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Preparation of 3,4-enynoindoles via directed lithiation and application to the synthesis of 3,4-carbocycloindoles

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Abstract—Lithiation at C4 of the indole nucleus is readily directed by several functional groups. The 4-substituted indoles thus obtained are transformed into suitable substrates for metathesis reactions. Ring-closing metathesis effected on these compounds lead to skeletons related to several indole alkaloids. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

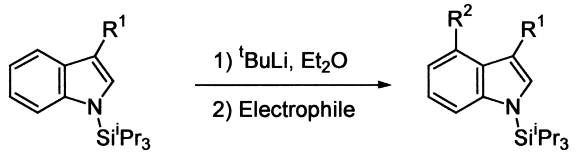
The synthesis of 3,4-disubstituted indoles is an important step to obtain several biologically active alkaloids, such as ergot alkaloids, hapalindoles and others. The formation of these compounds usually implies to construct the pyrrole ring from a suitable benzenoid precursor.[1] The direct functionalization of the 4 position in the indole has been scarcely done and normally goes via thallation[2] or mercuration[3] reactions. Directed lithiation[4] of the 4 position has only been reported in few substrates derived from gramine.[5] Functionalization at the 7 position of the indole has been reported using this methodology.[6] Additionally, the directed lithiation has been applied for the synthesis of claviciptic acid,[7] and other related alkaloids.[8] In this paper, we have extended the directed lithiation of indole at the 4 position of other substrates and we have transformed the resulting compounds into tricyclic indoles related to natural products, by means of metathesis reactions catalyzed by ruthenium complexes.[9]

2. Results and discussion

A modification of the methodology reported by Iwao[5] was applied to several substrates, bearing several directing groups (Scheme 1). Thus, lithiation at C4 of indoles **1**–**4** was accomplished with ^{t}BuLi in ether and after addition of different electrophiles the corresponding 3,4-disubstituted indoles **5**–**16** were obtained. The results are summarized in Table 1.

Several electrophiles were introduced successfully using dimethylaminomethyl and methoxymethyl as directing groups. Aldehydes reacted smoothly in good yields, and bromine and iodine were readily introduced. Reactive halides such as allyl bromide gave poor results in agreement with those reported in the literature for other halides.[10] Propylene oxide reacted with the gramine derivative **1** in excellent yield but with ether **3** it gave a mixture of the desired 4-substituted compound **15**, and compound **17** (Scheme 2). The formation of **17** can be explained if the lithiation of **3** occurs partially at C2. Then the silyl group migrates to that position as described recently for other indoles lithiated with BuLi.[11] Methoxide is then lost to give intermediate **C** which reacts with ^{t}BuLi to give **D**. Finally, the electrophile reacts with the anionic nitrogen to yield **17**. Selecting suitable reaction conditions, the formation of **17** can be minimized to only 10% (Scheme 2). We have not observed compounds analog to **17** in the reaction with DMF.

On the other hand, compounds **2** and **4**, with an extra methylene in the directing group, did not react, showing that in these cases the directing group is too far to effect its function. We also tried to use an amide to direct lithiation in the indole. Thus, compound **18a** was reacted under the same conditions using propylene oxide as electrophile. The major



1-4 **5-16**

Scheme 1.

Keywords: indoles; lithiation; enynes; metathesis; cyclizations.

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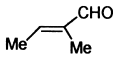
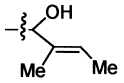
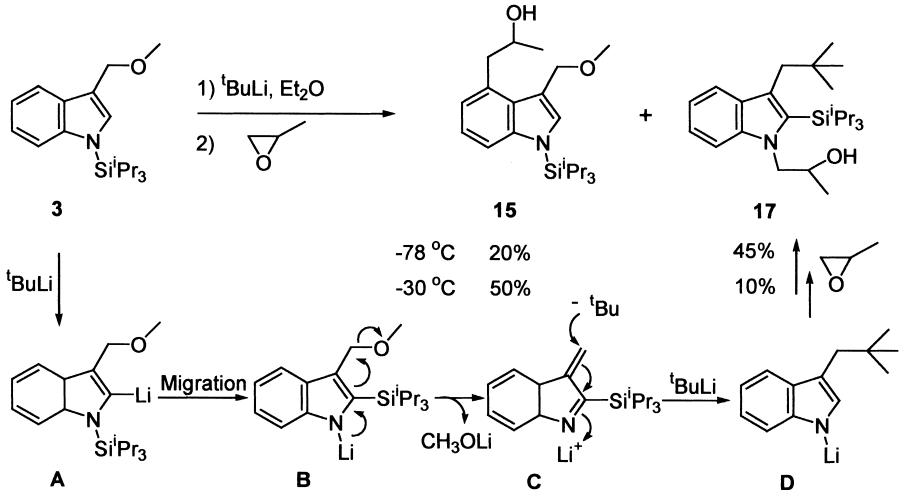
Table 1. Funtionalization at C4 in indoles by directed lithiation

Subs.	R^1	Electrophile	R^2	Prod.	Yield[a] (%)
1	CH_2NMe_2	I_2	I	**5**	80
1	CH_2NMe_2	CH_3CHO	$CHOHCH_3$	**6**	70
1	CH_2NMe_2	CH_2═$CHCHO$	$CHOHCH$═CH_2	**7**	80
1	CH_2NMe_2			**8**	90
1	CH_2NMe_2			**9**	98
1	CH_2NMe_2	CH_2═$CHCH_2Br$	CH_2CH═CH_2	**10**	20
1	CH_2NMe_2		$CH_2CHOHCH_3$	**11**	90
1	CH_2NMe_2	CBr_4	Br	**12**	60
2	$(CH_2)_2NMe_2$		$CH_2CHOHCH_3$	**13**	<5[b]
3	CH_2OMe	DMF	CHO	**14**	55
3	CH_2OMe		$CH_2CHOHCH_3$	**15**	50[c]
4	$(CH_2)_2OMe$	I_2	I	**16**	<5

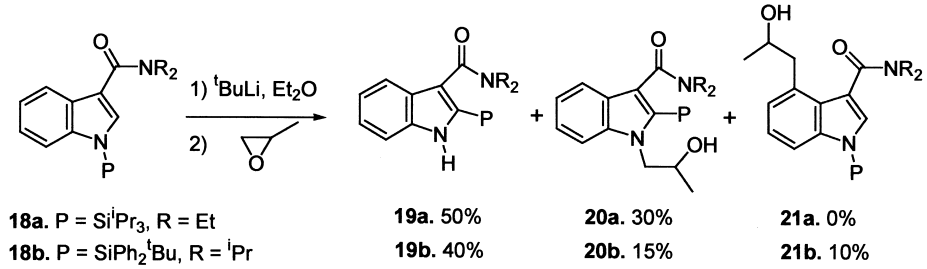
[a] Of pure material with correct spectroscopic data (^1H, ^{13}C NMR, IR).
[b] Another 60% of 2-substituted compound was obtained.
[c] See Scheme 2.

product in this reaction was the 2-silylated indole **19a** (50%), and also 30% of compound **20a** was formed. This implies a C2 lithiation, followed by migration of the triisopropylsilyl group, and partial reaction at the indole nitrogen.

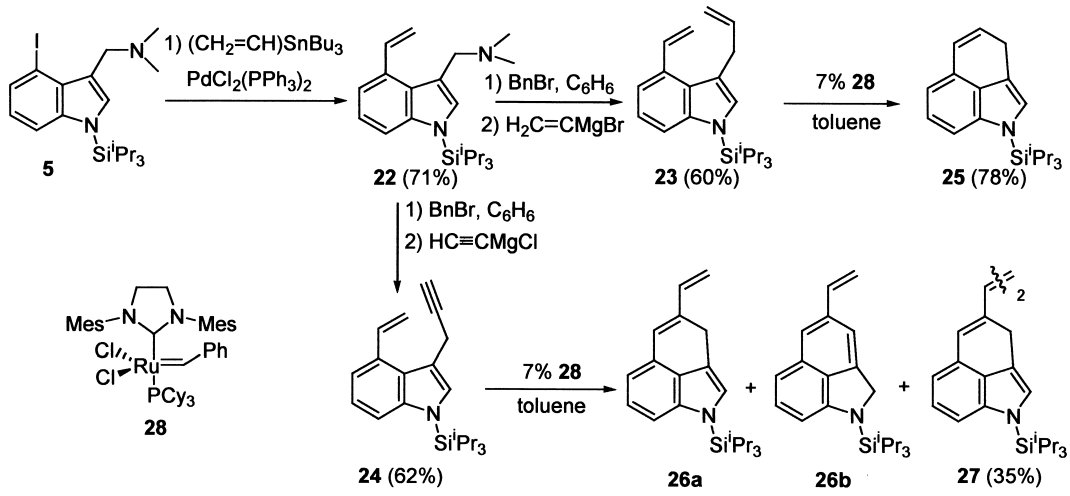
We tried to favor lithiation at C4 by increasing the steric demand of the substituents in the starting material, and thus prepared compound **18b**. The reaction of **18b** afforded 40% of the 2-silylated compound **19b**, 15% of compound **20b**



Scheme 2. The reaction of compound **3** with ^{t}BuLi and propylene oxide.



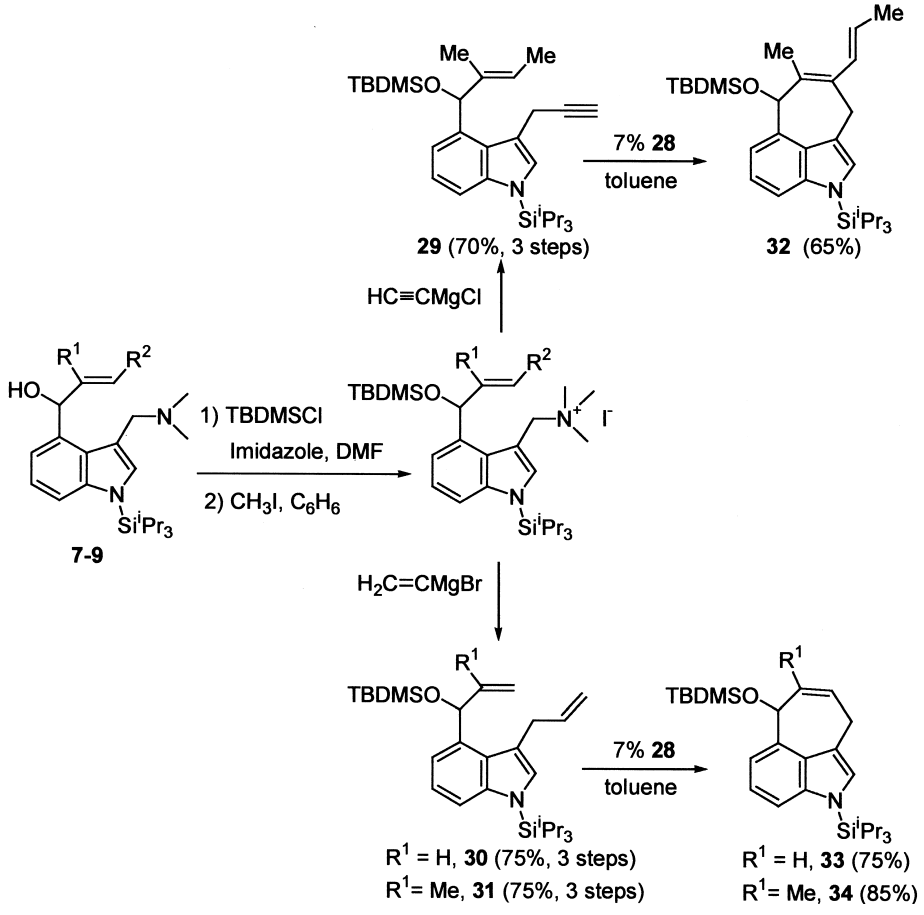
Scheme 3. The reaction of amides **18** with ^{t}BuLi and propylene oxide.



Scheme 4. Metathesis reactions of compounds **23** and **24**.

and only 10% of the desired 4-substituted compound **21b** (Scheme 3). From these results, we conclude that the amide is not a good directing group for the 4 position in the indole nucleus.

Some of the 3,4-disubstituted indoles described above were transformed into suitable precursors for metathesis reactions. Thus, a Stille coupling of compound **5** gave the 4-vinylindole **22** which was transformed into its ammonium salt by reaction with benzyl bromide. The parent salt obtained from **22** and methyl iodide was insoluble in ethereal solvents and was practically unreactive against Grignard reagents. Thus the benzyldimethylammonium salt was used and it was reacted with convenient Grignard reagents to yield **23** and **24** in good yields. These compounds were reacted with 7% second generation Grubbs' catalyst **28**. Ring-closing metathesis (RCM) of compound **23** yielded compound **25** readily, which however



Scheme 5. Metathesis reactions of compounds **29**–**31**.

decomposed partially after 15 min at room temperature. Enyne metathesis of **24** proceeded with total conversion in crude (^{1}H NMR), and led to a mixture of **26a**,**b** and **27**. Unfortunately, products **26** were unstable and decomposed even in a Florisil® column, so they could not be isolated. Attempts to effect a Diels–Alder reaction by adding maleic anhydride to the metathesis reaction mixture were also unsuccessful. After 3 days, no adduct was formed and when heating, or on addition of other Lewis acid type catalysts the result was decomposition. On the other hand, compound **27** could be isolated in 35% yield. It may be formed by cross-metathesis of compound **26a**. This compound is air-stable and can be chromatographed over silica gel. We have found these type of dimeric compounds in other enyne metathesis of indoles (Scheme 4).[12]

In the same way, compounds **7**–**9** were transformed into the enyne **29** and the dienes **30** and **31** via protection of the hydroxy group and displacement of the trimethylammonium salt with a Grignard reagent. Metathesis reactions using 7% of catalyst **28** afforded the diene **32** and compounds **33** and **34** in good yields. These compounds are stable and could be isolated and characterized (Scheme 5).

3. Conclusion

In conclusion, the functionalization at the position 4 of the indole nucleus has been investigated. This can be a good entry to 3,4-disubstituted indoles which can be readily transformed into adequate substrates for RCM and enyne metathesis reactions. The resulting products are related to ergot alkaloids like claviciptic acid.

4. Experimental

4.1. General methods

Melting points were determined on a Büchi 530 apparatus and are uncorrected. Thin layer chromatography (TLC) was accomplished using Merck TLC aluminum sheets (silica gel 60 F_{254}). Flash column chromatography was carried out on Merck silica gel (230–400 mesh) and Florisil®. All ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-300 instrument. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.00 ppm) or to the corresponding ^{13}C solvent signal. IR spectra were recorded on a Perkin–Elmer 1330 spectrophotometer and are given in cm^{-1}. Elemental analyses were performed in the UCM Microanalysis Service (Facultad de Farmacia, Universidad Complutense de Madrid, Spain). Ruthenium benzylidene complex **28** was obtained following literature methods.[13]

4.1.1. Dimethyl[2-(1-triisopropylsilyl-1*H*-indol-3-yl)-ethyl]-amine (2). Indole was transformed into *N*,*N*-dimethyltryptamine following the method described by Glennon.[14] 1.0 g (5.32 mmol) of this compound was added to a suspension of 0.19 g (6.38 mmol) of NaH (80% in paraffin) in THF (25 mL) at 0°C. After stirring for 3 h, 0.85 mL (6.38 mmol) of triisopropylsilyl chloride were added dropwise and the mixture was allowed to warm at room temperature overnight. The solution was quenched with water (25 mL) and extracted with ether (3×25 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. The crude was purified by flash chromatography ($CHCl_3$/MeOH 3:1) to obtain 1.2 g (65%) of **2** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.62–1.74 (m, 3H), 2.36 (s, 6H), 2.61–2.66 (m, 2H), 2.91–2.97 (m, 2H), 7.03 (s, 1H), 7.10–7.14 (m, 2H), 7.45–7.48 (m, 1H), 7.57–7.60 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 141.2, 130.8, 128.1, 121.2, 119.1, 118.4, 115.8, 113.8, 60.1, 45.3, 23.7, 18.0, 12.7; IR (neat) ν 1610, 1465, 1450 cm^{-1}; Anal. calcd for $C_{21}H_{36}N_2Si$: C, 73.19; H, 10.53; N, 8.13. Found: C, 73.38; H, 10.74; N, 7.96.

4.1.2. 3-Methoxymethyl-1-triisopropylsilyl-1*H*-indole (3). A solution of 3.0 g (18.60 mmol) of indole-3-carboxylic acid in MeOH (150 mL) was saturated with HCl (g). The mixture was heated under reflux for 24 h. The solvent was evaporated under vacuum and the crude purified by flash chromatography (hexane/EtOAc 1:1) to obtain 3.1 g (quantitative) of the corresponding methyl ester. 1.5 g (8.56 mmol) of this compound were added to a suspension of 0.31 g (10.27 mmol) of NaH (80% in paraffin) in THF (17 mL) at 0°C. After stirring for 3 h, 1.34 mL (10.27 mmol) of triisopropylsilyl chloride was added dropwise and the mixture was allowed to warm at room temperature overnight. The solution was quenched with water (15 mL), and extracted with ether (3×15 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. The crude was purified by flash chromatography (hexane/EtOAc 9:1) to obtain 3.7 g (60%) of 3-carboxymethyl-1-triisopropylsilylindole as a colorless oil. To 2.8 g (8.50 mmol) of this compound in dry THF (40 mL) and under argon, a solution of 14.1 mL (21.2 mmol) of DIBAL-H (1.5 M/Toluene) in dry THF (60 mL) was added dropwise at −78°C. The reaction mixture was stirred for 24 h. The reaction was then quenched by addition of saturated aqueous sodium tartrate (70 mL) and extracted with EtOAc (3×50 mL). The combined extracts were dried ($MgSO_4$) and evaporated under vacuum. Without further purification, a solution of this crude in 10 mL of dry THF was added to 0.3 g (10.15 mmol) of NaH (80% in paraffin) in 20 mL of dry THF at 0°C under argon. After vigorous stirring for 15 min, a solution of 0.17 mL (12.70 mmol) of iodomethane in 5 mL of dry THF was added dropwise and kept at 0°C for 1 h. The resulting mixture was then stirred at room temperature overnight. Then, water (15 mL) was added and the mixture was extracted with ether (3×15 mL). The organic layers were dried ($MgSO_4$) and the solvent was removed under vacuo. The crude was purified by flash chromatography (hexane/EtOAc 99:1) to obtain 1.6 g (60%, two steps) of **3** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.62–1.77 (m, 3H), 3.39 (s, 3H), 4.67 (s, 2H), 7.14–7.17 (m, 2H), 7.22 (s, 1H), 7.47–7.50 (m, 1H), 7.67–7.70 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 141.4, 130.6, 130.5, 121.6, 119.8, 119.0, 114.9, 113.9, 66.6, 57.4, 18.1, 12.7; IR (neat) ν 1615, 1470, 1450 cm^{-1}; Anal. calcd for $C_{19}H_{31}NOSi$: C, 71.87; H, 9.84; N, 4.41. Found: C, 72.03; H, 9.99; N, 4.24.

4.1.3. 3-(2-Methoxyethyl)-1-triisopropylsilyl-1*H*-indole (4). Following the same procedure employed for the synthesis of **3**, from 5.0 g (28.50 mmol) of 1*H*-indole-3-acetic acid, and after purification by flash chromatography

(hexane/EtOAc 1:1), 4.7 g (85%) of the corresponding methylester was obtained. From 4.3 g (23.70 mmol) of this ester, 0.78 g (26.7 mmol) of NaH and 3.42 mL (25.00 mmol) of tiisopropylsilyl chloride, and after purification by flash chromatography (hexane/EtOAc 10:1), 4.9 g (60%) of 3-carboxyethyl-1-triisopropylsilylindole was obtained. From 2.4 g (7.03 mmol) of this compound, 11.7 mL (17.60 mmol) of DIBAL-H and then by treatment with 0.25 g (8.44 mmol) of NaH and 1.6 mL (10.54 mmol) of MeI, and after purification by flash chromatography (hexane/EtOAc 99:1), 1.4 g (60%, two steps) of **4** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.61–1.76 (m, 3H), 3.04 (t, 2H, J=7.7 Hz), 3.40 (s, 3H), 3.67 (t, 2H, J=7.7 Hz), 7.07–7.16 (m, 3H), 7.46–7.49 (m, 1H), 7.58–7.61 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 141.1, 131.0, 128.7, 121.2, 119.2, 118.5, 114.5, 113.8, 73.0, 58.5, 25.7, 18.1, 12.8; IR (neat) ν 1610, 1465, 1450 cm^{-1}; Anal. calcd for $C_{20}H_{33}NOSi$: C, 72.45; H, 10.03; N, 4.22. Found: C, 72.65; H, 10.21; N, 4.05.

4.1.4. *N*,*N*-Diethyl-1-triisopropylsilyl-1*H*-indole-3-carboxamide (18a). Following the method described by Knight,[15] *N*-(*p*-toluenesulfonyl)indole was treated with oxalyl chloride and diethylamine to obtain the *N*,*N*-diethyl-1-phenylsulfonylindole-3-carboxamide. After hydrolysis of this tosylamide with 1.00 equiv. of KOH in MeOH and purification by flash chromatography (hexane/EtOAc 2:1), *N*,*N*-diethylindole-3-carboxamide (85%) was obtained. 0.18 g (0.83 mmol) of this compound was added to a suspension of 0.03 g (0.99 mmol) of NaH (80% in paraffin) in THF (5 mL) at 0°C. After stirring for 3 h, 0.81 mL (0.99 mmol) of triisopropylsilyl chloride was added dropwise and the mixture was allowed to warm to room temperature overnight. The solution was quenched with water (5 mL). The aqueous layers were extracted with ether (3×5 mL) and the combined organic phases dried ($MgSO_4$) and concentrated. The crude was purified by flash chromatography (hexane/EtOAc 4:1) to obtain 0.3 g (95%) of **18a** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.15 (d, 18H, J=7.7 Hz), 1.23 (t, 6H, J=7.1 Hz), 1.63–1.78 (m, 3H), 3.55 (q, 4H, J=7.1 Hz), 7.17–7.20 (m, 2H), 7.44 (s, 1H), 7.48–7.51 (m, 1H), 7.78–7.81 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 166.6, 140.2, 130.8, 129.3, 121.9, 120.5, 120.4, 114.1, 113.6, 41.1, 17.7, 13.6, 12.4; IR (neat) ν 1620, 1540, 1450, 1430 cm^{-1}; Anal. calcd for $C_{22}H_{36}N_2OSi$: C, 70.91; H, 9.74; N, 7.52. Found: C, 71.15; H, 9.95; N, 7.36.

4.1.5. *N*,*N*-Diisopropyl-1-(*tert*-butyldiphenylsilyl)-1*H*-indole-3-carboxamide (18b). Following same procedure described for **18a**, from 7.0 g (25.80 mmol) of 1-tosylindole, 1.25 mL (129.00 mmol) of oxalyl chloride, 17.2 g (129.00 mmol) of $AlCl_3$, 13.7 mL (98.00 mmol) of triisopropylamine and treatment of the corresponding carboxamide with KOH/MeOH, yielded after purification by flash chromatography (hexane/EtOAc 2:1), 1.4 g (32%, two steps) of *N*,*N*-diisopropylindole-3-carboxamide. The protection of this compound by treatment with 0.26 g (9.90 mmol) of NaH and 2.30 mL (9.90 mmol) of *tert*-butyldiphenylsilyl chloride, and after purification by flash chromatography (hexane/EtOAc 4:1), gave 2.0 g (56%) of **18b** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 9H), 1.37 (d, 12H, J=6.1 Hz), 3.96 (bs, 2H), 6.79 (d, 1H, J=8.2 Hz), 6.88 (t, 1H, J=7.1 Hz), 7.10 (t, 1H, J=8.2 Hz), 7.37 (t, 4H, J=7.1 Hz), 7.44–7.48 (m, 3H), 7.59 (dd, 4H, J_1=8.2 Hz, J_2=1.6 Hz), 7.77 (d, 1H, J=7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 166.6, 140.5, 135.7, 131.5, 130.8, 130.3, 129.7, 128.1, 121.8, 120.7, 120.2, 116.7, 115.4, 48.2, 28.2, 21.2, 19.8; IR (neat) ν 1610, 1540, 1450, 1430 cm^{-1}; Anal. calcd for $C_{31}H_{38}N_2OSi$: C, 77.13; H, 7.93; N, 5.80. Found: C, 77.34; H, 8.10; N, 5.63.

4.2. General procedure for the synthesis of compounds 5–17

^{t}BuLi (1.60 mmol) was added dropwise to a stirred solution of the corresponding indole (1.00 mmol) in dry ether (5 mL) at −78°C and under argon. After 15 min, the mixture was allowed to warm to 0°C (ca. 20 min), and stirred at 0°C for an additional 1.5 h. After cooling to −78°C, the electrophile (Table 1) (2.50 mmol) was added in small portions. The resulting mixture was stirred for 15 min at −78°C and then allowed to warm to room temperature for 1 h. 10 mL of water were added and the crude extracted with ether (3×10 mL). Evaporation of the solvent and purification by flash chromatography (hexane/EtOAc and $CHCl_3$/MeOH mixtures) yielded pure **5**–**17** compounds.

4.2.1. (4-Iodo-1-triisopropylsilyl-1*H*-indol-3-ylmethyl)-dimethylamine (5). Following the general procedure, from 0.50 g (1.50 mmol) of **1**, 1.40 mL (2.40 mmol) of ^{t}BuLi and 0.96 g (3.80 mmol) of iodine, and after purification by flash chromatography (hexane/EtOAc 1:1), 0.54 g (80%) of pure **5** was obtained as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 1.15 (d, 18H, J=7.7 Hz), 1.69–1.82 (m, 3H), 2.99 (s, 6H), 4.98 (s, 2H), 6.94 (t, 1H, J=7.7 Hz), 7.58 (d, 1H, J=8.2 Hz), 7.66 (d, 1H, J=8.2 Hz), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 141.7, 138.5, 132.6, 129.7, 123.9, 114.9, 106.4, 84.4, 52.2, 42.7, 18.1, 12.6; IR (neat) ν 1540, 1470, 1410 cm^{-1}; Anal. calcd for $C_{20}H_{33}IN_2Si$: C, 52.62; H, 7.29; N, 6.14. Found: C, 52.82; H, 7.50; N, 6.00.

4.2.2. 3-Dimethylaminomethyl-4-(1-hydroxyethyl)-1-triisopropylsilyl-1*H*-indole (6). Following the general procedure, from 0.50 g (1.50 mmol) of **1**, 1.40 mL (2.40 mmol) of ^{t}BuLi and 0.47 mL (3.80 mmol) of acetaldehyde, and after purification by flash chromatography (hexane/EtOAc 1:1), 0.39 g (70%) of pure **6** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.64–1.74 (m, 3H), 1.72 (d, 3H, J=6.6 Hz), 2.25 (s, 6H), 3.27 (d, 1H, J=13.0 Hz), 4.34 (d, 1H, J=13.0 Hz), 5.49 (q, 1H, J=6.6 Hz), 7.09 (s, 1H), 7.11–7.19 (m, 2H), 7.41 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 142.9, 138.5, 132.3, 127.5, 121.8, 116.2, 114.2, 113.7, 65.1, 57.9, 44.3, 20.6, 18.1, 12.7; IR (neat) ν 3180, 1460, 1420 cm^{-1}; Anal. calcd for $C_{22}H_{38}N_2OSi$: C, 70.53; H, 10.22; N, 7.48. Found: C, 70.75; H, 10.44; N, 7.25.

4.2.3. 1-(3-Dimethylaminomethyl-4-(1-hydroxy-2-propenyl)-1-triisopropylsilyl-1*H*-indole (7). Following the general procedure, from 0.50 g (1.50 mmol) of **1**, 1.40 mL (2.40 mmol) of ^{t}BuLi and 0.26 mL (3.80 mmol) of acrolein, and after purification by flash chromatography (hexane/EtOAc 4:1), 0.46 g (80%) of pure **7** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.12 (d, 18H, J=7.7 Hz), 1.63–1.74 (m, 3H), 2.23 (s, 6H), 3.56 (d, 1H, J=12.7 Hz), 3.97 (d, 1H, J=12.7 Hz), 5.33 (d, 1H, J=10.4 Hz), 5.45 (d, 1H,

J=17.0 Hz), 5.68–5.70 (m, 1H), 6.31–6.42 (m, 1H), 7.07–7.09 (m, 3H), 7.40–7.43 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 136.8, 140.9, 143.1, 132.4, 127.1, 121.6, 119.6, 114.4, 114.1, 114.0, 72.1, 57.4, 44.1, 18.0, 12.7; IR (neat) ν 3320, 1470, 1420 cm^{-1}; Anal. calcd for $C_{23}H_{38}N_2OSi$: C, 71.45; H, 9.91; N, 7.25. Found: C, 71.65; H, 10.21; N, 7.00.

4.2.4. 3-Dimethylaminomethyl-4-(1-hydroxy-2-methyl-2-propenyl)-1-triisopropylsilyl-1*H*-indole (8). Following the general procedure, from 2.50 g (7.57 mmol) of **1**, 7.12 mL (12.11 mmol) of ^{t}BuLi and 1.65 mL (18.92 mmol) of methacrolein, and after purification by flash chromatography ($CHCl_3$/MeOH 19:1), 3.25 g (90%) of pure **8** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.12 (d, 18H, J=7.7 Hz), 1.57 (bs, 1H), 1.63–1.73 (m, 3H), 1.80 (s, 3H), 2.22 (s, 6H), 3.55 (d, 1H, J=12.3 Hz), 3.96 (d, 1H, J=12.3 Hz), 5.13 (bs, 1H), 5.27 (bs, 1H), 5.52 (bs, 1H), 7.02 (t, 1H, J=7.1 Hz), 7.07–7.10 (m, 2H), 7.40 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 147.2, 143.2, 136.0, 132.3, 127.4, 121.7, 119.7, 114.2, 113.8, 111.1, 75.0, 57.5, 44.2, 21.3, 18.0, 12.7; IR (neat) ν 3310, 1550, 1470, 1420 cm^{-1}; Anal. calcd for $C_{24}H_{40}N_2OSi$: C, 71.94; H, 10.06; N, 6.99. Found: C, 72.16; H, 10.28; N, 6.80.

4.2.5. (*E*)-3-Dimethylaminomethyl-4-(1-hydroxy-2-methyl-2-butenyl)-1-triisopropylsilyl-1*H*-indole (9). Following the general procedure, from 2.57 g (7.79 mmol) of **1**, 7.3 mL (12.46 mmol) of ^{t}BuLi and 1.96 mL (19.47 mmol) of (*E*)-2-methyl-2-butenal, and after purification by flash chromatography ($CHCl_3$/MeOH 99:1), 3.1 g (98%) of pure **9** was obtained as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.63–1.73 (m, 3H), 1.69 (s, 3H), 1.75 (d, 3H, J=6.6 Hz), 2.21 (s, 6H), 3.44 (d, 1H, J=13.0 Hz), 4.03 (d, 1H, J=13.0 Hz), 5.52 (s, 1H), 5.78 (q, 1H, J=6.6 Hz), 6.95 (d, 1H, J=7.1 Hz), 7.04–7.08 (m, 2H), 7.39 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 143.1, 137.0, 136.7, 132.2, 127.6, 121.6, 119.7, 119.2, 114.1, 113.6, 75.5, 57.5, 44.2, 18.0, 15.0, 13.1, 12.7; IR (neat) ν 3360, 1470, 1420 cm^{-1}; Anal. calcd for $C_{25}H_{42}N_2OSi$: C, 72.41; H, 10.21; N, 6.76. Found: C, 72.62; H, 10.40; N, 6.57.

4.2.6. (4-Allyl-1-triisopropylsilyl-1*H*-indol-3-ylmethyl)-dimethylamine (10). Following the general procedure, from 0.25 g (0.76 mmol) of **1**, 0.72 mL (1.22 mmol) of ^{t}BuLi and 0.23 mL (1.90 mmol) of 3-bromo-1-propene, and after purification by flash chromatography (hexane/EtOAc 9:1), 0.54 g (20%) of pure **10** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.64–1.74 (m, 3H), 2.23 (s, 6H), 3.51 (s, 2H), 3.96 (d, 2H, J=6.0 Hz), 4.96–5.06 (m, 2H), 6.09–6.22 (m, 1H), 6.11 (d, 1H, J=7.1 Hz), 7.03–7.08 (m, 2H), 7.33 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 142.3, 138.9, 132.9, 131.6, 130.1, 129.0, 121.4, 120.6, 114.9, 112.0, 56.5, 45.0, 37.3, 18.1, 12.8; IR (neat) ν 1470, 1420 cm^{-1}; Anal. calcd for $C_{23}H_{38}N_2Si$: C, 74.53; H, 10.33; N, 7.56. Found: C, 74.71; H, 10.54; N, 7.38.

4.2.7. 1-(3-Dimethylaminomethyl-1-triisopropylsilyl-1*H*-indol-4-yl)-propan-2-ol (11). Following the general procedure, from 0.30 g (0.91 mmol) of **1**, 0.85 mL (1.45 mmol) of ^{t}BuLi and 0.16 mL (2.27 mmol) of propylene oxide, and after purification by flash chromatography ($CHCl_3$/MeOH 24:1), 0.32 g (90%) of pure **11** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.12 (d, 18H, J=7.7 Hz), 1.35 (d, 3H, J=6.0 Hz), 1.63–1.73 (m, 3H), 2.25 (s, 6H), 3.10 (d, 2H, J=6.6 Hz), 3.33 (d, 1H, J=12.9 Hz), 3.97 (d, 1H, J=12.9 Hz), 4.01 (q, 1H, J=6.0 Hz), 6.94 (d, 1H, J=7.1 Hz), 7.05 (s, 1H), 7.09 (t, 1H, J=7.1 Hz), 7.33 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 142.4, 132.5, 132.2, 129.3, 121.8, 121.5, 114.2, 111.9, 69.6, 56.5, 43.9, 41.6, 25.1, 18.0, 12.7; IR (neat) ν 3270, 1470, 1420 cm^{-1}; Anal. calcd for $C_{23}H_{40}N_2OSi$: C, 71.08; H, 10.37; N, 7.21. Found: C, 71.29; H, 10.56; N, 7.05.

4.2.8. (4-Bromo-1-triisopropylsilyl-1*H*-indol-3-ylmethyl)-dimethylamine (12). Following the general procedure, from 0.30 g (0.91 mmol) of **1**, 0.85 mL (1.45 mmol) of ^{t}BuLi and 0.75 g (2.27 mmol) of carbon tetrabromide, and after purification by flash chromatography ($CHCl_3$/MeOH 1:1), 0.22 g (60%) of pure **12** was obtained as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.63–1.75 (m, 3H), 2.42 (s, 6H), 4.03 (s, 2H), 6.96 (t, 1H, J=7.7 Hz), 7.29 (d, 1H, J=7.7 Hz), 7.39 (s, 1H), 7.44 (d, 1H, J=8.8 Hz); ^{13}C NMR (DMSO-d_6) δ 137.9, 127.9, 125.0, 123.3, 122.4, 113.0, 111.5, 110.4, 53.7, 44.1, 17.9, 12.2; IR (neat) ν 1540, 1470, 1420 cm^{-1}; Anal. calcd for $C_{20}H_{33}BrN_2OSi$: C, 71.08; H, 10.37; N, 7.21. Found: C, 71.29; H, 10.55; N, 7.03.

4.2.9. 3-Methoxymethyl-1-triisopropylsilyl-1*H*-indole-4-carbaldehyde (14). Following the general procedure, from 0.20 g (0.63 mmol) of **3**, 0.56 mL (1.01 mmol) of ^{t}BuLi and 0.12 mL (1.57 mmol) of *N*,*N*-dimethylformamide, and after purification by flash chromatography (hexane/EtOAc 24:1), 1.17 g (55%) of pure **14** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.14 (d, 18H, J=7.7 Hz), 1.63–1.76 (m, 3H), 3.44 (s, 3H), 4.78 (s, 2H), 7.27 (t, 1H, J=7.7 Hz), 7.42 (s, 1H), 7.73 (d, 1H, J=8.2 Hz), 7.79 (d, 1H, J=7.7 Hz), 10.52 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 194.5, 143.2, 134.6, 130.4, 130.1, 121.1, 119.4, 117.4, 115.8, 57.1, 44.8, 18.0, 12.7; IR (neat) ν 1680, 1600, 1460 cm^{-1}; Anal. calcd for $C_{20}H_{31}NO_2Si$: C, 69.52; H, 9.04; N, 4.05. Found: C, 69.70; H, 9.23; N, 3.91.

4.2.10. 4-(2-Hydroxypropyl)-1-(3-Methoxymethyl-1-triisopropylsilyl-1*H*-indole (15). Following the general procedure but at −30°C, from 0.20 g (0.63 mmol) of **3**, 0.56 mL (1.01 mmol) of ^{t}BuLi and 0.11 mL (1.57 mmol) of propylene oxide, and after purification (hexane/EtOAc 19:1 and then 3:1), 0.12 g (50%) of pure **15** and 0.021 g (10%) of pure **17** as colorless oil was obtained. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.35 (3H, d, J=6.0 Hz), 1.64–1.74 (m, 3H), 2.64 (bs, 1H), 3.04 (dd, 1H, J_1=13.7 Hz, J_2=8.8 Hz), 3.23 (dd, 1H, J_1=13.7 Hz, J_2=3.9 Hz), 3.39 (s, 3H), 3.99–4.10 (m, 1H), 4.67 (dd, 2H, J_1=30.2 Hz, J_2=11.5 Hz), 6.96 (d, 1H, J=7.1 Hz), 7.10 (t, 1H, J=8.2 Hz), 7.21 (s, 1H), 7.37 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 142.6, 132.7, 131.7, 129.0, 121.8, 121.6, 114.3, 112.4, 69.4, 68.0, 56.8, 42.7, 23.4, 18.1, 12.8; IR (neat) ν 3420, 1460, 1420 cm^{-1}; Anal. calcd for $C_{22}H_{37}NO_2Si$: C, 70.35; H, 9.93; N, 3.73. Found: C, 70.56; H, 10.15; N, 3.56.

4.2.11. 1-(2-Hydroxypropyl)-3-(2,2-dimethylpropyl)-2-triisopropylsilyl-1*H*-indole (17). Following the general procedure, from 0.20 g (0.63 mmol) of **3**, 0.56 mL (1.01 mmol) of ^{t}BuLi and 0.11 mL (1.57 mmol) of propylene

oxide, and after purification, 0.097 g (45%) of pure **17** and 0.047 g (20%) of pure **15** was obtained. ^{1}H NMR ($CDCl_3$) δ 0.96 (s, 9H), 1.09 (d, 6H, J=7.7 Hz), 1.16 (d, 12H, J=7.1 Hz), 1.22 (d, 3H, J=6.0 Hz), 1.60–1.71 (m, 3H), 2.83 (d, 1H, J=14.3 Hz), 2.90 (d, 1H, J=14.3 Hz), 4.11–4.30 (m, 3H), 7.04 (t, 1H, J=7.1 Hz), 7.16 (t, 1H, J=7.1 Hz), 7.32 (d, 1H, J=8.2 Hz), 7.64 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 139.4, 135.4, 131.0, 127.5, 121.8, 121.3, 118.3, 110.0, 66.7, 53.9, 38.3, 33.0, 31.0, 19.8, 19.4, 14.1; IR (neat) ν 3300, 1600, 1460, 1430 cm^{-1}; Anal. calcd for $C_{25}H_{43}NOSi$: C, 74.75; H, 10.79; N, 3.49. Found: C, 74.96; H, 10.92; N, 3.33.

4.3. Synthesis of compounds 19–21

Following the general procedure of funtionalization at C4, from 0.15 g (0.40 mmol) of **18a**, 0.38 mL (0.64 mmol) of ^{t}BuLi and 0.07 mL (1.00 mmol) of propylene oxide, and after purification by flash chromatography (hexane/EtOAc 4:1), 0.07 g (50%) of pure **19a** and 0.05 g (30%) of pure **20a** as colorless oils was obtained. From 0.2 g (0.43 mmol) of **18b**, 0.40 mL (0.68 mmol) of ^{t}BuLi and 0.07 mL (1.10 mmol) of propylene oxide, and after purification by flash chromatography (hexane/EtOAc 4:1), 0.08 g (40%) of pure **19b**, 0.03 g (15%) of pure **20b** and 0.02 g (10%) of pure **21b** as colorless oil were obtained.

4.3.1. *N*,*N*-Diethyl 2-triisopropylsilyl-1*H*-indole-3-carboxamide (19a). ^{1}H NMR ($CDCl_3$) δ 1.14 (d, 18H, J=7.7 Hz), 1.16–1.30 (bs, 6H), 1.46–1.60 (m, 3H), 3.20–3.40 (bs, 2H), 3.40–3.70 (bs, 2H), 7.11 (t, 1H, J=7.7 Hz), 7.19 (t, 1H, J=7.7 Hz), 7.39 (d, 1H, J=8.2 Hz), 7.49 (d, 1H, J=8.2 Hz), 8.25 (bs, 1H); ^{1}H NMR (C_6D_6) δ 0.99 (t, 6H, J=7.1 Hz), 1.16 (dd, 18H, J_1=7.7 Hz, J_2=1.6 Hz), 1.44–1.56 (m, 3H), 3.35 (q, 4H, J=7.1 Hz), 7.13–7.39 (m, 3H), 7.59 (d, 1H, J=7.1 Hz), 7.82 (bs, 1H); ^{13}C NMR (C_6D_6) δ 167.8, 138.1, 134.6, 127.1, 124.2, 122.9, 122.9, 120.5, 120.2, 111.4, 30.2, 19.2, 13.5, 12.0; IR (neat) ν 3300, 1600, 1460, 1430 cm^{-1}; Anal. calcd for $C_{22}H_{36}N_2OSi$: C, 70.91; H, 9.74; N, 7.52. Found: C, 71.09; H, 9.98; N, 7.34.

4.3.2. *N*,*N*-Diethyl 1-(2-hydroxypropyl)-2-triisopropylsilyl-1*H*-indole-3-carboxamide (20a). ^{1}H NMR ($CDCl_3$) δ 1.16 (d, 12H, J=7.7 Hz), 1.18 (d, 6H, J=7.7 Hz), 1.26–1.36 (m, 6H), 1.56–1.73 (m, 6H), 3.11–3.28 (m, 1H), 3.36–3.51 (m, 1H), 3.54–3.72 (m, 2H), 4.10–4.47 (m, 5H), 7.09 (t, 1H, J=7.1 Hz), 7.20 (td, 1H, J_1=8.2 Hz, J_2=1.6 Hz), 7.42 (d, 1H, J=8.2 Hz), 7.48 (d, 1H, J=8.1 Hz); ^{13}C NMR (DMSO-d_6) δ 165.2, 135.7, 129.0, 126.5, 121.1, 120.0, 119.3, 109.8, 109.7, 65.1, 52.7, 40.3, 20.3, 17.2, 13.2, 11.7; IR (neat) ν 3400, 1600, 1460 cm^{-1}; Anal. calcd for $C_{25}H_{42}N_2O_2Si$: C, 69.72; H, 9.83; N, 6.50. Found: C, 69.91; H, 9.99; N, 6.30.

4.3.3. *N*,*N*-Diisopropyl 2-(*tert*-butyldiphenylsilyl)-1*H*-indole-3-carboxamide (19b). ^{1}H NMR ($CDCl_3$) δ 0.97 (d, 12H, J=4.9 Hz), 1.15 (s, 9H), 1.50–1.60 (m, 2H), 7.01 (t, 1H, J=6.7 Hz), 7.13 (t, 1H, J=6.7 Hz), 7.30–7.38 (m, 6H), 7.50–7.53 (m, 4H), 10.26 (bs, 1H); ^{13}C NMR (DMSO-d_6) δ 166.5, 138.0, 135.7, 133.0, 128.7, 127.9, 127.0, 125.8, 125.5, 121.9, 118.6, 118.2, 111.7, 47.1, 28.2, 20.1, 17.3; IR (neat) ν 3440, 1610, 1450 cm^{-1}; Anal. calcd for $C_{31}H_{38}N_2OSi$: C, 77.13; H, 7.93; N, 5.80. Found: C, 77.32; H, 8.19; N, 5.62.

4.3.4. *N*,*N*-Diisopropyl 2-(*tert*-butyldiphenylsilyl)-1-(2-hydroxypropyl)-1*H*-indole-3-carboxamide (20b). ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 12H), 1.30–1.40 (bs, 12H), 3.90–4.00 (m, 3H), 4.09 (dd, 1H, J_1=13.7 Hz, J_2=6.1 Hz), 4.20 (q, 1H, J=6.0 Hz), 6.81 (dd, 1H, J_1=6.0 Hz, J_2=1.6 Hz), 7.06–7.16 (m, 3H), 7.28 (t, 2H, J=7.7 Hz), 7.34–7.44 (m, 3H), 7.49 (d, 2H, J=7.1 Hz), 7.65 (d, 2H, J=6.0 Hz), 7.72 (dd, 1H, J_1=6.0 Hz, J_2=1.6 Hz); ^{13}C NMR (DMSO-d_6) δ 165.0, 135.5, 134.8, 134.6, 133.4, 132.8, 129.2, 127.4, 127.1, 126.3, 121.2, 119.6, 119.2, 112.2, 109.6, 68.1, 52.6, 46.8, 26.3, 20.5, 20.2, 18.0; IR (neat) ν 3400, 1610, 1470 cm^{-1}; Anal. calcd for $C_{34}H_{44}N_2O_2Si$: C, 75.51; H, 8.20; N, 5.18. Found: C, 75.73; H, 8.38; N, 5.01.

4.3.5. *N*,*N*-Diisopropyl 1-(*tert*-butyldiphenylsilyl)-4-(2-hydroxypropyl)-1*H*-indole-3-carboxamide (21b). ^{1}H NMR δ 1.25 (s, 12H), 1.25–1.30 (bs, 6H), 1.34 (d, 6H, J=6.6 Hz), 2.90 (dd, 1H, J_1=13.7 Hz, J_2=8.8 Hz), 3.01–3.09 (m, 1H), 3.47 (q, 1H, J=7.1 Hz), 4.00–4.29 (m, 2H), 6.74 (d, 1H, J=7.7 Hz), 6.87 (t, 1H, J=7.7 Hz), 6.94 (d, 1H, J=7.1 Hz), 7.25 (d, 1H, J=6.0 Hz), 7.34–7.49 (m, 6H), 7.55–7.61 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 167.3, 140.7, 135.3, 134.5, 132.6, 131.5, 130.5, 129.0, 128.3, 127.9, 127.3, 121.8, 117.2, 112.7, 66.7, 47.8, 41.9, 28.0, 20.6, 20.5, 19.2; IR (neat) ν 3400, 1610, 1470 cm^{-1}; Anal. calcd for $C_{34}H_{44}N_2O_2Si$: C, 75.51; H, 8.20; N, 5.18. Found: C, 75.71; H, 8.39; N, 5.00.

4.4. Synthesis of compound 22

4.4.1. Dimethyl-(1-triisopropylsilyl-4-vinyl-1*H*-indol-3-ylmethyl)amine (22). Stille coupling[16] of **5** with vinyltributyltin yielded, after purification by flash chromatography (hexane/EtOAc 4:1 and then 1:1), pure **22** (71%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.7 Hz), 1.64–1.74 (m, 3H), 2.27 (s, 6H), 3.54 (s, 2H), 5.28 (dd, 1H, J_1=11.0 Hz, J_2=1.6 Hz), 5.70 (dd, 1H, J_1=17.6 Hz, J_2=1.6 Hz), 7.09 (s, 1H), 7.10 (t, 1H, J=7.7 Hz), 7.27 (d, 1H, J=8.2 Hz), 7.39 (d, 1H, J=8.2 Hz), 7.75 (dd, 1H, J_1=17.6 Hz, J_2=11.0 Hz) ^{13}C NMR ($CDCl_3$) δ 142.2, 136.8, 132.1, 131.8, 128.3, 121.5, 117.1, 116.1, 114.1, 113.2, 56.6, 45.0, 18.0, 12.7; IR (neat) ν 1460, 1410 cm^{-1}; Anal. calcd for $C_{22}H_{36}N_2Si$: C, 74.09; H, 10.17; N, 7.86. Found: C, 74.27; H, 10.38; N, 7.69.

4.5. Synthesis of compounds of 23 and 24

General procedure. The benzyldimethylammonium salt of **22** was prepared by reaction of this product with 2.0 equiv. of benzylbromide in dry benzene at room temperature. After 18 h of reaction, 4 equiv. of ethynylmagnesium chloride 0.5 M or vinylmagnesium bromide 1.0 M were slowly added to an ice-cooled solution of the ammonium salt in 10 mL of dry THF. The mixture was refluxed under argon overnight, and then was treated with 10 mL of a saturated aqueous NH_4Cl solution and extracted with EtOAc (3×10 mL). The organic phase was washed with brine, dried ($MgSO_4$) and concentrated. The crude thus obtained, was purified by flash chromatography (hexane) to obtain the corresponding diene **23** and enyne **24**.

4.5.1. 3-Allyl-1-triisopropylsilyl-4-vinyl-1*H*-indole (23). Following the general procedure, from 1.50 g (4.21 mmol) of **22**, 1.01 mL (8.42 mmol) of BnBr and 16.84 mL (16.84 mmol) of vinylmagnesium bromide, and after purification by flash chromatography, 0.86 g (60%) of pure **23** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 18H, J=7.1 Hz), 1.60–1.75 (m, 3H), 3.65 (d, 2H, J=5.5 Hz), 5.02 (dd, 1H, J_1=17.0 Hz, J_2=1.6 Hz), 5.09 (dd, 1H, J_1=9.9 Hz, J_2=1.6 Hz), 5.26 (dd, 1H, J_1=11.0 Hz, J_2=1.6 Hz), 5.67 (dd, 1H, J_1=17.0 Hz, J_2=1.6 Hz), 6.07–6.20 (m, 1H), 7.00 (s, 1H), 7.09 (t, 1H, J=7.7 Hz), 7.23 (d, 1H, J=8.8 Hz), 7.40 (d, 1H, J=7.7 Hz), 7.44 (dd, 1H, J_1=17.0 Hz, J_2=11.0 Hz); ^{13}C NMR ($CDCl_3$) δ 142.1, 137.9, 136.0, 131.8, 130.0, 128.1, 121.4, 117.1, 116.3, 115.6, 114.5, 113.4, 31.9, 18.1, 12.8; IR (neat) ν 1460, 1410 cm^{-1}; Anal. calcd for $C_{22}H_{33}NSi$: C, 77.81; H, 9.79; N, 4.12. Found: C, 77.99; H, 9.98; N, 4.00.

4.5.2. 3-(2-Propynyl)-1-triisopropylsilyl-4-vinyl-1*H*-indole (24). Following the general procedure, from 1.50 g (4.21 mmol) of **22**, 1.01 mL (8.42 mmol) of BnBr and 33.68 mL (16.84 mmol) of ethynylmagnesium chloride, and after purification by flash chromatography, 0.88 g (62%) of pure **24** was obtained as a colorless oil. ^{1}H NMR (CD_3OD) δ 1.02 (d, 18H, J=7.3 Hz), 1.54–1.64 (m, 3H), 2.35 (t, 1H, J=2.1 Hz), 3.67 (d, 2H, J=2.1 Hz), 5.16 (dd, 1H, J_1=11.0 Hz, J_2=1.6 Hz), 5.53 (dd, 1H, J_1=17.0 Hz, J_2=1.6 Hz), 6.95 (t, 1H, J=7.3 Hz), 7.08 (d, 1H, J=7.3 Hz), 7.19 (s, 1H), 7.29 (d, 1H, J=8.5 Hz), 7.41 (dd, 1H, J_1=17.0 Hz, J_2=11.0 Hz) ^{13}C NMR ($CDCl_3$) δ 142.2, 135.6, 131.7, 130.4, 127.3, 121.6, 117.3, 115.3, 113.6, 112.9, 82.9, 69.6, 18.2, 18.1, 12.8; IR (neat) ν 3320, 2120, 1470, 1420 cm^{-1}; Anal. calcd for $C_{22}H_{31}NSi$: C, 78.27; H, 9.26; N, 4.15. Found: C, 78.50; H, 9.47; N, 4.01.

4.6. Synthesis of compounds 29–31

General procedure. Compounds **7**–**9** were protected as their TBDMS derivatives.[17] Using the same procedure employed in the synthesis of **23** and **24**, these compounds were transformated into their trimethylammonium salts by reaction with CH_3I. Conversion to **29**–**31** was achieved by treatment of these salts with ethynylmagnesium chloride or vinylmagnesium bromide. Usual work-up and purification by flash chromatography (hexane) yielded pure enyne **29** (70%, three steps) and dienes **30** (75%, three steps) and **31** (75%, three steps).

4.6.1. 4-[1-(*tert*-Butyldimethylsilyloxy)-2-methylbut-2-enyl]-3-prop-2-ynyl-1-triisopropylsilyl-1*H*-indole (29). ^{1}H NMR ($CDCl_3$) δ −0.25 (s, 3H), 0.02 (s, 3H), 0.86 (s, 9H), 1.14 (dd, 18H, J_1=7.7 Hz, J_2=1.1 Hz), 1.57 (d, 3H, J=6.6 Hz), 1.63–1.73 (m, 3H), 1.66 (s, 1H), 2.20 (t, 1H, J=2.2 Hz), 3.69 (d, 1H, J=19.2 Hz), 3.88 (dd, 1H, J_1=19.2 Hz, J_2=2.2 Hz), 5.23 (q, 1H, J=6.6 Hz), 5.58 (bs, 1H), 7.07 (t, 1H, J=7.7 Hz), 7.17 (d, 1H, J=7.7 Hz), 7.28 (s, 1H), 7.37 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 142.4, 139.2, 135.4, 130.1, 127.3, 121.1, 120.6, 119.8, 113.1, 112.7, 83.8, 78.1, 69.3, 25.9, 18.3, 18.2, 18.1, 13.6, 13.4, 12.9, −4.8, −4.9; IR (neat) ν 1460, 1420 cm^{-1}; Anal. calcd for $C_{31}H_{51}NOSi_2$: C, 73.02; H, 10.08; N, 2.75. Found: C, 73.20; H, 10.26; N, 2.60.

4.6.2. 3-Allyl-4-[1-(*tert*-butyldimethylsilanyloxy)allyl]-1-triisopropylsilanyl-1*H*-indole (30). ^{1}H NMR ($CDCl_3$) δ −0.09 (s, 3H), 0.01 (s, 3H), 0.91 (s, 9H), 1.12 (d, 18H, J=7.7 Hz), 1.62–1.72 (m, 3H), 3.60–3.64 (m, 2H), 4.94–5.21 (m, 4H), 5.83–5.85 (m, 1H), 6.05–6.18 (m, 2H), 6.97 (s, 1H), 7.09 (t, 1H, J=7.7 Hz), 7.24 (d, 1H, J=8.2 Hz), 7.35 (d, 1H, J=7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 142.2, 142.1, 138.2, 136.3, 130.1, 127.1, 121.2, 117.4, 115.6, 115.1, 112.7, 71.9, 31.9, 26.0, 18.4, 18.2, 12.9, −4.5, −4.7; IR (neat) ν 1470, 1430 cm^{-1}; Anal. calcd for $C_{29}H_{49}NOSi_2$: C, 71.98; H, 10.21; N, 2.89. Found: C, 72.20; H, 10.38; N, 2.71.

4.6.3. 3-Allyl-4-[1-(*tert*-butyldimethylsilyloxy)-2-methyl-allyl]-1-triisopropylsilyl-1*H*-indole (31). ^{1}H NMR ($CDCl_3$) δ −0.22 (s, 3H), −0.01 (s, 3H), 0.88 (s, 9H), 1.12 (d, 18H, J=7.7 Hz), 1.64–1.72 (m, 3H), 1.76 (s, 3H), 3.50–3.66 (m, 2H), 4.70 (s, 1H), 4.84 (s, 1H), 5.00 (dd, 1H, J_1=19.2 Hz, J_2=1.6 Hz), 5.10 (dd, 1H, J_1=11.5 Hz, J_2=1.6 Hz), 5.67 (s, 1H), 6.04–6.18 (m, 1H), 6.94 (s, 1H), 7.08 (t, 1H, J=7.7 Hz), 7.24 (d, 1H, J=7.7 Hz), 7.35 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 148.6, 142.0, 138.3, 135.6, 130.0, 128.0, 120.7, 118.9, 115.6, 115.5, 112.8, 112.1, 75.1, 32.0, 25.9, 20.0, 18.3, 18.2, 12.9, −4.6, −4.9; IR (neat) ν 1460, 1420 cm^{-1}; Anal. calcd for $C_{30}H_{51}NOSi_2$: C, 72.37; H, 10.32; N, 2.81. Found: C, 72.55; H, 10.14; N, 2.63.

4.7. General procedure for the ring-closing metathesis

The corresponding diene or enyne (1.00 mmol) was dissolved in 20 mL of dry toluene under argon. To this solution, ruthenium catalyst **28** (0.05 mmol) was added and the reaction was refluxed for 4–6 h (TLC). The mixture was filtered through celite and the solvent evaporated under vacuum. The crude thus obtained was purified by flash chromatography (hexane) to obtain the corresponding 3,4-carbocycloindoles.

4.7.1. 1-Triisopropylsilyl-1,3-dihydrobenzo[*cd*]indole (25). Following the general procedure, from 0.10 g (0.29 mmol) of **23**, 17 mg (0.02 mmol) of **28**, and after a short Florisil® column, 0.07 g (78%) of **25** was obtained as a colorless oil which turned dark in ca. 15 min. ^{1}H NMR ($CDCl_3$) δ 1.12 (d, 18H, J=7.7 Hz), 1.57–1.70 (m, 3H), 3.85 (bs, 2H), 5.93 (dt, 1H, J_1=9.9 Hz, J_2=3.8 Hz), 6.54 (dt, 1H, J_1=9.9 Hz, J_2=2.2 Hz), 6.65 (d, 1H, J=6.6 Hz), 6.85 (s, 1H), 6.95 (t, 1H, J=8.2 Hz), 7.15 (d, 1H, J=8.2 Hz).

4.7.2. Bis-1,2-[1-triisopropylsilyl-1,3-dihydrobenzo[*cd*]-indol-4-yl]ethylene (27). Following the general procedure, from 0.10 g (0.30 mmol) of **24**, 18 mg (0.020 mmol) of **28** and after purification, 35 mg (35%) of pure **27** was obtained as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 1.15 (d, 18H, J=7.7 Hz), 1.62–1.72 (m, 3H), 4.05 (bs, 2H), 6.64 (s, 1H), 6.67 (s, 1H), 6.76 (d, 1H, J=7.1 Hz), 6.95–7.02 (m, 2H), 7.17 (d, 1H, J=8.2 Hz);^{13}C NMR ($CDCl_3$) δ 137.9, 137.1, 130.2, 129.5, 128.1, 127.1, 125.2, 122.9, 115.2, 114.0, 113.4, 29.7, 18.1, 12.7; IR (neat) ν 1460, 1440 cm^{-1}; Anal. calcd for $C_{42}H_{58}N_2Si_2$: C, 77.96; H, 9.03; N, 4.33. Found: C, 78.17; H, 9.19; N, 4.06.

4.7.3. 6-(*tert*-Butyldimethylsilyloxy)-7-methyl-8-propenyl-2-triisopropylsilyl-6,9-dihydro-2*H*-2-aza-benzo[*cd*]-azulene (32). Following the general procedure, from 0.07 g

(0.15 mmol) of **29**, 9 mg (0.010 mmol) **28**, and after purification, 0.05 g (65%) of pure **32** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 6H), 1.02 (s, 9H), 1.12 (dd, 18H, J_1=7.7 Hz, J_2=3.8 Hz), 1.58–1.70 (m, 3H), 1.81 (s, 3H), 1.84 (s, 3H), 3.64 (d, 1H, J=15.4 Hz), 3.89 (d, 1H, J=15.4 Hz), 5.78–5.89 (m, 1H), 6.39–6.43 (m, 2H), 6.87 (s, 1H), 7.00 (t, 1H, J=8.2 Hz), 7.08 (d, 1H, J=7.1 Hz), 7.21 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 140.7, 138.3, 135.7, 130.0, 129.2, 128.6, 124.9, 123.4, 121.2, 115.7, 112.8, 112.3, 71.9, 26.1, 26.0, 18.7, 18.6, 18.2, 12.8, 12.1, −5.0, −5.1; IR (neat) ν 1460, 1430 cm^{-1}; Anal. calcd for $C_{31}H_{51}NOSi_2$: C, 73.02; H, 10.08; N, 2.75. Found: C, 73.23; H, 10.25; N, 2.59.

4.7.4. 6-(*tert*-Butyldimethylsilyloxy)-2-triisopropylsilyl-6,9-dihydro-2*H*-2-azabenzo[*cd*]azulene (33). Following the general procedure, from 0.10 g (0.21 mmol) of **30**, 12.5 mg (0.015 mmol) of **28**, and after purification, 0.07 g (75%) of pure **33** was obtained as a colorless oil. ^{1}H NMR δ ($CDCl_3$) 0.14 (s, 3H), 0.15 (s, 3H), 1.00 (s, 9H), 1.12 (dd, 18H, J_1=7.7 Hz, J_2=1.1 Hz), 1.61–1.71 (m, 3H), 3.27–3.35 (m, 1H), 3.70 (d, 1H, J=14.8 Hz), 5.97 (t, 1H, J=2.7 Hz), 6.11 (s, 1H), 6.90 (s, 1H), 7.08 (t, 1H, J=7.1 Hz), 7.16 (d, 1H, J=7.1 Hz), 7.29 (d, 1H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 141.2, 138.9, 134.6, 127.9, 125.9, 121.4, 118.6, 114.2, 113.9, 112.7, 70.5, 31.7, 25.9, 18.4, 18.2, 12.8, −4.6, −4.9; IR (neat) ν 1460, 1430 cm^{-1}; Anal. calcd for $C_{27}H_{45}NOSi_2$: C, 71.14; H, 9.95; N, 3.07. Found: C, 71.32; H, 10.16; N, 2.91.

4.7.5. 6-(*tert*-Butyldimethylsilyloxy)-7-methyl-2-triisopropylsilyl-6,9-dihydro-2*H*-2-aza-benzo[*cd*]azulene (34). Following the general procedure, from 0.10 g (0.20 mmol) of **31**, 12 mg (0.014 mmol) of **28** and after purification, 0.08 g (85%) of pure **34** was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 3H), 0.33 (s, 3H), 1.20 (s, 9H), 1.34 (d, 18H, J=7.1 Hz), 1.79–1.94 (m, 3H), 2.00 (s, 3H), 3.50–3.57 (m, 1H), 3.84 (dd, 1H, J_1=14.8 Hz, J_2=4.4 Hz), 5.91–5.96 (m, 1H), 6.26 (bs, 1H), 7.09 (s, 1H), 7.21–7.30 (m, 2H), 7.48 (d, 1H, J=7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 148.7, 143.4, 141.2, 134.8, 128.6, 125.3, 121.1, 120.9, 115.6, 112.7, 72.5, 31.6, 26.0, 24.7, 18.5, 18.2, 12.9, −4.9, −5.0; IR (neat) ν 1460, 1430 cm^{-1}; Anal. calcd for $C_{28}H_{47}NOSi_2$: C, 71.58; H, 10.08; N, 2.98. Found: C, 71.79; H, 10.26; N, 2.80.

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