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A New Acyl Radical-based Route to the 1,5-Methanoazocino[4,3-*b*]indole Framework of Uleine and *Strychnos* Alkaloids

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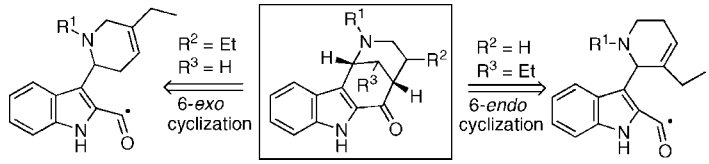

C-4 or C-12 ethyl substituted 1,5-methanoazocino[4,3-*b*]indoles, which constitute the tetracyclic framework of uleine alkaloids as well as the ABDE substructure of the *Strychnos* alkaloid family, have been synthesized by novel 6-*exo* and 6-*endo* cyclizations of selenoester-derived 2-indolylacyl radicals upon 5-ethyl-1,2,3,6- and 3-ethyl-1,2,5,6-tetrahydropyridines, respectively.

Introduction

In the last years we have been involved in the development of a novel general synthetic entry to indole compounds taking advantage of the reactions of phenyl selenoester derived 2-indolylacyl radicals.[1,2] In particular, we have shown that several alkaloid structures embodying the 2-acylindole moiety can be efficiently assembled by intramolecular reactions of these radical intermediates with a variety of indole-tethered carbon−carbon double bond acceptors.[2b,3] On the basis of our earlier work, we considered extending this methodology for the construction of the 1,5-methanoazocino[4,3-*b*]indole system, which constitutes the bridged arrangement of the indole alkaloids of the uleine group[4] (uleine, dasycarpidone and their C-20 epimers, Figure 1) as well as the ABDE substructure of the *Strychnos* alkaloid family,[5] exemplified by the pentacyclic components tubifolidine or strychnopivotine (strychnan biogenetic type) and tubotaiwine (aspidospermatan biogenetic type). Although these natural products have long attracted the attention of the synthetic community and, consequently, a great variety of synthetic approaches have been reported,[4,5] radical methodologies have been little explored in this field.[6]

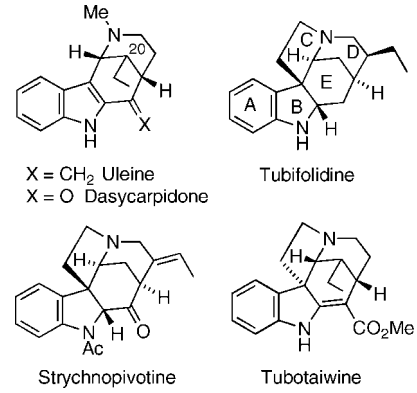

FIGURE 1. Uleine and *Strychnos* Alkaloids.

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(1) For a review on the chemistry of acyl radicals, see: (a) Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, I. *Chem. Rev.* **1999**, *99*, 1991–2069.

(2) (a) Bennasar, M.-L.; Roca, T.; Griera, R.; Bosch, J. *Org. Lett.* **2001**, *3*, 1697–1700. (b) Bennasar, M.-L.; Roca, T.; Ferrando, F. *Org. Lett.* **2004**, *6*, 759–762.

(3) (a) Bennasar, M.-L.; Roca, T.; Ferrando, F. *J. Org. Chem.* **2005**, *70*, 9077–9080. (b) Bennasar, M.-L.; Roca, T.; Ferrando, F. *J. Org. Chem.* **2006**, *71*, 1746–1749. (c) Bennasar, M.-L.; Roca, T.; Ferrando, F. *Org. Lett.* **2006**, *8*, 561–564. (d) Bennasar, M.-L.; Roca, T.; García-Díaz, D. *J. Org. Chem.* **2007**, *72*, 4562–4565.

(4) For reviews, see: (a) Joule, J. A. In *Indoles. The Monoterpenoid Indole Alkaloids*, Saxton, J. E., Ed.; The Chemistry of Heterocyclic Compounds; Weissberger, A., Taylor, E. C., Eds.; Wiley: New York, 1983; Vol. 25, Part 4, Ch 6. (b) Alvarez, M.; Joule, J. A. In *Monoterpenoid Indole Alkaloids*; Saxton, J. E., Ed.; The Chemistry of Heterocyclic Compounds; Taylor, E. C., Ed.;Wiley: Chichester, 1994; Supplement to Vol. 25, Part 4, Ch 6. (c) Alvarez, M.; Joule, J. A. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: New York, 2001; Vol. 57, Ch 4.

(5) For reviews, see: (a) Bosch, J.; Bonjoch, J. In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, , Ed.; Elsevier: Amsterdam, 1988; pp 31−88. (b) Sapi, J.; Massiot, G. In *Monoterpenoid Indole Alkaloids*; Saxton, J. E., Ed.; The Chemistry of Heterocyclic Compounds; Taylor, E. C., Ed.; Wiley: Chichester, 1994; Supplement to Vol. 25, Part 4, Ch 7. (c) Bosch, J.; Bonjoch, J.; Amat, M. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: New York, 1996; Vol. 48, pp 75−189.

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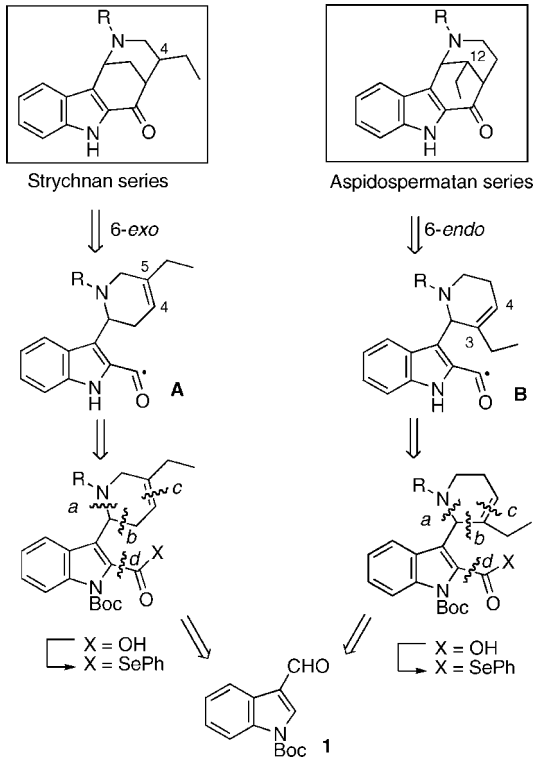
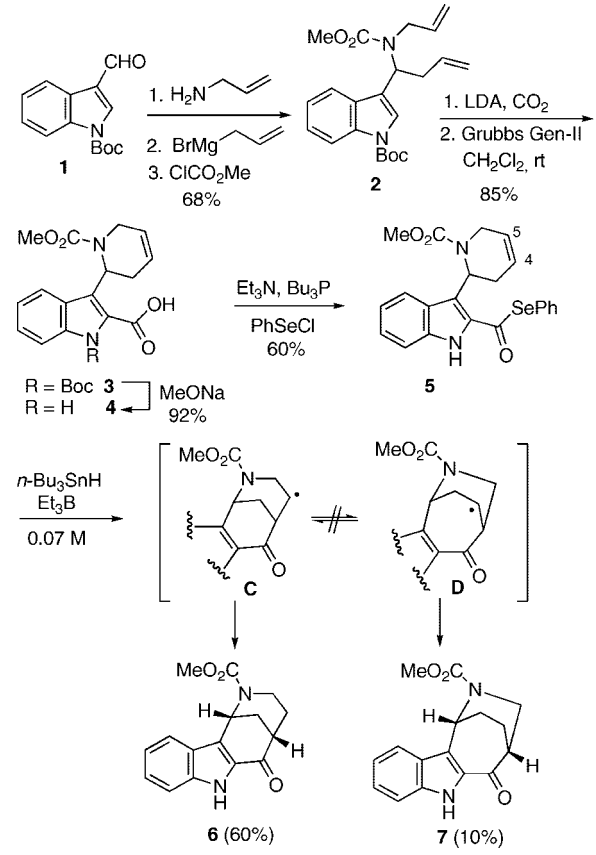
SCHEME 1. Synthetic Strategy



As depicted in Scheme 1, our strategy for the assembly of this bridged tetracyclic framework relies on the closure of the carbocyclic 6-membered ring by cyclization of 3-(tetrahydro-2-pyridyl)-2-indolylacyl radicals.[7,8] We anticipated that placing both the double bond acceptor and the required two-carbon appendage at different positions of the pyridine ring (as depicted in **A** and **B**) would enable two radical cyclization pathways to generate complementary substituted tetracycles. Thus, either strychnan (C-4 ethyl) or aspidospermatan (C-12 ethyl) substructures would be produced by regioselective 6-exo or 6-endo cyclizations upon 1,2,3,6- or 1,2,5,6-tetrahydropyridines, respectively. Critical to the success of our synthetic plan was the efficient construction of the cyclization substrates. To this end, we devised two closely related flexible routes starting from the *N*-protected indole-3-carbaldehyde **1**, which involve an amination (bond *a*)-imine allylation or alkenylation (bond *b*)-ring closing metathesis (RCM, bond *c*) sequence. In addition, carboxylation of a 2-lithioindole derivative (bond *d*) at some stage would install the carboxylic acid function from which the acyl radical precursor selenoester would be prepared.

SCHEME 2. Model 6-Exo Cyclization



Results and Discussion

We set out to study the construction of the 6-oxo-1,5-methanoazocino[4,3-*b*]indole system by 6-exo cyclization of 2-indolylacyl radicals upon 1,2,3,6-tetrahydropyridines (6-heptenoyl radicals **A**). To test the feasibility of the proposal we first targeted the model selenoester **5**, which incorporated an unsubstituted tetrahydropyridine moiety at the indole 3-position.[9] As anticipated, this compound was available from the *N*-Boc-protected indole **1**, following the synthetic sequence depicted in Scheme 2. Thus, reaction of **1** with allylamine and alkylation of the resulting imine with allylmagnesium bromide led to an unstable secondary amine, which was not isolated[10] but was subsequently acylated with methyl chloroformate to give carbamate **2** in 68% overall yield. At this point, the carboxy group could be introduced with high efficiency by treatment with LDA and reaction of the intermediate 2-lithioindole derivative with carbon dioxide. The next closure of the tetrahydropyridine ring of the resulting sensitive carboxylic acid by RCM was accomplished uneventfully by reaction with the second generation Grubbs catalyst $(Im)(PCy_3)_2(Cl)_2Ru{=}CHPh$

(6) (a) Kuehne, M. E.; Wang, T.; Seraphin, D. *J. Org. Chem.* **1996**, *61*, 7873–7881. (b) Kuehne, M. E.; Bandarage, U. K.; Hammach, A.; Li, Y.-L.; Wang, T. *J. Org. Chem.* **1998**, *63*, 2172–2173. (c) Eichberg, M. J.; Dorta, R. L.; Grotjahn, D. B.; Lamottke, K.; Schmidt, M.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **2001**, *123*, 9324–9337.

(7) For a leading review on the synthesis of nitrogen heterocycles by radical cyclization, see: Bowman, W. R.; Fletcher, A. J.; Potts, G. B. S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2747–2762.

(8) For relevant radical cyclizations leading to bridged nitrogen heterocycles, see: (a) Della, E. W.; Knill, A. M. *J. Org. Chem.* **1996**, *61*, 7529–7533. (b) Quirante, J.; Escolano, C.; Massot, M.; Bonjoch, J. *Tetrahedron* **1997**, *53*, 1391–1402. (c) Quirante, J.; Escolano, C.; Merino, A.; Bonjoch, J. *J. Org. Chem.* **1998**, *63*, 968–976. (d) Della, E. W.; Smith, P. A. *J. Org. Chem.* **2000**, *65*, 6627–6633. (e) Hoepping, A.; George, C.; Flippen-Anderson, J.; Kozikowski, A. P. *Tetrahedron Lett.* **2000**, *41*, 7427–7432. (f) Tamura, O.; Yanagimachi, T.; Kobayashi, T.; Ishibashi, H. *Org. Lett.* **2001**, *3*, 2427–2429. (g) Quirante, J.; Vila, X.; Escolano, C.; Bonjoch, J. *J. Org. Chem.* **2002**, *67*, 2323–2328. (h) Yu, J.; Wang, T.; Liu, X.; Deschamps, J.; Flippen-Anderson, J.; Liao, X.; Cook, J. M. *J. Org. Chem.* **2003**, *68*, 7565–7581. (i) Bower, J. F.; Szeto, P.; Gallagher, T. *Chem. Commun.* **2005**, 5793–5795. (j) Bower, J. F.; Szeto, P.; Gallagher, T. *Org. Biomol. Chem.* **2007**, *5*, 143–150. (k) Grainger, R. S.; Welsh, E. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 5377–5380. (l) Dandapani, S.; Duduta, M.; Panek, J. S.; Porco, Jr., J. A. *Org. Lett.* **2007**, *9*, 3849–3852. (m) Yoshimitsu, T.; Atsumi, C.; Iimori, E.; Nagaoka, H.; Tanaka, T. *Tetrahedron Lett.* **2008**, *49*, 4473–4475. (n) See also ref 6.

(9) For a preliminary report of this part of the work, see: Bennasar, M.-L.; Roca, T.; García-Díaz, D. *Synlett* **2008**, 1487–1490.

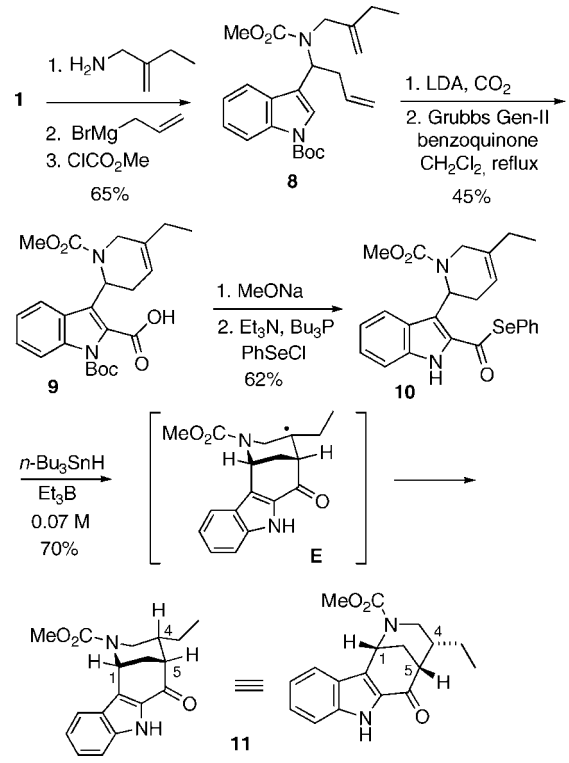
(10) All attempts to carry out the amination-imine allylation sequence from an indole-3-carbaldehyde already incorporating a carboxylic ester at the 2-position resulted in lactamization.

at room temperature in CH_2Cl_2 to give tetrahydropyridine **3** in 85% overall yield from **2**. Selective removal of the indole protecting group under the usual acid (TFA) conditions resulted in intensive decomposition, but it was also achieved in high yield (92%) using a basic protocol (MeONa, reflux). Finally, the resulting tetrahydropyridine carboxylic acid **4** was converted into selenoester **5** by phenylselenation under Batty and Crich conditions[11] (60%).

With a reliable route to the radical precursor in hand, attention was focused on the key cyclization step. Satisfactorily, treatment of selenoester **5** with 2 equiv of *n*-Bu_3SnH in the presence of Et_3B as the initiator at room temperature in benzene (concentration 0.07 M) led to azocinoindole **6** as the major product in 60% yield. The formation of **6** was consistent with the predicted 6-exo cyclization of the initially formed 2-indolylacyl radical to give a bridged azabicyclo[3.3.1]nonane ring system after reduction of the cyclized secondary radical **C**. Minor amounts of tetracycle **7**, containing the regioisomeric bicyclo[3.2.2]nonane system derived from the radical attack at the C-5 tetrahydropyridine position instead of C-4, were also obtained (10% yield). No evidence of acyl radical reduction (i.e., formation of an aldehyde), either from direct hydrogen abstraction from the hydride or an eventual [1,5]-hydrogen transfer, was observed. We experimented with different hydride concentrations to ascertain if the regiochemical outcome was a reflection of the kinetic composition of the initially formed cyclized radicals **C** and **D** or the result of a partial equilibration between these intermediates through one-carbon ring expansion.[12] As compounds **6** and **7** were invariably obtained in the same 6:1 ratio (combined yields 30−40%) working at a higher (0.14 M) or lower (0.005 M) hydride concentration, we assumed that the aforementioned equilibration was not included in the reaction pathway.

Following the success in the model deethyl series, we endeavored to complete the strychnan core structure (C-4 ethyl) by extending the chemistry outlined above to a more elaborated radical precursor (e.g., selenoester **10**, Scheme 3). We expected that the presence of an ethyl substituent at the site of attack on the tetrahydropyridine double bond would preclude the undesired cyclization pathway, thus favoring the exclusive formation of the 6-membered ring. Our synthetic route to **10** began with the sequential reaction of aldehyde **1** with 2-ethylallylamine,[13] allylmagnesium bromide, and methyl chloroformate to give carbamate **8** in 65% yield. Introduction of the α-carboxy group was less efficient than in the above series as it suffered from competitive interaction of the intermediate 2-lithioindole with the *N*-(methoxycarbonyl) group, resulting in partial lactamization.[14] Indeed, after RCM of the rather unstable carboxylic acid, performed in the presence of benzoquinone to prevent the unwanted isomerization of the terminal double bond,[15] the *N*-Boc tetrahydropyridine **9** was obtained in a modest 45% yield from **8**. Changing the order of the synthetic steps, that is, first performing the RCM of **8** and then the carboxylation at the tetrahydropyridine stage, resulted in an even higher undesired

SCHEME 3. Cyclization of Selenoester 10



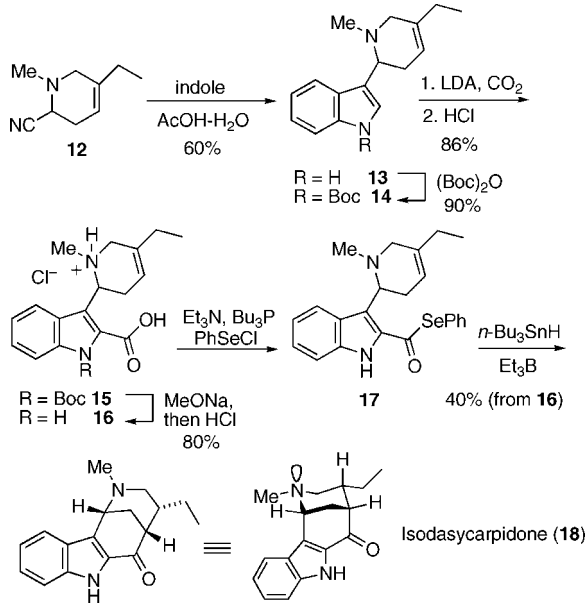
lactamization and, consequently, a lower yield of **9** (<10%).[14] Finally, removal of the *N*-Boc group followed by phenylselenation led to selenoester **10** in 62% yield.

We were pleased to find that selenoester **10** upon exposure to the *n*-Bu_3SnH-Et_3B reductive protocol led to tetracycle **11**[16] (70%), which embodied the expected 4-ethyl-6-oxo-1,5-methanoazocino[4,3-*b*]indole framework with the H-4/H-5 cis relative configuration of the indole alkaloid tubifolidine. The formation of **11** as a single regio- and stereoisomer can be rationalized by considering that, after the predicted 6-exo cyclization of the initially formed 2-indolylacyl radical upon the less substituted alkene carbon, the resulting tertiary radical (**E**) undergoes stereoselective axial hydrogen abstraction from the stannane.

This satisfactory result motivated us to examine a more concise approach to an alternative 6-exo cyclization substrate en route to the so-called isodasycarpidone[17,18] (**18**, Scheme 4). This approach features the rapid assembly of the required 3-(2-tetrahydropyridyl)indole moiety by exploiting the venerable chemistry of *N*-alkyl-2-cyano-1,2,3,6-tetrahydropyridines,[19] which are synthons for dihydropyridinium salts able to react with the indole ring.[18,20] Thus, tetrahydropyridine **13** could be easily synthesized in 60% yield by reaction of 2-cyanotetrahydropyridine **12**[21] with indole in acidic aqueous medium. After protection of the indole NH with a Boc group, the α-lithiation-carboxylation sequence cleanly afforded the expected amino acid (86%), which was isolated as the hydrochloride salt (**15**). The

(11) Batty, D.; Crich, D. *Synthesis* **1990**, 273–275.
(12) For discussions, see: (a) Beckwith, A. L. J.; O'Shea, D. M.; Westwood, S. W. *J. Am. Chem. Soc.* **1987**, *110*, 2565–2575. (b) Boger, D. L.; Mathvink, R. J. *J. Org. Chem.* **1992**, *57*, 1429–1443. (c) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091–2115. (d) Chatgilialoglu, C.; Ferreri, C.; Lucarini, M.; Venturini, A.; Zavitsas, A. A. *Chem.—Eur. J.* **1997**, *3*, 376–387.
(13) Prepared from 2-ethylallyl methanesulfonate: (a) Plamondon, L.; Wuest, J. D. *J. Org. Chem.* **1991**, *56*, 2066–75, See Supporting Information.
(14) See Supporting Information for details.
(15) Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160–17161.
(16) Gràcia, J.; Casamitjana, N.; Bonjoch, J.; Bosch, J. *J. Org. Chem.* **1994**, *59*, 3939–3951.
(17) Kametani, T.; Suzuki, T. *J. Org. Chem.* **1971**, *36*, 1291–1293.
(18) Bosch, J.; Rubiralta, M.; Domingo, A.; Bolós, J.; Linares, A.; Minguillón, C.; Amat, M.; Bonjoch, J. *J. Org. Chem.* **1985**, *50*, 1516–1522.
(19) Fry, E. M. *J. Org. Chem.* **1964**, *29*, 1647–1650.
(20) Feliz, M.; Bosch, J.; Mauleón, D.; Amat, M.; Domingo, A. *J. Org. Chem.* **1982**, *47*, 2435–2440.
(21) Chapman, R. F.; Phillips, N. I. J.; Ward, R. S. *Tetrahedron* **1985**, *41*, 5229–5234.

SCHEME 4. Synthesis of Isodasycarpidone



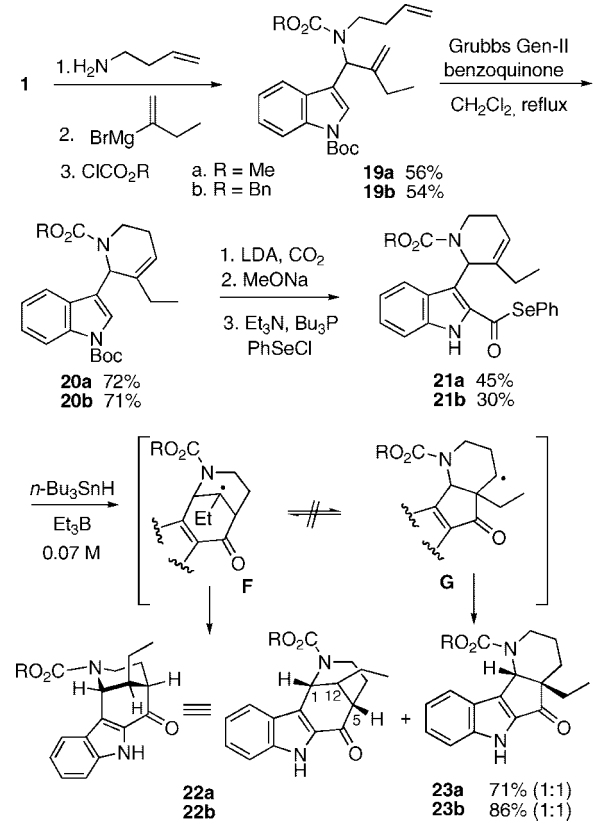
subsequent indole deprotection under the usual basic conditions followed by phenylselenation of the resulting amino acid **16** led to the highly unstable *N*-methyl selenoester (**17**), which was directly subjected to our standard radical protocol. Satisfactorily, the initially formed 2-indolylacyl radical underwent the expected regio- and stereoselective cyclization leading to isodasycarpidone (**18**), once again possessing the H-4/H-5 cis relationship, in 40% overall yield from **16**.

Following our general plan, we sought to elaborate the aspidospermatan core structure (C-12 ethyl) by tackling the more challenging 6-endo cyclizations of 2-indolylacyl radicals upon 1,2,5,6-tetrahydropyridines (5-hexenoyl radicals **B**, Scheme 1). In this series we planned to directly study the behavior of 3-ethyl substituted radical precursors since the presence of the two-carbon appendage was expected to be crucial to sterically prevent the otherwise favored competitive 5-exo closure.

With the final aim of reaching dasycarpidone alkaloids, we first targeted selenoesters **21a,b** bearing an easily removable acyl (methoxycarbonyl or benzyloxycarbonyl) group at the tetrahydropyridine nitrogen. These compounds were prepared from indole-3-carbaldehyde **1**, following the synthetic sequence outlined in Scheme 5. Reaction of **1** with 3-butenylamine followed by addition of 1-buten-2-ylmagnesium bromide[22] to the resulting imine led to a secondary allyl homoallyl amine, which was acylated with methyl or benzyl chloroformate to give carbamates **19a** (56%) or **19b** (54%). Since the indole α-lithiation-carboxylation of **19a** suffered from competitive lactamization as in the above series, we decided to first close the tetrahydropyridine ring by RCM. Thus, treatment of **19a** or **19b** with the second generation Grubbs catalyst in the presence of benzoquinone led to 1,2,5,6-tetrahydropyridines **20a** (72%) or **20b** (71%), which were then elaborated into selenoesters **21a** or **21b** by carboxylation, indole deprotection, and phenylselenation. Without any intermediate being isolated, the overall yield of the three-step sequence was 45 or 30%, respectively.

With selenoesters **21** in hand, we were ready to attempt the key cyclization step. Disappointingly, upon subjection to a

SCHEME 5. Cyclization of Selenoesters 21

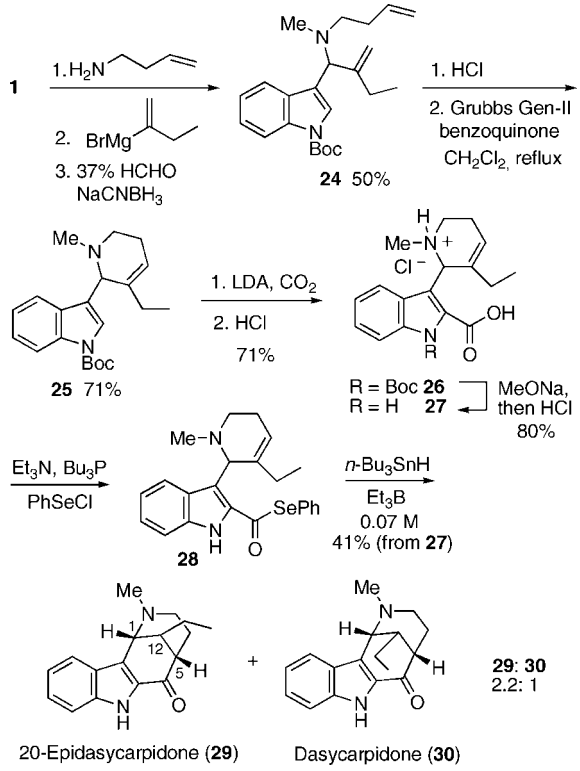


reductive protocol identical to that used in the above exo series (*n*-Bu_3SnH, Et_3B, concentration 0.07 M) selenoester **21a** led to a nearly equimolecular mixture of 6-endo (**22a**) and 5-exo (**23a**) tetracycles, which could not be separated. We explored the possibility of increasing the amount of endo product by carrying out the radical cyclization at lower hydride concentrations (0.01 M, 0.005 M), giving opportunities to an eventual equilibration of the intermediate cyclized radicals **F** and **G** in favor of the most stable tertiary radical **F**. However, the product ratio was not significantly modified and, consequently, we assumed that the observed exo−endo regioselectivity was a reflection of the initial kinetic composition of cyclized radicals. On the other hand, cyclization of the *N*-(benzyloxycarbonyl) selenoester **21b** was not regioselective either, but the mixture of cyclized products **22b** and **23b** could now be separated by column chomatography. Tetracycle **22b** was shown by NMR to embody the expected 12-ethyl-6-oxo-1,5-methanoazocino[4,3-*b*]indole framework with the H-5/H-12 trans relative configuration (12-ethyl axial with respect to the piperidine ring), which is the result of the stereoselective equatorial hydrogen abstraction of the cyclized radical **F** from the stannane.

At this point we considered examining the behavior of the 2-indolylacyl radical derived from *N*-methyl selenoester **28** (Scheme 6) to see if changing the carbamate nitrogen atom for an amine nitrogen atom in the acceptor ring would have any influence in the regiochemical course of the cyclization. To this end, aldehyde **1** was allowed to react as above with 3-butenylamine and 1-buten-2-ylmagnesium bromide,[22] and the resulting secondary amine was converted into the tertiary amine **24** in 50% yield by reductive alkylation with formaldehyde. The assembly of the tetrahydropyridine moiety was accomplished in 71% yield by RCM of **24**, which required its previous

(22) Sinha, S. C.; Li, L.-S.; Watanabe, S.; Kaltgrad, E.; Tanaka, F.; Rader, C.; Lerner, R. A.; Barbas, C. F. *Chem.—Eur. J.* **2004**, *10*, 5467–5472.

SCHEME 6. Synthesis of Dasycarpidones



conversion into the hydrochloride salt.[23] The subsequent indole α-carboxylation of **25** (71% yield), indole deprotection of **26** (80% yield), and phenylselenation of amino acid **27** led to the highly unstable *N*-methyl selenoester **28**, which was directly subjected to the standard radical cyclization protocol. To our delight, the 5-exo route was completely suppressed since a 2.2:1 mixture of stereoisomeric azocinoindoles **29** and **30** was obtained in 41% overall yield from **27**. After chromatographic separation, the major product **29** was assigned as (±)-20-epidasycarpidone[17,24] (H-5/H-12 trans relative configuration), which was identical to the material produced by hydrogenolysis-methylation of the benzyl carbamate **22b**.[14] On the other hand, the minor product **30** was assigned as (±)-dasycarpidone[16,17] (H-5/H-12 cis relative configuration, 12-ethyl equatorial with respect to the piperidine group). This stereochemical result indicated that the 6-endo cyclization was now followed by an incompletely stereoselective hydrogen abstraction of the resulting cyclized radical.

Conclusion

A conceptually new route to the bridged tetracyclic framework of uleine and *Strychnos* alkaloids, featuring 6-exo or 6-endo cyclizations of 2-indolylacyl radicals upon tetrahydropyridines, has been developed. The usefulness of the approach is established by the synthesis of isodasycarpidone and dasycarpidones, thus illustrating the considerable potential of 2-indolylacyl radical intermediates for the total synthesis of indole alkaloids.

(23) For a recent review discussing RCM of amine-containing dienes, see: Compain, P. *Adv. Synth. Catal.* **2007**, *349*, 1829–1846.

(24) Forns, P.; Diez, A.; Rubiralta, M.; Solans, X.; Font-Bardia, M. *Tetrahedron* **1996**, *52*, 3563–3574.

Experimental Section

Phenyl 3-[(1-Methoxycarbonyl)-1,2,3,6-tetrahydro-2-pyridyl]indole-2-carboselenoate (5). A suspension of carboxylic acid **4** (0.25 g, 0.83 mmol) in anhydrous CH_2Cl_2 (6 mL) was treated with Et_3N (0.24 mL, 1.68 mmol). After 15 min at rt, the mixture was concentrated to give the triethylammonium salt. In another flask, tributylphosphine (1.0 mL, 4.20 mmol) was added under Ar to a solution of PhSeCl (0.80 g, 4.20 mmol) in anhydrous THF (6 mL), and the mixture was stirred at rt for 10 min (yellow solution). The above ammonium salt in THF (6 mL) was added to this solution, and the resulting mixture was stirred overnight. The reaction mixture was partitioned between Et_2O (20 mL) and H_2O (20 mL) and was extracted with Et_2O (3 × 15 mL). The solvent was removed and the crude product was chromatographed (hexanes and then 75:25 hexanes−AcOEt) to give selenoester **5** as a white solid: 0.22 g (60%); mp 174−5 °C; ^{1}H NMR (400 MHz) δ 2.48 (br d, J = 17.2 Hz, 1H), 2.79 (m, 1H), 3.59 (s, 3H), 4.02 (d, J = 17.6 Hz, 1H), 4.29 (d, J = 18.0 Hz, 1H), 6.00 (m, 3H), 7.10 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 8 Hz, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.44 (m, 3H), 7.62 (m, 2H), 7.68 (d, J = 8 Hz, 1H), 8.74 (br s, 1H); ^{13}C NMR (75.4 MHz) δ 30.3 (CH_2), 42.4 (CH_2), 46.9 (CH), 52.7 (CH_3), 112.4 (CH), 121.1 (CH), 122.8 (CH), 124.9 (CH), 125.5 (C), 126.0 (C), 126.1 (2 CH), 129.2 (CH), 129.4 (CH), 130.7 (C), 136.2 (CH), 136.8 (C), 156.6 (C), 183.4 (C), indole C-3 not observed. Anal. calcd for $C_{22}H_{20}N_2O_3Se\cdot 1H_2O$: C, 57.77; H, 4.84; N, 6.12. Found: C, 57.92; H, 4.52; N, 5.92.

Cyclization of Selenoester 5. *n*-Bu_3SnH (0.18 mL, 0.65 mmol) and Et_3B (1 M in hexanes, 0.65 mL, 0.65 mmol) were added to a solution of selenoester **5** (0.14 g, 0.32 mmol, previously dried azeotropically with anhydrous C_6H_6) in anhydrous C_6H_6 (9 mL). The reaction mixture was stirred at rt for 3 h with dry air constantly supplied by passing compressed air through a short tube of Drierite. The reaction mixture was concentrated. The residue was partitioned between hexanes (15 mL) and acetonitrile (15 mL), and the polar layer was washed with hexanes (3 × 15 mL). The acetonitrile solution was concentrated, and the crude product was chromatographed (hexanes and then 7:3 hexanes−AcOEt) to give the following compounds:

Methyl 6-oxo-1,2,3,4,5,6-hexahydro-1,5-methanoazocino[4,3-*b*]indole-2-carboxylate (6): 55 mg (60%); ^{1}H NMR (400 MHz, assignment aided by HSQC and COSY, mixture of rotamers) δ 2.02 (m, 2H, 4-H), [2.22 (dt, J = 12.8, 2.8 Hz) and 2.55 (br d, J = 10.8 Hz), 2H, 12-H], [2.78 (br t, J = 12.8 Hz) and 3.8−4.0 (masked), 2H, 3-H], 2.89 (s, 1H, 5-H), 3.68 and 3.88 (2 s, 3H, OMe), 5.78 and 5.94 (2 s, 1H, 1-H), 7.18 (t, J = 7.2 Hz, 1H, 10-H), 7.39 (t, J = 8.4 Hz, 1H, 9-H), 7.48 (d, J = 8 Hz, 1H, 8-H), [7.69 (br d, J = 6.8 Hz) and 7.91 (d, J = 7.6 Hz), 1H, 11-H], 9.60 and 9.64 (2 s, 1H, 7-H); ^{13}C NMR (100.6 MHz, assignment aided by HSQC and HMBC, mixture of rotamers) δ 29.0 (C-4), 35.4 (C-12), 36.5 (C-3), 41.3 (C-5), 43.6 and 44.1 (C-1), 52.7 (OMe), 112.5 and 112.8 (C-8), 121.3 (C-10), 121.7 and 122.7 (C-11), 124.3 (C-11a), 125.4 (C-11b), 127.5 (C-9), 132.6 (C-6a), 138.4 (C-7a), 155.9 and 156.2 (CO_2), 193.3 (C-6); ESI-HRMS $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_3$: 285.1233. Found: 285.1232.

Methyl 5-Oxo-2,3,4,5-tetrahydro-1,4-ethanoazepino[4,3-*b*]indole-2-carboxylate (7): 9 mg (10%); ^{1}H NMR (400 MHz, assignment aided by HSQC and COSY, mixture of rotamers) δ 1.90 (m, 2H, 11-H, 12-H), 2.13 (m, 1H, 12-H), 2.41 (m, 1H, 11-H), [3.21 (t, J = 5.2 Hz) and 3.26 (br t), 1H, 4-H], [3.51 (d, J = 12.8 Hz) and 3.65 (m), 2H, 3-H], 3.64 and 3.65 (2 s, 3H, OMe), [5.79 (dd, J = 2.4, 5.6 Hz) and 5.98 (dd, J = 2, 5.2 Hz), 1H, 1-H], 7.22 (t, J = 7.6 Hz, 1H, 9-H), 7.41 (m, 2H, 7-H, 8-H), [7.79 (d, J = 8 Hz) and 7.91 (d, J = 7.6 Hz), 1H, 10-H], 8.96 and 8.99 (2 s, 1H, 6-H); ^{13}C NMR (100.6 MHz, assignment aided by HSQC and HMBC, mixture of rotamers) δ 18.7 (C-12), 26.9 and 27.0 (C-11), 42.3 and 42.5 (C-3), 45.0 and 45.5 (C-1), 46.5 (C-4), 52.6 and 52.7 (OMe), 112.2 and 112.4 (C-7), 120.7 and 121.0 (C-10), 121.2 (C-9), 124.6 and 124.8 (C-10a), 127.0 and 127.2 (C-8), 130.7 and 131.2

(C-10b), 132.8 and 132.9 (C-5a), 137.2 and 137.3 (C-6a), 155.6 and 155.9 (CO_2), 194.0 (C-5); ESI-HRMS $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_3$: 285.1233. Found: 285.1233.

Phenyl 3-[5-Ethyl-(1-methoxycarbonyl)-1,2,3,6-tetrahydro-2-pyridyl]indole-2-carboselenoate (10). Tetrahydropyridine **9** (0.16 g, 0.37 mmol) in MeOH (2 mL) was allowed to react with a solution of MeONa, previously prepared from Na (42 mg, 1.85 mmol) in MeOH (10 mL), at reflux temperature overnight. The reaction mixture was concentrated, and the residue was partitioned between 2 M aqueous HCl (15 mL) and CH_2Cl_2 (15 mL) and extracted with CH_2Cl_2 (2 × 10 mL). After concentration of the organic extracts, the resulting material (0.11 g) was dissolved in anhydrous CH_2Cl_2 (3 mL) and then treated with Et_3N (0.09 mL, 0.66 mmol), tributylphosphine (0.40 mL, 1.65 mmol), and PhSeCl (0.32 g, 1.65 mmol) as described for the preparation of selenoester **5**. After flash chromatography of the crude product (hexanes and 8:2 hexanes−AcOEt), selenoester **10** was obtained as an oil: 0.11 g (62%); ^{1}H NMR (300 MHz) δ 1.08 (t, J = 7.2 Hz, 3H), 2.15 (q, J = 7.2 Hz, 2H), 2.44 (dt, J = 16.5, 5.1 Hz, 1H), 2.75 (m, 1H), 3.59 (s, 3H), 3.95 (d, J = 16.8 Hz, 1H), 4.20 (d, J = 16.5 Hz, 1H), 5.64 (m, 1H), 5.91 (dd, J = 7.2, 4.5 Hz, 1H), 7.08 (ddd, J = 8.1, 6.6, 1.2 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.43 (m, 3H), 7.58 (d, J = 8.1 Hz, 1H), 7.61 (m, 2H), 8.87 (s, 1H); ^{13}C NMR (75.4 MHz) δ 11.8 (CH_3), 28.0 (CH_2), 30.5 (CH_2), 45.4 (CH_2), 47.4 (CH), 52.7 (CH_3), 112.3 (CH), 118.4 (CH), 120.9 (CH), 122.7 (CH), 125.4 (C), 126.2 (CH), 126.6 (C), 129.2 (CH), 129.4 (CH), 130.5 (C), 136.2 (CH), 136.7 (C), 138.4 (C), 156.6 (C), 183.2 (C), indole C-3 not observed; ESI-HRMS $[M + H]^+$ calcd for $C_{24}H_{25}N_2O_3Se$: 469.1024. Found: 469.1022.

(1*RS*, 4*RS*, 5*RS*) Methyl 4-Ethyl-6-oxo-1,2,3,4,5,6-hexahydro-1,5-methanoazocino[4,3-*b*]indole-2-carboxylate (11).[16] Following the protocol described for selenoester **5**, selenoester **10** (0.10 g, 0.21 mmol) gave tetracycle **11** after flash chromatography (8:2 hexanes−AcOEt): 46 mg (70%); ^{1}H NMR (400 MHz, assignment aided by HSQC, mixture of rotamers) δ 1.06 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.24 and 1.40 (2 m, 2H, CH_2CH_3), 1.94 (m, 1H, 4-H), 2.19 (dt, J = 13.2, 3.2 Hz, 1H, 12-H), 2.41 (q, J = 12.8 Hz, 1H, 3-H), 2.60 (br d, J = 12 Hz, 1H, 12-H), 2.91 (q, J = 3.2 Hz, 1H, 5-H), 3.70 and 3.89 (2 s, 3H, OMe), [3.86 (masked dd) and 4.02 (dd, J = 4.8, 13.6 Hz), 1H, 3-H], 5.77 and 5.92 (2 s, 1H, 1-H), 7.18 (t, J = 7.6 Hz, 1H, 10-H), 7.39 (t, J = 8.4 Hz, 1H, 9-H), 7.48 (d, J = 8.4 Hz, 1H, 8-H), [7.68 (d, J = 8 Hz) and 7.91 (d, J = 8 Hz), 1H, 11-H], 9.67 and 9.71 (2 s, 1H, 7-H); ^{13}C NMR (100.6 MHz, assignment aided by HSQC, mixture of rotamers) δ 11.4 (CH_2CH_3), 24.4 (CH_2CH_3), 36.2 and 36.5 (C-12), 41.3 (C-4), 42.4 and 42.6 (C-3), 43.6 and 44.0 (C-1), 44.9 (C-5), 52.7 and 52.9 (OMe), 112.5 and 112.9 (C-8), 121.2 (C-10), 121.6 and 122.6 (C-11), 124.2 (C-11a), 124.4 and 124.9 (C-11b), 127.3 (C-9), 133.0 (C-6a), 138.3 (C-7a), 155.7 and 155.9 (CO_2), 191.9 (C-6); ESI-HRMS $[M + H]^+$ calcd for $C_{18}H_{21}N_2O_3$: 313.1546. Found: 313.1552.

Isodasycarpidone (18).[17,18] Amino acid hydrochloride **16** (0.13 g, 0.41 mmol) was treated with Et_3N (0.14 mL, 1.02 mmol), tributylphosphine (0.50 mL, 2.05 mmol), and PhSeCl (0.39 g, 2.05 mmol) following the protocol described for the preparation of **5**. The reaction mixture was partitioned between CH_2Cl_2 (10 mL) and H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were concentrated, and the resulting residue was dissolved in Et_2O (10 mL) and then treated with a saturated solution of HCl in Et_2O (0.5 mL). The solvent was removed and the resulting oil was successively triturated with hexanes (4 × 10 mL) and Et_2O (4 × 10 mL) to give crude selenoester **17** as the hydrochloride salt (0.12 g, impurified with 15% tributylphosphine oxide). As this compound slowly underwent hydrolisis on standing, it was immediately converted into the free base and then subjected to the cyclization protocol described for selenoester **5**. After flash chromatography (98:2 AcOEt−diethylamine), isodasycarpidone (**18**) was obtained: 44 mg (40% from **16**); ^{1}H NMR (400 MHz, assignment aided by HSQC) δ 1.02 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.20 and 1.41 (2 m, 2H, CH_2CH_3), 1.74 (t, J = 12.4 Hz, 1H, 3-H), 2.00 (m, 1H, 4-H), 2.29 (dt, J = 12, 3.2 Hz, 1H, 12-H), 2.30 (s, 3H, NMe), 2.56 (dt, J = 12.7, 3.2 Hz, 1H, 12-H), 2.61 (dd, J = 12.4, 4.8 Hz, 1H, 3-H), 2.77 (q, J = 3.2 Hz, 1H, 5-H), 4.34 (t, J = 3.2 Hz, 1H, 1-H), 7.18 (t, J = 8 Hz, 1H, 10-H), 7.37 (t, J = 8 Hz, 1H, 9-H), 7.48 (d, J = 8 Hz, 1H, 8-H), 7.70 (d, J = 7.6 Hz, 1H, 11-H), 9.56 (s, 1H, 7-H); ^{13}C NMR (100.6 MHz, assignment aided by HSQC and HMBC) δ 11.6 (CH_2CH_3), 24.8 (CH_2CH_3), 38.2 (C-12), 44.1 (NMe), 41.5 (C-4), 44.8 (C-5), 52.0 (C-1), 52.6 (C-3), 112.6 (C-8), 121.0 (C-10), 121.8 (C-11b), 122.0 (C-11), 126.7 (C-9), 126.8 (C-11a), 133.5 (C-6a), 137.8 (C-7a), 192.5 (C-6); ESI-HRMS $[M + H]^+$ calcd for $C_{17}H_{21}N_2O$: 269.1648. Found: 269.1653. Anal. calcd for $C_{17}H_{20}N_2O \cdot HCl \cdot {}^1/_2H_2O$: C, 65.06; H, 7.07; N, 8.92. Found: C, 64.94; H, 7.12; N, 8.56.

Phenyl 3-[(3-Ethyl-1-(methoxycarbonyl)-1,2,5,6-tetrahydro-2-pyridyl]indole-2-carboselenoate (21a). *n*-BuLi (1.6 M in hexane, 0.52 mL, 0.82 mmol) was added under Ar to a cooled (−78 °C) solution of diisopropylamine (0.12 mL, 0.82 mmol) in anhydrous THF (5 mL), and the resulting solution was stirred at −78 °C for 30 min. Tetrahydropyridine **20a** (0.21 g, 0.55 mmol) in anhydrous THF (5 mL) was then added, and the resulting red mixture was stirred at −78 °C for 30 min. CO_2 (gas) was bubbled through the reaction mixture, which immediately turned orange. After 15 min at −78 °C, the reaction mixture was quenched with H_2O (5 mL), acidified with 1 M aqueous HCl, and extracted with CH_2Cl_2 (3 × 10 mL). Concentration of the organic extracts gave the crude carboxylic acid (0.20 g). A solution of this acid in MeONa, previously prepared from Na (56 mg, 2.40 mmol) in MeOH (10 mL), was heated at reflux overnight. The reaction mixture was concentrated, and the residue was partitioned between 2 M aqueous HCl (15 mL) and CH_2Cl_2 (15 mL) and extracted with CH_2Cl_2 (2 × 15 mL). The organic extracts were concentrated, and the resulting residue (0.13 g) was dissolved in CH_2Cl_2 (3 mL) and then treated with Et_3N (0.11 mL, 0.78 mmol), tributylphosphine (0.48 mL, 1.95 mmol), and PhSeCl (0.37 g, 1.95 mmol) as described for the preparation of selenoester **5**. After flash chromatography of the crude product (hexanes and then 8:2 hexanes−AcOEt), selenoester **21a** was obtained as a white solid: 0.11 g (45%); ^{1}H NMR (400 MHz) δ 0.97 (t, J = 7.6 Hz, 3H), 1.88 (m, 2H), 2.30 (m, 1H), 2.43 (m, 1H), 3.34 (m, 1H), 3.65 (s, 3H), 4.25 (m, 1H), 5.83 (d, J = 4 Hz, 1H), 6.25 (s, 1H), 7.10 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 8 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.45 (m, 3H), 7.63 (m, 2H), 7.89 (d, J = 8 Hz, 1H), 8.88 (s, 1H); ^{13}C NMR (100.6 MHz) δ 12.1 (CH_3), 24.7 (CH_2), 26.8 (CH_2), 38.9 (CH_2), 49.7 (CH), 52.6 (CH_3), 112.3 (CH), 119.0 (CH), 119.3 (C), 121.0 (CH), 122.7 (CH), 125.8 (C), 125.9 (CH), 127.4 (C), 129.3 (CH), 129.5 (CH), 133.5 (C), 136.0 (CH), 136.4 (C), 138.0 (C), 156.1 (C), 184.2 (C). Anal. calcd for $C_{24}H_{24}N_2O_3Se$: C, 61.67; H, 5.18; N, 5.99. Found: C, 61.39; H, 5.24; N, 6.12.

Phenyl 3-[1-(Benzyloxycarbonyl)-3-ethyl-1,2,5,6-tetrahydro-2-pyridyl]indole-2-carboselenoate (21b). Operating as above, tetrahydropyridine **20b** (0.28 g, 0.62 mmol) was allowed to react with *n*-BuLi (1.6 M in hexane, 0.58 mL, 0.93 mmol), diisopropylamine (0.13 mL, 0.93 mmol), and CO_2 (gas) to give a crude carboxylic acid (0.26 g). After the usual deprotection with MeONa (2.30 mmol), the resulting crude material was treated with Et_3N (0.14 mL, 1.0 mmol), tributylphosphine (0.62 mL, 2.50 mmol), and PhSeCl (0.48 g, 2.50 mmol) as described for the preparation of selenoester **5**. After flash chromatography (hexanes and then 8:2 hexanes−AcOEt), selenoester **21b** was obtained as an oil: 0.10 g (30%); ^{1}H NMR (300 MHz) δ 0.95 (t, J = 7.5 Hz, 3H), 1.87 (m, 2H), 2.27 (m, 1H), 2.40 (m, 1H), 3.41 (m, 1H), 4.20 (m, 1H), 5.02 (d, J = 12.6 Hz, 1H), 5.21 (br d, J = 12.3 Hz, 1H), 5.79 (br s, 1H), 6.32 (s, 1H), 7.09 (ddd, J = 8.1, 6.9, 0.9 Hz, 1H), 7.20−7.43 (m, 10H), 7.52 (m, 2H), 7.89 (d, J = 8.1 Hz, 1H), 8.77 (s, 1H); ^{13}C NMR (75.4 MHz) δ 12.0 (CH_3), 24.7 (CH_2), 26.7 (CH_2), 38.7 (CH_2), 50.1 (CH), 66.8 (CH_2), 112.2 (CH), 118.9 (CH), 121.0 (CH), 122.7 (CH), 125.7 (C), 125.9 (C), 127.3 (C), 127.6 (CH), 127.8 (CH), 128.2 (CH), 129.1 (C), 129.4 (CH), 133.4 (C), 136.0 (CH),

136.3 (C), 137.1 (C), 138.1 (C), 155.4 (C), 183.8 (C), indole C-3 not observed; ESI-HRMS $[M + H]^+$ calcd for $C_{30}H_{29}N_2O_3Se$: 545.1337. Found: 545.1331.

Cyclization of Selenoester 21a. Selenoester **21a** (0.12 g, 0.25 mmol) was subjected to the protocol described for selenoester **5**. After flash chromatography (hexanes and then 85:15 hexanes−AcOEt), a nearly equimolecular mixture of tetracycles **22a** and **23a** was obtained: 55 mg (71%).

Cyclization of Selenoester 21b. Selenoester **21b** (0.13 g, 0.25 mmol) was subjected to the protocol described for selenoester **5**. After flash chromatography (hexanes and then 7:3 hexanes−AcOEt), a 1:1 mixture of tetracycles **22b** and **23b** was obtained: 83 mg (86%). Additional flash chromatography (9:1 hexanes−AcOEt to 8:2 hexanes−AcOEt) gave pure samples of both compounds.

(1*RS*, 5*RS*, 12*SR*)-Benzyl 12-ethyl-6-oxo-1,2,3,4,5,6-hexahydro-1,5-methanoazocino[4,3-*b*]indole-2-carboxylate (22b): ^{1}H NMR (400 MHz, assignment aided by HSQC, mixture of rotamers) δ 1.01 and 1.06 (2 t, $J = 7.2$ Hz, 3H, CH_3CH_2), 1.58 and 1.82 (2 m, 2H, CH_3CH_2), 1.65 and 2.20 (2 m, 2H, 4-H), 2.32 and 2.41(2 m, 1H, 12-H), 2.65−2.80 (m, 2H, 3-H, 5-H), [3.85 (dd, $J = 14.7$, 6.9 Hz) and 3.97 (dd, $J = 13.2$, 6.3 Hz), 1H, 3-H], [5.08 (d, $J = 12.3$ Hz), 5.17 (d, $J = 12.6$ Hz), 5.24 (d, $J = 12$ Hz) and 5.34 (d, $J = 12.3$ Hz), 2H, $PhCH_2$], 5.67 and 5.81 (2 br s, 1H, 1-H), [7.01 (t, $J = 7.2$ Hz) and 7.20 (t, $J = 7.6$ Hz), 1H, 10-H], 7.30−7.50 (m, 7.5 H, 8-, 9-, 11-H, Ph), 7.92 (d, $J = 8$ Hz, 0.5 H, 11-H), 9.08 (s, 1H, 7-H); ^{13}C NMR (signals from the HSQC experiment, mixture of rotamers, only CH, CH_2, and CH_3 are shown) δ 11.5 (CH_3CH_2), 22.6 (CH_3CH_2), 23.0 (C-4), 36.3 (C-3), 44.0 (C-12), 45.1 (C-5), 46.3 and 46.4 (C-1), 67.4 and 67.5 ($PhCH_2$), 112.8 (C-8), 121.4 and 121.5 (C-10), 122.1 and 122.8 (C-11), 128.0−128.5 (C-9 and Ph); ESI-HRMS $[M + H]^+$ calcd for $C_{24}H_{25}N_2O_3$: 389.1859. Found: 389.1864.

Benzyl 4a-ethyl-3,4,4a,5,6,10c-hexahydro-5-oxo-2*H*-pyrido[2′,3′:3,4]cyclopenta[1,2-*b*]indole-1-carboxylate (23b, cis relative configuration tentatively assigned): ^{1}H NMR (400 MHz, mixture of rotamers) δ [0.85 (t, $J = 7.2$ Hz) and 0.87 (t, $J = 7.6$ Hz), 3H], 1.60−2.05 (m, 6H), 2.85 and 2.97 (2 m, 1H), 3.78 and 3.93 (m, 1H), [5.23 (d, $J = 12.4$ Hz), 5.30 (d, $J = 12$ Hz), 5.37 (d, $J = 12$ Hz), and 5.42 (d, $J = 12.4$ Hz), 2H], 5.72 and 5.78 (2 br s, 1H), [7.08 (t, $J = 8$ Hz) and 7.13 (t, $J = 7.6$ Hz), 1H], 7.30−7.50 (m, 7H), 7.55 (d, $J = 7.6$ Hz, 1H), 9.18 and 9.22 (2 s, 1H); ^{13}C NMR (signals from the HSQC experiment, mixture of rotamers, only CH, CH_2, and CH_3 are shown) δ 8.43 (CH_3), 18.3 (CH_2), 29.5 (CH_2), 29.7 (CH_2), 39.8 and 40.0 (CH_2), 52.7 (CH), 67.5 (CH_2), 112.8 and 113.5 (CH), 121.6 (CH), 122.0 (CH), 122.9 (CH), 128.0−128.5 (3 CH); ESI-HRMS $[M + H]^+$ calcd for $C_{24}H_{25}N_2O_3$: 389.1859. Found: 389.1867.

Cyclization of Selenoester 28. Amino acid hydrochloride **27** (0.11 g, 0.34 mmol) was treated with Et_3N (0.11 mL, 0.77 mmol), tributylphosphine (0.48 mL, 1.93 mmol), and PhSeCl (0.37 g, 1.93 mmol) following the protocol described for the preparation of **5**. The reaction mixture was partitioned between CH_2Cl_2 (10 mL) and H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were treated with a saturated solution of HCl in Et_2O (0.5 mL). The solvent was removed, and the resulting oil was triturated with Et_2O (4 × 10 mL) to give crude selenoester **28** as the hydrochloride salt (0.10 g, impurified with 20% tributylphosphine oxide). This material was immediately converted into the free base and then subjected to the cyclization protocol described for selenoester **5**. Flash chromatography (hexanes and then 80:19:1 hexanes−AcOEt−diethylamine) gave the following compounds.

(±)-20-Epidasycarpidone (29):[17,24] 26 mg (28% from **27**); ^{1}H NMR (400 MHz, assignment aided by HSQC) δ 1.08 (t, $J = 7.6$ Hz, 3H, CH_2CH_3), 1.67 (br d, $J = 13.6$ Hz, 1H, 4-H), 1.71 (m, 1H, CH_2CH_3), 2.01 (m, 2H, CH_2CH_3, 3-H), 2.25 (m, 2H, 3-H, 12-H), 2.26 (s, 3H, NMe), 2.47 (dd, $J = 10.8$, 5.2 Hz, 1H, 3-H), 2.59 (s, 1H, 5-H), 4.15 (s, 1H, 1-H), 7.20 (ddd, $J = 8.0$, 6.8, 1.2 Hz, 1H, 10-H), 7.37 (td, $J = 7.2$, 7.2, 1.2 Hz, 1H, 9-H), 7.45 (d, $J = 8$ Hz, 1H, 8-H), 7.71 (d, $J = 7.6$ Hz, 1H, 11-H), 8.87 (br s, 1H, 7-H); ^{13}C NMR (100.6 MHz, assignment aided by HSQC and HMBC) δ 11.7 (CH_2CH_3), 23.3 (CH_2CH_3), 23.9 (C-4), 44.6 (NMe), 45.0 (C-5), 46.1 (C-12), 46.2 (C-3), 54.8 (C-1), 112.4 (C-8), 121.0 (C-10), 122.1 (C-11), 124.2 (C-11a), 126.8 (C-9), 126.9 (C-11b), 133.3 (C-6a), 137.6 (C-7a), 194.9 (C-6); ESI-HRMS $[M + H]^+$ calcd for $C_{17}H_{21}N_2O$: 269.1648. Found: 269.1658.

(±)-Dasycarpidone (30):[16,17] 12 mg (13% from **27**); ^{1}H NMR (400 MHz, assignment aided by HSQC) δ 0.88 (t, $J = 7.2$ Hz, 3H, CH_2CH_3), 1.29 (m, 2H, CH_2CH_3), 1.92 (br d, $J = 10.4$ Hz, 1H, 4-H), 2.15 (m, 2H, 3-H, 4-H), 2.36 (s, 3H, NMe), 2.49 (tm, $J = 7.2$, 1H, 12-H), 2.65 (m, 1H, 3-H), 2.70 (m, 1H, 5-H), 4.35 (d, $J = 2.4$ Hz, 1H, 1-H), 7.20 (t, $J = 7.6$ Hz, 1H, 10-H), 7.39 (ddd, $J = 8.0$, 7.2, 1.2 Hz, 1H, 9-H), 7.49 (d, $J = 8.4$ Hz, 1H, 8-H), 7.70 (d, $J = 8$ Hz, 1H, 11-H), 9.39 (br s, 1H, 7-H); ^{13}C NMR (100.6 MHz, assignment aided by HSQC) δ 11.7 (CH_2CH_3), 24.9 (CH_2CH_3), 29.7 (C-4), 43.8 (NMe), 46.0 (C-3), 46.1 (C-5), 49.1 (C-12), 56.4 (C-1), 112.7 (C-8), 119.0 (C-11b), 121.3 (C-10), 121.7 (C-11), 126.9 (C-9), 127.5 (C-11a), 132.9 (C-6a), 138.0 (C-7a), 192.9 (C-6); ESI-HRMS $[M + H]^+$ calcd for $C_{17}H_{21}N_2O$: 269.1648. Found: 269.1661.

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Supporting Information Available: General experimental protocols and detailed experimental procedures for synthetic intermediates **2**−**4**, **8**, **9**, **13**−**16**, **19a**,**b**, **20a**,**b**, and **24**−**27**. Characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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