Diastereoselective Alkylation of 2,3,4,6-Di-*O*-isopropylidene-2-keto-L-gulonic Amides. Application to the Asymmetric Synthesis of 1-Substituted-1,2,3,4-tetrahydroisoquinolines and 1-Substituted-1,2,3,4,-tetrahydro-*β*-carbolines

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Received February 9, 2001

The diastereoselective alkylation of amides **3a**,**b** and **7a**,**b** derived from gulonic acid is described. Substituted compounds are obtained in good yield and high diastereoselectivity. A mechanistic investigation establishes that the diastereoselectivity did not arise from an initial asymmetric deprotonation. The stereochemistry is then determined during the alkylation step.

Introduction

Carbanions with a negative charge alpha to nitrogen are valuable intermediates in organic synthesis.[1] The asymmetric version of this methodology received considerable attention due to the numerous applications in interesting natural or biological products. α-Lithiation of amines is possible when the nitrogen atom is substituted by a suitable electron-withdrawing group which can both increase the kinetic acidity of an α-proton and stabilize the carbanion by complex-induced proximity effects.[2] α-Aminoalkyl carbanions are readily accessible from aminooxazolines,[3] formamidines,[4] and carbamates[5] deprotonation methodologies. The resulting lithio species can then react with typical carbonyl and halide electrophiles.

A number of cases have been reported which involve a dipole-stabilized carbanion adjacent to the nitrogen of an amide.[6] These results indicate that carboxylic acids can be regarded as suitable activating agents for α-lithiation of amines. A few years ago the C-1 diastereoselective alkylation of *N*-pivaloyl-tetrahydroisoquinoline was reported by Seebach.[7] In the same time, Meyers reported[8] that *N*-benzyl lactams can be deprotonated α to nitrogen depending on the size of the ring, suggesting that lithiation of the benzylic carbon is possible provided that the corresponding protons are suitably placed for metalation. However, to the best of our knowledge, the asymmetric version of this reaction received only very few applications. In the known examples described in the tetrahydroisoquinoline series, the asymmetric center inducing diastereoselection was located α to the nitrogen (on the C-3 position) limiting this strategy to the corresponding substituted derivatives.[7,9]

Surprisingly, despite the facility to prepare various amides and to deprotect them to amines, and with regard to the great variety of available chiral carboxylic acids, the strategy involving chiral acids as chiral inducers for the diastereoselective alkylation of amines has never been reported.

With these results in mind, we decided to explore the generation of α-aminoalkyl carbanions derived from amides and their reactivity toward electrophiles. To prevent α-carbonyl deprotonation, we decided to choose α-trisubstituted carboxylic acid, with chirality being located on the quaternary center. The stabilization of the carbanion can then be envisaged by a chelation process involving either the oxygen atom of the amide group or another heteroatom present in the carboxylic acid, which could generate a five- or six-membered ring (Scheme 1).

Here, we report our first results of a general stereospecific route to 1-substituted tetrahydroisoquinolines and 1-substituted tetrahydro-*β*-carbolines using electrophilic attack at the corresponding α-aminoalkyl carbanion generated from a chiral amide derived from inexpensive commercially available 2,3,4,6-di-*O*-isopropylidene-2-keto-L-gulonic acid (DIGA) **2** which possesses all the features required for an evaluation of our strategy.

1-Substituted-1,2,3,4-tetrahydroisoquinolines are abundant in plant products, and many exhibit interesting biological activity.[10] They constitute the largest family

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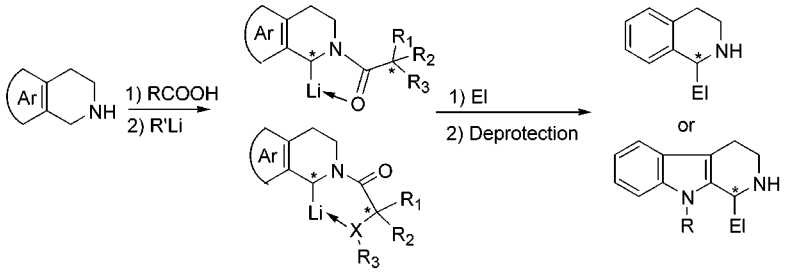
10.1021/jo0155658 CCC: $20.00
Published on Web 11/29/2001

Scheme 1



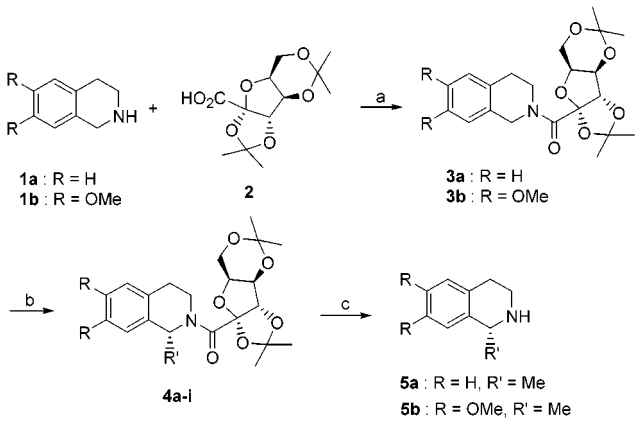
of alkaloids in the plant kingdom and occupy a pivotal place from which numerous structural groups are derived. On the other hand, the presence of 1-substituted-1,2,3,4-tetrahydro-*β*-carbolines in numerous indole alkaloids and biological active compounds also generated intensive investigations for new synthetic methods. Since many of the products encountered in these families are chiral, several original methodologies for the synthesis of chiral 1-substituted compounds have been reported.[9,11,12] The diastereoselective Pictet−Spengler and Bischler−Napieralski reactions are well established but require the presence of an activated aromatic system. Asymmetric reduction and alkylation of the dihydroisoquinoline and dihydro-*β*-carboline derivatives are the most recently explored technologies. Most of these methods are hampered by the lack of generality, low chemical or optical yields, and the number of synthetic operations involved. In this respect, the Meyers amidines[4] in which 1-lithiated tetrahydroisoquinolines or tetrahydro-*β*-carbolines are diastereoselectively alkylated have provided by far the best results.

Results and Discussion

Alkylation of Tetrahydroisoquinolines. The amides **3a**,**b** are easily prepared in one step from commercially available amines **1a**,**b** and 2,3,4,6-di-*O*-isopropylidene-2-keto-L-gulonic acid (DIGA) **2** by using classical methods (IBCF, NMM) in good yields (73 and 75%, respectively). The alkylation reactions of amides **3a**,**b** were best carried out by treatment with 1.3 equiv of *tert*-butyllithium in THF at −78 °C (Scheme 2, Table 1).

The resulting orange-red anion was then allowed to react with different electrophiles furnishing substituted products in 41−57% yield. Despite our efforts to improve the yields, starting material (ca. 30%) was always recovered. Increasing the temperature led only to the formation of degradation products. Neither the use of other bases (*s*-BuLi, LiHMDS, LDA) nor the addition of additives (HMPA, TMEDA, DMPU) led to an increase in the yields. However, when the reaction was performed in the presence of LiBr (1.2 equiv), a 10−14% increase of de was observed, furnishing a high level of selectivity (Table 1, entries 1, 3, and 4). Substituted products were obtained with high diastereoselectivity (66−98%) with the exception of the allylated derivatives (entries 2 and 6). The absence of diastereoselectivity during allylation was previously reported by Beak and may be explained by low facial selectivity in the substitution step.[13]

Scheme 2[a]



[a] Conditions: (a) IBCF, NMM, CH_2Cl_2, −10 °C, 70%. (b) *t*-BuLi, THF, −78 °C, 30 min., then R′X, 41 to 57%. (c) KOH, MeOH, 70%.

Table 1. Diastereoselective Alkylation of Tetrahydroisoquinoline Gulonic Amides (Scheme 2)

entry	substrate	electrophile	product	yield[a] (%)	selectivity[b] (de, %)
1	**3a**	MeI	**4a**	53	82 (93)[c]
2	**3a**	CH_2=$CHCH_2Br$	**4b**	41	4
3	**3a**	$PhCH_2Br$	**4c**	50	84 (98)[c]
4	**3a**	$PhCH_2CH_2Br$	**4d**	41	66 (78)[c]
5	**3b**	MeI	**4e**	55	78
6	**3b**	CH_2=$CHCH_2Br$	**4f**	50	16
7	**3b**	$PhCH_2CH_2Br$	**4g**	57	72

[a] Yields represent a mass balance of the isolated mixture of diastereomers; in all cases ca. 30% of unreacted product was recovered. [b] Diastereomeric ratios were determined by GC-MS analysis of unpurified mixtures. [c] Selectivity obtained in the presence of LiBr.

Diastereomeric compounds **4** were easily separated from the starting amide by flash chromatography; a single recrystallization generally furnished the pure major isomer. The stereochemistry of major isomer **4a** was assigned by X-ray crystallography.[14] The stereochemistry of other C-1 substituted products was made by analogy to **4a** and confirmed by preparation of simple tetrahydroisoquinolines (vide infra).

Alkylation of Tetrahydro-*β*-carbolines. In this series, two *N*-indole-substituted gulonic amides **7a** and **7b** were prepared (Scheme 3). The same alkylation

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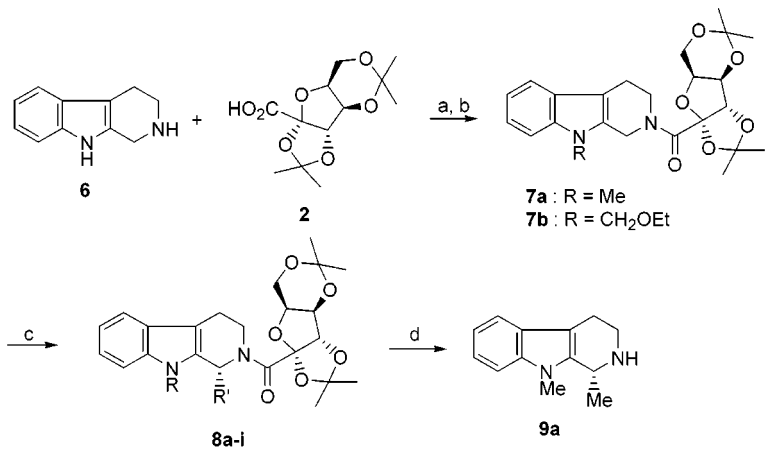
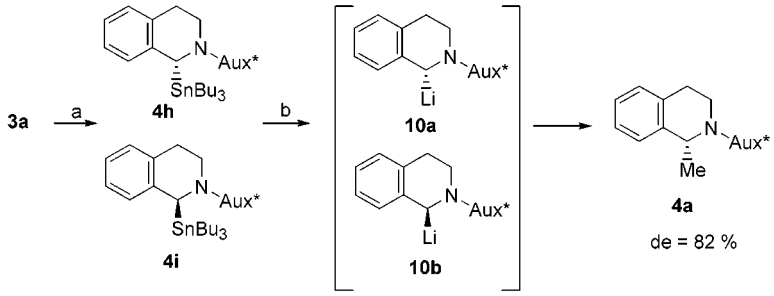
Scheme 3[a]



[a] Conditions: (a) IBCF, NMM, CH_2Cl_2, −10 °C, 78%. (b) KH, THF, MeI, or $EtOCH_2Cl$, 84% and 88%. (c) *t*-BuLi, THF, −78 °C, 30 min., then R′X, 40 to 57%. (d) KOH, MeOH, 70%.

Scheme 4[a]



[a] Conditions: (a) *t*-BuLi, THF, −78 °C, 30 min., then Bu_3SnCl, 46%. (b) n-BuLi, THF, −78 °C then MeI, 65%.

Table 2. Diastereoselective Alkylation of Tetrahydro-*β*-carboline Gulonic Amides (Scheme 3)

entry	substrate	electrophile	product	yield[a] (%)	selectivity[b] (de, %)
1	**7a**	MeI	**8a**	51	82
2	**7a**	CH_2=$CHCH_2Br$	**8b**	41	26
3	**7a**	$PhCH_2Br$	**8c**	57	72
4	**7a**	$PhCH_2CH_2Br$	**8d**	57	68
5	**7b**	MeI	**8e**	40	36
6	**7b**	CH_2=$CHCH_2Br$	**8f**	40	12
7	**7b**	$PhCH_2Br$	**8g**	42	80
8	**7b**	$PhCH_2CH_2Br$	**8h**	41	14

[a] Yields represent a mass balance of the isolated mixture of diastereomers; in all cases ca. 30% of unreacted product was recovered. [b] Diastereomeric ratios were determined by HPLC analysis of unpurified mixtures.

procedure as previously described for tetrahydroisoquinolines was applied to these compounds. Results are reported in Table 2.

Surprisingly, in this series, the diastereoselectivity was not modified by the addition of LiBr. Moderate to good diastereoselectivities (68−82%) in the *N*-Me series (entries 1−4) were observed with the exception of the allylic electrophiles. The same absolute configuration was attributed to C-1; this hypothesis was further confirmed by comparison of optical rotation of deprotected compounds. Replacement of the methyl substituent by an ethoxymethyl protecting group results in lower yields and uneven diastereoselectivities (entries 5−8) suggesting the modification of the reactive intermediate by participation of the oxygen atom of the *N*-indole protecting group to the chelation process.

Cleavage of the Chiral Appendage. Synthesis of 1-substituted tetrahydroisoquinolines or 1-substituted tetrahydro-*β*-carbolines required removal of the gulonic acid appendage of compounds **4** and **8**. Cleavage of the chiral auxiliary proved to be more difficult than expected. Acidic conditions furnished the desired compounds in very low yield. Finally, removal of the gulonic acid was achieved in satisfactory yield (60−70%) by basic treatment (KOH/MeOH, reflux). To verify the preservation of the configuration integrity during this step, the methyl derivatives **4a**, **4e**, and **8a** were deprotected, and the resulting products **5a**, **5b**, and **9** were compared to literature data (IR, NMR, $[\alpha]_D$). A complete agreement was observed which confirmed the absolute configuration of the asymmetric center. The optical purity of the final products was confirmed by chiral GC (ee > 98%).

Mechanism. The two different pathways for asymmetric alkylation which are possible for this sequence are asymmetric deprotonation and asymmetric substitution. To get information concerning the mechanism involved during this reaction, we studied the results of tin−lithium exchange and reaction with electrophiles of two epimeric stannanes. Scheme 4 outlines the preparation, transmetalation, and electrophilic quench of these compounds. Tetrahydroisoquinoline **3a** was alkylated to a separable mixture of stannanes **4h** and **4i** in 46% yield and 36% de. After separation of the diastereomeric stannanes by flash chromatography, both diastereomers were transmetalated and then quenched by MeI. The transmetalation was complete in less than 30 min at −78 °C and furnished the same isomer **4a** in 65% yield with

the same diastereoselectivity (82%) as that observed after direct lithiation (Table 1, entry 1).

As far as we know, tin−lithium exchange is known to proceed with retention of configuration.[15] The results that we observed suggested that the substitution proceeded via rapidly equilibrating diastereomeric organolithium intermediates. Consequently, the enantioselectivity is determined during the post-deprotonation step.

Conclusion

In this paper, we describe the first application of chiral carboxylic acids as activating agents and chiral inducers for α-lithiation of two important families of nitrogen heterocyclic compounds. 2,3,4,6-Di-*O*-isopropylidene-2-keto-L-gulonic acid is an inexpensive chiral auxiliary which can be used to prepare 1-substituted tetrahydroisoquinolines and tetrahydro-β-carbolines. The mechanism involved during this process is far from clear. Experiments are currently in progress to confirm the mechanism hypothesis and to study the possibility of introducing functionalized electrophiles. While the diastereoselectivity presently observed for alkylation of cyclic benzylic amines is still moderate, the search for new candidates derived from low molecular weight acids will furnish information on the mechanism involved during this reaction and could lead to a more efficient chiral auxiliary.

Experimental Section

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) was distilled under argon from sodium benzophenone kethyl prior to use, and CH_2Cl_2 was distilled from CaH_2. Flash column chromatography purification was carried out using silica gel (70−230 mesh). ^{1}H NMR and ^{13}C NMR were recorded at 300.13 and 75.47 MHz, respectively, in $CDCl_3$. Coupling constants (*J*) are reported in Hz. NMR chemical shifts are reported in ppm downfield from an internal solvent peak. IR spectra were recorded using KBr pellets or NaCl plates, and only partial data are reported. GC−mass spectroscopy was done on a HEWLETT PACKARD HP 5890 equipped with an apolar capillary column of 25 m. Chiral chromatography was achieved on a β-Dex-120 Supelco 0.25 mm × 0.25 μm × 15 m column.

(2′,2′,5′,5′-Tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydroisoquinoline (3a). In a flask under argon, cooled to −10 °C and fitted with a magnetic stirrer, isobutyl chloroformate (IBCF) (1.16 mL, 8.96 mmol), *N*-methylmorpholine (NMM) (1.09 mL, 9.95 mmol), and 2 mL of anhydrous CH_2Cl_2 were introduced. To this solution was added 2,3,4,6-di-*O*-isopropylidene-2-keto-L-gulonic acid monohydrate (DIGA) (3 g, 10.9 mmol) in 6 mL of anhydrous CH_2Cl_2, followed 20 min later by a solution of tetrahydroisoquinoline (1.12 mL, 8.96 mmol) and *N*-methylmorpholine (3.26 mL, 2.98 mmol) in 30 mL of anhydrous CH_2Cl_2. The mixture was stirred for 2 h at −10 °C. After dilution of the solution with 200 mL of CH_2Cl_2, the organic layers were washed with aqueous solutions saturated with NaCl (3 × 50 mL). The organic layers were then dried ($MgSO_4$) and concentrated under vacuum. The residue was then purified by flash column chromatography using 40% ethyl acetate in cyclohexane as eluent, affording **3a** as a white powder (2.54 g, 6.54 mmol, 73%). mp 81 °C. $[\alpha]^{20}_D$ −4.2° (*c* 0.45, $CHCl_3$). IR: 2991, 2936, 1651 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.25 (s, 3H), 1.25 (s, 3H), 1.35 (s, 3H), 1.45 (s, 3H), 2.83 (m, 2H), 4.00 (d, 2H, *J* = 13.2), 4.05 (m, 2H), 4.11 (m, 1H), 4.20 (s, 1H), 4.70 (dd, 2H, *J* = 32.1, *J* = 17.3), 5.30 (m, 1H), 7−7.15 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 19.1, 26.3, 27.1, 29.1, 29.9, 43.8, 45.4, 60.3, 73.3, 74.5, 87.7, 97.8, 112.8, 113.4, 126.5, 126.6, 127.0, 129.0, 133.5, 135.1, 165.6. Anal. Calcd for $C_{21}H_{27}NO_6$, $^1/_2$ H_2O: C, 63.30; H, 6.83; N, 3.51. Found: C, 63.24; H, 7.02; N, 3.64. MS *m*/*z* (relative intensity) (M): 389 (4), 374 (13), 230 (100), 171 (28), 132 (45), 43 (47).

(2′,2′,5′,5′-Tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (3b). The synthesis was done using the same procedure as for compound **3a**. Flash chromatography (40% EtOAC in cyclohexane) yielded a white powder (1.08 g, 2.40 mmol, 75%). mp 79 °C. $[\alpha]^{20}_D$ +2.4° (*c* 0.75, $CHCl_3$). IR: 2993, 2937, 2866, 1651 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.25 (s, 3H), 1.25 (s, 3H), 1.35 (s, 3H), 1.45 (s, 3H), 2.75 (m, 2H), 3.78 (s, 3H), 3.78 (s, 3H), 4.00 (m, 2H), 4.01 (m, 2H), 4.20 (m, 1H), 4.60 (dd, 2H, *J* = 30.2, *J* = 16.9), 5.28 (m, 1H), 6.55 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 19.1, 26.3, 27.2, 29.1, 29.4, 44.0, 45.0, 56.3, 56.3, 60.3, 73.3, 74.5, 87.7, 97.8, 109.6, 111.8, 112.8, 113.4, 125.3, 126.8, 147.9, 148.0, 165.5. Anal. Calcd for $C_{23}H_{31}NO_8$, $^1/_2$ H_2O: C, 60.25; H, 6.71; N, 3.05. Found: C, 60.18; H, 6.85; N, 3.18. MS *m*/*z* (relative intensity) (M): 449 (6), 434 (5), 290 (100), 191 (52), 43 (36).

1-Methyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydroisoquinoline (4a). Starting material **3a** (0.1 g, 0.26 mmol) was first dried using Dean−Starck apparatus with toluene for 4 h. Toluene was replaced by THF (15 mL). At −78 °C, *t*-BuLi (222 μL, 0.33 mmol) was slowly added. After 15 min, methyl iodide (77 μL, 1.23 mmol) was introduced, and the agitation was continued for 2 h. The mixture was then quenched with saturated $NaHCO_3$ aqueous solution (1 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (54 mg, 0.13 mmol, 53%). Recrystallization in a mixture of AcOEt/cyclohexane afforded **4a** as the major diastereomer. mp 102 °C. $[\alpha]^{20}_D$ −81.3° (*c* 0.75, $CHCl_3$). IR: 2936, 2866, 1644 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 3H), 1.29 (s, 3H), 1.31 (s, 3H), 1.40 (d, 3H, *J* = 6.7), 1.45 (s, 3H), 2.66 (m, 1H), 3.06 (m, 1H), 3.32 (td, 1H, *J* = 10.2, *J* = 3.1), 3.95 (m, 2H), 4.12 (m, 1H), 4.18 (m, 1H), 4.43 (dt, 1H, *J* = 10.2, *J* = 3.1), 5.31 (m, 1H), 5.46 (q, 1H, *J* = 6.9), 7.07 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 19.2, 21.4, 26.2, 27.2, 29.0, 30.0, 39.8, 49.5, 60.4, 73.2, 74.6, 87.8, 97.8, 112.9, 113.6, 126.5, 126.6, 127.5, 129.2, 134.7, 138.7, 165.1. Anal. Calcd for $C_{22}H_{29}NO_6$: C, 65.49; H, 7.24; N, 3.47. Found: C, 65.48; H, 7.18; N, 3.38. MS *m*/*z* (relative intensity) (M): 403 (8), 388 (60), 244 (100), 171 (31), 132 (26), 43 (23).

1-Allyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydroisoquinoline (4b). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAC in cyclohexane) yielded a white powder (45 mg, 0.10 mmol, 41%). IR: 1651, 1493, 1454, 1129, 1073 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 3H), 1.27 (s, 3H), 1.30 (s, 3H), 1.45 (s, 3H), 2.55 (t, 2H, *J* = 7.5), 2.65−3.00 (m, 2H), 3.40 (ddd, 1H, *J* = 37.5, *J* = 12.1, *J* = 3.7), 3.90 (m, 2H), 4.05 (m, 1H), 4.15 (m, 1H), 4.42 (m, 1H), 4.96 (m, 2H), 5.26 (m, 2H), 5.55 (m, 1H), 5.80 (m, 1H), 7.10 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 19.2, 26.4, 27.2, 28.9, 29.6, 40.0, 41.6, 52.7, 60.4, 73.4, 74.5, 87.7, 97.8, 112.7, 113.6, 117.4, 126.3, 126.7, 127.7, 129.2, 134.7, 135.3, 137.2, 165.6. MS *m*/*z* (relative intensity) (M): 414 (4), 388 (100), 171 (21), 132 (40), 43 (4).

1-Benzyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydroisoquinoline (4c). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAC in cyclohexane) yielded a white powder (62 mg, 0.13 mmol, 50%). IR: 3061, 2995, 1651, 1510, 1462, 1175, 1121 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ

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1.19 (s, 3H), 1.32 (s, 3H), 1.38 (s, 3H), 1.41 (s, 3H), 2.38 (m, 1H), 2.70 (m, 1H), 2.90−3.20 (m, 2H), 4.02 (d, 2H, J = 7.0), 4.09 (m, 1H), 4.15 (m, 2H), 4.23 (m, 1H), 5.32 (m, 1H), 5.61 (t, 1H, J = 4.6), 7.00 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 19.2, 26.3, 27.2, 29.3, 29.7, 41.4, 41.7, 54.9, 60.4, 73.3, 74.5, 87.6, 97.9, 112.7, 113.4, 126.3, 126.8, 127.9, 128.4, 128.5, 128.8, 129.1, 130.5, 130.7, 135.4, 136.4, 138.0, 165.6. MS *m*/*z* (relative intensity) (M): 464 (4), 388 (100), 171 (22), 132 (33), 43 (11).

1-Phenethyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,-4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydroisoquinoline (4d). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAC in cyclohexane) yielded a white powder (52 mg, 0.10 mmol, 41%). IR: 3062, 2990, 1650, 1496, 1453, 1179, 1130 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.16 (s, 3H), 1.30 (s, 3H), 1.30 (s, 3H), 1.48 (s, 3H), 2.05 (m, 2H), 2.66 (m, 2H), 2.66 (m, 1H), 3.10 (m, 1H), 3.43 (m, 1H), 3.95 (m, 2H), 4.05 (m, 1H), 4.12 (m, 1H), 4.54 (m, 1H), 5.34 (m, 1H), 5.62 (m, 1H), 7.13 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 19.2, 26.4, 27.2, 28.9, 30.0, 32.8, 39.2, 39.7, 53.1, 60.4, 73.3, 74.6, 87.8, 97.8, 112.7, 113.7, 126.1, 126.3, 126.7, 127.7, 128.6, 128.7, 128.8, 129.0, 129.3, 134.6, 137.9, 142.6, 165.9. MS *m*/*z* (relative intensity) (M): 478 (4), 388 (100), 171 (14), 132 (24), 91 (7), 43 (8).

1-Methyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4e). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (66 mg, 0.144 mmol, 55%). Recrystallization in a mixture of AcOEt/cyclohexane afforded **4e** as the major diastereomer. mp 103 °C. $[\alpha]^{20}_D$ −71.3° (*c* 0.75, $CHCl_3$). IR: 2992, 2836, 1644 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.16 (s, 3H), 1.30 (s, 3H), 1.32 (s, 3H), 1.35 (d, 3H, J = 5.1), 1.46 (s, 3H), 2.56 (m, 1H), 3.00 (m, 1H), 3.25 (td, 1H, J = 12.0, J = 3.6), 3.78 (s, 3H), 3.78 (s, 3H), 4.04 (m, 2H), 4.10 (m, 1H), 4.17 (m, 1H), 5.30 (m, 1H), 5.37 (m, 1H), 6.52 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 19.2, 21.3, 26.1, 27.2, 29.0, 29.5, 39.8, 49.1, 56.4, 60.4, 73.2, 74.5, 87.8, 97.8, 110.2, 111.7, 112.9, 113.5, 126.6, 130.5, 147.8, 147.9, 165.0. Anal. Calcd for $C_{24}H_{33}NO_8$, $^1/_8$ H_2O: C, 61.88; H, 7.14; N, 3.00. Found: C, 61.88; H, 7.02; N, 2.94. MS *m*/*z* (relative intensity) (M): 463 (4), 448 (8), 304 (32), 281 (70), 207 (100), 44 (52).

1-Allyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4f). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (55 mg, 0.11 mmol, 50%). IR: 1651, 1454, 1179, 1125 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 3H), 1.28 (s, 3H), 1.32 (s, 3H), 1.45 (s, 3H), 2.51 (m, 2H), 2.55 (m, 2H), 2.90 (m, 1H), 3.35 (m, 1H), 3.78 (s, 3H), 3.78 (s, 3H), 4.00 (m, 2H), 4.04 (m, 1H), 4.16 (dd, 1H, J = 10.0, J = 2.1), 4.45 (m, 1H), 5.00 (m, 2H), 5.29 (m, 1H), 5.45 (m, 1H), 5.83 (m, 1H), 6.51 (m, 1H), 6.56 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 19.2, 26.4, 27.2, 29.0, 29.5, 40.0, 41.5, 52.2, 56.2, 56.4, 60.4, 73.4, 74.5, 87.7, 97.8, 110.5, 111.8, 112.7, 113.6, 117.4, 126.7, 129.0, 135.4, 147.6, 147.9, 165.5. MS *m*/*z* (relative intensity) (M): 474 (4), 448 (100), 281 (35), 192 (80), 171 (25), 43 (26).

1-Phenethyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,-4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4g). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (70 mg, 0.13 mmol, 57%). IR: 3060, 2992, 1648, 1453, 1178, 1108 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.16 (s, 3H), 1.33 (s, 3H), 1.33 (s, 3H), 1.47 (s, 3H), 2.05 (m, 2H), 2.57 (m, 1H), 2.59 (m, 1H), 2.75 (m, 1H), 3.05 (m, 1H), 3.40 (m, 2H), 3.76 (s, 3H), 3.77 (s, 3H), 3.95 (m, 2H), 4.11 (m, 1H), 4.18 (m, 1H), 5.34 (m, 1H), 5.52 (q, 1H, J = 4.8), 6.50 (s, 2H), 7.18 (m, 5H). ^{13}C NMR ($CDCl_3$): δ 19.2, 26.4, 27.2, 29.0, 29.5, 32.8, 39.0, 39.8, 52.7, 56.2, 56.4, 60.4, 73.3, 74.6, 87.8, 97.8, 110.5, 111.8, 112.7, 113.7, 126.1, 126.5, 128.7, 129.8, 130.1, 130.4, 130.9, 142.6, 147.7, 147.9, 165.9. MS *m*/*z* (relative intensity) (M): 538 (4), 448 (100), 394 (16), 192 (33), 43 (20).

1-Tributyltin-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,-4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydroisoquinoline (4h,i). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a colorless oil **4h** (54.5 mg, 0.08 mmol, 31%) and **4i** (25.5 mg, 0.04 mmol, 15%).

4h. IR: 2928, 2871, 1490, 1454, 1382, 1254, 1180, 1128, 1073 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.83 (m, 18H), 1.24 (m, 9H), 1.36 (s, 3H), 1.38 (s, 3H), 1.41 (s, 3H), 1.43 (s, 3H), 2.71 (m, 1H), 3.10 (m, 1H), 3.46 (m, 1H), 4.03 (m, 2H), 4.17 (m, 1H), 4.25 (m, 1H), 4.38 (m, 1H), 5.35 (m, 1H), 5.49 (m, 1H), 7.02 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 10.9, 14.0, 19.2, 26.3, 26.8, 27.1, 27.3, 27.5, 27.6, 27.8, 29.0, 29.1, 29.3, 29.4, 29.5, 30.1, 30.6, 44.2, 50.3, 60.5, 73.0, 74.6, 87.9, 97.7, 113.3, 113.6, 124.2, 124.6, 126.6, 128.7, 132.4, 139.6, 163.4.

4i. IR: 2928, 2871, 1490, 1454, 1382, 1254, 1180, 1128, 1073 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.83 (m, 18H), 1.24 (m, 9H), 1.36 (s, 3H), 1.38 (s, 3H), 1.41 (s, 3H), 1.43 (s, 3H), 2.71 (m, 1H), 3.10 (m, 1H), 3.46 (m, 1H), 4.03 (m, 2H), 4.17 (m, 1H), 4.25 (m, 1H), 4.38 (m, 1H), 5.35 (m, 1H), 5.61 (m, 1H), 7.02 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 10.9, 14.0, 19.2, 26.3, 26.8, 27.1, 27.3, 27.5, 27.6, 27.8, 29.0, 29.1, 29.3, 29.4, 29.5, 30.1, 30.6, 44.2, 49.9, 60.5, 73.0, 74.6, 87.9, 97.7, 113.3, 113.6, 124.2, 124.6, 126.6, 128.7, 132.4, 139.6, 163.4. MS *m*/*z* (relative intensity) (M): 678 (4), 622 (29), 388 (92), 179 (58), 132 (100), 43 (17).

***(R)*-1-Methyl-1,2,3,4-tetrahydroisoquinoline (5a).** To a solution of KOH in methyl alcohol (6 N) was added **4a** (195 mg, 0.48 mmol). The mixture was warmed at reflux for 96 h. Methyl alcohol was removed under vacuum and replaced by brine saturated solution. The amine was extracted by ethyl acetate (4 × 30 mL). The organic layers were then dried (Na_2SO_4) and concentrated under vacuum. Flash chromatography (30% EtOAc in cyclohexane) yielded an oil (49 mg, 0.33 mmol, 70%). ^{1}H NMR ($CDCl_3$): δ 1.37 (d, 3H, J = 6.6), 2.66 (dt, 1H, J = 16.4, J = 4.9), 2.77 (m, 1H), 2.95 (m, 1H), 3.15 (m, 1H), 4.02 (q, 1H, J = 6.9), 7.02 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 22.8, 30.1, 41.9, 51.8, 126.3, 126.3, 126.4, 129.6, 134.9, 140.5. MS *m*/*z* (relative intensity) (M): 146 (11), 144 (3), 132 (100), 117 (18), 105 (9), 77 (8).

1-Methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (5b). Deprotection was done using the same procedure as for compound **5a**. Flash chromatography (30% EtOAc in cyclohexane) yielded an oil (71 mg, 0.34 mmol, 72%). ^{1}H NMR ($CDCl_3$): δ 1.40 (d, 3H, J = 6.7), 2.31 (m, 1H), 2.59 (m, 1H), 2.74 (m, 1H), 2.95 (m, 1H), 3.18 (m, 1H), 3.78 (s, 6H), 4.00 (m, 1H), 6.50 (s, 1H), 6.55 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 23.0, 29.6, 42.0, 51.6, 56.4, 56.4, 109.4, 112.1, 126.9, 132.2, 147.7, 147.8. MS *m*/*z* (relative intensity) (M): 206 (8), 192 (100), 176 (13), 148 (7), 91 (6).

(2′,2′,5′,5′-Tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9methyl*-pyrido[3,4]indole (7a). A THF solution of amide (0.63 g, 1.47 mmol) coming from the condensation of **6** and **2** (same protocol as **3a**) was added to a stirred suspension of potassium hydride (71 mg, 1.77 mmol) in THF (6 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h, tetramethylethylenediamine (266 μL, 1.77 mmol) was added, and stirring was continued for 30 min. Methyl iodide (183 μL, 2.95 mmol) was added slowly, and stirring was continued for an additional hour. The reaction was shaken with water (30 mL), and the organic layer was separated. The aqueous layer was extracted with diethyl ether (2 × 20 mL). The combined organic layers were washed with water (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was chromatographed (40% EtOAc in cyclohexane) and yielded a yellow powder (0.55 g, 1.23 mmol, 84%). mp 80 °C. $[\alpha]^{20}_D$ +8.1° (*c* 0.75, $CHCl_3$). IR: 2992, 2924, 1651 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.23 (s, 3H), 1.26 (s, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 2.80 (m, 2H), 3.57 (s, 3H), 3.89 (m, 2H), 4.02 (d, 2H,

J = 8.2), 4.12 (m, 1H), 4.19 (m, 1H), 4.58 (d, 1H, J = 16.7), 4.94 (d, 1H, J = 16.7), 5.31 (m, 1H), 7.02 (m, 1H), 7.11 (m, 1H), 7.22 (d, 1H, J = 8.0), 7.42 (d, 1H, J = 7.6). ^{13}C NMR ($CDCl_3$): δ 19.1, 22.4, 26.3, 27.2, 29.8, 40.8, 44.8, 60.3, 73.4, 74.6, 87.8, 97.9, 108.1, 109.2, 112.8, 113.4, 118.4, 119.4, 121.5, 126.8, 131.8, 137.5, 166.3. Anal. Calcd for $C_{24}H_{30}N_2O_6$, $^1/_8$ H_2O: C, 64.81; H, 6.79; N, 6.30. Found: C, 64.89; H, 6.56; N, 6.15. MS *m*/*z* (relative intensity) (M): 442 (40), 427 (20), 283 (100), 184 (54), 157 (19), 43 (28).

(2′,2′,5′,5′-Tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9ethoxymethyl*-pyrido[3,4]indole (7b). The synthesis was done using the same procedure as for compound **7a**. Flash chromatography (40% EtOAC in cyclohexane) yielded a yellow powder (0.68 g, 1.40 mmol, 88%). IR: 3054, 2989, 1656, 1452, 1130 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.04 (t, 3H, J = 7.0), 1.23 (s, 3H), 1.24 (s, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 2.79 (m, 2H), 3.37 (q, 2H, J = 7.0), 3.95 (m, 2H), 4.00 (d, 2H, J = 9.2), 4.12 (m, 1H), 4.20 (m, 1H), 4.62 (d, 1H, J = 16.9), 4.90 (d, 1H, J = 16.8), 5.30 (m, 1H), 5.34 (m, 2H), 7.13 (m, 2H, J = 7.1), 7.33 (d, 1H, J = 7.9), 7.41 (d, 1H, J = 7.5). ^{13}C NMR ($CDCl_3$): δ 15.3, 19.1, 22.4, 26.3, 27.2, 29.1, 40.7, 44.6, 60.3, 64.1, 73.2, 73.3, 74.6, 87.8, 97.9, 109.8, 109.9, 112.9, 113.4, 118.5, 120.3, 122.2, 127.5, 131.7, 137.6, 166.3. MS *m*/*z* (relative intensity) (M): 486 (14), 471 (8), 327 (82), 281 (80), 228 (100), 171 (45), 43 (93).

1-Methyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9methyl*-pyrido[3,4]indole (8a). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (59 mg, 0.129 mmol, 57%). Recrystallization in a mixture of AcOEt/cyclohexane afforded **8a** as the major diastereomer. mp 170 °C. $[\alpha]^{20}_D$ −68.6° (*c* 0.75, $CHCl_3$). IR: 2990, 2936, 1646 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.11 (s, 3H), 1.30 (s, 3H), 1.32 (s, 3H), 1.41 (d, 3H, J = 4.0), 1.47 (s, 3H), 2.70 (m, 2H), 3.36 (td, 1H, J = 13.6, J = 3.8), 3.59 (s, 3H), 3.98 (m, 2H), 4.12 (m, 1H), 4.16 (m, 1H), 4.68 (m, 1H), 5.31 (m, 1H), 5.62 (q, 1H, J = 6.6), 7.01 (m, 1H), 7.14 (m, 1H), 7.20 (d, 1H, J = 8.0), 7.39 (d, 1H, J = 7.6). ^{13}C NMR ($CDCl_3$): δ 18.9, 19.2, 22.4, 26.2, 27.1, 28.9, 30.2, 40.2, 45.3, 60.4, 73.3, 74.8, 87.9, 97.9, 107.7, 109.2, 112.9, 113.6, 118.6, 119.5, 121.7, 126.8, 136.4, 137.7, 165.5. Anal. Calcd for $C_{25}H_{32}N_2O_6$, $^1/_8$ H_2O: C, 65.44; H, 7.03; N, 6.10. Found: C, 65.37; H, 6.92; N, 5.96. MS *m*/*z* (relative intensity) (M): 456 (53), 441 (42), 297 (100), 199 (63), 59 (28), 43 (28).

1-Allyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9methyl*-pyrido[3,4]indole (8b). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (45 mg, 0.09 mmol, 41%). IR: 1649, 1470, 1180, 1129 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.14 (s, 3H), 1.29 (s, 3H), 1.35 (s, 3H), 1.44 (s, 3H), 2.56 (m, 2H), 2.70 (m, 2H), 3.45 (m, 1H), 3.62 (s, 3H), 4.00 (m, 2H), 4.15 (m, 1H), 4.20 (m, 1H), 4.70 (m, 1H), 5.04 (m, 2H), 5.30 (m, 1H), 5.77 (m, 1H), 5.85 (m, 1H), 7.05 (m, 1H), 7.13 (m, 1H), 7.20 (m, 1H), 7.39 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 19.3, 22.5, 26.3, 27.2, 28.9, 30.5, 39.0, 40.1, 48.3, 60.3, 73.2, 74.7, 87.9, 97.8, 108.1, 109.3, 112.7, 113.5, 117.8, 118.5, 119.6, 121.8, 126.8, 134.0, 135.5, 137.8, 166.1. MS *m*/*z* (relative intensity) (M): 482 (6), 467 (4), 441 (100), 283 (28), 185 (51), 43 (20).

1-Benzyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9methyl*-pyrido[3,4]indole (8c). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (69 mg, 0.13 mmol, 57%). IR: 1639, 1454, 1260, 1181, 1077 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.12 (s, 3H), 1.30 (s, 3H), 1.36 (s, 3H), 1.41 (s, 3H), 2.62 (m, 2H), 3.12 (m, 2H), 3.42 (m, 3H), 3.99 (m, 2H), 4.09 (m, 1H), 4.18 (m, 1H), 4.56 (m, 2H), 5.24 (m, 1H), 5.87 (m, 1H), 7.10 (m, 8H), 7.41 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 20.1, 23.0, 27.0, 27.9, 29.9, 31.4, 41.2, 41.6, 50.9, 61.2, 74.3, 75.4, 88.5, 98.7, 109.2, 110.2, 113.5, 114.2, 119.3, 120.3, 122.6, 127.7, 127.8, 129.6, 129.7, 131.1, 131.2, 135.8, 138.1, 138.8, 166.6. MS *m*/*z* (relative intensity) (M): 532 (1), 517 (3), 441 (100), 185 (30), 43 (8).

1-Phenethyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,-4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9methyl*-pyrido[3,4]indole (8d). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (70 mg, 0.13 mmol, 57%). IR: 1651, 1432, 1265, 1179, 1071 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.20 (s, 3H), 1.30 (s, 3H), 1.35 (s, 3H), 1.50 (s, 3H), 2.10 (m, 2H), 2.65 (m, 1H), 2.75 (m, 2H), 3.00 (m, 1H), 3.45 (m, 1H), 3.49 (s, 3H), 3.95 (m, 2H), 4.13 (m, 1H), 4.20 (m, 1H), 4.75 (m, 1H), 5.37 (m, 1H), 5.80 (m, 1H), 7.21 (m, 8H), 7.40 (d, 1H, J = 7.7). ^{13}C NMR ($CDCl_3$): δ 19.3, 22.7, 26.4, 27.2, 28.9, 30.1, 32.5, 36.6, 40.3, 48.5, 60.4, 73.4, 74.8, 87.9, 97.9, 107.8, 109.3, 112.8, 113.8, 118.6, 119.5, 121.7, 126.4, 126.8, 128.6, 128.8, 128.9, 129.2, 135.7, 137.7, 142.2, 166.5. MS *m*/*z* (relative intensity) (M): 546 (11), 531 (4), 441 (100), 185 (24), 43 (13).

1-Methyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9ethoxymethyl*-pyrido[3,4]indole (8e). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (41 mg, 0.08 mmol, 40%). IR: 3061, 2993, 1644, 1461, 1130 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.07 (m, 3H), 1.11 (s, 3H), 1.30 (s, 3H), 1.32 (s, 3H), 1.47 (s, 3H), 1.50 (m, 3H), 2.69 (m, 1H), 2.95 (m, 1H), 3.37 (m, 2H), 3.41 (m, 2H), 3.98 (m, 2H), 4.13 (m, 1H), 4.17 (m, 1H), 4.67 (m, 1H), 5.30 (m, 1H), 5.40 (m, 2H), 5.69 (m, 1H), 7.10 (m, 2H), 7.33 (d, 1H, J = 7.1), 7.40 (d, 1H, J = 7.3). ^{13}C NMR ($CDCl_3$): δ 15.4, 19.3, 22.4, 26.2, 27.2, 28.9, 30.1, 39.9, 45.3, 60.4, 64.1, 72.9, 73.2, 74.7, 87.9, 97.8, 109.6, 109.9, 113.0, 113.6, 118.7, 120.4, 122.4, 127.7, 136.4, 137.9, 165.4. MS *m*/*z* (relative intensity) (M): 500 (13), 485 (17), 454 (30), 295 (54), 242 (81), 43 (100).

1-Allyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9ethoxymethyl*-pyrido[3,4]indole (8f). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (43 mg, 0.08 mmol, 40%). IR: 3055, 2990, 1648, 1454, 1181, 1129 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.08 (m, 3H), 1.10 (s, 3H), 1.29 (s, 3H), 1.31 (s, 3H), 1.44 (s, 3H), 2.60 (m, 2H), 2.81 (m, 2H), 3.43 (m, 1H), 3.45 (m, 2H), 4.01 (m, 2H), 4.12 (m, 1H), 4.21 (m, 1H), 4.66 (m, 1H), 4.99 (m, 1H), 5.29 (m, 1H), 5.36 (m, 2H), 5.81 (m, 1H), 5.85 (m, 1H), 7.12 (m, 1H, 2H), 7.38 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 15.4, 19.3, 22.5, 26.4, 27.2, 28.8, 38.9, 40.0, 48.3, 60.4, 64.1, 73.2, 73.4, 74.7, 87.7, 97.8, 109.6, 110.0, 112.8, 113.5, 117.5, 120.4, 122.5, 127.5, 134.3, 135.2, 137.9, 166.0. MS *m*/*z* (relative intensity) (M): 526 (2), 485 (100), 229 (67), 171 (39), 59 (40), 43 (64).

1-Benzyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9ethoxymethyl*-pyrido[3,4]indole (8g). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (67 mg, 0.12 mmol, 57%). IR: 3060, 2991, 1648, 1455, 1181, 1129 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^{1}H NMR ($CDCl_3$): δ 1.09 (m, 3H), 1.11 (s, 3H), 1.31 (s, 3H), 1.37 (s, 3H), 1.41 (s, 3H), 2.55 (m, 1H), 2.70 (m, 1H), 2.95 (m, 1H), 3.28 (t, 2H, J = 6.7), 3.41 (q, 2H, J = 6.9), 4.00 (d, 2H, J = 13.5), 4.09 (m, 1H), 4.19 (m, 1H), 4.46 (m, 1H), 5.16 (d, 1H, J = 11.3), 5.23 (m, 1H), 5.38 (d, 1H, J = 11.3), 5.69 (t, 1H, J = 5.3), 7.11 (m, 5H), 7.16 (m, 2H), 7.36 (d, 2H, J = 8.1). ^{13}C NMR ($CDCl_3$): δ 15.4, 19.3, 22.1, 26.1, 27.2, 29.1, 39.7, 40.7, 50.1, 60.4, 64.3, 73.3, 73.5, 74.6, 87.0, 97.9, 110.0, 110.4, 112.6, 113.4, 118.6, 120.4, 122.5, 126.9, 127.4, 128.6, 128.7, 130.4,

130.5, 134.9, 137.7, 138.2, 165.8. MS *m*/*z* (relative intensity) (M): 485 (100), 229 (46), 171 (38), 59 (36), 43 (90).

1-Phenethyl-2-(2′,2′,5′,5′-tetramethyl-tetrahydro-1′,3′,-4′,6′,8′-pentaxo-cyclopenta[a]-indene-8′a-carbonyl)-1,2,3,4-tetrahydro-*9ethoxymethyl*-pyrido[3,4]indole (8h). The synthesis was done using the same procedure as for compound **4a**. Flash chromatography (10% EtOAc in cyclohexane) yielded a white powder (69 mg, 0.12 mmol, 57%). IR: 3058, 2988, 1651, 1455, 1180, 1129 cm^{-1}. The product was isolated as a diastereomeric mixture of compounds. NMR of the major isomer, ^1H NMR ($CDCl_3$): δ 1.02 (m, 3H), 1.12 (s, 3H), 1.18 (s, 3H), 1.30 (s, 3H), 1.50 (s, 3H), 2.15 (m, 1H), 2.20 (m, 1H), 2.64 (m, 1H), 2.69 (m, 2H), 2.90 (m, 1H), 3.33 (m, 2H), 3.45 (m, 1H), 4.04 (m, 2H), 4.15 (m, 1H), 4.25 (m, 1H), 4.70 (t, 1H, J = 14.2), 5.16 (m, 1H), 5.35 (m, 1H), 5.86 (t, 1H, J = 9.3), 7.14 (m, 2H), 7.20 (m, 5H), 7.29 (d, 1H, J = 8.0), 7.37 (d, 1H, J = 7.5). ^{13}C NMR ($CDCl_3$): δ 15.3, 19.3, 22.6, 26.4, 27.2, 28.8, 32.6, 36.4, 40.0, 48.5, 60.4, 64.0, 73.1, 73.3, 74.8, 87.7, 97.8, 109.6, 109.9, 112.8, 113.8, 118.7, 120.4, 122.4, 126.3, 127.5, 128.7, 128.8, 128.9, 129.2, 135.7, 137.8, 142.3, 166.4. MS *m*/*z* (relative intensity) (M): 590 (6), 485 (100), 441 (35), 315 (75), 229 (53), 171 (45), 59 (51), 43 (74).

1-Methyl-1,2,3,4-tetrahydro-*9methyl*-pyrido[3,4-b]indole (9). The deprotection was done using the same procedure as for compound **5a**. Flash chromatography (30% EtOAc in cyclohexane) yielded an oil (67 mg, 0.33 mg, 70%). ^1H NMR ($CDCl_3$): δ 1.41 (d, 3H, J = 6.6), 2.66 (t, 2H, J = 5.6), 3.13 (m, 2H), 3.60 (s, 3H), 4.16 (q, 1H, J = 6.4), 7.02 (m, 1H), 7.11 (m, 1H), 7.21 (d, 1H, J = 8.2), 7.43 (d, 1H, J = 7.7). ^{13}C NMR ($CDCl_3$): δ 21.4, 23.3, 30.3, 39.8, 46.7, 107.8, 109.0, 118.4, 119.3, 121.5, 127.3, 137.4, 137.4. MS *m*/*z* (relative intensity) (M): 200 (40), 185 (100), 170 (30), 158 (9), 144 (10), 115 (10).

Acknowledgment. We thank Dr. L. Toupet for providing X-ray analysis of compound **4a**.

JO0155658