Strain-Barrier Stabilized Products from the Fischer Indole Synthesis. Compounds Containing the 4*H*-Imidazo[1,2-*a*]pyrrolo[3,4-*b*]indole and Dipyrrolo [3,4-*b*:3′,4′-*b*′][1,3]diazeto[1,2-*a*:3,4-*a*′]diindole Ring Systems

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The angular 3a-amino groups of 3a-amino-1,3a,4,8b-tetrahydro-pyrrolo[3,4-*b*]indol-3(2*H*)-ones fail to undergo the expected spontaneous elimination (as ammonia) which would introduce a 3a–4 double bond. The resistance of the amino group to elimination is such that reaction with oxalyl chloride bridges that group to the 4-nitrogen to create a stable dioxoimidazole ring. Replacement of the amino group by methoxy takes place in methanolic sulfuric acid. 3a-amino-1,2,3,3a,4,8b-hexahydropyrrolo[3,4-*b*]indoles undergo ammonia elimination in acid solution, but yield expected 1,2,3,8b-tetrahydropyrrolo[3,4-*b*]indoles only as transient precursors of stable products, apparently their symmetrical dimers (dipyrrolo[3,4-*b*:3′,4′-*b*′][1,3]diazeto[1,2-a:3,4-*a*′]diindoles).

Compounds in the pyrrolo[3,4-*b*]indole series were earlier found to show an unexpected resistance to the introduction of unsaturation at the 3a–4 position[1,2,3]. Compounds of type **9**, incorporating a 3*H*-indole structure, are presently unknown, probably because of the bond-angle strain which would be associated with a trigonal C atom located at the 3a position. The results reported here reinforce the conclusions developed in the earlier work[2], in which the unexpected persistence of normally unstable structures (such as **2**) was seen as a consequence of the interference of such a strain barrier with the expected facile elimination reactions which would yield 3*H*-indoles. Three previously unreported reactions illustrating such behavior and leading to new types of products are reported here. These observations have much in common with those reported[4,5] for studies of the chemistry of conjugated enones incorporating a strained double bond at a bridgehead location. Other phenomena in indole chemistry which may be interpreted on a similar basis have recently been reviewed[6].

Formation of 3a-Methoxy Derivatives

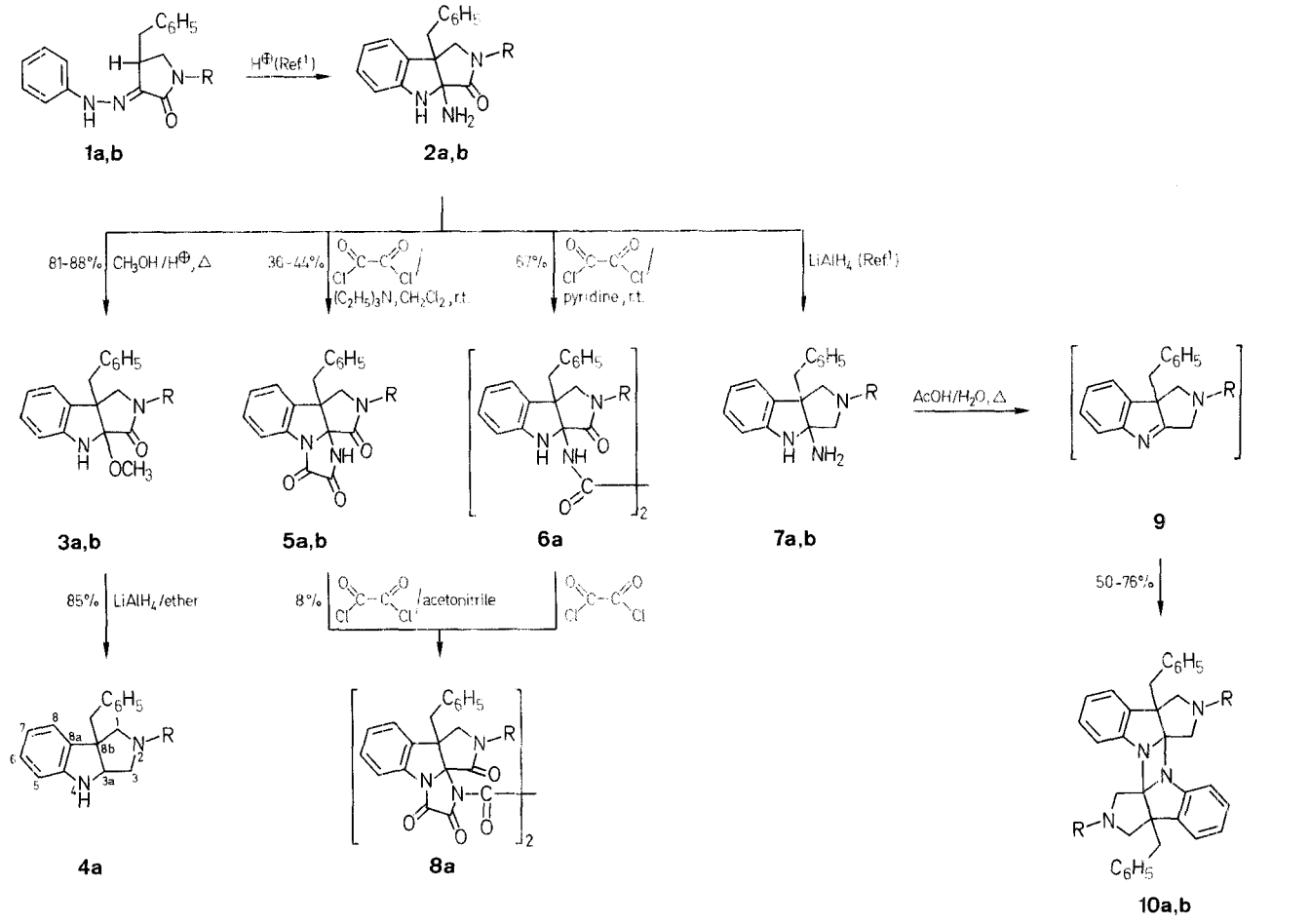
Compounds of type **2** are obtained when phenylhydrazones of 4-benzyl-2,3-dioxopyrrolidines (**1**) are subjected to the acid-catalyzed rearrangement of the Fischer indole synthesis[1]. Treatment of these products with strong acids dissolved in methanol (or other primary alcohols) fails to cause elimination of ammonia to form a C=N double bond, but results in nucleophilic replacement of the angular amino group by a methoxy (or other alkoxy) group. The exchange process takes place cleanly and in good yield. Lithium aluminum hydride reduction of a resulting 3a-methoxy derivative (**3a**) provides the best method for obtaining a compound (**4a**) containing the unfunctionalized 1,2,3,4,5,6-hexahydropyrrolo[3,4-*b*]indole ring structure.

Incorporation of Angular Amino Groups into a New Ring Structure

When treated with oxalyl chloride, compounds of type **2** were found to react either at the angular amino group alone or at that position and the indoline nitrogen as well. Elimination to form a C=N double bond was not facilitated by these acylations. Under one set of conditions (in dichloromethane containing triethylamine), an oxalyl group connecting the two nitrogens is introduced to form a new five-membered ring. The resulting stable products **5** contain the novel 4*H*-imidazo[1,2-*a*]pyrrolo[3,4-*b*]indole ring system. Bis-oxamides **6** from reaction only at the angular amino group are formed instead in pyridine solution. In some experiments, small amounts of a third product (**8**) were formed as a result of a sequence of both types of acylation.

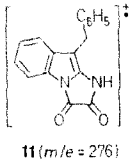
Formation of Dimers (10) of the 3*H*-Indole Structure 9

It was previously demonstrated that the lactam carbonyl group of compounds of type **2** could be removed by lithium aluminum hydride reduction while preserving the angular amino function[1]. When the resulting products **7** are heated with 60% aqueous acetic acid, elimination of the elements of ammonia does occur, but the expected 3*H*-indoles of structure **9** are not obtained. Instead, the products isolated show properties expected for dimers derivable from **9**. In the mass spectra, the molecular ions correspond to a dimeric molecular formula. The rather simple ^{1}H-NMR spectra of the compounds seem to require their formulation as symmetrical dimers (**10**), derived from **9** via a [2 + 2]-cycloaddition, and described by the names 2,10-dicyclohexyl- or 2,10-dimethyl-3a,11a-dibenzyl-1,2,3,3a,9,10,11,11a-octahydrodipyrrolo[3,4-*b*:3′4′-*b*′] [1,3]diazeto[1,2-*a*:3,4-*a*′]-diindole. The configuration of these products has not been established. However, it may be supposed that the structure depicted (**10**, *meso* form with center of symmetry present) would be favored as minimizing steric interactions within the dimer molecule. (Structural formula **10** is not intended to specify the undetermined configurational relationship between the two carbons at each of the pyrrolo-indole ring junctions, although *cis* configurations seem likely). Another procedure yielded a lower-melting product from **7a** with properties indicating that it represents the same type of structure as **10a**, but in a mixture of configurations. Prolonged heating of this material in 75% aqueous acetic converts it at least in part to **10a**, mp 250°C, which is presumed therefore to represent a favored stable configuration. The compounds evidently do not dissociate readily to **9**, however; they do not, for example, undergo reduction with lithium aluminum hydride. An analogous dimerization via [2 + 2]-cycloaddition has been characteristic of an unisolable strained enone studied by House et al.[4,5]. Thermally reversible trimerizations of less strained, isolable 3*H*-indoles have been observed previously, but the established instances are with 3*H*-indoles which are unsubstituted at the 2-position and free of bulky groups in the 3-position[6–9]. The susceptibility of the trimers to thermal dissociation does not prevent them from displaying the trimeric molecular ion in their mass spectra[7,8]. Hence, the absence of any ions larger than the dimeric molecular ion from the mass spectra of **10a** and **10b** tends to favor their formulation as dimers rather than trimers. The low solubilities of **10a** und **10b** in suitable solvents is an obstacle to obtaining their molecular weights



by other means. The fact that **9a** and **9b**, although they would be 3*H*-indoles with bulky subsitituents in positions 2 and 3, undergo this type of self addition suggests the operation of a different process that that leading to the dissociable trimers. The facts that **10a** and **10b** fail to show typical UV spectra of protonated 3*H*-indoles in acid solution or to give the complex ^{1}H-NMR spectra of the trimers also seem to differentiate them from such trimers[7,8,9].

Fragmentation patterns seen in mass spectra of some of these compounds may have a bearing on the question of whether strained structures such as **9** could ever be obtained as isolable compounds. Compounds **5a** and **5b** both yield an ion of *m/e* = 276 which is best explained by structure **11**, strain having been relieved by decomposition to yield an indole derivative. Fragments corresponding to **9** are not produced from **5a** or **5b**, nor from **6a** or **8a**. The latter compounds fragment at the middle of the linking oxalyl group and undergo loss of carbon monoxide from the resulting ions. The apparent dimers **10a** and **10b**, on the other hand, do yield fragment ions corresponding to **9**, which, in the case of the mixed diastereomers of **10a**, are formed five times as abundantly at 70 ev as at 12 ev. The generation of an ion of structure **9** from the dimer has evidently required a significant input of energy.



11 (*m/e* = 276)

Microanalyses were performed by Drs. G. Weiler and F. B. Strauss, Oxford, England and M. H. W. Laboratories, Phoenix, Arizona. Mass spectra were taken by James Boal of Mellon Institute. ^{1}H-NMR spectra were measured with a Varian A-60 instrument. Recommendations from Dr. Kurt L. Loening of Chemical Abstracts Service were followed in naming the new ring structures.

2-Substituted 3a-Alkoxy-8b-benzyl-1,3a,4,8*b*-tetrahydropyrrolo-[*3,4-b*]indol-3(2*H*)-ones (3):

2-Cyclohexyl-3a-methoxy-8b-benzyl-1,3a,4,8b-tetrahydropyrrolo-[3,4-b]indol-3(2H)-one **(3a)**:

A solution of 3a-amino-8b-benzyl-2-cyclohexyl-1,3a,4,8b-tetrahydropyrrolo[3,4-*b*]indol-3(2*H*)-one **(2a)** (4.0 g) in absolute methanol (100 ml) containing 95% sulfuric acid (1.0 ml) is refluxed with stirring for 2 h. The mixture is then cooled and 2.5 normal sodium hydroxide (20 ml) and water (100 ml) are added. The mixture is extracted with dichloromethane (100 ml, then 50 ml). The extract is washed with water (75 ml), dried with magnesium sulfate, and filtered. It is then concentrated by distillation with simultaneous addition of Skellysolve-B (brand of petroleum ether, mainly *n*-hexane). From this solution, a white granular solid crystallizes upon cooling; yield: 3.65 g (88%); m.p. 127–129°C. The analytical sample is prepared by three successive recrystallizations from Skellysolve-B, using ether to aid in the dissolution of the compound; m.p. 127–128.5°C.

$C_{24}H_{28}B_2O_2$	calc.	C 76.56	H 7.50	N 7.44
(376.5)	found	76.68	7.75	7.15

IR (nujol): ν = 3360 (N—H); 1678 (C=O); 1608, 1460, 1442, 752, 745 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 240 (3.75); 292.5 nm (3.34).

^{1}H-NMR ($CDCl_3$/TMS_{int}): δ = 7.47–6.30 (m, 9 H_{arom}); 5.57 (s, 1 H, N—H); 4.06–3.58 (m, 1 H, 1-position of cyclohexyl); 3.69 (d, 1 H J = 10 Hz, ring HCH); 3.67 (s, 3 H, OCH_3); 3.28 (d, 1 H, J = 10 Hz ring HCH), 3.19 (d, 1 H, J = 13 Hz, benzyl HCH); 2.98 (d, 1 H J = 13 Hz, benzyl HCH); 2.14–0.81 (m, 10 H, cyclohexyl).

2-Methyl-3a-methoxy-8b-benzyl-1,3a,4,8b-tetrahydropyrrolo-[3,4-b]indol-3(2H)-one **3b**):
3a-amino-8b-benzyl-2-methyl-1,3a,4,8b-tetrahydropyrrolo[3,4-*b*]-indol-3(2*H*)-one (**2b**; 2.0 g) is refluxed in a mixture of absolute methanol (50 ml) and 95% sulfuric acid (0.5 ml) for 2 h. The reaction mixture worked up as in the procedure described above for **3a**. The resulting Skellysolve-B solution is concentrated by distillation to ~ 10 ml. From this solution, a white granular solid is obtained; yield: 1.80 g (81%); m.p. 142–143°C. The analytical sample is prepared by two successive recrystallizations of this from ether and Skellysolve-B, followed by one recrystallization from methanol; m.p. 142–143°C.

$C_{19}H_{20}N_2O_2$	calc.	C 74.00	H 6.54	N 9.09
(308.4)	found	74.19	6.56	9.05

IR (nujol): ν = 3360, 1680, 1605, 1458, 1125, 1113, 742, 705 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 239 (3.73), 292.5 nm (3.34).

^{1}H-NMR ($CDCl_3$/TMS_{int}): δ = 7.36–6.28 (m, 9 H_{arom}); 5.52 (s, 1 H, N—H exchangeable with D_2O); 3.78 (d, 1 H, J = 10 Hz, ring HCH); 3.65 (s, 3 H, OCH_3); 3.21 (d, 1 H, J = 10 Hz, ring HCH); 3.16 (d, 1 H, J = 13 Hz, benzyl HCH); 2.97 (d, 1 H, J = 13 Hz, benzyl HCH); 2.71 ppm (s, 3 H, N—CH_3).

2-Substituted 11b-Benzyl-1,11b-dihydro-4*H*-imidazo[*1,2-a*]-pyrrolo-[3,4-*b*]indole-3,5,5,6(2*H*)-triones (5):

*11b-Benzyl-2-cyclohexyl-1,11b-dihydro-4*H*-imidazo[1,2-a]-pyrrolo[3,4-b]indole-3,5,6(2H)-trione* **(5a):**
To a solution of 3a-amino-8b-benzyl-2-cyclohexyl-1,3a,4,8b-tetrahydropyrrolo[3,4-*b*]indol-3(2*H*)-one (**2a**; 3.0 g, 8.32 mmol) and triethylamine (9 ml) in dry dichloromethane (150 ml), a solution of oxalyl chloride (1.28 g, 10 mmol) in dry dichloromethane (30 ml) is added slowly with stirring in an apparatus protected from moisture. The clear pale yellow mixture is stirred for 18–24 h and then extracted twice with 1.2 normal hydrochloric acid (90 ml) and with water (2 × 90 ml). The reaction mixture is dried with magnesium sulfate, then the filtrate is distilled to remove dichloromethane while methanol is added. The resulting mixture, while still boiling, is diluted with small portions of water until crystallization is induced, then cooled in a mixture of methanol, ice, and water to complete the crystallization; yield: 1.37 g (37%) of colorless fine prisms, m.p. 336–338°C (dec). A second smaller crop is obtained by addition of water to the concentrated mother liquor and agitating the resultant oil until it solidifies. Recrystallization from 95% ethanol affords 155 mg more of the product; total yield: 1.51 g (44%); m.p. 336–338°C. The recrystallizations from methanol did not change the melting point.

$C_{25}H_{25}N_3O_3$	calc.	C 72.27	H 6.07	N 10.12
(415.5)	found	72.03	6.26	10.00

MS (70 eV): *m/e* (rel. int. %) = 415 (10), 387 (4), 276 (4), 199 (6), 171 (10), 112 (3), 91 (22), 83 (3), 69 (7), 58 (3), 57 (4), 55 (8), 43 (8), 41 (7), 32 (21), 28 (100), 18 (77), 17 (18), 14 (3).

IR (nujol): ν = 3370, 1765, 1740, 1685, 1477, 1454, 1415, 756 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 264 (3.88), 286 (3.76) (inflection), 306 nm (350) (inflection).

^{1}H-NMR ($CDCl_3$/CF_3COOH/TMS_{int}): δ = 7.73–6.58 (m, 9 H_{arom}); 4.35 (d, 1 H, J = 10.5 Hz, ring HCH); 4.15–3.58 (m, 1 H, 1-cyclohexyl position); 3.82 (d, 1 H, J = 10.5 Hz, ring HCH); 3.29 (d, 1 H, J = 13 Hz, benzyl HCH); 2.98 (d, 1 H, J = 13 Hz, benzyl HCH); 2.20–0.88 ppm (m, 10 H, cyclohexyl).

*11b-Benzyl-2-methyl-1,11b-dihydro-4*H*-imidazo[1,2-a]pyrrolo[3,4-b]indol-3,5,6(2H)-trione* **(5b)**:
3a-amino-8b-benzyl-2-methyl-1,3a,4,8b-tetrahydropyrrolo[3,4-b]-indol-3(2*H*)-one (**2b**; 1 g, 3.42 mmol) and triethylamine (3 ml) are dissolved in dry dichloromethane (50 ml). To this solution, a solution of oxalyl chloride (0.521 g, 4.10 mmol) in dichloromethane (10 ml) is slowly added with stirring. The clear pale yellow mixture is stirred at room temperature for 21.5 h. The product is isolated in the same manner as the 2-cyclohexyl compound (**5a**). It separates initially as an oil from the methanol-water mixture, but gradually crystallizes. It is collected by filtration and recrystallized from methanol to give a pale-yellow granular product; yield: 430 mg (36%); m.p. 307–308°C (dec). A final recrystallization from methanol yields colorless crystals, m.p. 308–309°C (dec).

$C_{20}H_{17}N_3O_3$	calc.	C 69.15	H 4.93	N 12.10
(347.4)	found	69.17	5.03	12.16

MS (70 eV): *m/e* (rel. int. %) = 347 (20), 319 (7), 276 (5), 256 (3), 248 (6), 218 (3), 205 (6), 199 (5), 171 (20), 170 (5), 152 (3), 116 (5), 91 (21), 69 (8), 65 (4), 57 (4), 55 (3), 44 (6), 43 (4), 42 (4), 41 (4), 32 (22), 31 (6), 29 (4), 28 (100), 18 (93), 17 (22), 14 (4).

IR (nujol): ν = 3370, 1770, 1740, 1720, 1698, 1482, 1455, 770, 703 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 264 (3.88), 286 (3.75) (inflection), 306 nm (3.50) (inflection).

^{1}H-NMR ($CDCl_3$/CF_3COOH/TMS_{int}): δ = 7.70–6.55 (m, 9 H_{arom}); 4.41 (d, 1 H, 10.5 Hz, ring HCH); 3.74 (d, 1 H, J = 10.5 Hz, ring HCH); 3.26 (d, 1 H, J = 13 Hz, benzyl HCH); 3.08 (d, 1 H, J = 13 Hz, benzyl H—CH); 2.97 ppm (s, 3 H, N—CH_3, covers downfield peak of δ 3.08 benzyl doublet).

***N,N'*-Bis(11b-Benzyl-2-cyclohexyl-1,11b-dihydro-4*H*-imidazo-[1,2-*a*]pyrrolo[3,4-*b*]indol-3,5,6(2*H*)-trione-4-yl)-oximide (8a):**
A procedure similar to that used in the preparation of **5a** is applied to 1 g of **2a**. The amount of oxalyl chloride used is increased to 1.42 g (0.42 g added at the start and 1.0 g after 7 h) and acetonitrile is used in place of dichloromethane as the solvent. After a reaction period of 20.5 h at room temperature, the mixture is diluted to 700 ml with water. The precipitated product is collected by filtration and washed with 2.5 normal sodium hydroxide, then water. Colorless needles are obtained following crystallization from chloroform/methanol (chloroform is distilled out until crystallization begins); yield: 0.10 g (8.2%); m.p. 376–380°C. A second crystallization raises the m.p. to 387–388°C (dec).

$C_{52}H_{48}N_6O_8$	calc.	C 70.58	H 5.47	N 9.50
(884.964)	found	70.28	5.62	9.23

MS (70 eV): *m/e* (rel. int. %) = 884 (0.04), 803 (0.2), ~ 442 (0.05), 415 (2, impurity), 414 (1), 387 (1), 199 (2), 171 (4), 95 (3), 91 (12), 85 (5), 82 (8), 81 (4), 71 (4), 69 (4), 57 (6), 44 (5), 43 (5), 41 (7), 32 (5), 28 (31), 27 (3), 20 (6), 18 (100), 17 (31).

IR (nujol): ν = 1780, 1750, 1720, 1700, 1480, 1460, 1408, 1290, 707 cm^{-1}.

UV (ethanol): λ = 265 nm, 286 nm (inflection), 305 nm (inflection) (Saturated solution, ε values not determined).

The filtrate from the first crystallization yields 0.110 g of **5a**.

***N,N'*-Bis(8b-benzyl-2-cyclohexyl-3-oxo-1,2,3,3a,4,8b-hexahydropyrrolo[3,4-*b*]indol-3a-yl)-oxamide (6a):**
To a solution of compound **2a** (0.1 g, 2.78 mmol) in dry pyridine (10 ml) in an apparatus protected from moisture, oxalyl chloride (0.39 g, 3.05 mmol) is added slowly with stirring. The mixture is stirred for 40 min longer at room temperature. Water (~ 30 ml) is added to the mixture, and the precipitated product is collected by filtration, then digested thoroughly with hot methanol. The product is filtered from the cooled methanol extract, dried, and recrystallized from dichloromethane/methanol to give colorless needles; yield: 730 mg (67%); m.p. 300.5–302°C (dec). An analytical sample is obtained by recrystallizing the product twice from dichloromethane/methanol (dichloromethane is removed by distillation until crystallization begins); m.p. 301–302° (dec).

$C_{48}H_{52}N_6O_4 \cdot 1/2\ H_2O$	calc.	C 73.35	H 6.80	N 10.69
(786.0 = 776.96 + 9.02)	found	73.46	6.78	10.76

MS (70 eV): *m/e* (rel. int. %) = 776 (0.03), 433 (1), 432 (2), 416 (0.06), 415 (0.2), 361 (0.5), 360 (1), 345 (2), 344 (7), 394 (8), 262 (5), 248 (3), 234 (4), 233 (4), 219 (3), 218 (6), 216 (4), 206 (3), 205 (8), 204 (4), 171 (7), 156 (3), 128 (4), 112 (3), 92 (3), 91 (23), 83 (2), 65 (3), 55 (6), 43 (3), 41 (6), 30 (4), 28 (10), 18 (100), 17 (22).

IR (nujol): ν = 3330, 1710, 1667, 1493 (sh), 1480, 1460, 754 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 242.5 (4.23) (shoulder), 294 m, (3.70).

^{1}H-NMR ($CDCl_3$/TMS_{int}; proton count is for half of the *bis* structure): δ = 8.03 (s, 1 H, exchanges with D_2O + NaOH,

—N—H); 7.42–6.17 (m, 9 H); 5.22 (s, 1 H, exchanges with D_2O, —N—H; 4.33–3.75 (m, 1 H, 1-cyclohexyl position); 4.07 (d, 1 H, J = 9.5 Hz, ring HCH); 3.46 (d, 1 H, J = 9.5 Hz, ring HCH); 3.04 (d, 1 H, J = 13 Hz, benzyl HCH); 2.85 (d, 1 H, J = 13 Hz, benzyl HCH); 2.33–0.83 ppm (br. m, 10 H, cyclohexyl).

2,10-Disubstituted 3a,11a-Dibenzyl-1,2,3,3a,9,11,11a-octahydrodipyrrolo[3,4-*b*:3′,4′-*b*′][1,3]diazeto[1,2-*a*:3,4-*a*′]diindoles – Dimers of 2-Substituted 8b-Benzyl-1,2,3-8b-tetrahydropyrrolo[3,4-*b*]indole (10a and 10b):

2-Cyclohexyl- or 2-methyl-3a-amino-8b-benzyl-1,2,3,3a,4,8b-hexahydropyrrolo[3,4-*b*]indole (**7a** or **7b**) is dissolved in 60% aqueous acetic acid (10 ml of 60% acetic acid per gram of **10a** or **10b**) and heated under reflux with stirring for 15 to 30 min. The mixture is cooled to room temperature and then added to a stirred, cold 2.5 normal solution of sodium hydroxide (50 ml per gram of **7**). The product is immediately precipitated as a white flocculent solid, which is collected by filtration, washed with water, air-dried, and recrystallized from chloroform or dichloromethane/ethanol. Exposure to light causes yellowing of the colorless crystals and lowering of the melting point.

3a,11a-Dibenzyl-1,2,3,3a,9,10,11,11a-octahydro-2,10-dicyclohexyldipyrrolo[3,4-b:3′,4′-b′][1,3]-diazeto-[1,2-a:3,4-a′]diindole (**10a**): Yield from 1.0 g of **7a**: 0.47 g (50%); colorless prisms, m.p. 249–250°C (dec), following crystallization from dichloromethane/95% ethanol. Allowing the substance to stand for 1–2 days in the light lowered the m.p. to ~ 241–242°C (dec).

$C_{46}H_{52}N_4$	calc.	C 83.59	H 7.93	N 8.48
(660.9)	found	83.27	7.82	8.21

MS (70 eV): *m/e* (rel. int. %) = 661 (4), 660 (8), 577 (1), 569 (4), 549 (5), 458 (6), 454 (3), 426 (3), 363 (3), 362 (9), 347 (4), 331 (6), 330 (4), 251 (4), 239 (4), 220 (7), 169 (12), 157 (7), 130 (6), 113 (4), 112 (37), 111 (4), 110 (4), 91 (10), 83 (5), 82 (5), 81 (3), 55 (13), 43 (3), 42 (3), 41 (8), 30 (13), 28 (10), 18 (100), 17 (23).

IR (nujol): ν = 1592, 1475, 1450, 764, 710 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 264 (4.33), 317 nm (3.70).

UV (ethanolic hydrochloric acid): λ_{max} (log ε) = 248 (4.29); 300 nm (3.72).

^{1}H-NMR($CDCl_3$/TMS_{int}; proton count is for half of the symmetrical dimer): 7.40–6.18 (m, 9 H_{arom}); 3.95 (d, 1 H, J = 5 Hz, ring HCH); 3.88 (d, 1 H, J = 5 Hz, ring HCH); 3.24 (d, 1 H, J = 14 Hz, benzyl HCH); 3.01 (d, 1 H, J = 9 Hz, ring HCH); 2.92 (d, 1 H, J = 14 Hz, benzyl HCH); 2.78 (d, 1 H, 9 Hz, ring HCH); ~ 2.59–2.00 (br. s, 1 H, 1-position of cyclohexyl), 1.86–0.71 ppm (br. m, 10 H, cyclohexyl).

3a,11a-Dibenzyl-1,2,3,3a,9,10,11,11a-octahydro-2,10-dimethyldipyrrolo[3,4-b:3′,4′-b′][1,3]diazeto[1,2-a:3,4-a′]diindole (**10b**): Yield of recrystallized dimer from 0.50 g of **7b**: 0.358 g (76%); colorless prisms, m.p. 235–237°C (dec). Two more recrystallizations from dichloromethane/ethanol give an analytical sample; m.p. 238–239°C (dec).

$C_{36}H_{36}N_4$	calc.	C 82.40	H 6.92	N 10.58
(524.8)	found	82.25	7.10	10.61

MS (70 eV): *m/e* (rel. int. %) = 525 (3), 524 (7), 481 (2), 438 (3), 437 (3), 433 (1), 391 (3), 390 (8), 347 (7), 342 (0.1), 318 (4), 263 (4), 262 (3), 226 (3), 220 (3), 183 (7), 171 (5), 130 (3), 91 (5), 57 (3), 44 (7), 43 (2), 42 (4), 28 (7), 18 (100), 17 (22).

High resolution MS: Formula (calc. *m/e*, measured *m/e*) = $C_{36}H_{36}N_4$ (524.2940, 524.2942); $C_{34}H_{31}N_3$ (481.2518, 481.2530); $C_{32}H_{26}N_2$ (438.2096, 438.2070), $C_{32}H_{25}N_2$ (437.2018, 437.2028).

IR (nujol): ν = 1600, 1478, 1453, 1242, 1228, 733, 704 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 261 (4.43), 311 (3.79) nm.

UV (ethanolic hydrochloric acid): λ_{max} (log ε) = 245 (4.34), 296 (3.74) nm.

^{1}H-NMR($CDCl_3$/TMS_{int}; proton count is for half of the symmetrical dimer): 7.69–6.54 (m, 9 H_{arom}); 4.18 (d, 1 H, J = 5 Hz, ring HCH); 3.53 (d, 1 H, J = 5 Hz, ring HCH); 3.34 (d, 1 H, J = 15 Hz, benzyl HCH); 3.34 (d, 1 H, J = 9.5 Hz, ring HCH); 3.14 (d, 1 H, J = 15 Hz, benzyl HCH); 2.62 (d, 1 H, J = 9.5 Hz, ring HCH); 2.21 ppm (s, 3 H, N—CH_3).

Mixed Diasteriomers of 3a,11a-Dibenzyl-1,2,3,3a,9,10,11,11a-octahydro-2,10-dicyclohexyldipyrrolo[3,4-*b*:3′,4′-*b*′][1,3]diazeto[1,2-*a*:3,4-*a*′]diindole (10a):

Compound **7a** (2.0 g) is dissolved in a solution of potassium hydroxide (40 g) in methanol (200 ml) and water (200 ml). The mixture is stirred at room temperature for 16.5 h, then extracted with chloroform (3 × 100 ml). The chloroform solution is extracted with water (80 ml), dried with magnesium sulfate, and concentrated under reduced pressure. The resulting oily residue is dissolved in methanol (40 ml) and a solid is obtained by concentrating and cooling the methanolic solution. A yellow brown powdery solid (0.4 g) is collected by filtration. After recrystallization from methanol the product melts at 105–115°C to a cloudy viscous oil, which turns clear at ~ 145°C. After another recrystallization the product melts in a similar manner but does not give a clear melt below ~ 200°C. Fractional recrystallization from 95% ethanol yields a first crop, m.p. 95–110°C and a second crop, m.p. 125–150°C. Both are colorless crystalline powders with essentially identical IR spectra that are very similar to the spectrum of the isomer of 241–242°C; total yield: ~ 0.2 g (10%).

$C_{46}H_{52}N_4$ (First Crop)	calc.	C 83.59	H 7.93	N 8.48
(660.9)	found	83.37	8.06	8.26
$C_{46}H_{52}N_4$ (Second Crop)	calc.	C 83.59	H 7.93	N 8.48
(660.9)	found	83.29	7.98	8.56

MS (70 eV): *m/e* (rel. int. %) 661 (2), 660 (5), 578 (.04), 577 (1), 570 (3), 569 (7), 550 (2), 549 (3), 535 (2), 534 (2), 458 (8), 445 (8), 444 (20), 362 (4), 353 (3), 347 (4), 333 (3), 332 (6), 331 (32), 330 (100), 329 (5), 284 (4), 371 (6), 270 (7), 269 (3), 257 (3), 256 (4), 240 (4), 239 (16), 238 (4), 221 (5), 220 (13), 219 (7), 218 (19), 217 (5), 206 (3), 169 (10), 158 (3), 157 (17), 156 (7), 155 (13), 144 (4), 143 (3), 142 (3), 130 (12), 129 (4), 126 (9), 127 (27), 124 (3), 111 (3), 110 (10), 96 (16), 92 (4), 91 (24), 83 (16), 82 (60), 81 (2), 68 (5), 67 (5), 65 (3), 57 (3), 56 (5), 55 (24), 44 (23), 43 (15), 42 (11), 41 (24), 39 (4), 30 (15), 29 (4), 28 (7), 27 (4), 18 (81), 17 (26). (The ratio of the intensity of the 330 mass peak to that of the 660 mass peak decreases from a value of 20 at 70 eV to 5 at 12 eV.)

IR (nujol): ν = 1600, 1475, 1451, 1368, 747, 737, 697 cm^{-1}.

UV (ethanol): λ_{max} (log ε) = 257 (4.28), 302 (3.70) nm.

UV (ethanolic hydrochloric acid): λ_{max} (log ε) = 244 (4.02), 290 nm (3.61).

^{1}H-NMR ($CDCl_3$/TMS_{int}; proton count is for one-half of the *bis*-structure): δ = 7.43–7.04 (m, ~ 9 H_{arom}); 4.23 (d, ~ 1 H, J = 5 Hz, ring HCH); 3.99 (d, ~ 1 H, J = 5 Hz, ring HCH); 3.80–2.76 (m, ~ 4 H); 2.48–2.17 (m, ~ 1 H); 2.10–0.95 ppm (m, ~ 10 H, cyclohexyl ring).

Conversion of Mixed Diastereomers of Dimer 10a to the High-Melting Form: A sample (150 mg; m.p. ~ 105–115°) of the product from the potassium hydroxide treatment of **7a** described above is heated under reflux in 20 ml of 75% aqueous acetic acid (20 ml). Following addition of the mixture to excess 2.5 normal sodium hydroxide, collection of the product by filtration, and crystallization from dichloromethane/ethanol, the form of **10a** melting at 246–248°C is obtained, identical to the product from **7a** produced by heating with 60% aqueous acetic acid; yield: 50 mg.

8b-Benzyl-2-cyclohexyl-1,2,3,3a,4,8b-hexahydropyrrolo[3,4-*b*]indole (4a):

A solution of compound **3a** (1 g) in anhydrous ether (50 ml) is added to a stirred solution of lithium aluminum hydride (1 g) in anhydrous ether (100 ml). The mixture is stirred and refluxed for 4.25 h. A 20% aqueous solution of sodium potassium tartrate (~ 3 ml) is added to destroy excess lithium aluminum hydride, the solids are removed by filtration, and then these are extracted with ether (2 × 50 ml). To the combined filtrate and ether extract, Skellysolve B is added and the solution distilled until no ether remains. The resulting clear Skellysolve B solution is concentrated to 5 ml. Following cooling

with a methanol-water-ice mixture, scratching the walls of the flask causes crystallization of a white solid, which is collected by filtration; yield: 0.750 g (85%); m.p. 96–98°C. The IR spectrum identifies the compound as **4a** (Ref. 1).

IR (nujol): ν = 3470, 2790, 1605, 1475, 1460, 1450, 1253, 1132, 749, 742, 693 cm^{-1}.

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