5, 125.8, 128.1, 129.5, 132.5, 150.5, 151.2, 152.5, 153.8, 193.2. Anal. Calcd for $C_{18}H_{18}N_4O_5$: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.41; H, 4.89; N, 14.99.

Luche Reduction of 5. To a stirred solution of 120 mg (0.376 mmol) of **5** in 20 mL of MeOH was added 154 mg (0.413 mmol) of cerium trichloride heptahydrate. After the solution was stirred for 5 min, 18 mg (0.476 mmol) of sodium borohydride was added and stirring was continued for 10 min. The reaction mixture was diluted with water and extracted with CH_2Cl_2, and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by radial PLC (silica gel, EtOAc/hexanes). The first product to elute (18 mg, 15%) was identified as (2*R**,4*R**)-4-hydroxy-1-((phenoxy)carbonyl)-2-phenyl-5-vinyl-3,4-dihydro-2*H*-pyridine **(36)** and was isolated as a colorless oil; IR (neat) 3565, 3060, 2922, 1727, 1643, 1493, 1423, 1376, 1327, 1195 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.80 (d, 1H, J = 9.3 Hz), 2.38 (m, 1H), 2.70 (d, 1H, J = 14.7 Hz), 4.46 (m, 1H), 5.05 (d, 1H, J = 10.6 Hz), 5.33 (d, 1H, J = 17.4 Hz), 5.67 (m, 1H), 6.36 (dd, 1H, J = 17.4 and 11.4 Hz), 6.90 (m, 1H), 7.29 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 36.4, 32.7, 53.4, 60.7, 111.5, 111.9, 121.6, 125.2, 126.1, 126.6, 127.6, 129.3, 129.6, 135.0, 140.2, 152.5; HRMS calcd for $C_{20}H_{19}NO_3$ ([M + H]$^+$) 321.1365, found 321.1352.

The second product to elute (90 mg, 74%) was identified as (2*R**,4*S**)-4-hydroxy-1-((phenoxy)carbonyl)-2-phenyl-5-vinyl-3,4-dihydro-2*H*-pyridine (**35**): colorless foam; IR (thin film) 3400, 3049, 2924, 1723, 1636, 1493, 1339, 1198 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.86 (d, 1H, J = 5.4 Hz), 2.26 (m, 1H), 2.47 (m, 1H), 4.36 (m, 1H), 5.05 (d, 1H, J = 11.2 Hz), 5.32 (d, 1H, J = 17.7 Hz), 5.42 (t, 1H, J = 4.8 Hz), 6.29 (dd, 1H, J = 17.7 and 11.2 Hz), 6.91 (m, 1H), 7.30 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 38.5, 55.2, 60.9, 112.5, 121.6, 125.3, 126.0, 126.8, 127.5, 128.9, 129.5, 134.1, 141.0, 150.8, 152.1; HRMS calcd for $C_{20}H_{19}NO_3$ ([M]$^+$) 321.1365, found 321.1364.

(2*R,4*S**,6a*S**,9a*S**,9b*R**)-4-Hydroxy-7,9-dioxo-2,8-diphenyl-1-((phenyoxy)carbonyl)-2,3,4,6,6a,7,8,9,9a,9b-decahydropyrrolo[3,4-*h*]quinoline (37).** To a solution of 46 mg (0.143 mmol) of **35** in 10 mL of toluene was added 32 mg (0.186 mmol) of *N*-phenylmaleimide. The mixture was heated at reflux for 30 min, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 62 mg (87%) of **37** as a colorless solid: mp 202−203 °C (EtOAc/hexane); IR (thin film) 3473, 3063, 2958, 1709, 1596, 1495, 1381, 1359, 1208, 1180 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.72 (d, 1H, J = 5.4 Hz), 2.03 (m, 2H), 2.26 (m, 1H), 3.00 (dd, 1H, J = 15.0 and 7.0 Hz), 3.31 (t, 1H, J = 7.7 Hz), 4.36 (m, 2H), 5.11 (m, 1H), 5.53 (m, 1H), 6.10 (m, 1H), 6.64 (d, 1H, J = 8.2 Hz), 7.10−7.50 (m, 14H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.9, 38.7, 39.6, 41.8, 55.4, 58.6, 62.7, 118.9, 121.7, 125.4, 125.6, 126.7, 127.1, 128.8, 129.0, 129.2, 129.4, 132.0, 140.2, 144.8, 151.0, 154.6, 177.1, 178.7. Anal. Calcd for $C_{30}H_{26}N_2O_5$: C, 72.86; H, 5.30; N, 5.66. Found: C, 72.65; H, 5.29; N, 5.68.

(2*R,4*R**,6a*S**,9a*S**,9b*R**)-4-Hydroxy-7,9-dioxo-2,8-diphenyl-1-((phenyoxy)carbonyl)-2,3,4,6,6a,7,8,9,9a,9b-decahydropyrrolo[3,4-*h*]quinoline (38).** To a solution of 35 mg (0.109 mmol) of **36** in 7 mL of toluene was added 25 mg (0.144 mmol) of *N*-phenylmaleimide. The mixture was heated at reflux for 30 min, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexane) to give 50 mg (93%) of **38** as a colorless solid: mp 115−116 °C (EtOAc/hexane); IR (thin film) 3479, 3060, 2919, 1711, 1596, 1494, 1383, 1204 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.34 (m, 3H), 2.92 (dd, 1H, J = 15.2 and 7.5 Hz), 3.34 (t, 1H, J = 8.0 Hz), 4.39 (s, 1H), 4.51 (m, 1H), 5.09 (s, 1H), 5.50 (m, 1H), 6.07 (m, 1H), 6.64 (d, 1H, J = 7.5 Hz), 7.05−7.49 (m, 15H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.4, 36.4, 39.7, 41.7, 52.5, 55.5, 66.6, 121.8, 125.5, 125.6, 126.0, 126.6, 127.0, 128.9, 129.0, 129.3, 129.4, 131.9, 138.7, 146.8, 151.8, 155.0, 176.9, 178.6. Anal. Calcd for $C_{30}H_{26}N_2O_5$: C, 72.86; H, 5.30; N, 5.66. Found: C, 72.70; H, 5.31; N, 5.70.

(3a*R,6*S**,8*R**,9a*S**,9b*R**)-6-Hydroxy-1-oxo-9-((phenoxy)carbonyl)-8-phenyl-1,2,3,3a,4,6,7,8,9a,9b-decahydro-9-azacyclopenta[*a*]naphthalene (39).** To a solution of 25 mg (0.07 mmol) of **35** was added 10 mg (0.12 mmol) of 2-cyclopentenone. The mixture was heated at 200 °C in a sealed tube for 36 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 21 mg (68%) of **39** as a colorless solid: mp 172−173 °C (EtOAc/hexane); IR (thin film) 3448, 2931, 1731, 1707, 1495, 1348, 1202 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.41 (m, 1H), 1.71 (m, 1H), 2.02−2.59 (m, 6H), 2.94 (m, 1H), 3.58 (m, 1H), 4.31 (m, 1H), 4.97 (s, 1H), 5.56 (m, 1H), 5.88 (m, 1H), 6.53 (d, 1H, J = 7.7 Hz), 7.24 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.4, 29.2, 33.4, 38.5, 38.8, 50.5, 55.8, 59.0, 63.7, 119.1, 121.8, 125.7, 125.8, 127.0, 128.7, 129.2, 129.5, 138.7, 145.6, 154.7, 219.7; HRMS calcd for $C_{25}H_{25}NO_4$ ($[M + H]^+$) 404.1862, found 404.1862.

(2*R,4*S**)-(2-Benzyloxypropyl)-4-hydroxy-1-(phenoxycarbonyl)-5-vinyl-3,4-dihydro-2*H*-pyridine (40)**. To a mixture of 932 mg (2.38 mmol) of **21** and 975 mg (2.62 mmol) of $CeCl_3 \cdot 7H_2O$ in 43 mL of MeOH at −20 °C was added portionwise 117 mg (3.09 mmol) of $NaBH_4$. After 45 min at −20 °C, the reaction was quenched with water (5 mL), and the MeOH was removed under reduced pressure. The remaining aqueous solution was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried over K_2CO_3, filtered, and concentrated under reduced pressure. Purification of the residue by radial PLC (silica gel, 5% EtOAc/hexanes/1% TEA) gave 861 mg (92%) of **40** as a clear oil: IR (neat) 3435, 3054, 3030, 2930, 2863, 1722, 1637, 1494, 1424, 1344, 1199 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.67−1.76 (m, 5H), 1.89−1.99 (m, 2H), 2.38−2.45 (m, 1H), 3.52 (dd, 2H, J = 10.2, 9.4 Hz), 4.44 (s, 1H), 4.50 (s, 2H), 4.65−4.72 (m, 1H), 5.12 (d, 1H, J = 11.0 Hz), 5.38 (d, 1H, J = 18.3 Hz), 6.26 (dd, 1H, J = 17.6 and 11.0 Hz), 7.02 (s, 1H), 7.14 (d, 2H, J = 8.8 Hz), 7.22−7.42 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.6, 28.3, 35.2, 52.2, 61.3, 70.0, 73.1, 112.8, 120.9, 121.7, 125.7, 126.0, 127.7, 127.8, 128.6, 129.6, 134.4, 138.6, 151.0, 151.8; HRMS calcd for $C_{24}H_{27}NO_4$ ($[M]^+$) 393.1904, found 393.1942.

The minor product (**41**, 36.4 mg, 4%) was isolated as a clear oil: IR (neat) 3475, 2923, 2855, 2359, 1723, 1643, 1336, 1197, 1054 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.68−1.96 (m, 6H), 2.28 (d, 1H, J = 15.2 Hz), 3.50 (br s, 2H), 4.41−4.49 (m, 3H), 4.58 (s, 1H), 5.05 (t, 1H, J = 16.8 Hz), 5.31 (t, 1H, J = 16.8), 6.27−6.34 (m, 1H), 7.06−7.37 (m, 11H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.1, 28.8, 29.2 (due to rotamers), 31.7, 50.5, 51.2 (due to rotamers), 60.2, 70.3, 73.1, 110.4, 110.8, 119.3, 119.8 (due to rotamers), 121.8, 126.0, 126.6, 127.8, 128.5, 129.6, 135.5, 138.7, 151.0, 151.6, 152.3 (due to rotamers); HRMS calcd for $C_{24}H_{27}NO_4$ ($[M]^+$) 393.1904, found 393.1937.

(2*R,4*S**)-(2-Benzyloxypropyl)-4-hydroxy-1-(phenoxycarbonyl)-5-vinyl-3,4-dihydro-2*H*-pyridine (41). Method A.** A solution of 10.18 mL (10.1 mmol, 1.0 M in toluene) of diisopropyl aluminum hydride was added dropwise to 4.48 g (20.3 mmol) of 2,6-di-*tert*-butyl-4-methylphenol in 48 mL of toluene at 0 °C. The solution was stirred at 0 °C for 1 h and then cooled to −78 °C. A solution of 797 mg (2.0 mmol) of **21** in 5 mL of toluene was added, and the resulting red solution was allowed to stir at −78 °C for 1 h and then placed in a −30 °C freezer for 3 h. The resulting yellow solution was quenched with 5 mL of saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (5 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by radial PLC (silica gel, 5−20% EtOAc/hexanes) to give 583 mg (73%) of **41** as a clear oil, which was identical with the minor product isolated by Luche reduction of **21**.

Method B. A solution of 10.95 mL (10.9 mmol, 1.0 M in toluene) of diisopropyl aluminum hydride was added dropwise to 4.83 g (21.9 mmol) of 2,6-di-*tert*-butyl-4-methylphenol in 50 mL toluene at 0 °C. The solution was stirred at 0 °C for 1 h and then cooled to −78 °C. A solution of 538 mg (1.1 mmol) of **42** in 5 mL of toluene was added dropwise to give a red solution that was stirred at −78 °C for 1 h and then placed in a −30 °C freezer for 3 h. The resulting yellow solution was poured into ice cold 1% HCl (30 mL) and extracted with EtOAc (3 × 10 mL), and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by radial PLC (silica gel, 10% EtOAc/hexanes) to give 409.3 mg (76%) of (2*R**,4*R**)-2-(3-benzyloxypropyl)-4-hydroxy-5-iodo-1-(phenoxycarbonyl)-3,4-dihydro-2*H*-pyridine as a clear oil: IR (neat) 3447, 3085, 3028, 2992, 2860, 1724, 1630, 1597, 1493, 1553, 1391, 1308, 1198, 1094, 1057 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.63−1.92 (m, 4H), 2.07−2.11 (m, 5H), 2.34 (d, 1H, J = 14.8 Hz), 2.42 (s, 1H), 3.48−3.50 (m, 2H), 4.19 (s, 1H), 4.46−4.48 (m, 3H), 7.11 (d, 2H, J = 7.6 Hz), 7.21−7.45 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 28.4, 33.8, 52.4, 65.2, 69.8, 73.1, 83.6, 121.6, 126.0, 127.8, 128.5, 129.6, 131.0, 138.4, 150.7; HRMS calcd for $C_{22}H_{24}INO_4$ ($[M]^+$) 493.0750, found 493.0736.

A solution of the above iodide (2.355 g, 4.775 mmol) and palladium tetrakis(triphenyl)phosphine (386 mg, 0.334 mmol, 7%) in toluene (11 mL) was degassed with argon. Tributyl(vinyl)tin (1.81 mL, 6.207 mmol, 1.3 equiv) was added dropwise at room temperature and then the mixture was warmed to 90 °C and stirred for 12 h (monitored by thin-layer chromatography). The reaction mixture was cooled to room temperature and poured into a 1:1 mixture of EtOAc:H_2O. The product was extracted with EtOAc. The combined organic layers were dried over sodium sulfate, filtered, and concentrated in vacuo. The product was purified by radial PLC (1% TEA/5% EtOAc/hexanes) to afford 68% (1.272 g) of **41** as a clear oil.

(2*R,4*R**)-(2-Benzyloxypropyl)-(2,2-dimethylpropionyloxy)-4-hydroxy-1-(phenoxycarbonyl)-5-vinyl-3,4-dihydro-2*H*-pyridine (43).** To a stirred solution (292 mg,

0.74 mmol) of **41** in 2 mL of THF at −78 °C was added 888 μL (0.09 mmol, 1.0 M) of NaHMDS in THF. The solution was stirred for 30 min and then 182 μL (1.48 mmol) of pivaloyl chloride was added. After the solution was stirred for 2 h at −78 °C, the reaction was quenched with saturated aqueous $NaHCO_3$ (1 mL). The aqueous layer was extracted with Et_2O (3 × 1 mL). The combined organic extracts were washed with brine (1 mL) and dried over K_2CO_3. The solvent was removed under reduced pressure and the residue was purified by radial PLC (silica gel, 5% EtOAc/hexanes) to afford 235 mg (70%) of **43** as a clear oil: IR (neat) 2959, 2866, 2360, 2340, 1721, 1650, 1645, 1311, 1196 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.20 (s, 9H), 1.61−2.26 (m, 7H), 3.45−3.51 (m, 2H), 4.42−4.50 (m, 3H), 4.94 (m, 2H), 5.73 (d, 1H, *J* = 4.0 Hz), 6.26 (m, 1H), 7.11−7.41 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.3, 28.9, 29.3 (due to rotamers), 30.6, 39.1, 50.1, 50.7 (due to rotamers), 62.1, 70.1, 73.3, 77.4, 110.7, 111.0 (due to rotamers), 116.1, 116.6 (due to rotamers), 121.7, 126.0, 127.7, 127.8, 128.2, 128.5, 129.7, 134.7, 138.5, 151.0, 151.7, 152.2 (due to rotamers), 178.1; HRMS calcd for $C_{29}H_{35}NO_5$ ([M]$^+$) 477.2515, found 477.2523.

Diels−Alder Reaction of 43 with Benzodithiin Tetraoxide. To a solution of 33 mg (0.07 mmol) of **43** in 2 mL of toluene was added 16 mg (0.07 mmol) of benzodithiin tetraoxide.[17] The solution was degassed with argon and then heated to reflux for 12 h. After being cooled to room temperature, the solution was concentrated under reduced pressure and the residue was purified by radial PLC (silica gel, 5−10% EtOAc/hexanes) to give 29 mg (60%) of (2*R**,4*S**,6a*R**,12a*S**,12b*S**)-2-(3-benzyloxypropyl)-4-(2,2-dimethylpropionyloxy)-1-(phenoxycarbonyl)-7,7,12,12-tetraoxa-3,4,6,6a,7,7,12,12a,12b-octahydro-2*H*-7λ^6,12λ^6-dithia-1-azabenzo[α]anthracene (**44**) as a white solid: mp 164.5−165.0 °C; IR (neat) 2966, 2926, 2857, 1726, 1457, 1326, 1279, 1203, 1149, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.10−1.40 (m, 9H), 1.70−1.90 (q, 2H, *J* = 5.3 Hz), 1.95−2.20 (m, 2H), 2.23−2.40 (m, 3H), 2.80−3.01 (m, 2H), 3.45−3.65 (m, 2H), 3.85 (t, 1H, *J* = 9.6), 4.16 (q, 1H, *J* = 7.3), 4.55 (s, 2H), 5.17−5.30 (br s, 1H), 5.62 (d, 1H, *J* = 9.2 Hz), 6.13 (s, 1H), 7.10−7.60 (m, 10H), 7.78−8.00 (m, 2H), 8.04, (d, 2H, *J* = 8.0 Hz); ^{13} CNMR ($CDCl_3$) 400 MHz) δ 22.0, 26.1, 27.7, 34.2, 37.0, 50.2, 51.0, 58.4, 62.0, 69.4, 70.6, 73.3, 82.9, 118.0, 121.4, 124.9, 125.4, 127.9, 128.0, 128.3, 128.5, 129.1, 130.9, 133.4, 134.0, 136.9, 138.4, 150.7, 152.1, 154.6; HRMS calcd for $C_{37}H_{41}NO_9S_2$ ([M + H]$^+$) 708.2301, found 708.2315.

The minor isomer (9 mg, 19%) was identified as (2*S**,6a*R**,12a*S**,12b*S**)-2-(3-benzyloxypropyl)-4,7,7,12,12-pentaoxo-3,4,6,6a,7,12,12a,12b-octahydro-2*H*-7λ^6,12λ^6-dithia-1-azabenzo[*a*]anthracene-1-carboxylic acid phenyl ester (**45**) and was isolated as a white solid: mp 148.0−149.0 °C; IR (neat) 2985, 2924, 2871, 2359, 2341, 1721, 1324, 1205, 1150, 751, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.45−1.56 (s, 9H), 1.58−1.68 (m, 1H), 2.01−2.08 (m, 2H), 2.33 (d, 1H, *J* = 17.2 Hz), 2.77−2.93 (m, 2H), 3.43 (t, 1H, *J* = 9.6 Hz), 3.62−3.66 (m, 1H), 4.43 (d, 1H, *J* = 11.2 Hz), 4.55−4.62 (m, 6H), 5.19 (br s, 1H), 5.54 (br s, 1H), 5.94 (s, 1H), 7.00 (d, 2H, *J* = 7.2 Hz), 7.14 (t, 1H, *J* = 6.8 Hz), 7.25−7.40 (m, 8H), 7.62 (t, 2H, *J* = 7.6 Hz), 7.92 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.2, 26.0, 27.9, 29.9, 34.6, 39.4, 50.5, 51.3, 59.1, 62.2, 66.8, 69.7, 73.6, 77.4, 116.8, 121.6, 124.9, 125.1, 125.5, 128.1, 128.6, 129.2, 133.5, 134.2, 135.6, 136.1, 137.3, 138.5, 150.9, 155.0, 176.9; HRMS calcd for $C_{37}H_{41}NO_9S_2$ ([M + H]$^+$) 708.2301, found 708.2355.

(2*S,4*R**,6a*S**,12a*R**,12b*R**)-2-(3-Benzyloxypropyl)-4-hydroxy-1-(phenoxy carbonyl)-7,7,12,12-tetraoxa-3,4,6,6a,7,7,12,12a,12b-octahydro-2*H*-7λ^6,12λ^6-dithia-1-azabenzo-[α]anthracene (46)**. To a −78 °C solution of 20 mg (0.028 mmol) of **44** in 2 mL of CH_2Cl_2 was added 70.6 μL (0.070 mmol) of 1.0 M DIBALH in toluene. After 2 h at −78 °C, the reaction was quenched with MeOH (1 mL) and diluted with brine (1 mL). The solution was extracted with CH_2Cl_2 (3 × 1 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by radial PLC (silica gel, 40% EtOAc/hexanes) gave 13 mg (78%) of **46** as a white solid, mp 132.0−132.5 °C; IR (neat) 2360, 1717, 1322, 1204, 1148, 1130, 738, 698, 668 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ1.25−1.71 (m, 4H), 2.00−2.06 (m, 2H), 2.33 (d, 1H, *J* = 17.4 Hz), 2.75−2.86 (m, 2H), 3.47 (m, 1H), 3.65 (m, 1H), 4.32 (br s, H), 4.44 (d, 1H, *J* = 11.2 Hz), 4.35−4.59 (m, 4H), 5.48 (br s, 1H), 5.97 (s, 1H), 6.98 (d, 1H, *J* = 8.0 Hz), 7.15 (t, 2H, *J* = 7.6 Hz), 7.26−7.41 (m, 8H), 7.67 (t, 2H, *J* = 7.6 Hz), 7.90 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.3, 26.3, 28.0, 29.9, 34.7, 39.5, 50.6, 51.3, 59.1, 62.3, 66.8, 69.7, 73.6, 116.8, 121.6, 125.0, 125.5, 128.2, 128.6, 129.3, 133.6, 134.2, 135.6, 136.1, 137.4, 138.5, 150.9, 155.0; HRMS calcd for $C_{32}H_{33}NO_8S_2$ ([M + H]$^+$) 624.1726, found 624.1761.

(2*R,5*S**,6a*S**,12a*R**,12b*R**)-2-(3-Benzyloxypropyl)-5-ethoxycarbonylmethyl-1-(phenoxycarbonyl)-7,7,12,12-tetraoxo-3,5,6,6a,7,12,12a,12b-octahydro-2*H*-7λ^6,12 l^6-dithiabenzo[α]anthracene (47).** To a solution of 10.5 mg (0.017 mmol) of **46** (10.5 mg, 0.017 mmol) in 2 mL of triethyl orthoacetate was added 1 drop of a 1:10 propionic acid:triethyl orthoacetate solution. The resulting mixture was refluxed for 3 h and then concentrated under reduced pressure. Purification by radial PLC (silica gel, 5% EtOAc/5% CH_2Cl_2/ 90% hexanes) gave 7.8 mg of **47** (67%) as a white solid, mp 180.5−181.5 °C; IR (neat) 2979, 2938, 2863, 1716, 1686, 1495, 1455, 1355, 1320, 1194, 1148, 748, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, 3H, *J* = 7.2 Hz), 1.58−1.80 (m, 4H), 2.15−2.26 (m, 1H), 2.48−2.61 (m, 3H), 2.42 (br d, 1H, *J* = 12.9 Hz), 3.37 (q, 1H, *J* = 5.1 Hz), 3.50 (s, 2H), 3.85 (dt, 1H, *J* = 10.8 and 2.7 Hz), 4.04−4.18 (m, 2H), 4.48 (s, 2H), 4.59−4.63 (m, 2H), 5.98 (d, 1H, *J* = 5.4 Hz), 6.21 (s, 1H), 7.13−7.36 (m, 11H), 7.74−7.82 (m, 2H), 7.96 (t, 2H, *J* = 4.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.5, 26.7, 27.3, 27.6, 31.0, 37.0, 39.4, 52.3, 53.1, 59.1, 59.7, 61.1, 70.1, 73.2, 122.1, 124.6, 124.9, 125.2, 126.0, 127.8, 127.9, 128.6, 129.7, 133.6, 134.2, 134.7, 138.6, 140.9, 151.3, 156.2, 171.2; HRMS for $C_{36}H_{39}NO_9S_2$ ([M + H]$^+$) 694.4125, found 694.2147.

(1*R)-[3-(9,10-Dioxo-9,10-dihydroanthracen-2-yl)-3-oxo-1-phenylpropyl]carbamic Acid Phenyl Ester (50).** To a solution of 70 mg (0.219 mmol) of **5** in 10 mL of toluene was added 41 mg (0.259 mmol) of 1,4-naphthoquinone. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The residue was rapidly purified by radial PLC (silica gel, EtOAc/hexanes) to give 87 mg (84%) of (2*R**,6a*S**,12a*S**,12b*R**)-4,7,12-trioxo-1-((phenoxy)carbonyl)-2-phenyl-3,4,6,6a,7,12,12a,12b-octahydro-2*H*-naphtho[2,3-*h*]quinoline (**48**) as a colorless foam: IR (thin film) 3027, 2910, 1699, 1623, 1592, 1483, 1350, 1255, 1203 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.31 (m, 1H), 2.78 (m, 1H), 3.00 (dt, 1H, *J* = 16.0 and 3.7 Hz), 3.58 (m, 1H), 3.82 (m, 1H), 5.00 (m, 1H), 6.10 (m, 1H), 6.66 (m, 1H), 6.76 (m, 2H), 7.21 (m, 9H), 7.77 (m, 2H), 7.96 (m, 1H), 8.05 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.1, 43.7, 47.3, 49.7, 55.9, 57.8, 121.7, 125.8, 126.2, 126.6, 127.6, 128.0, 129.3, 129.4, 132.5, 133.8, 134.7, 134.9, 135.0, 141.1, 150.8, 155.3, 194.8, 196.3, 196.6; HRMS calcd for $C_{30}H_{23}NO_5$ ([M + H]$^+$) 478.1654, found 478.1652.

To a solution of 85 mg (0.178 mmol) of **48** in 10 mL of CH_2Cl_2 was added 1.0 g of silica gel. The mixture was stirred at room temperature for 18 h, filtered, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 75 mg (88%) of **50** as a light yellow foam: IR (thin film) 3338, 1694, 1672, 1590, 1523, 1485, 1361, 1291, 1199 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.70 (dd, 1H, *J* = 16.8 and 5.8 Hz), 3.97 (m, 1H), 5.45 (m, 1H), 6.02 (br s, 1H), 7.29 (m, 11H), 7.85 (m, 2H), 8.35 (m, 3H), 8.80 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.9, 44.6, 52.2, 121.8, 125.6, 126.7, 127.2, 127.7, 128.2, 129.1, 129.5, 133.1, 133.6, 134.0, 134.8, 140.7, 151.1, 154.2, 182.6, 189.0, 196.8; HRMS calcd for $C_{30}H_{21}NO_5$ ([M + H]$^+$) 476.1498, found 476.1516.

(1*R)-[3-(5,8-Dioxo-5,8-dihydronaphthalen-2-yl)-3-oxo-1-phenylpropyl]carbamic Acid Phenyl Ester (51).** To a solution of 30 mg (0.094 mmol) of **5** in 7 mL of toluene was added 12 mg (0.111 mmol) of 1,4-benzoquinone. The mixture was heated at reflux for 12 h, cooled to room temperature, and

concentrated under reduced pressure. The residue was rapidly purified by radial PLC (silica gel, EtOAc/hexanes) to give 37 mg (93%) of (2*R**,6a*S**,10a*S**,10b*R**)-4,7,10-trioxo-1-((phenoxy)carbonyl)-2-phenyl-3,4,6,6a,7,10,10a,10b-octahydro-2*H*-benzo[*h*]quinoline as a clear oil: IR (thin film) 3048, 3919, 1689, 1622, 1493, 1351, 1262, 1203 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.38 (m, 1H), 2.70 (m, 1H), 2.97 (dd, 1H, J = 15.7 and 3.8 Hz), 3.41 (m, 1H), 3.71 (dd, 1H, J = 15.7 and 5.8 Hz), 4.69 (t, 1H, J = 3.0 Hz), 4.38 (m, 1H), 6.02 (m, 1H), 6.56−6.72 (m, 2H), 6.77 (d, 1H, J = 7.9 Hz), 7.30 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.0, 43.6, 46.6, 55.7, 57.9, 116.4, 121.7, 125.9, 126.2, 128.1, 129.4, 129.5, 134.1, 135.0, 138.1, 139.2, 141.0, 150.9, 155.3, 194.4, 197.6, 198.7; HRMS calcd for $C_{26}H_{21}NO_5$ ($[M + H]^+$) 428.1498, found 428.1500.

To a solution of 35 mg (0.0819 mmol) of the above intermediate in 5 mL of CH_2Cl_2 was added 1.0 g of silica gel. The mixture was stirred at room temperature for 18 h, filtered, and concentrated under reduced pressure. The residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 24 mg (69%) of **51** as a light yellow foam: IR (thin film) 3332, 3060, 2919, 1714, 1668, 1602, 1513, 1486, 1297, 1205 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.62 (dd, 1H, J = 17.1 and 5.8 Hz), 3.85 (d, 1H, J = 17.1 Hz), 5.39 (m,1H), 5.96 (br s, 1H), 7.03−7.42 (m, 12H), 8.13 (d, 1H, J = 7.9 Hz), 8.24 (d, 1H, J = 7.9 Hz), 8.53 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.7, 52.2, 116.3, 121.7, 125.6, 126.3, 126.7, 127.3, 128.2, 129.1, 129.5, 132.3, 133.0, 134.7, 139.1, 139.2, 140.6, 151.1, 154.1, 184.2, 184.3, 196.7; HRMS calcd for $C_{26}H_{19}NO_5$ ($[M + H]^+$) 426.1341, found 426.1364.

(1*R,3*R**)-[3-(5,8-Dioxo-5,8-dihydronaphthalen-2-yl)-3-hydroxy-1-phenylpropyl]carbamic Acid Phenyl Ester (52).** To a solution of 28 mg (0.087 mmol) of **35** in 5 mL of toluene was added 12 mg (0.111 mmol) of 1,4-benzoquinone. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The residue was rapidly purified by radial PLC (silica gel, EtOAc/hexanes) to give 32 mg (86%) of (2*R**,4*S**,6a*S**,10a*S**,10b*R**)-4-hydroxy-7,10-dioxo-1-((phenoxy)carbonyl)-2-phenyl-3,4,6,-6a,7,10,10a,10b-octahydro-1*H*-benzo[*h*]quinoline as a colorless oil: IR (neat) 3456, 3061, 2935, 1701, 1691, 1597, 1494, 1352, 1262, 1205, 1102 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.63 (m, 1H), 2.13 (m, 1H), 2.28 (m, 1H), 2.56 (m, 1H), 2.77 (m, 1H), 3.41 (m, 1H), 4.41 (m, 1H), 4.66 (m, 1H), 4.91 (s, 1H), 5.59 (m, 1H), 5.70 (s, 1H), 6.45 (m, 1H), 6.60 (m, 1H), 7.05−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 39.0, 47.0, 48.7, 55.7, 59.5, 64.1, 115.4, 121.6, 125.4, 125.6, 127.1, 129.0, 129.2, 137.2, 137.8, 140.6, 145.8, 150.9, 155.1, 198.1, 199.9; HRMS calcd for $C_{26}H_{23}NO_5$ ($[M + H]^+$) 430.1654, found 430.1635.

To a solution of 32 mg (0.0745 mmol) of the above intermediate in 8 mL of CH_2Cl_2 was added 1.0 g of silica gel. The mixture was stirred at room temperature for 18 h, filtered, and concentrated under reduced pressure. The residue was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 28 mg (88%) of **52** as a light yellow oil: IR (thin film) 3353, 3063, 2923, 1714, 1666, 1600, 1530, 1489, 1306, 1206 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.18 (m, 1H), 2.39 (m, 1H), 4.76 (m, 1H), 4.99 (q, 1H, J = 6.6 Hz), 5.76 (m, 1H), 6.95 (s, 1H), 7.06 (m, 1H), 7.17 (m, 1H), 7.33 (m, 11H), 7.71 (d, 1H, J = 7.8 Hz), 8.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 45.8, 54.3, 71.8, 121.7, 123.7, 125.6, 126.8, 127.2, 128.3, 129.3, 129.5, 131.3, 132.2, 138.8, 139.0, 141.3, 151.0, 151.2, 154.4, 184.9, 185.2; HRMS calcd for $C_{26}H_{21}NO_5$ ($[M + H]^+$) 428.1498, found 428.1517.

(3*R)-4-(3-Phenoxycarbonylamino-3-phenylpropionyl)-phthalic Acid Dimethyl Ester (54).** To a solution of 60 mg (0.186 mmol) of **5** in 8 mL of toluene was added 34 mg (0.241 mmol) of dimethyl acetylenedicarboxylate. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The residue was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 60 mg (71%) of **54** as a colorless solid: mp 65−66 °C; IR (thin film) 3354, 3025, 2942, 1731, 1525, 1484, 1437, 1290, 1202, 1125, 1072 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.53 (dd, 1H, J = 17.3 and 6.1 Hz), 3.83 (m, 1H), 3.92 (s, 6H), 5.40 (m, 1H), 6.10 (br s, 1H), 7.15 (m, 3H), 7.39 (m, 7H), 7.72 (d, 1H, J = 8.0 Hz), 8.05 (d, 1H, J = 8.0 Hz), 8.26 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.3, 52.0, 53.1, 53.2, 121.7, 125.5, 126.6, 128.0, 128.2, 128.9, 129.0, 129.4, 130.9, 132.0, 136.7, 138.3, 140.7, 151.0, 154.1, 166.9, 167.6, 196.4. Anal. Calcd for $C_{26}H_{23}NO_7$: C, 67.67; H, 5.02; N, 3.04. Found: C, 67.41; H, 5.10; 3.05.

(3*R)-4-(3-Phenoxycarbonylamino-3-phenylpropionyl)-phthalic Acid Di-*tert*-butyl Ester (55).** To a solution of 85 mg (0.266 mmol) of **5** in 10 mL of toluene was added 78 mg (0.346 mmol) of di-*tert*-butyl acetylenedicarboxylate. The mixture was heated at reflux for 12 h, cooled to room temperature, and concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 122 mg (85%) of **55** as a colorless foam: IR (thin film) 3342, 2979, 1722, 1503, 1491, 1368, 1309, 1205 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.59 (s, 18H), 3.49 (dd, 1H, J = 16.8 and 6.0 Hz), 3.78 (d, 1H, J = 16.8 Hz), 5.38 (m, 1H), 6.17 (br s, 1H), 7.13 (m, 3H), 7.36 (m, 7H), 7.64 (d, 1H, J = 7.8 Hz), 7.96 (d, 1H, J = 7.8 Hz), 8.14 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.2, 44.2, 52.1, 82.8, 82.9, 121.7, 125.5, 126.6, 128.0, 129.0, 129.3, 129.4, 130.1, 134.2, 137.8, 138.3, 140.8, 151.1, 154.1, 165.9, 166.3, 196.7; HRMS calcd for $C_{32}H_{35}NO_7$ ($[M + H]^+$) 546.2492, found 546.2502.

(1*R)-(3-Naphthalen-2-yl-3-oxo-1-phenylpropyl)carbamic Acid Phenyl Ester (57).** To a solution of 30 mg (0.939 mmol) of **4** in 7 mL of acetonitrile at room temperature was added 36 mg (0.122 mmol) of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**56**) followed by 0.122 mL of a 1.0 M solution of TBAF. After 10 min, the reaction mixture was concentrated under reduced pressure. The residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 23 mg (62%) of **57** as a white solid: mp 137−138 °C; IR (thin film) 3333, 2922, 1733, 1682, 1626, 1603, 1486, 1369, 1313, 1248, 1203 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.64 (dd, 1H, J = 16.8 and 6.0 Hz), 3.93 (m, 1H), 5.44 (m, 1H), 6.22 (br s, 1H), 7.15 (m, 3H), 7.32 (m, 4H), 7.40 (m, 2H), 7.57 (m, 3H), 7.92 (m, 4H), 8.43 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 43.9, 52.4, 121.8, 123.9, 125.5, 126.7, 127.1, 127.9, 128.0, 128.8, 129.0, 129.4, 129.9, 130.3, 132.7, 134.2, 136.0, 141.1, 141.2, 151.2, 154.3, 198.1. Anal. Calcd for $C_{26}H_{21}NO_3$: C, 78.97; H, 5.35; N, 3.54. Found: C, 78.91; H, 5.47; N, 3.59.

(1*R,2*R**)-(2-Acetoxy-3-naphthalen-2-yl-3-oxo-1-phenylpropyl)carbamic Acid Phenyl Ester (60).** To a solution of 265 mg (0.75 mmol) of acetate **58**[22] in 20 mL of CH_2Cl_2 was added 254 mg (1.13 mmol) of *N*-iodosuccinimide followed by 30 mg (0.08 mmol) of hydroxy(tosyloxy)iodobenzene. The reaction mixture was stirred at room temperature in the dark for 18 h, filtered through a plug of silica gel, and concentrated under reduced pressure. The product was purified by radial PLC (silica gel, EtOAc/hexanes) to give 280 mg (78%) of (2*S**,3*S**)-3-acetoxy-5-iodo-1-((phenoxy)carbonyl)-2-phenyl-2,3-dihydro-4-pyridon as a colorless foam: IR (thin film) 3064, 1748, 1682, 1577, 1493, 1386, 1297, 1200, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.14 (s, 3H), 5.57 (s, 1H), 5.87 (s, 1H), 7.00 (m, 2H), 7.33 (m, 8H), 8.80 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.0, 62.3, 71.0, 74.4, 121.0, 126.0, 126.8, 129.1, 129.6, 129.7, 132.9, 148.4, 150.1, 150.3, 169.4, 181.1; HRMS calcd for $C_{20}H_{16}INO_5$ ($[M + H]^+$) 478.0151, found 478.0167.

To a solution of 260 mg (0.545 mmol) of the above iodide in 15 mL of toluene was added 225 mg (0.710 mmol) of tributylvinyltin followed by 44 mg (0.038 mmol) of tetrakis-(triphenylphosphine)palladium(0). The mixture was heated at reflux for 15 h, filtered through Celite, and concentrated under reduced pressure. The crude product was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 117 mg (57%) of (2*R**,3*S**)-3-acetoxy-1-((phenoxy)carbonyl)-2-phenyl-5-vinyl-2,3-dihydro-4-pyridone (**59**) as a white solid: mp 129−130 °C (EtOAc/hexane); IR (thin film) 3065, 1744, 1681, 1592, 1493, 1309, 1194, 1017, 915 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.17

(s, 3H), 5.22 (d, 1H, J = 11.4 Hz), 5.34 (s, 1H), 5.80 (s, 1H), 5.89 (d, 1H, J = 17.5 Hz), 6.40 (dd, 1H, J = 17.5 and 11.4 Hz), 7.00 (m, 2H), 7.34 (m, 8H), 8.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 61.8, 73.5, 115.9, 116.3, 121.2, 126.2, 126.7, 128.7, 129.0, 129.6, 129.8, 133.7, 140.4, 150.4, 151.5, 169.8, 185.2. Anal. Calcd for $C_{22}H_{19}NO_5$: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.85; H, 5.18; N, 3.59.

To a solution of 43 mg (0.114 mmol) of **59** in 10 mL of acetonitrile at room temperature was added 51 mg (0.171 mmol) of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate followed by 0.170 mL of a 1.0 M solution of TBAF. After 10 min the reaction mixture was concentrated under reduced pressure. The crude residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 32 mg (62%) of **60** as a clear oil: IR (thin film) 3330, 2919, 1740, 1694, 1488, 1370, 1203 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.24 (s, 3H), 5.54 (m, 1H), 6.22 (d, 1H, J = 8.0 Hz), 6.61 (d, 1H, J = 3.4 Hz), 7.11−7.40 (m, 11H), 7.57 (m, 2H), 7.88 (m, 3H), 8.41 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.0, 56.6, 75.4, 121.7, 124.0, 125.7, 127.1, 127.6, 128.0, 128.7, 129.0, 129.2, 129.6, 130.2, 131.0, 132.6, 136.1, 151.7, 154.4, 170.4, 194.6; HRMS calcd for $C_{28}H_{23}NO_5$ ([M + H]$^+$) 454.1654, found 454.1639.

(1*R)-[1-(2-Naphthalen-2-yl-2-oxoethyl)allyl]carbamic Acid Phenyl Ester (63).** To a solution of 1.20 g (4.66 mmol) of dihydropyridone **61**[23] in 50 mL of CH_2Cl_2 was added 1.57 g (6.78 mmol) of *N*-iodosuccinimide followed by 183 mg (0.48 mmol) of hydroxy(tosyloxy)iodobenzene. The reaction mixture was stirred at room temperature in the dark for 18 h, filtered through a plug of silica gel, and concentrated under reduced pressure. The product was purified by radial PLC (silica gel, EtOAc/hexanes) to give 1.20 g (67%) of (2*R**)-5-iodo-1-((benzyloxy)carbonyl)-2-phenyl-2,3-dihydro-4-pyridone as a light yellow oil: IR (neat) 3061, 1723, 1671, 1579, 1388, 1286, 1250, 1135 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.83 (d, 1H, J = 16.4 Hz), 2.96 (dd, 1H, J = 16.4 and 6.5 Hz), 5.24 (m, 5H), 5.74 (m, 1H), 7.37 (m, 5H), 8.31 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 38.8, 55.2, 69.7, 75.8, 118.2, 128.7, 129.1, 132.4, 134.7, 143.7, 146.9, 151.5, 186.3; HRMS calcd for $C_{15}H_{14}INO_3$ ([M + H]$^+$) 384.0097, found 384.0104.

To a solution of 1.13 g (2.95 mmol) of the above iodide in 25 mL of toluene was added 1.22 g (3.84 mmol) of tributylvinyltin followed by 0.24 g (0.21 mmol) of tetrakis(triphenylphosphine)-palladium(0). The mixture was heated at reflux for 15 h, filtered through Celite, and concentrated under reduced pressure. The crude product was purified by radial PLC (silica gel, EtOAc/hexanes) to afford 0.34 g (41%) of (2*R**)-1-((benzyloxy)-carbonyl)-2,5-divinyl-2,3-dihydro-4-pyridone (**62**) as a light yellow oil: IR (neat) 3066, 2960, 1731, 1672, 1606, 1397, 1303, 1258, 1132 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.57 (d, 1H, J = 16.3 Hz), 2.91 (dd, 1H, J = 16.3 and 7.0 Hz), 5.05−5.32 (m, 6H), 5.69 (d, 1H, J = 17.6 Hz), 5.78 (m, 1H), 6.33 (dd, 1H, J = 17.6 and 11.4 Hz), 7.38 (s, 5H), 7.91 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.6, 54.8, 69.4, 114.4, 116.7, 117.9, 129.0, 129.3, 132.2, 133.1, 135.1, 138.6, 152.7, 191.1; HRMS calcd for $C_{17}H_{17}NO_3$ ([M + H]$^+$) 284.1287, found 284.1273.

To a solution of 48 mg (0.169 mmol) of **62** in 12 mL of acetonitrile at room temperature was added 76 mg (0.254 mmol) of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate followed by 0.254 mL of a 1.0 M solution of TBAF. After 10 min, the reaction mixture was concentrated under reduced pressure. The residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 40 mg (66%) of **63** as a white solid: mp 98−99 °C (EtOAc/pentane); IR (thin film) 3335, 3060, 1713, 1508, 1468, 1251, 1184 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.36 (dd, 1H, J = 16.9 and 5.7 Hz), 3.57 (d, 1H, J = 16.9 Hz), 4.80 (m, 1H), 5.11 (s, 2H), 5.14 (d, 1H, J = 10.7 Hz), 5.24 (d, 1H, J = 17.2 Hz), 5.67 (br s, 1H), 6.00 (m, 1H), 7.33 (s, 5H), 7.58 (m, 2H), 7.88 (m, 2H), 7.99 (m, 2H), 8.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 42.9, 50.5, 67.0, 115.8, 123.8, 127.1, 128.0, 128.3, 128.8, 129.8, 130.2, 132.7, 134.3, 135.9, 136.7, 137.6, 139.1, 155.9, 174.1. Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.90. Found: C,76.68; H, 5.98; N, 3.79.

(1*R)-(1-Formyl-3-naphthalen-2-yl-3-oxopropyl)carbamic Acid Benzyl Ester (64).** To a stirred solution of 30 mg (0.835 mmol) of **63** in 8 mL of a 1:1 mixture of THF/water was added 89 mg (0.416 mmol) of sodium periodate. After the solution was stirred for 5 min, 3 drops of osmium tetroxide (4 wt % solution in water) was added and the solution was stirred for 5 h. The reaction mixture was filtered through a pad of Celite and extracted with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by radial PLC (silica gel, EtOAc/hexanes) to give 29 mg (97%) of **64** as a colorless oil: IR (neat) 3354, 3060, 2919, 2825, 1715, 1678, 1507, 1373, 1255 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.75 (dd, 1H, J = 18.2 and 3.9 Hz), 3.91 (dd, 1H, J = 18.2 and 4.2 Hz), 4.60 (m, 1H), 5.14 (s, 2H), 6.03 (d, 1H, J = 7.8 Hz), 7.34 (m, 5H), 7.60 (m, 2H), 7.93 (m, 4H), 8.47 (s, 1H), 9.83 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 40.1, 56.4, 67.5, 123.7, 127.3, 128.1, 128.4, 128.5, 128.8, 128.9, 129.2, 129.6, 129.9, 130.7, 132.6, 133.3, 136.2, 156.5, 197.6, 199.8.

(2*R)-2-Benzyloxycarbonylamino-4-naphthalen-2-yl-4-oxobutyric Acid (65).** To a solution of 30 mg (0.083 mmol) of **64** in 1 mL of 2-methyl-2-butene was added 2 mL of *tert*-butyl alcohol. To this solution was added 15 mg (0.166 mmol) of sodium chlorite and 20 mg (0.166 mmol) of NaH_2PO_4 in 0.5 mL of water. The resulting mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated to one-half volume, diluted with 15 mL of water, and washed with pentane. The aqueous layer was acidified, extracted with ether, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was recrystallized from $CHCl_3$/pentane to afford 26 mg (86%) of **65** as a colorless solid: mp 169−170 °C; IR (thin film) 3389, 2942, 1731, 1695, 1672, 1519, 1431, 1372, 1219 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.70 (d, 1H, J = 17.2 Hz), 3.97 (d, 1H, J = 17.2 Hz), 4.87 (m, 1H), 5.13 (s, 2H), 5.96 (m, 1H), 7.33 (s, 5H), 7.60 (m, 2H), 7.93 (m, 4H), 8.48 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 41.4, 50.1, 67.5, 123.7, 127.3, 128.1, 128.3, 128.4, 128.8, 129.0, 129.3, 129.9, 130.7, 131.7, 132.6, 133.3, 136.2, 149.9, 184.0, 198.4. Anal. Calcd for $C_{22}H_{19}NO_5$: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.68; H, 5.03; N, 3.67.

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Supporting Information Available: Spectroscopic and analytical data for compounds **9**−**11**, **13a/b**, **14a/b**, **15a/b**, **16a**, **17**, **21**−**22**, **24**−**25**, **35**−**36**, **39**−**48**, **50**−**52**, **55**, **60**, **62**, **64**−**65**; ORTEP plots and X-ray crystal data for compounds **22** and **47** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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