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Palladium-catalysed cyclization of 2-alkynylanilines to 2-substituted indoles under an acidic two-phase system

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Abstract

The cyclization of 2-alkynylanilines in the presence of $PdCl_2$ and $^nBu_4NCl$ under an acidic CH_2Cl_2–HCl two-phase system affords 2-substituted indoles in good to high yield, at room temperature. The reaction is particularly suited to the one-flask preparation of 2-substituted indoles from 2-ethynylaniline.

Key words: Palladium; Two-phase catalysis; Indole

1. Introduction

Because of their potential as synthetic intermediates for the preparation of many alkaloids and pharmacologically active compounds [1,2], 2-substituted indoles represent a target of current interest. Amongst the methods reported in the literature, the palladium-catalysed cyclization of 2-alkynylanilines [3] or 2-anilides [3b,4] appear to play a valuable role in the synthesis of this class of compounds and our report on the utilization of this reaction in combination with the palladium-catalysed coupling of 2-ethynylaniline with vinyl and aryl triflates or halides [3a] provided a significant widening of the scope of the methodology. A crucial step in the cyclization mechanism requires the protolytic cleavage of the carbon–palladium bond of the supposed σ-vinylpalladium intermediate **1** (Scheme 1). Under widely used conditions (acetonitrile; 60–80°C; $PdCl_2L_2$ [3,4]; neutral conditions from now on) protons necessary for that arise from the hydrochloric acid generated in the conversion of the starting 2-alkynylanilines or 2-anilides into the σ-vinylpalladium complex **1**.

We have previously found that, under acidic CH_2Cl_2–3 N HCl two-phase conditions, the $PdCl_2$–$^nBu_4NCl$ combination can successfully promote the formation of conjugate addition-type products from arylmercury or aryltin compounds and α,β-enones and α,β-enals [5] as well as the conversion of 4-hydroxy-1-alkynes into γ-hydroxy-α,β-enones [6] at room temperature, most probably favouring the protic cleavage of σ-vinylpalladium intermediates. Therefore, as part of our continuing effort to develop synthetic procedures for the preparation of the indole nucleus [3a,7] and speculating that the acidic medium could favour the protic cleavage of the σ-vinylpalladium intermediates **1** as well, we decided to explore the possible utilization of this catalytic system in the cyclization of 2-alkynylanilines **2** to 2-substituted indoles **3**.

In the following, we report the results of this study.

2. Results and discussion

2-Alkynylanilines **2**, prepared through the palladium-catalysed coupling of readily available 2-ethynyl-

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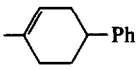
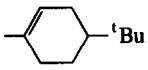
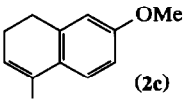
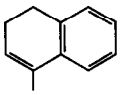
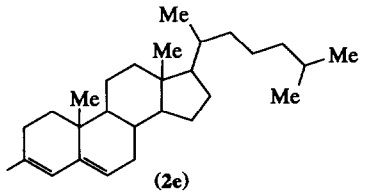
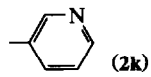
aniline and a variety of vinyl and aryl halides or triflates [3a], have been reacted in the presence of the $PdCl_2$–$^nBu_4NCl$ combination under an acidic CH_2Cl_2–HCl two-phase system at room temperature to give 2-substituted indoles **3** with a good to high yield. Our results are summarized in Table 1.

The hydrochloric acid concentration was found to affect the reaction outcome. For example, **2d** gave the

TABLE 1. Palladium-catalysed cyclization of 2-alkynylanilines **2** to 2-substituted indoles **3** in an acidic CH_2Cl_2–HCl two-phase system (Scheme 2) [a]

Number	2-Alkynylaniline **2** R	Reaction time (h)	Aqueous HCl (N)	Yield of **3** [b] (%)	
1		20	0.5	**3a**	98
2		3	–	**3a**	87 [c]
3		20	0.5	**3a**	62 [d]
4		20	0.5	**3a**	40 [e]
5	(**2a**)	20	–	**3a**	10
6	 (**2b**)	16	0.5	**3b**	97
7		72	2.0	**3c**	70
8	(**2c**)	3.5	–	**3c**	64 [c]
9		36	–	**3d**	92
10	(**2d**)	3.5	–	**3d**	76 [c]
11	 (**2e**)	10	0.5	**3e**	89 [f]
12	$-C_6H_4$-4-Me (**2f**)	48	3.0	**3f**	82
13	$-C_6H_4$-4-Me (**2f**)	3	–	**3f**	80 [c]
14	$-C_6H_4$-4-OMe (**2g**)	21	3.0	**3g**	68
15	$-C_6H_4$-3-F (**2h**)	72	3.0	**3h**	45
16	$-C_6H_4$-3-F (**2h**)	6	–	**3h**	51 [c]
17	$-C_6H_4$-3-F (**2h**)	72	3.0	**3h**	22 [d]
18	$-C_6H_4$-3-F (**2h**)	72	3.0	**3h**	14 [e]
19	$-C_6H_4$-4-COOMe (**2i**)	72	3.0		–
20	–CH=CH–Ph (**2j**)	72	3.0	**3j**	57
21	–CH=CH–Ph (**2j**)	2.5	–	**3j**	74 [c]
22		48	3.0	**3k**	–
23	(**2k**)	36	–	**3k**	38 [c]
24		5	–	**3k**	56 [g]

[a] Unless otherwise stated, reactions were carried out at room temperature under an argon atmosphere, using the following molar ratios: **2**: $PdCl_2$: $^nBuN_4Cl$ = 1 : 0.05 : 0.01.

[b] Yields refer to single runs and are given on pure isolated products.

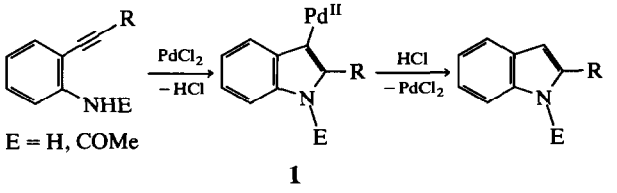
[c] Carried out at 70°C in acetonitrile in the presence of $PdCl_2$ (5 mol.%) [3a].

[d] Carried out in the presence of $NaAuCl_4$ (5 mol.%).

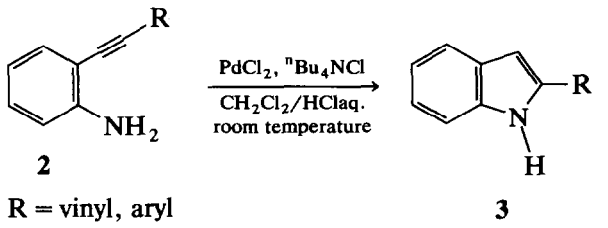
[e] Carried out in the presence of $NaAuCl_4$ (5 mol.%) and $^nBu_4NCl$ (10 mol.%).

[f] In the presence of $PdCl_2$ (10 mol.%) and $^nBuN_4Cl$ (20 mol.%).

[g] Carried out at 80°C in acetonitrile in the presence of $NaAuCl_4$ (5 mol.%) [3b].



Scheme 1.



Scheme 2.

highest yield of the corresponding indole derivative in the presence of 2 N HCl (Table 2). In many cases, however, 0.5 N HCl provided good results.

Usually our acidic two phase conditions (room temperature) gave yields comparable with or higher than those obtained with $PdCl_2$ in acetonitrile (60–80°C) (Table 1, compare numbers 1, 7 and 9 with numbers 2, 8 and 10 respectively). The use of $NaAuCl_4$ with or without $^nBu_4NCl$ under the same two-phase conditions afforded lower yields (Table 1, numbers 3, 4, 17 and 18). Limitations on the generality of the methodology arise when 2-alkynylanilines containing electron-withdrawing substituents are subjected to cyclization conditions (Table 1, numbers 19 and 22). With these substrates the use of neutral conditions was found to afford better results (Table 1, compare number 15 with 16 and number 22 with 23). In the effect, the highest yield with **2k** was obtained by using $NaAuCl_4$ under neutral conditions [3b] (Table 1, number 24). Since it seems likely that electron-withdrawing substituents may exert a closely similar influence on the step(s) leading

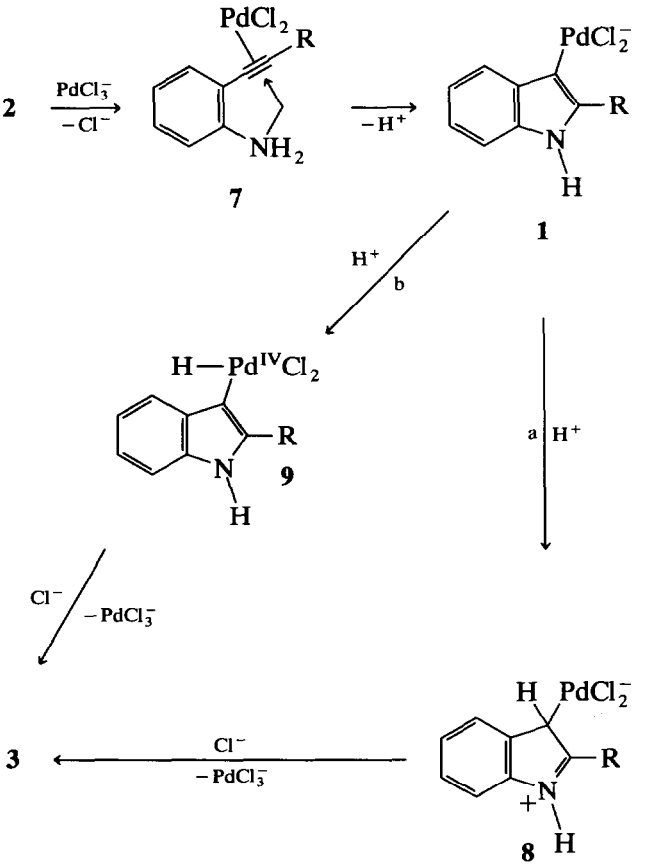
TABLE 2. Acid concentration and synthesis of **3d** from **2d** in a CH_2Cl_2–HCl two-phase system in the presence of $PdCl_2$–$^nBu_4NCl$ [a]

Acid concentration (N)	Recovered **2d** yield [b] (%)	**3d** yield [b] (%)
0.1	55	9
0.5	26	35
1.0	17	45
2.0	–	92 [c]

[a] Unless otherwise stated, reactions were carried out at room temperature (48 h), under a nitrogen atmosphere, using the following molar ratios: **2d**:$PdCl_2$:$^nBu_4NCl$ = 1:0.05:0.10.

[b] Yields refer to single run and are given on pure isolated products.

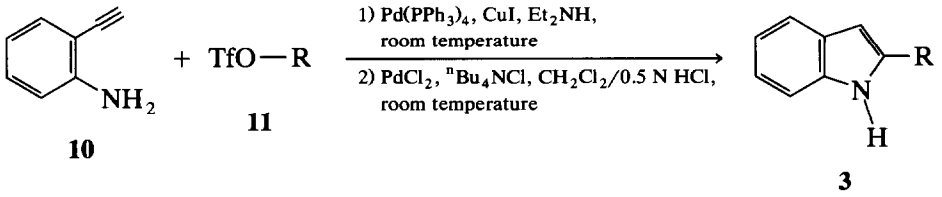
[c] 36 h.



Scheme 3.

to the protic cleavage of the carbon–palladium bond of σ-vinylpalladium intermediates **1** under both neutral and acidic conditions, a reasonable working hypothesis accounting for the differences in reactivity observed with 2-alkynylanilines containing acetylenic π electrons conceivably less prone to coordinate palladium can be based on the assumption that they arise in the step leading to the formation of the π-alkynylpalladium complex **7** (Scheme 3). The idea is that in the presence of $PdCl_2$ and $^nBu_4NCl$ this step involves a palladium(II) species less reactive than that operating under neutral conditions. In this respect, it may be worth mentioning that $PdCl_2$ and $^nBu_4NCl$ have been reported to react in dichloromethane to produce a palladium complex whose minimal chemical structure may be represented as $^nBu_4NPdCl_3$ [8]. The possible presence of this dichloromethane soluble complex along the reaction coordinate leading to 2-substituted indoles appears to reconcile our results.

Based on these considerations, the reaction may be supposed to proceed through (a) nucleophilic attack of nitrogen on the complexed carbon–carbon triple bond, (b) protonation of the σ-vinylpalladium complex **1** and



10 11 3

Scheme 4.

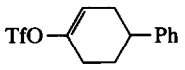
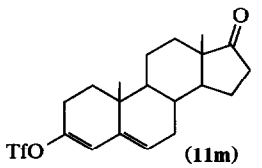
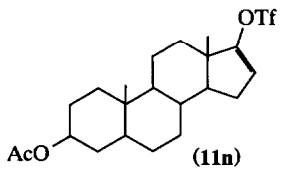
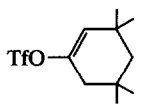
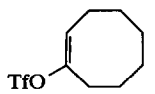
(c) elimination of palladium(II) species from the resultant intermediate **8** to afford the indole derivative and the palladium(II) catalyst (Scheme 3a). It is also possible to envisage the formation of **3** through the alternative or parallel (b′) protonation of **1** to give the σ-vinylpalladium(IV) complex **9** [9] followed by (c′) reductive elimination (Scheme 3b).

It is of interest to note that the acidic medium does not prevent the unprotected amino group from attacking the coordinated carbon–carbon triple bond.

The present procedure proved to be especially convenient for the one-flask conversion of 2-ethynylaniline **10** into 2-substituted indoles, without the isolation of the intermediate 2-alkynylanilines (Scheme 4).

For example, **3a** was isolated with 64% yield when the crude mixture obtained from the palladium-catalysed coupling of 2-ethynylaniline with 4-phenylcyclohex-1-enyl triflate was reacted, after evaporation under vacuum at the rotary evaporator, with $PdCl_2$ in acetonitrile (80°C, for 3.5 h). Treating the reaction mixture derived from the coupling step with the $PdCl_2$–$^nBu_4NCl$ combination under our CH_2Cl_2–3 N HCl

TABLE 3. One-flask palladium-catalysed conversion of 2-ethynylaniline **10** into 2-substituted indoles **3** (Scheme 4) [a]

Number	Vinyl triflate **11**	Reaction time (coupling) (h)	Reaction time (cyclization) (h)	Overall yield of **3** [b] (%)
1		5	14	**3a** 98
2	 **(11a)**	5	3.5	**3a** 64 [c]
3	 **(11m)**	5.5	14	**3l** 65
4	 **(11n)**	6	48	**3m** 96
5	 **(11o)**	5.5	40	**3n** 81
6	 **(11p)**	5.5	14	**3o** 62

[a] Unless otherwise stated, reactions were carried out according to the procedure reported in the experimental section.

[b] Yields refer to single runs and are given on pure isolated products.

[c] The crude mixture obtained from the palladium-catalysed coupling of **10** with **11a** was reacted, after evaporation at the rotary evaporator, with $PdCl_2$ in acetonitrile (80°C for 3.5 h).

two-phase system (room temperature for 14 h), again after evaporation under vacuum at the rotary evaporator, led to the isolation of **3a** with 98% yield.

Our results are summarized in Table 3.

In conclusion, we have shown that our protocol, based on the utilization of the $PdCl_2$–$^nBu_4NCl$ combination in a CH_2Cl_2–HCl two-phase system, allows an easy access to 2-substituted indole derivatives from 2-alkynylanilines under mild conditions. No protection of the amino group is needed. The possibility of preparing 2-substituted indoles through an efficient one-flask process from 2-ethynylaniline is of particular interest from a synthetic standpoint. In the most favourable cases, it is possible to synthesize 2-substituted indoles from 2-ethynylaniline at room temperature.

3. Experimental details

Melting points were determined with a Büchi apparatus and are uncorrected. $PdCl_2$, $NaAuCl_4$ and $^nBuN_4Cl$ are commercially available and were used as purchased, without further purification. 2-Alkynylanilines **2** were prepared as reported in reference [3a]. Vinyl triflates **11a**, **m** [10], **n** [11], **o** and **p** [6] were prepared according to reference [12] and purified by flash chromatography on silica gel eluting with n-hexane–EtOAc mixtures. Palladium-catalysed cyclization of 2-alkynylanilines and one-flask conversion of 2-ethynylaniline into 2-substituted indoles were carried out on a 0.3–1.2 mmol scale. The products were purified by flash chromatography on silica gel eluting with n-hexane–EtOAc mixtures.

NMR spectra ($CDCl_3$, unless otherwise indicated; tetramethylsilane as internal standard) were recorded with a Bruker AC 200 spectrometer. IR spectra (KBr, unless otherwise indicated) were recorded with a Perkin–Elmer 683 spectrometer. Electron impact (EI) and chemical ionization (CI) (CH_4) mass spectra were recorded on a HP 59970 spectrometer workstation formed by an HP 5890 gas chromatograph equipped with a methyl silicone capillary column and by an HP 5970 mass detector. All the isolated products gave satisfactory microanalyses.

3.1. 2-Alkynylanilines 2a–2k

3.1.1. 2-(4-Phenylcyclohex-1-enyl)ethynylaniline (2a)

M.p., 125–127°C, IR: ν 3500, 3400, 2190 cm^{-1}. ^1H NMR: δ 7.35–7.15 (m, 6H), 7.10–7.03 (m, 1H), 6.69–6.62 (m, 2H), 6.25 (bs, 1H), 4.15 (bs, 2H), 2.82–2.73 (m, 1H), 2.48–2.26 (m, 4H), 2.01–1.76 (m, 2H). ^{13}C NMR: δ 147.5, 146.3, 134.0, 131.9, 129.2, 128.4, 126.8, 126.2, 120.6, 117.7, 114.2, 108.3, 96.2, 83.8, 39.1, 33.8, 30.1, 29.5. Mass spectroscopy (MS) (CI): *m/e* (relative intensity) 274 (MH^+, 100).

3.1.2. 2-(4-tert-Butylcyclohex-1-enyl)ethynylaniline (2b)

M.p., 93–94°C. IR: ν 3450, 3350, 2180 cm^{-1}. ^1H NMR: δ 7.25 (d, $J = 7.8$ Hz, 1H), 7.10–7.02 (m, 1H), 6.68–6.61 (m, 2H), 6.18 (bs, 1H), 4.16 (bs, 2H), 2.31–2.10 (m, 3H), 1.95–1.75 (m, 2H), 1.30–1.20 (m, 2H), 0.87 (s, 9H). ^{13}C NMR: δ 147.5, 135.0, 131.9, 129.1, 120.5, 117.8, 114.1, 108.5, 96.4, 83.3, 43.2, 32.2, 31.0, 27.5, 27.1, 23.8. MS (CI): *m/e* (relative intensity) 254 (MH^+, 100).

3.1.3. 2-(6-Methoxy-3,4-dihydro-1-naphthyl)ethynylaniline (2c)

Oil. IR (neat): ν 3460, 3370, 2200 cm^{-1}. ^1H NMR: δ 7.59 (d, $J = 8.4$ Hz, 1H), 7.38–7.26 (m, 1H), 7.15–7.04 (m, 1H), 6.77–6.64 (m, 4H), 6.38 (t, $J = 4.8$ Hz, 1H), 4.20 (bs, 2H), 3.76 (s, 3H), 2.77 (t, $J = 8.4$ Hz, 2H), 2.42–2.31 (m, 2H). ^{13}C NMR: δ 159.1, 147.8, 136.9, 132.8, 132.1, 129.5, 126.2, 125.8, 121.3, 117.9, 114.3, 113.2, 111.2, 108.2, 92.8, 86.5, 55.2, 27.6, 23.6. MS (CI): *m/e* (relative intensity): 276 (MH^+, 100).

3.1.4. 2-(3,4-Dihydro-1-naphthyl)ethynylaniline (2d)

Oil. IR (neat): ν 3500, 3400, 2200 cm^{-1}. ^1H NMR: δ 7.66 (d, $J = 7.3$ Hz, 1H), 7.37–7.33 (m, 1H), 7.24–7.03 (m, 4H), 6.70–6.60 (m, 2H), 6.48 (t, $J = 4.8$ Hz, 1H), 4.20 (bs, 2H), 2.76 (t, $J = 8.0$ Hz, 2H), 2.40–2.29 (m, 2H). ^{13}C NMR: δ 135.3, 135.1, 132.6, 132.1, 129.5, 127.7, 127.4, 126.6, 124.9, 121.7, 117.8, 114.3, 108.0, 92.5, 86.8, 27.1, 23.6. MS (CI): *m/e* (relative intensity): 246 (MH^+, 100).

3.1.5. 2-(Cholesta-3,5-dien-3-yl)ethynylaniline (2e)

M.p., 207–209°C. IR: ν 3350, 3450 cm^{-1}. ^1H NMR: δ 7.29–7.24 (m, 1H), 7.09 (t, $J = 7.7$ Hz, 1H), 6.71–6.63 (m, 2H), 6.36 (s, 1H), 5.55 (bs, 1H), 4.20 (bs, 2H). ^{13}C NMR: δ 147.5, 141.4, 135.2, 131.9, 129.2, 126.5, 117.9, 117.1, 114.2, 108.6, 97.0, 85.5. MS (CI): *m/e* (relative intensity) 484 (MH^+, 100).

3.1.6. 2-(4-Methylphenyl)ethynylaniline (2f)

M.p., 100–102°C. IR: ν 3400, 3500, 2210 cm^{-1}. ^1H NMR: δ 7.44–7.32 (m, 3H), 7.21–7.07 (m, 3H), 6.74–6.66 (m, 2H), 4.25 (bs, 2H), 2.35 (s, 3H). ^{13}C NMR: δ 147.7, 138.3, 132.0, 131.3, 129.5, 129.1, 120.2, 117.9, 114.3, 108.1, 94.8, 85.2, 21.5. MS (CI): *m/e* (relative intensity) 208 (MH^+, 100).

3.1.7. 2-(4-Methoxyphenyl)ethynylaniline (2g)

M.p., 104–106°C. IR: ν 3500, 3400 cm^{-1}. ^1H NMR: δ 7.45 (AA′ part of an AA′BB′ system, $J = 8.6$ Hz, 2H),

7.35 (d, $J = 7.4$ Hz, 1H), 7.11 (t, $J = 7.8$ Hz, 1H), 6.86 (BB' part of an AA'BB' system, $J = 8.6$ Hz, 2H), 6.74–6.66 (m, 2H), 4.03 (bs, 2H), 3.80 (s, 3H). ^{13}C NMR: δ 159.5, 147.6, 132.9, 131.9, 129.4, 117.9, 115.4, 114.3, 114.0, 108.2, 94.6, 84.5, 55.2. MS (CI): *m/e* (relative intensity) 224 (MH^+, 100).

3.1.8. 2-(3-Fluorophenyl)ethynylaniline (2h)

M.p., 70–72°C. IR 3500, 3400, 2190 cm^{-1}. ^{1}H NMR: δ 7.37–6.99 (m, 6H), 6.73–6.66 (m, 2H), 4.27 (bs, 2H). ^{13}C NMR: δ 162.4 (d, $J = 246$ Hz), 147.9, 132.2, 130.1, 129.9, 127.3, 127.2, 118.1 (d, $J = 23$ Hz), 118.0, 115.5 (d, $J = 21$ Hz), 114.4, 107.3, 93.4, 86.9. MS (CI): *m/e* (relative intensity): 212 (MH^+, 100).

3.1.9. 2-(4-Carbomethoxyphenyl)ethynylaniline (2i)

M.p., 127–129°C. IR: ν 3490, 3390, 2200, 1720 cm^{-1}. ^{1}H NMR: δ 8.02 (AA' part of an AA'BB' system, $J = 7.9$ Hz, 2H), 7.57 (BB' part of an AA'BB' system, $J = 7.9$ Hz, 2H), 7.39–7.35 (m, 1H), 7.21–7.12 (m, 1H), 6.76–6.69 (m, 2H), 4.30 (bs, 2H), 3.93 (s, 3H). ^{13}C NMR: δ 166.5, 150.0, 132.3, 131.3, 130.3, 129.5, 129.3, 128.0, 118.0, 114.4, 107.2, 94.0, 89.1, 52.2. MS (CI): *m/e* (relative intensity) 252 (MH^+, 100).

3.1.10. 2-(2-Phenyleth-1-enyl)ethynylaniline (2j)

M.p., 95–97°C. IR: ν 3490, 3390, 2180 cm^{-1}. ^{1}H NMR: δ 7.44–7.26 (m, 6H), 7.16–7.08 (m, 1H), 7.02 (AA' part of an AA'BB' system, $J = 16.2$ Hz, 1H), 6.75–6.66 (m, 2H), 6.43 (BB' part of an AA'BB' system, $J = 16.2$ Hz, 1H), 4.20 (bs, 2H). ^{13}C NMR: δ 147.7, 140.6, 136.2, 132.0, 129.6, 128.7, 128.5, 126.2, 117.9, 114.3, 108.1, 94.2, 88.3. MS (CI): *m/e* (relative intensity) 220 (MH^+, 100).

3.1.11. 2-(3-Pyridyl)ethynylaniline (2k)

M.p., 104–106°C. IR: ν 3470, 3330, 2200 cm^{-1}. ^{1}H NMR: δ 8.76–8.74 (m, 1H), 8.54–8.50 (m, 1H), 7.79–7.73 (m, 1H), 7.39–7.34 (m, 1H), 7.27–7.10 (m, 2H), 6.74–6.67 (m, 2H), 4.36 (bs, 2H). ^{13}C NMR: δ 151.9, 148.4, 148.0, 138.2, 132.3, 130.3, 123.1, 120.5, 117.9, 114.4, 106.9, 91.2, 89.4. MS (CI): *m/e* (relative intensity) 195 (MH^+, 100).

3.2. General procedure for the cyclization of 2-alkynylanilines (2): synthesis of 2-(3,4-dihydro-1-naphthyl)indole (3d)

To a solution of **2d** (0.200 g, 0.81 mmol) in dichloromethane (15 ml) were added 2.0 N HCl (5 ml), $PdCl_2$ (0.007 g, 0.040 mmol) and $^nBu_4NCl$ (0.024 g, 0.081 mmol). The reaction mixture was stirred for 36 h at room temperature under nitrogen and poured into a separatory funnel containing diethyl ether and saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were dried (Na_2SO_4) and evaporated under vacuum. The residue was separated on silica gel eluting with a 90/10 n-hexane/EtOAc mixture to afford 0.185 g of **3d** (92% yield).

3.3. General procedure for one-flask conversion of 2-ethynylaniline (10) into 2-substituted indoles (3): synthesis of 2-(3α-acetoxyandrost-16-en-17-yl)indole (3m)

To a stirred solution of 3α-acetoxy-androst-16-en-17-yl triflate **11n** (0.230 g, 0.49 mmol) in dimethylformamide (0.5 ml) and diethylamine (2 ml) were added 2-ethynylaniline **10** (0.058 g, 0.49 mmol), $Pd(PPh_3)_4$ (0.011 g, 0.009 mmol) and CuI (0.004 g, 0.020 mmol). The reaction mixture was stirred for 6 h at room temperature under a nitrogen atmosphere, and then evaporated under vacuum at the rotary evaporator (warm water bath). The residue was dissolved in dichloromethane (13 ml) and 0.5 N HCl (5 ml), $PdCl_2$ (0.05 g, 0.028 mmol), and $^nBu_4NCl$ (0.015 g, 0.051 mmol) were added. The reaction mixture was stirred at room temperature for 48 h under a nitrogen atmosphere. Work-up as before afforded a residue wich was purified by silica gel chromatography eluting with a 80/20 *n*-hexane/EtOAc mixture to give 0.205 g of **3m** (96% yield).

3.3.1. 2-(4-Phenylcyclohex-1-enyl)indole (3a)

M.p., 201–203°C. IR 3450 cm^{-1}. ^{1}H NMR: δ 8.08 (bs, 1H), 7.56 (d, $J = 7.5$ Hz, 1H), 7.36–7.02 (m, 8H), 6.47 (d, $J = 1.5$ Hz, 1H), 6.15 (bs, 1H), 2.95–2.80 (m, 1H), 2.61–2.36 (m, 4H), 2.15–1.85 (m, 2H). ^{13}C NMR: δ 146.5, 138.9, 136.2, 129.0, 128.9, 128.5, 126.9, 126.2, 122.1, 121.9, 120.4, 119.8, 110.4, 99.2, 39.8, 33.6, 29.6, 26.7. MS (EI): *m/e* (relative intensity): 273 (M^+, 73).

3.3.2. 2-(4-tert-Butylcyclohex-1-enyl)indole (3b)

M.p., 148–150°C. IR 3390 cm^{-1}. ^{1}H NMR: δ 8.05 (bs, 1H), 7.55 (d, $J = 7.4$ Hz, 1H), 7.30–7.05 (m, 3H), 6.42 (s, 1H), 6.06 (t, $J = 2.8$ Hz, 1H), 2.70–2.55 (m, 1H), 2.45–2.15 (m, 2H), 2.10–1.90 (m, 2H), 1.40–1.20 (m, 2H), 0.92 (s, 9H). ^{13}C NMR: δ 139.2, 136.2, 128.9, 128.8, 122.8, 121.9, 120.3, 119.7, 110.4, 98.7, 43.9, 32.2, 27.5, 27.2, 27.1, 23.9. MS (EI): *m/e* (relative intensity) 253 (M^+, 78).

3.3.3. 2-(6-Methoxy-3,4-dihydro-1-naphthyl)indole (3c)

M.p., 122–124°C. IR 3390 cm^{-1}. ^{1}H NMR: δ 7.98 (bs, 1H), 7.58 (d, $J = 7.7$ Hz, 1H), 7.31–7.03 (m, 4H), 6.76–6.75 (m, 1H), 6.67–6.61 (m, 1H), 6.53 (d, $J = 1.9$ Hz, 1H), 6.12 (t, $J = 4.8$ Hz, 1H), 3.75 (s, 3H), 2.74 (t, $J = 8$ Hz, 2H), 2.36–2.26 (m, 2H). ^{13}C NMR: δ 158.8,

138.8, 137.2, 135.8, 131.2, 128.6, 126.6, 126.5, 125.8, 121.8, 120.3, 119.8, 114.0, 110.8, 110.7, 101.7, 55.2, 28.4, 23.1. MS (EI): *m/e* (relative intensity) 275 (M^+, 100).

*3.3.4. 2-(3,4-Dihydro-1-naphthyl)indole (**3d**)*

M.p., 157–159°C. IR: ν 3440 cm^{-1}. ^1H NMR: δ 8.01 (bs, 1H), 7.61 (d, $J = 8.0$ Hz, 1H), 7.40–7.28 (m, 2H), 7.22–7.08 (m, 5H), 6.58 (d, $J = 2.0$ Hz, 1H), 6.33 (t, $J = 4.8$ Hz, 1H), 2.82 (t, $J = 7.8$ Hz), 2.44–2.33 (m, 2H). ^{13}C NMR: δ 136.9, 135.8, 133.6, 131.7, 128.6, 128.5, 127.8, 127.5, 126.5, 125.3, 121.9, 120.4, 119.9, 110.7, 101.9, 28.0, 23.2. MS (EI): *m/e* (relative intensity) 245 (M^+, 61).

*3.3.5. 2-(Cholesta-3,5-dien-3-yl)indole (**3e**)*

M.p., 213–216°C. IR: ν 3450 cm^{-1}. ^1H NMR: δ 8.17 (bs, 1H), 7.55 (d, $J = 7.5$ Hz, 1H), 7.32–7.28 (m, 1H), 7.14–7.05 (m, 2H), 6.53 (d, $J = 1.6$ Hz, 1H), 6.34 (s, 1H), 5.60 (bs, 1H). ^{13}C NMR: δ 141.7, 139.0, 136.5, 129.0, 125.7, 125.6, 123.8, 122.2, 120.3, 119.9, 110.4, 99.9. MS (EI): *m/e* (relative intensity) 483 (M^+, 100).

*3.3.6. 2-(4-Methylphenyl)indole (**3f**)*

M.p., 212–214°C. IR: ν 3450 cm^{-1}. ^1H NMR (acetone-d_6): δ 10.60 (bs, 1H), 7.75 (AA' part of an AA'BB' system, $J = 8.1$ Hz, 2H), 7.55 (d, $J = 7.5$ Hz, 1H), 7.40 (d, $J = 7.7$ Hz, 1H), 7.26 (BB' part of an AA'BB' system, $J = 8.1$ Hz, 2H), 7.12–6.96 (m, 2H), 6.84 (d, $J = 2.1$ Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (acetone-d_6): δ 137.9, 130.3, 125.8, 122.3, 120.9, 120.3, 111.9, 99.3, 21.1. MS (EI): *m/e* (relative intensity) 207 (M^+, 100).

*3.3.7. 2-(4-Methoxyphenyl)indole (**3g**)*

M.p., 219–221°C. IR: ν 3450 cm^{-1}. ^1H NMR (DMSO-d_6): δ 11.43 (bs, 1H), 7.80 (AA' part of an AA'BB' system, $J = 8.7$ Hz, 2H), 7.49 (d, $J = 7.5$ Hz, 1H), 7.38 (d, $J = 7.8$ Hz, 1H), 7.10–7.00 (m, 4H), 6.76 (d, $J = 1.9$ Hz), 3.80 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 158.7, 137.7, 136.9, 128.8, 126.3, 124.9, 121.0, 119.7, 119.2, 114.3, 111.1, 97.3, 55.1. MS (EI): *m/e* (relative intensity) 223 (M^+, 100), 208 (45).

*3.3.8. 2-(3-Fluorophenyl)indole (**3h**)*

M.p., 127–130°C. IR: ν 3450 cm^{-1}. ^1H NMR: δ 8.26 (bs, 1H), 7.63 (d, $J = 7.4$ Hz, 1H), 7.38–7.10 (m, 7H), 6.81 (d, $J = 2.2$ Hz, 1H). ^{13}C NMR: δ 163.2 (d, $J = 245$ Hz), 130.7, 130.5, 122.8, 120.9, 120.7, 120.6, 120.5, 114.4 (d, $J = 21$ Hz), 112.0 (d, $J = 23$ Hz), 111.0, 100.9. MS (EI): *m/e* (relative intensity) 211 (M^+, 100).

*3.3.9. 2-(2-Phenyleth-1-enyl)indole (**3j**)*

M.p., 198–201°C. IR: ν 3420 cm^{-1}. ^1H NMR (acetone-d_6): δ 10.60 (bs, 1H), 7.58–7.49 (m, 3H), 7.41–7.21 (m, 6H), 7.15–6.96 (m, 2H), 6.62 (d, $J = 1.2$ Hz, 1H). ^{13}C NMR (acetone-d_6) 138.2, 129.6, 128.3, 127.9, 127.0, 123.1, 121.0, 120.3, 120.2, 111.6, 104.1. MS (EI): *m/e* (relative intensity) 219 (M^+, 100).

*3.3.10. 2-(3-Pyridyl)indole (**3k**)*

M.p., 163–166°C. IR: ν 3170 cm^{-1}. ^1H NMR: δ 9.10 (bs, 1H), 9.00 (d, $J = 1.9$ Hz, 1H), 8.54–8.51 (m, 1H), 7.98 (dt, $J = 7.9$ Hz, $J = 1.8$ Hz, 1H), 7.65 (d, $J = 7.6$ Hz, 1H), 7.44–7.33 (m, 2H), 7.23–7.10 (m, 2H), 6.89 (d, $J = 1.5$ Hz, 1H). ^{13}C NMR: δ 148.2, 146.2, 137.3, 134.4, 132.6, 128.9, 128.7, 123.9, 123.0, 120.9, 120.6, 111.2, 101.3. MS (CI): *m/e* (relative intensity) 195 (MH^+, 100).

*3.3.11. 2-(17-Oxoandrosta-3,5-dien-3-yl)indole (**3l**)*

M.p., 259–261°C. IR: ν 3480, 1730 cm^{-1}. ^1H NMR: δ 8.18 (bs, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.32 (d, $J = 7.6$ Hz, 1H), 7.19–7.02 (m, 2H), 6.55 (d, $J = 1.3$ Hz, 1H), 6.36 (s, 1H), 5.62 (bs, 1H), 1.03 (s, 3H), 0.93 (s, 3H). ^{13}C NMR: δ 221.1, 141.7, 138.7, 136.5, 129.0, 126.0, 124.4, 123.4, 122.3, 120.3, 119.9, 110.4, 100.1. MS (CI): *m/e* (relative intensity) 386 (MH^+, 100).

*3.3.12. 2-(3β-Acetoxy-androst-16-en-17-yl)indole (**3m**)*

M.p., 119–121°C. IR: ν 3400, 1740 cm^{-1}. ^1H NMR: δ 8.16 (bs, 1H), 7.55 (d, $J = 8.2$ Hz, 1H), 7.31–7.01 (m, 3H), 6.53 (d, $J = 1.6$ Hz, 1H), 5.95 (bs, 1H), 5.03 (bs, 1H), 2.05 (s, 3H), 1.03 (s, 3H), 0.86 (s, 3H). ^{13}C NMR: δ 170.8, 146.7, 136.0, 134.1, 129.0, 124.9, 122.1, 120.4, 119.8, 110.3, 99.9, 70.1. MS (EI): *m/e* (relative intensity) 431 (M^+, 100), 372 (46).

*3.3.13. 2-(3,3,5,5-Tetramethylcyclohex-1-enyl)indole (**3n**)*

M.p., 79–82°C. IR: ν 3480 cm^{-1}. ^1H NMR: δ 8.15 (bs, 1H), 7.54 (d, $J = 6.9$ Hz, 1H), 7.30–7.00 (m, 3H), 6.45 (d, $J = 1.3$ Hz, 1H), 5.80 (s, 1H), 2.20 (d, $J = 1.1$ Hz, 2H), 1.43 (s, 2H), 1.11 (s, 6H), 1.04 (s, 6H). ^{13}C NMR: δ 139.4, 136.2, 131.4, 128.9, 125.4, 122.0, 120.3, 119.7, 110.3, 99.4, 49.6, 39.8, 33.0, 31.6, 30.6, 30.0.

*3.3.14. 2-(Cyclooct-1-enyl)indole (**3o**)*

M.p., 88–90°C. IR: 3400 cm^{-1}. ^1H NMR: δ 8.05 (bs, 1H), 7.54 (d, $J = 8$ Hz, 1H). 7.22–7.04 (m, 3H), 6.46 (d, $J = 1.8$ Hz, 1H), 7.01 (t, $J = 8.2$ Hz, 1H), 2.63 (t, $J = 6.2$ Hz, 2H), 2.35–2.25 (m, 2H). ^{13}C NMR: δ 139.2, 136.4, 132.4, 129.1, 125.1, 122.0, 120.3, 119.7, 110.3, 99.6, 30.3, 29.4, 27.1, 27.0, 26.8, 26.0. MS (CI): *m/e* (relative intensity) 226 (MH^+, 100).

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