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A New Access to 2'-Amino-substituted Vinylindoles as Donor-activated Heterocyclic Dienes and their First Diels-Alder Reactions

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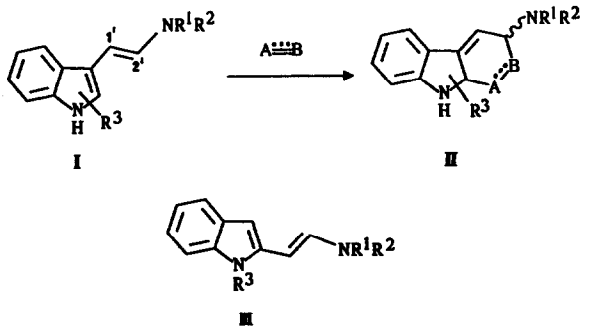
Abstract: Reactions of the 3-acylindoles **5**, **10**, and **15** with α-amino-α'-diphenylphosphinoyl-substituted carbanions gave rise to the 2'-amino-substituted 3- and 2-vinylindoles **7**, **12**, and **17** by way of the isolable carbinols **6**, **11**, and **16**. The heterocyclic dienes **7**, **12**, and **17** readily underwent Diels-Alder reactions with *N*-phenylmaleimide.

Diels-Alder reactions of 2- and 3-vinylindoles as 4π-electron components are now well established as a highly versatile procedure for regio- and stereocontrolled syntheses of [*b*]annellated indoles and/or carbazoles, including alkaloids.[1-7] This methodology should also constitute an attractive concept for new syntheses of heteroatom-functionalized carbazoles and annellated indoles, i.e. compounds selectively functionalized with alkoxy, alkylthio, or amino groups.[4-6] In this context, 2'-amino-functionalized 3-vinylindoles of the type I are of special interest[6] since they possess the structural feature (indole-C-C-NR_2) of dehydrotryptamine and some alkaloids of *Aristotelia* genera.[8] On the other hand, indolylenamines of the type I should also be of interest as building blocks for the synthesis of compounds exhibiting antidepressive and/or antitumor activity as well as of indole alkaloids biogenetically derived from L-tryptophan/tryptamine.[8,9]

Furthermore, isomeric 2-vinylindoles of the type III are also of general interest for the development of novel concepts for the synthesis of 2-amino-substituted carbazoles by a related Diels-Alder process. However, AM1 calculations on the parent compounds **IV** and **V** revealed[10] that these species can, in principle, be involved in HOMO(diene)-LUMO(dienophile) controlled [4 + 2]-cycloadditions[6] to produce [*b*]-annellated indoles. According to charge calculations[10] on the other hand, simple, one-bond formation reactions are also possible at the C1' position of **IV** or at the C3 and C1' positions of **V** in accordance with the general reactivity patterns of enamines.[11]

However as described previously,[6] the synthetic elaboration of I, e.g. from indole-3-acetaldehyde and morpholine or pyrrolidine, is a very laborious procedure and the relatively unstable species thus obtained were very difficult to characterize and underwent polymerization reactions instead of Diels-Alder reactions.[6,11]

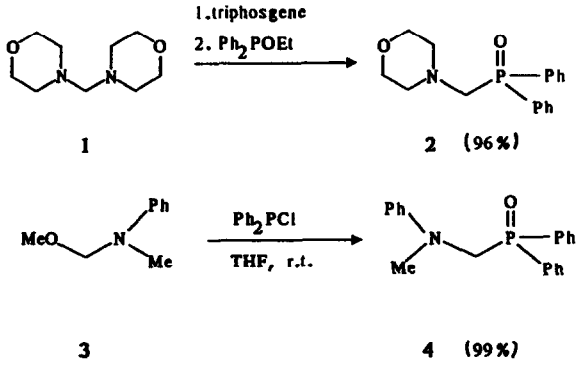


Scheme 1

In the present article, we report on a new synthesis of previously unknown 2'-amino-functionalized 3-vinylindoles of the types I and III starting from aminal or aminal ether substrates and demonstrate the enophilic reactivity of the electron-rich systems I and III towards *N*-phenylmaleimide (NPMI). The key synthetic step is a variant of the Horner-Wadsworth-Emmons reaction involving 2- or 3-acylindoles and *in situ* generated. highly reactive α-amino-α'-diphenylphosphinoyl-substituted carbanions.

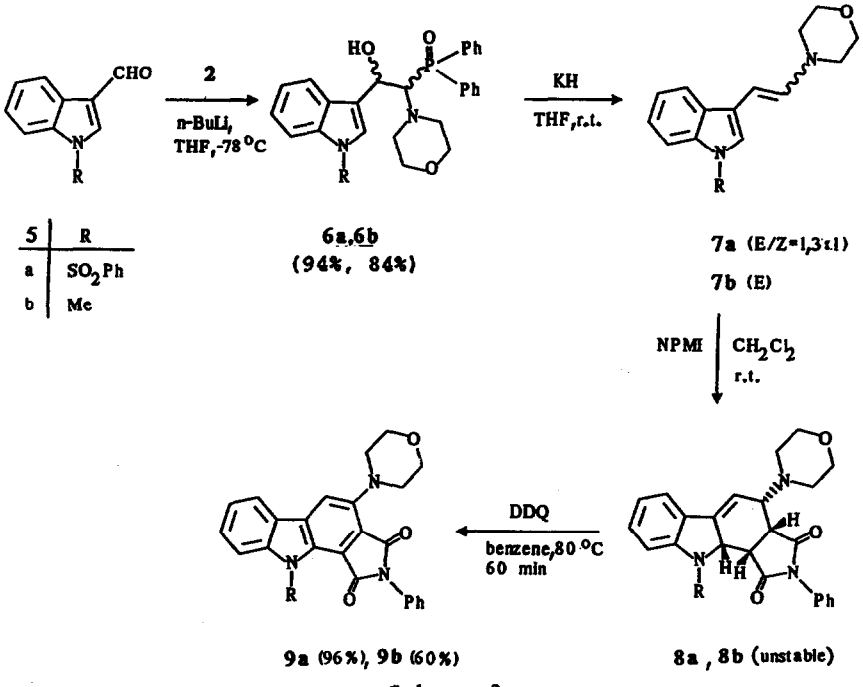
Thus, the diphenyl(*N*-morpholinomethyl)phosphine oxide (**2**)[12] required for the synthesis of the corresponding 3-vinylindoles was obtained easily by an aminal cleavage reaction[13] of **1** with phosgene (reagent used: triphosgene ≡ bis[trichloromethyl] carbonate) under an inert gas atmosphere in a special reaction vessel.[19] Subsequent reaction of the *N*-chloromethylmorpholine intermediate with ethyl diphenylphosphinite[14] gave **2** (Scheme 2) in a high yield. In a related procedure, the aminal ether **3**[15] was converted directly to **4** (99%) by an Arbuzov reaction with chloro(diphenyl)phosphine.[16]

In the key step, the indole-3-carbaldehydes **5a,b** each reacted with the *in situ* generated carbanion of **2** to produce a diastereoisomeric mixture of the indole-3-carbinols **6a,b** (Scheme 3). Potassium hydride-catalyzed 1,2-elimination on **6a,b** furnished the *N*-substituted 3-[2-(morpholin-4-yl)vinyl]indoles **7a,b** with a preference for (*E*)-stereoselectivity. Compounds **7a,b**, however, are extremely unstable (like the *N*-unsubstituted indole analogue[6]) and undergo rapid oligomerization and polymerization. The pattern of the vinylic protons (^{1}H-NMR) is indicative for the constitution and stereochemistry of **7** [*E*-**7a**: δ = 5.86 and 6.64 ppm (d, J = 14.2 Hz), *Z*-**7a**: δ = 5.29 and 5.94 ppm (d, J = 9.2 Hz); *E*-**7b**: δ = 5.65 and 6.57 ppm (d,



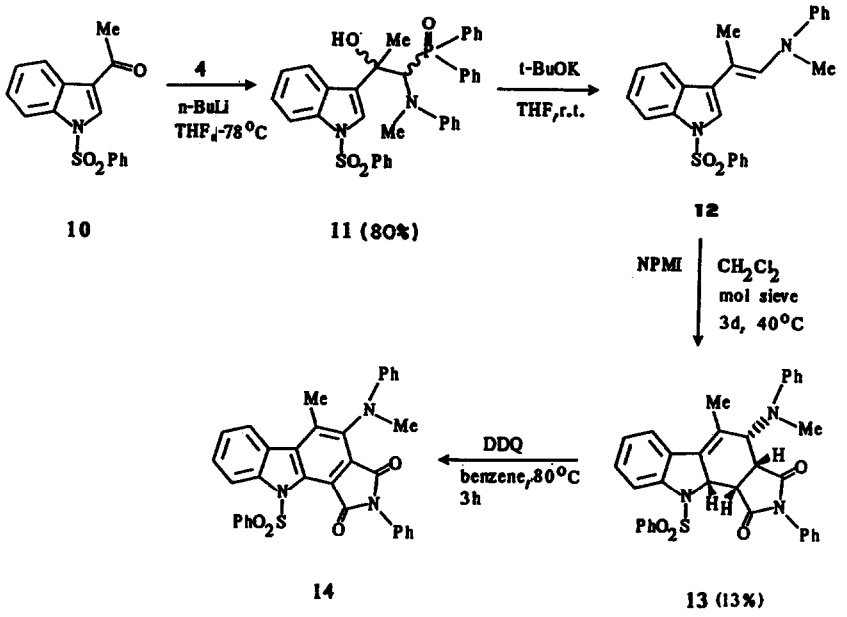
Scheme 2

J = 14.2 Hz)]. However, freshly prepared **7a,b** did participate in HOMO(diene)-LUMO(dienophile) controlled, stereoselective Diels-Alder reactions with NPMI (Scheme 3) to furnish the "endo"-cycloadduct **8a** and the less stable and difficult to purify **8b**, respectively. ^{1}H-NMR configurational analyses of **8** revealed that the "*E*"-stereochemistry of **7** is retained which is suggestive of a concerted process. In both cases, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ)-catalyzed dehydrogenation of **8** furnished the respective 14π-carbazoles **9a,b** in good yields.



Scheme 3

In a related procedure (Scheme 4), the 3-acetylindole **10** also reacted with the *in situ* generated carbanion of **4** to furnish a mixture of diastereomers of **11** (the reaction of **10** with the more basic anion of **2** failed because of enolate formation of **10**). Potassium *tert*-butoxide-induced 1,2-elimination of **11** gave rise to the *E*-3-vinylindole **12** as an oily product stereoselectively. The electron-rich **12** exhibits the same instability as mentioned for **7a,b**. However, freshly prepared **12** also underwent a Diels-Alder reaction with NPMI to give exclusively the "endo"-cycloadduct **13**. As outlined in Scheme 3, DDQ-catalyzed dehydrogenation of **13** led directly to the carbazole **14**.

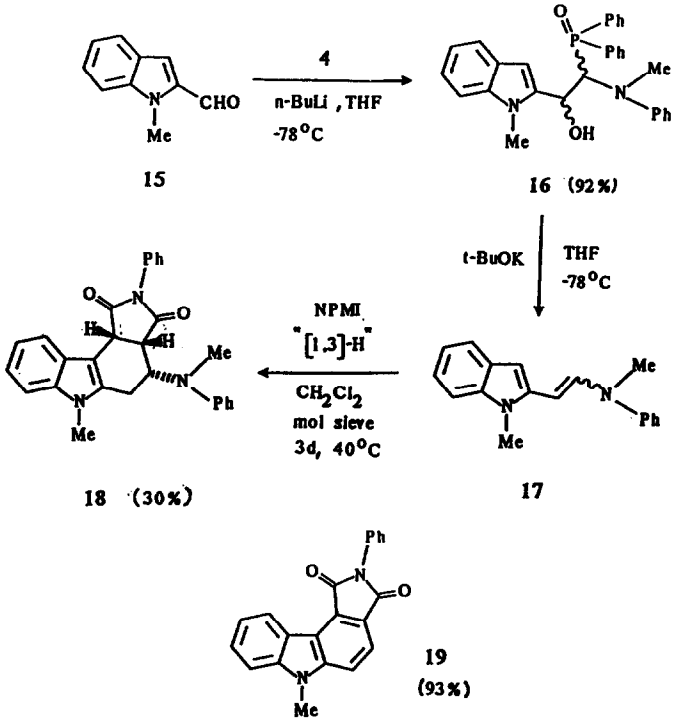


Scheme 4

In an analogous procedure, the indole-3-carbaldehyde **15** reacted with the carbanion of **4** to furnish the isomeric carbinols **16** which were transformed to the 2-vinylindole **17** by treatment with *t*-BuOK (Scheme 5). This heterocyclic diene **17**, which is also rather unstable and difficult to purify, again underwent a Diels-Alder reaction with *N*-phenylmaleimide to furnish the [*c*]annellated carbazole **18**. As is typical for cycloaddition reactions of 2-vinylindoles, the primarily formed [4 + 2]-cycloadduct is subsequently stabilized by a formal [1,3]-H shift (indolization process).[3] In addition, the carbazole **18** was dehydrogenated by DDQ to furnish the coplanar compound **19** by way of an additional elimination of *N*-methylaniline.

The vinylindoles **7**, **12**, and **16** were also subjected to reactions with a variety of other carbo- and heterodienophiles (e.g. dimethyl acetylenedicarboxylate, methyl acrylate, 4-phenyl-4*H*-1,2,4-triazoline-3,5-

dione, tetracyanoethylene) but we have not yet been able to isolate any identifiable compounds from the complex product spectra obtained. This is probably due to an enhanced ambident nucleophilic reactivity of the integrated enamine structures.



Scheme 5

The constitutions of products **6**, **9**, **11**, and **16** as well as the configurations of **7a,b**, **8a**, **13**, and **18** (**8b**, **12**, and **17** were too unstable) were elucidated by 400 MHz ^{1}H-NMR and, in some cases, by 100.6 MHz ^{13}C-NMR as well as ^{1}H,^{1}H-NOE experiments. The configuration given for product **12** is based on its relation to the configuration of the cycloadduct **13** which should be the result of a concerted Diels-Alder reaction. The diagnostically relevant NOE's calculated on an energy-minimized molecular structure (MMX molecular mechanics method)[17] for an "endo"-cycloadduct with an annellated *N*-methylsuccinimide ring and the same stereochemistry as **13** are depicted in Fig. 1

In summary, a new synthetic strategy for some 2'-amino-substituted 2- and 3-vinylindoles and, above all, the first Diels-Alder reactions of these classes of vinylindoles are presented. It should be mentioned that the carbazoles **8**, **14**, and **18** with a coplanar framework (chromophoric group) are of general interest as antitumor active intercalators to human B-DNA.[18]

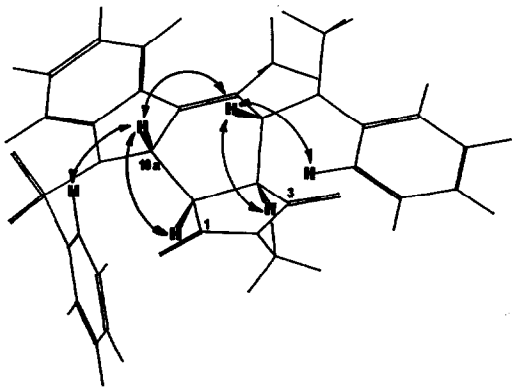


Fig. 1. MMX minimized molecular structure of the N^2-methyl derivative of **13**. The *N*-methyl derivative was chosen in order to reduce the computation time and for the sake of better clarity. The bis-annellated cyclohexene ring adopts a twisted boat conformation which is fully compatible with the ^{1}H-NMR data. The diagnostic ^{1}H,^{1}H-NOE's for clarification of the relative configuration are depicted with double arrows indicating magnetization transfer.

EXPERIMENTAL SECTION

Melting points were determined on a Büchi SMP-20 apparatus and are uncorrected. Mass spectra were recorded on a Varian MAT CH 7 spectrometer at an ionization voltage of 70 eV; FD-mass spectra were recorded on a Finnigan MAT 90 spectrometer. ^{1}H- and ^{13}C-NMR spectra (400 and 100.6 MHz) were obtained on a Bruker WM 400 spectrometer and 200 MHz ^{1}H-NMR spectra on a Bruker AC 200 spectrometer (δ, ppm scale, TMS as internal standard). The C,H,N analyses were performed with a Carlo Erba Strumentazione 1164 apparatus. For flash chromatography, Merck silica gel 60 (grain size 0.040-0.063 mm) was used; for column chromatography, Merck silica gel 60 (grain size 0.063-0.200 mm) was used. All reactions were performed in highly pure, anhydrous solvents under a nitrogen atmosphere. In those reactions in which racemic products are formed the nomenclature and structures of only one of the enantiomers are given.

Diphenyl(N-morpholinomethyl)phosphine Oxide (**2**).

A solution of the aminal **1** (3.24 g, 17.4 mmol) in 10 ml *n*-hexane was placed in a nitrogen-flushed special reaction vessel (for details of the apparatus, see ref.[19]). A solution of triphosgene (2.15 g, 7.25 mmol) in 30 ml *n*-hexane was added through the rubber septum and the reaction mixture was warmed gently until colourless crystals began to separate. After crystal formation was complete, the nitrogen flow to the apparatus was changed, the solvent was forced out, and the crystals were washed several

times with *n*-hexane. The crystals were then dissolved in 20 ml benzene, the solution was cooled in a water bath, and a solution of ethyl diphenylphosphinite (4.3 g, 18.24 mmol) in 40 ml benzene was added dropwise. The resultant mixture was heated under reflux for about 1 h and then, while still hot, forced under a nitrogen atmosphere through the sintered glass pad into a flask. Colourless crystals formed spontaneously, the crystals were separated from the solvent, and dried. Yield: 5.03 g (96%), m.p. 160 °C (benzene). Anal. calcd. for $C_{17}H_{20}NO_2P$ (301.22): C 67.76, H 6.69, N 4.65; found: C 67.70, H 6.71, N 4.71. MS (*m/e*): 301 ($M^{+\cdot}$, 0.4%), 283 (10%), 100 (100%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.62 (s, 4H), 3.21 (d, ^3J = 6.7 Hz, 2H), 3.60 (mc, 4H), 7.47 (mc, 6H, aromatic), 7.76 (mc, 4H, aromatic).

Diphenyl(N-methyl-N-phenylaminomethyl)phosphine Oxide (**4**).

Chlorodiphenylphosphine (1.46 g, 6.6 mmol) and *N*-methoxymethyl-*N*-methylaniline (**3**; 1 g, 6.6 mmol) in 20 ml THF were stirred at room temperature for 2 h. After removal of the solvent, colourless crystals remained. Yield: 2.1 g (99%), m.p. 122 °C (THF). Anal. calcd. for $C_{20}H_{20}NOP$ (321.36): C 74.75, H 6.27, N 4.36; found: C 74.45, H 5.99, N 4.48. MS (*m/e*): 321 ($M^{+\cdot}$, 2.8%), 120 (100%), 77 (9%). ^{1}H-NMR (DMSO-d_6, 200 MHz): δ 2.80 (s, 3H, CH_3), 4.40 (d, ^2J = 1.7 Hz, 2H, CH_2), 6.60 (t, ^3J = 7.1 and 7.0 Hz, 1H, aromatic), 6.78 (d, ^3J = 8.4 Hz, 2H, aromatic), 7.06 (t, ^3J = 7.6 and 7.4 Hz, 2H, aromatic), 7.41-7.61 (m, 6H, aromatic), 7.84-7.93 (m, 4H, aromatic).

Diphenyl[2-hydroxy-2-[(N-phenylsulfonyl)-indol-3-yl]-1-morpholino-ethyl]phosphine Oxide (**6a**).

A suspension of **2** (1.65 g, 5.5 mmol) in 20 ml anhydrous THF at -30 °C was treated under a nitrogen atmosphere with 3.5 ml of a 1.6 molar solution of *n*-BuLi in *n*-hexane. After 30 min, *N*-phenylsulfonylindole-3-carbaldehyde (**5a**; 1.54 g, 5.4 mmol) in 20 ml THF was added. After a further 30 min, the mixture was allowed to warm to room temperature and saturated sodium chloride solution was added with stirring. A spontaneous yellow coloration formed. The organic phase was separated and the aqueous phase was extracted several times with dichloromethane. After drying with $MgSO_4$ and evaporation of the organic phases, an amorphous mass was obtained. Yield: 3.02 g (94%; diastereomeric mixture). The first fraction was separated from this crude product by flash chromatography (petroleum ether/ethyl acetate, 4/1) as colourless crystals. M.p. 189 °C (diethyl ether). Anal. calcd. for $C_{32}H_{31}N_2O_5SP$ (586.65): C 65.51, H 5.33, N 4.78; found: C 65.46, H 5.40, N 4.78. FD-MS (*m/e*): 586 ($M^{+\cdot}$, 42%), 542 (24%), 367 (100%), 300 (80%), 284 (27%). ^{1}H-NMR (CD_2Cl_2, 400 MHz): δ 2.76 (mc, 4H), 3.10 (mc, 2H), 3.25 (mc, 2H), 3.84 (mc, 1H), 4.90 (d, ^3J = 4.0 Hz, 1H, OH, exchangeable with D_2O), 5.48 (mc, 1H), 7.17-7.90 (m, 20H, aromatic).

Diphenyl{2-hydroxy-2-[(N-methyl)-indol-3-yl]-1-morpholinoethyl}phosphine Oxide (**6b**).

Prepared as described for **6a** from *N*-methylindole-3-carbaldehyde (860 mg, 5.4 mmol) and obtained as a colourless, amorphous mass. Yield: 2.13 g (84%), m.p. 163 °C. FD-MS (*m/e*): 460 ($M^{+\cdot}$, 100%).

(E/Z)-3-(2-Morpholinoethenyl)-N-*phenylsulfonylindole* (**7a**).

Compound **6a** (3.02 g, 5.1 mmol) was dissolved in 30 ml anhydrous THF and the solution was purged with nitrogen. Potassium hydride (241 mg, 6 mmol; the mineral oil suspension was previously washed with three 10 ml portions of *n*-hexane) was added. After 2 h, 200 ml *n*-hexane and 50 ml water were added and the mixture was stirred for 1 h more. The organic phase was then separated, dried with $MgSO_4$, and concentrated to furnish the crude product. Yield: 1.35 g. $C_{20}H_{20}N_2O_3S$ (368.46). FD-MS (*m/e*): 368 ($M^{+\cdot}$, 100%). ^{1}H-NMR ($CDCl_3$, 400 MHz, *E/Z* = 1.3:1): δ 5.86 and 6.64 (each d, ^3J = 14.2 Hz, vinyl protons of *E*-**7a**), 5.29 and 5.94 (each d, ^3J = 9.2 Hz, vinyl protons of *Z*-**7a**).

(E)-3-(2-Morpholinoethenyl)-N-*methylindole* (**7b**).

Prepared as described for **7a** from **6b** (2.13 g, 0.46 mmol) in 30 ml dimethoxyethane. Yield of crude product: 1.3 g. $C_{15}H_{18}N_2O$ (242.32). FD-MS (*m/e*): 242 ($M^{+\cdot}$, 100%). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 5.65 and 6.75 (each d, ^3J = 14.2 Hz, vinyl protons of *E*-**7b**).

4a-Morpholino-2-phenyl-10-phenylsulfonyl-1,2,3,3aß,4ß,10,10aß-octahydropyrrolo[3,4-a]carbazole-1,3-dione (**8a**).

The crude product **7a** (350 mg, 0.95 mmol) was dissolved in 30 ml anhydrous CH_2Cl_2, *N*-phenylmaleimide (320 mg, 2 mmol) was added, and the mixture was stirred at room temperature for 3 h. Separation by column chromatography (ethyl acetate) gave rise to colourless crystals. Yield: 95 mg (18% based on the crude substrate), m.p. 198 °C (ethyl acetate). Anal. calcd. for $C_{30}H_{27}N_3O_5S$ (541.63): C 66.53, H 5.02, N 7.76; found: C 66.42, H 5.17, N 7.81. FD-MS (*m/e*): 541 ($M^{+\cdot}$, 4%), 386 (100%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.40 (m_c, 2H, morpholine-CH_2), 2.91 (m_c, 3H, morpholine-CH_2 and C4-H), 3.72 (dd, ^3J = 8.5 and 6.2 Hz, 1H, C3a-H), 3.83 (m_c, 4H, morpholine-CH_2), 4.15 (pseudo-t, ^3J = 8.4 and 7.4 Hz, 1H, C10b-H), 4.74 (dd, ^3J = 7.4 Hz, ^4J = 1.0 Hz, 1H, C10a-H), 6.19 (dd, ^3J = 8.5 Hz, ^4J = 1.0 Hz, 1H, C5-H), 6.90-7.90 (m, 14H, aromatic). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 38.4, 43.8, 52.9 (2 × CH_2), 61.3, 66.7 (2 × CH_2), 115.3, 115.8, 120.9, 124.1, 125.7, 126.4, 127.2, 128.4, 128.8, 129.3, 130.8, 131.6, 133.6, 136.3, 137.6, 144.9, 172.0 (CO), 173.1 (CO).

4-Morpholino-2-phenyl-10-phenylsulfonyl-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-1,3-dione (**9a**).

The carbazole **8a** (50 mg, 0.09 mmol) and DDQ (25 mg, 0.11 mmol) in 20 ml benzene were heated under reflux for 30 min. The benzene was then evaporated under reduced pressure and the residue was separated by column chromatography (petroleum ether/ethyl acetate, 1/1) to furnish fluorescent

yellow crystals. Yield 46 mg (96%), m.p. 212 °C (ethyl acetate/*n*-hexane). Anal. calcd. for $C_{30}H_{23}N_3O_5S$ (537.60): C 67.03, H 4.31, N 7.82; found: C 66.95, H 4.40, N 7.86. MS (*m/e*): 537 ($M^{+\cdot}$, 60%), 396 (100%). ^{1}H-NMR (CD_2Cl_2, 400 MHz): δ 3.37 (m_c, 4H, morpholine-CH_2), 4.01 (m_c, 4H, morpholine-CH_2), 7.30-7.60 (m, 12H, aromatic), 7.67 (s, 1H, C5-H), 7.84-7.95 (m, 2H, aromatic).

10-Methyl-4-morpholino-2-phenyl-1,2,3,10-tetrahydropyrrolo[3,4-a]-carbazole-1,3-dione (**9b**).

The crude product **7b** (245 mg, 1mmol) was dissolved in anhydrous CH_2Cl_2, *N*-phenylmaleimide (175 mg, 1.01 mmol) was added, and the mixture was stirred for 3 h. The primarily formed adduct could not be worked-up by column chromatography. Hence, the reaction solution was concentrated, the residue was dissolved in 25 ml benzene, DDQ (454 mg, 2 mmol) was added, and the resultant mixture was heated under reflux for 1 h. The benzene was evaporated and the residue worked-up by column chromatography (ethyl acetate) to furnish red crystals. Yield: 245 mg (60%), m.p. 231 °C (ethyl acetate). Anal. calcd. for $C_{25}H_{21}N_3O_3$ (411.46): C 72.98, H 5.15, N 10.21; found: C 73.08, H 5.23, N 10.10. FD-MS (*m/e*): 411 ($M^{+\cdot}$, 100%), 342 (5%). ^{1}H-NMR (CD_2Cl_2, 400 MHz): δ 3.30 (m_c, 4H, morpholine-CH_2), 3.93 (m_c, 4H, morpholine-CH_2), 4.41 (s, 3H, NCH_3), 7.30-7.63 (m, 8H, aromatic), 8.01 (s, 1H, C5-H), 8.13 (d, ^3J = 7.8 Hz, 1H, aromatic).

Diphenyl[2-hydroxy-1-(N-methyl-N-phenylamino)-2-(N-phenylsulfonylindol-3-yl)propyl]phosphine Oxide (**11**).

Diphenyl(*N*-methyl-*N*-phenylaminomethyl)phosphine oxide (**4**; 1 g, 3.1 mmol) was dissolved in 20 ml THF and the solution was purged with nitrogen. The solution was cooled to -30 C and 2 ml *n*-BuLi (1.6 molar solution in *n*-hexane) were added. After cooling to -78 °C, a solution of **10** (900 mg, 3 mmol) in 20 ml THF was added dropwise. The mixture was allowed to warm to room temperature after 30 min and then concentrated to leave a brown, amorphous mass. Yield: 1.55 g (80%, diastereomeric mixture). Separation by flash chromatography (petroleum ether/ethyl acetate, 1/1) gave 2 fractions. *Fraction 1*: colourless crystals, m.p. 192 °C (toluene); *Fraction 2*: colourless crystals, m.p. 173 °C (ethyl acetate). Anal. calcd. for $C_{36}H_{33}N_2O_4SP$ (620.71): C 69.66, H 5.36, N 4.51; found for fraction 1: C 69.60, H 5.42, N 4.50; found for fraction 2: C 69.57, H 5.47, N 4.61. FD-MS (*m/e*): fraction 1: 620 ($M^{+\cdot}$, 100%), 600 (19%), 321 (5%); fraction 2: 620 ($M^{+\cdot}$, 100%), 600 (13%), 402 (3%), 321 (16%). ^{1}H-NMR (acetone-d_6, 200 MHz): δ fraction 1: 1.41 (d, ^4J = 0.8 Hz, 3H, CH_3), 2.95 (br. s, 1H, OH, exchangeable with D_2O), 3.08 (s, 3H, NCH_3), 5.41 (dd, ^2J = 10.6 Hz, ^4J = 0.8 Hz, 1H, propyl-H), 6.72-8.04 (m, 25H, aromatic), δ fraction 2: 1.95 (d, ^4J = 0.5 Hz, 3H, CH_3), 2.83 (s, 3H, NCH_3), 2.92 (br. s, 1H, OH, exchangeable with D_2O), 5.54 (dd, ^2J = 9.6 Hz, ^4J = 0.5 Hz, 1H, propyl-H), 6.46-7.98 (m, 25H, aromatic).

5-Methyl-4α-(N-methyl-N-phenylamino)-2-phenyl-10-phenylsulfonyl-1,2,3,3aß,4ß,10,10aß,10bß-octahydropyrrolo[3,4-a]carbazole-1,3-dione (**13**).

The diastereomeric mixture **11** (1 g, 1.6 mmol) was dissolved in 15 ml THF and then added dropwise under nitrogen to a suspension of potassium *t*-butoxide (350 mg) in 10 ml THF at -78 °C. The mixture was allowed to warm to room temperature and stirred for 45 min. It was then treated with 75 ml saturated sodium chloride solution, the phases were separated, and the aqueous phase was washed several times with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and concentrated. Since flash chromatographic work-up was not possible because of the instability of the product, the crude mixture (230 mg) was dissolved in 20 ml CH_2Cl_2 and treated with molecular sieve (3 g, 4 Å). *N*-Phenylmaleimide (150 mg, 0.87 mmol) was then added and the mixture was warmed at 40 °C for 3 days. After filtration, concentration, and column chromatographic separation (petroleum ether/ethyl acetate), colourless crystals were obtained. Yield: 70 mg (13% based on compound **11**), m.p. 219 °C (ethyl acetate). Anal. calcd. for $C_{34}H_{29}N_3O_4S$ (575.69): C 70.94, H 5.08, N 7.30; found: C 70.90, H 5.13, N 7.34. FD-MS (*m/e*): 575 ($M^{+\cdot}$, 100%), 530 (9%), 402 (11%). ^{1}H-NMR (DMSO-d_6, 400 MHz): δ 1.85 (s, 3H, C5-CH_3), 3.07 (s, 3H, NCH_3), 4.00 (m_c, 1H, C3a-H), 4.18 (pseudo-t, ^3J = 8.05 and 7.2 Hz, 1H, C10b-H), 4.65 (d, ^3J = 5.18 Hz, 1H, C4-H), 5.26 (dd, ^3J = 7.2 Hz, ^5J = 1.9 Hz, 1H, C10a-H), 6.72-7.68 (m, 17H, aromatic), 8.00 (d, ^3J = 7.5 Hz, 2H, SO_2-phenyl-H_{ortho}).

5-Methyl-4-(N-methyl-N-phenylamino)-2-phenyl-10-phenylsulfonyl-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-1,3-dione (**14**).

Prepared as described for **9a** from **13** (30 mg, 0.052 mmol) in 10 ml benzene and DDQ (20 mg, 0.088 mmol), reaction time 3 h, and obtained as yellow crystals. Yield: 28 mg (95%), m.p. 252 °C (ethyl acetate). Anal. calcd. for $C_{34}H_{25}N_3O_4S$ (571.66): C 71.44, H 4.41, N 7.35; found: C 71.39, H 4.51, N 7.40. FD-MS (*m/e*): 571 ($M^{+\cdot}$, 12%), 557 (100%), 466 (6%). ^{1}H-NMR (acetone-d_6, 400 MHz): δ 2.13 (s, 3H, CH_3), 2.96 (s, 3H, NCH_3), 6.96-8.08 (m, 19H, aromatic).

Diphenyl[2-hydroxy-2-(N-methylindol-2-yl)-1-(N-methyl-N-phenylamino)-ethyl]phosphine Oxide (**16**).

Prepared as described for **11** from **4** (1.74 g, 5.4 mmol) in 30 ml THF and **15** (850 mg, 5.34 mmol) in 10 ml THF and obtained as a light brown, amorphous mass. Yield: 2.39 g (92%). Flash chromatography (ethyl acetate) resulted in the separation of two fractions. *Fraction 1*: colourless crystals, m.p. 167 °C (ethyl acetate); *Fraction 2*: colourless crystals, m.p. 149 °C (ethyl acetate). Anal. calcd. for $C_{30}H_{29}N_2O_2P$ (480.55): C 74.98, H 6.08, N 5.83; found for fraction 1: C 74.79, H 6.09, N 5.69; found for fraction 2: C 74.90, H 5.98, N 5.80. FD-MS (*m/e*): fraction 1: 480 ($M^{+\cdot}$, 100%), 320 (4%); fraction 2: 480 ($M^{+\cdot}$, 100%), 320 (6%). ^{1}H-NMR (acetone-d_6, 200 MHz): δ fraction 1: 2.92 (br. s, 1H OH, exchangeable with D_2O), 3.13 (s, 3H, NCH_3), 3.85 (s, 3H, indole NCH_3), 5.32 (pseudo-t, ^3J = 8.1 and 8.2 Hz, 1H, ethyl C2-H), 5.80 (m_c, 1H, ethyl C1-H), 6.40 (s, 1H, indole C3-H), 6.59-7.79 (m, 19H, aromatic); δ fraction 2: 2.83 (s, 3H,

NCH_3), 2.92 (br. s, 1H, OH, exchangeable with D_2O), 3.89 (s, 3H, indole NCH_3), 5.54 (dd, ^3J = 5.7 and 9.6 Hz, 1H, ethyl C2-H), 5.96 (m_c, 1H, ethyl C1-H), 6.42 (s, 1H, indole C3-H), 6.47-8.18 (m, 19H, aromatic).

6-Methyl-4α-(N-methyl-N-phenylamino)-2-phenyl-1,2,3,3aß,4ß,5,6,10cß-octahydropyrrolo[3,4-c]carbazole-1,3-dione (**18**).

Prepared as described for **13** from compound **16** (950 mg, 1.98 mmol) in 40 ml THF, with potassium *t*-butoxide (500 mg, 4.45 mmol) and *N*-phenylmaleimide (695 mg, 4 mmol) and separated by flash chromatography (petroleum ether/ethyl acetate, 5/1) to give colourless crystals. Yield: 260 mg (30%), m.p. 244 °C (ethyl acetate). Anal. calcd. for $C_{28}H_{25}N_3O_2$ (435.52): C 77.22, H 5.79, N 9.65; found: C 77.12, H 5.87, N 9.70. FD-MS (*m/e*): 435 ($M^{+\cdot}$, 100%), 326 (2%), 218 (9%). ^{1}H-NMR (CD_2Cl_2, 400 MHz): δ 3.09 (dd, ^2J = 15.3 Hz, ^3J = 4.6 Hz, 1H, C5-Hα), 3.14 (s, 3H, NCH_3), 3.32 (ddd, ^2J = 15.3 Hz, ^3J = 7.7 Hz, , ^4J = 1.8 Hz, 1H, C5-Hß), 3.68 (s, 3H, indole NCH_3), 3.93 (ddd, ^3J = 7.8 and 3.7 Hz, ^4J = 1.8 Hz, 1H, C3a-H), 4.58-4.63 (m_c, 2H, C4-H, C10c-H), 6.78 (pseudo-t, ^3J = 7.3 and 7.2 Hz, 1H, aromatic), 6.90 (d, ^3J = 8.3 Hz, 2H, aniline phenyl-H_{ortho}), 7.09-7.95 (m, 11H, aromatic).

6-Methyl-2-phenyl-1,2,3,6-tetrahydropyrrolo[3,4-c]carbazole-1,3-dione (**19**).

Prepared as described for compound **9a** from **18** (100 mg, 0.23 mmol) and DDQ (75 mg, 0.33 mmol), reaction time 24 h, and obtained as light yellow crystals. Yield: 70 mg (93%), m.p. 263 °C (ethyl acetate). Anal. calcd. for $C_{21}H_{14}N_2O_2$ (326.36): C 77.29, H 4.32, N 8.58; found: C 77.34, H 4.50, N 8.62. MS (*m/e*): 326 ($M^{+\cdot}$, 100%), 282 (36%), 179 (24%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.88 (s, 3H, CH_3), 7.33-7.63 (m, 9H, aromatic), 7.96 (d, ^3J = 8.3 Hz, 1H, C5-H), 9.01 (d, ^3J = 8.3 Hz, 1H, C4-H).

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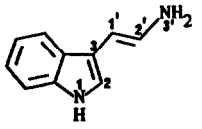
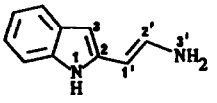


IV



V

HOMO coefficients (total charges) from **IV**: N1 = 0.3299 (-0.22), C2 = -0.3882 (-0.09), C3 = - 0.4062 (-0.08), C1′ = 0.3736 (-0.18), C2′ = 0.3760 (-0.06), N3′ = -0.3111 (-0.33); HOMO coefficients (total charges) from **V**: N1 = 0.0792 (-0.22), C2 = -0.3859 (0.05), C3 = -0.4692 (-0.22), C1′ = 0.3381 (-0.25), C2′ = 0.3163 (±0.00), N3′= -0.2852 (-0.34).

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