Iridium- and ruthenium-catalysed synthesis of 2,3-disubstituted indoles from anilines and vicinal diols†

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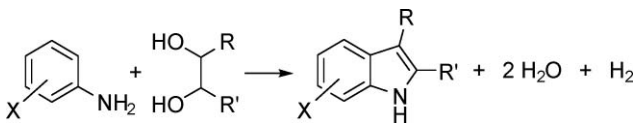
A straightforward and atom-economical method is described for the synthesis of 2,3-disubstituted indoles. Anilines and 1,2-diols are condensed under neat conditions with catalytic amounts of either $[Cp^*IrCl_2]_2$/MsOH or $RuCl_3 \cdot xH_2O$/phosphine (phosphine = PPh_3 or xantphos). The reaction does not require any stoichiometric additives and only produces water and dihydrogen as byproducts. Anilines containing methyl, methoxy, chloro and fluoro substituents can participate in the cyclocondensation. Meta-substituted anilines give good regioselectivity for 6-substituted indoles, while unsymmetrical diols afford excellent regioselectivity for the indole isomer with an aryl or large alkyl group in the 2-position. The mechanism for the cyclocondensation presumably involves initial formation of the α-hydroxyketone from the diol. The ketone subsequently reacts with aniline to generate the α-hydroxyimine which rearranges to the corresponding α-aminoketone. Acid- or metal-catalysed electrophilic ring-closure with the release of water then furnishes the indole product.

Introduction

The indole skeleton is one of the most important heterocyclic ring systems which is found in many natural products[1] and biologically active molecules.[2] Substituted indoles are capable of binding to a number of receptors with high affinity and the indole substructure is found in a variety of different drugs.[3] This has stimulated intense research into the chemical synthesis of indoles for more than a century.[4] The Fischer indole synthesis from 1883[5] is still a widely applied method where aryl hydrazines are reacted with enolisable aldehydes/ketones to afford the heterocycle after a sigmatropic rearrangement of the corresponding hydrazone.[6] Another classical but less commonly used procedure is the Bischler indole synthesis from 1892[7] where anilines are alkylated with α-haloketones and the resulting α-anilinoketones then cyclised to the target molecule.[8] More recently, a variety of new procedures have been developed for assembling the indole ring system particularly by the use of various palladium-catalysed cyclisations.[9] However, the starting materials are often 1,2-disubstituted aromatic compounds such as 2-haloanilines, which may not be widely available, but have to be prepared in separate steps. A more straightforward protocol with simple starting materials involve condensation of anilines with 1,2-diols to afford indoles after liberating two molecules of water and one molecule of dihydrogen (Scheme 1). This procedure is also a very environmentally friendly and atom-economical method for synthesis of the heterocycle.[10] The reaction has previously been achieved with anilines and $RuCl_2(PPh_3)_3$ in dioxane at 180 °C[11] or with 1-naphthylamine and $IrCl_3 \cdot 3H_2O$/BINAP in mesitylene at 169 °C under air.[12] However, in both cases a significant excess of the arylamine is employed. A related indole synthesis has been described with anilines, alkanolammonium chlorides and $RuH_2(PPh_3)_4$, but in this case an additional stoichiometric amount of $SnCl_2 \cdot 2H_2O$ is required.[13]



Scheme 1 Indole synthesis from anilines and 1,2-diols.

Recently, we have shown that piperazines can be formed by cyclocondensation of primary amines with 1,2-diols in the presence of the iridium catalyst $[Cp^*IrCl_2]_2$.[14] The C–N bond is generated by dehydrogenation of the alcohol to the carbonyl compound followed by imine formation and hydrogenation to the product amine with the liberated dihydrogen from the first step.[15,16] We have also shown that oxindoles can be alkylated in the 3-position with alcohols in the presence of $RuCl_3 \cdot xH_2O$ and PPh_3.[17] We speculated that with anilines the iridium or the ruthenium catalyst would mediate both the C–N and the C–C bond formation to furnish the indole skeleton. Herein, we describe an expedient procedure for synthesis of substituted indoles by cyclocondensation of anilines with 1,2-diols in the presence of either $[Cp^*IrCl_2]_2$ or $RuCl_3 \cdot xH_2O$/phosphine.

Results and discussion

The initial experiments were carried out with aniline, butane-2,3-diol and 1% $[Cp^*IrCl_2]_2$ in a toluene solution. In the absence of any other additives very little conversion was observed at 110 °C while increasing the temperature to 170 °C led to a very complex mixture. With 5% K_2CO_3, which is known to co-catalyse the C–N bond formation,[15] a complex mixture of products was still obtained with no visible cyclisation to the indole. Our previous work had shown that the C–N bond formation could also be mediated by an acidic co-catalyst.[14] We reasoned that the acid would also

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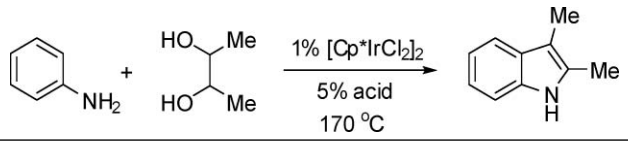
† Electronic supplementary information (ESI) available: NMR spectra for all products. See DOI: 10.1039/c0ob00106f

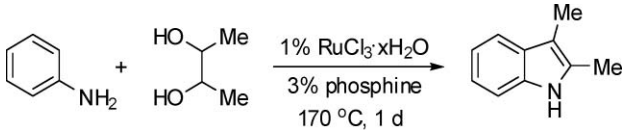
Table 1 Synthesis of 2,3-dimethylindole with different acid co-catalysts[a]



Entry	Acid	Reaction time	Yield[b]
1	H_2SO_4[c]	1 d	48%
2	H_2SO_4[c]	4 d	59%
3	none	2 d	16%
4	conc. HCl	5 d	53%
5	conc. HBr	5 d	53%
6	ZnI_2	1 d	18%
7	$MgBr_2$	2 d	53%
8	$AlCl_3$	3 d	58%
9	TMSOTf	2 d	52%
10	$BF_3{\cdot}OEt_2$	2 d	70%
11	MsOH	2 d	76%
12	conc. H_3PO_4	3 d	75%
13	AcOH	2 d	20%
14	CF_3CO_2H	2 d	46%
15	CF_3SO_3H	2 d	59%

[a] Performed with aniline (90 µL, 1 mmol), butane-2,3-diol (90 µL, 1 mmol), $[Cp^*IrCl_2]_2$ (8 mg, 0.01 mmol) and acid (0.05 mmol) in a closed vial at 170 °C. [b] Isolated yield. [c] With 2.5% H_2SO_4.

Table 2 Synthesis of 2,3-dimethylindole with ruthenium trichloride and different phosphines[a]



Entry	Phosphine	Yield[b]
1	PPh_3	65% (60%)
2	PCy_3	27% (20%)
3	$P(OEt)_3$	11%
4	$P(2\text{-furyl})_3$	9%
5	$(4\text{-}MeOC_6H_4)_3P$	64%
6	$(4\text{-}FC_6H_4)_3P$	70%
7	DPEphos[c]	60%
8	BINAP[c]	35%
9	dppe[c]	38%
10	dppp[c]	70%
11	dppb[c]	73% (66%)
12	dpppentane[c]	62%
13	dppf[c]	53%
14	xantphos[c]	76% (71%)

[a] Performed with aniline (90 µL, 1 mmol), butane-2,3-diol (90 µL, 1 mmol), $RuCl_3{\cdot}xH_2O$ (2.3 mg, 0.01 mmol) and phosphine (0.03 mmol) in a closed vial at 170 °C. [b] GC yields (isolated yields in parenthesis). [c] 1.5% bidentate phosphine.

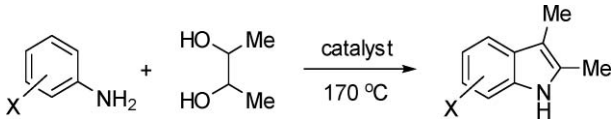
facilitate the C–C bond formation to the indole. Indeed, when the substrates were reacted in toluene at 170 °C with 5% sulfuric acid, 2,3-dimethylindole was obtained as the main product. The reaction was rather slow and only gave 34% yield after 2 days. The main problem seems to be precipitation of the ammonium salt between aniline and the acid. Under neat conditions, however, a homogeneous mixture was obtained and a faster conversion was observed giving rise to the indole in 48–59% isolated yield (Table 1, entries 1 and 2). The reaction was performed in a closed vial with equimolar amounts of aniline and butane-2,3-diol and catalytic amounts of the additives. Although, dihydrogen is released and the pressure increases, no reduction to 2,3-dimethylindoline was observed. Not surprisingly, the reaction did not proceed in the absence of the iridium catalyst.

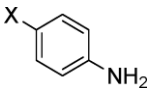
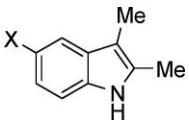
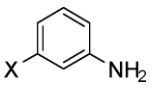
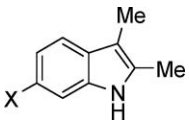
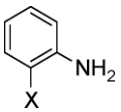
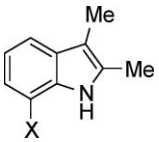
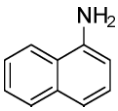
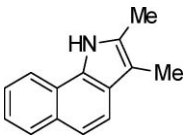
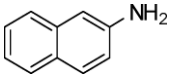
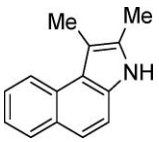
Even though sulfuric acid is a very convenient co-catalyst, the reaction was still rather slow and gave rise to a few minor byproducts. Therefore, a number of experiments were performed with different acids in order to identify the optimum co-catalyst. The acid was necessary since the reaction otherwise gave a complex mixture from which the indole could only be isolated in a low yield (entry 3). Concentrated hydrochloric acid and hydrobromic acid led to essentially the same result as sulfuric acid while several Lewis acids gave faster conversion, but without significantly improving the yield (entries 4–10). The best result was obtained with methanesulfonic acid which gave very clean conversion into the indole with no visible byproducts or starting material remaining according to GC (entry 11). Concentrated phosphoric acid also afforded a good yield, but the reaction was slower while other Brønsted acids were less effective (entries 12–15). As a result the favoured catalyst system consisted of 1% $[Cp^*IrCl_2]_2$ and 5% methanesulfonic acid.

Since ruthenium is significantly cheaper than iridium it was decided also to investigate the cyclocondensation in the presence of various ruthenium catalysts. Based on our previous experience with alkylation of oxindole[17] we focused our attention on ruthenium trichloride and various phosphines in the absence of a solvent. The first experiment was performed with aniline, butane-2,3-diol, $RuCl_3{\cdot}xH_2O$ (1%), PPh_3 (3%) and methanesulfonic acid (5%). After heating the mixture to 170 °C for 1 day, 2,3-dimethylindole was isolated in ~50% yield. When the experiment was repeated in the absence of the sulfonic acid the indole was obtained in 60% yield (Table 2, entry 1). Contrary to the iridium experiment the acid is not necessary in this case to promote the cyclisation. A number of phosphines were then investigated to identify the optimum ligand for the reaction (entries 2–14).

The best results were achieved with the two bidentate ligands dppb and xantphos which gave 66 and 71% isolated yield, respectively. The ratio between ruthenium and phosphorus was further investigated with PPh_3 and dppb, but in both cases the 1 : 3 ratio was found to give the highest yield. However, when repeating the same experiment several times we did in some cases observe a variation in the yield. This appears to be caused by differences in the size of the ruthenium trichloride crystals. The active catalyst is presumably a ruthenium(II) complex generated *in situ* by reduction of ruthenium trichloride with the phosphine. Thus it seems that this process may vary slightly from one experiment to another depending on the ruthenium trichloride batch. When the cyclocondensation was performed with the more soluble $RuCl_2(PPh_3)_3$ complex, consistent yields around 50% were obtained. Due to the convenience of the *in situ* generated catalyst we opted for a solution where this could be generated in a more reproducible way. It turned out that if the reaction mixture was stirred at 110 °C for 1 h and then heated to 170 °C more consistent results were obtained. At 110 °C the cyclocondensation does not proceed, but ruthenium trichloride reacts with the phosphine and the active catalyst is generated. Subsequent heating to the reaction

Table 3 Synthesis of indoles from substituted anilines and butane-2,3-diol[a]



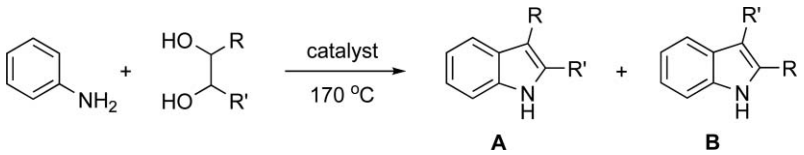
Entry	Aniline	X	Indole	Yield[b] $[Cp^*IrCl_2]_2$	Yield[b] $RuCl_3/PPh_3$	Yield[b] $RuCl_3$/xantphos
1		Me		61%	48%	50%
2		OMe		59%	56%	53%
3		Cl		66%	57%	69%
4		F		46%	45%	52%
5		Me		34%	49%	51%
6		OMe		64%	48%	58%
7		Cl		47%[c]	57%[d]	69%[d]
8		F		47%[e]	48%	52%
9		Me		65%	72%	87%
10		OMe		41%	41%	34%
11		—		65%	60%	72%[f]
12		—		76%	58%	63%[f]

[a] See experimental section for reaction procedures. [b] Isolated yield. [c] Isolated as a 4 : 1 mixture of the 6-chloro and the 4-chloro isomer. [d] Isolated as a 6 : 1 mixture of the 6-chloro and the 4-chloro isomer. [e] Minor amounts of the corresponding 4-fluoroindole was observed, but not isolated. [f] Reaction time 2 days.

temperature furnishes a more reproducible yield of the indole product .

With these optimised conditions in place the stage was now set to explore the substrate scope and limitation of the cyclocondensation method. For each substrate the reaction was performed with both the iridium catalyst ($[Cp^*IrCl_2]_2$/MsOH) and with the ruthenium catalyst ($RuCl_3/PPh_3$ and $RuCl_3$/xantphos). First, regioselectivity and functional groups in the aniline were investigated by reacting various substituted anilines with butane-2,3-diol (Table 3). Methyl and methoxy substituents were compatible with the reaction conditions and yielded the corresponding indoles without any major byproducts (entries 1, 2, 5, 6, 9 and 10). Chloro and fluoro substituents were allowed in the *para* and the *meta* positions (entries 3, 4, 7 and 8) while *o*-chloro- and *o*-fluoroaniline reacted sluggishly and gave less than 25% yield of the corresponding indole (results not shown). With the chloroanilines small amounts of 2,3-dimethylindole was observed as a byproduct, but not isolated. Bromo and boronic ester substituents, on the other hand, were completely reduced off with both the iridium and the ruthenium catalyst and carboxylic acids underwent decarboxylation. Methyl ester groups were partially cleaved off while anilines with cyano, dimethylamino, acetamido, nitro or trifluoromethyl substituents either decomposed or reacted very poorly. Meta-substituted anilines gave a good regioselectivity in the cyclisation to the *para* position (entries 5–8). The same regioselectivity is observed for the sigmatropic rearrangement in the Fischer indole synthesis when the directing group is *ortho-para* directing.[6] The two naphthyl amines gave good yields of the corresponding benzindoles (entries 11 and 12) while 2-aminopyridine gave a complex mixture and 4-aminopyridine did not react. In all cases, the three different catalysts gave comparable yields of the indole product. However, the reactions with the ruthenium catalysts were performed in a shorter time and with a lower catalyst loading than with the iridium catalyst and the ruthenium system is therefore recommended for general use. With this system the xantphos ligand

Table 4 Synthesis of indoles from aniline and various diols[a]



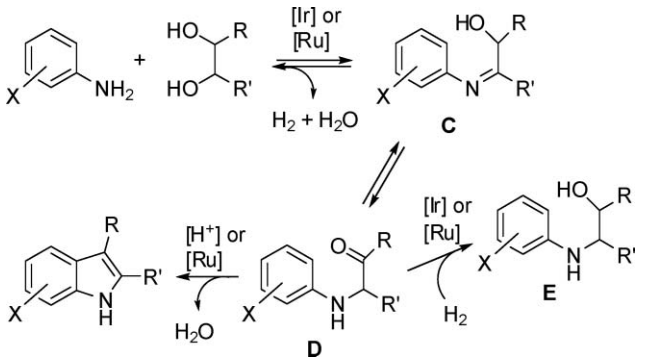
Entry	R	R′	Yield[b] $[Cp^*IrCl_2]_2$	Yield[b] $RuCl_3/PPh_3$	Yield[b] $RuCl_3$/xantphos
1	Me	Et	70% (5 : 1)[c]	49% (1 : 0)[c,d]	57% (1 : 0)[c,d]
2	Me	*n*Bu	65% (7 : 1)[c]	54% (7 : 1)[c]	61% (1 : 0)[c,d]
3	Me	*i*Pr	58% (1 : 0)	32% (1 : 0)[e]	—
4	Me	Ph	31% (1 : 0)[c]	27% (1 : 0)	28% (1 : 0)
5	$-(CH_2)_4-$		53%	50%[f]	52%[f]
6	Ph	Ph	29%	—	—

[a] See experimental section for reaction procedures. [b] Isolated yield (**A** : **B** ratio in parenthesis). [c] Aniline : diol ratio 2 : 3. [d] Minor isomer not isolated. [e] Reaction time 3 days. [f] 3% MsOH was also added.

usually gives a slightly better yield than the triphenylphosphine ligand.

The regioselectivity was also investigated with respect to the diol by reacting different diols with aniline in the presence of the iridium and the ruthenium catalyst. Remarkably, unsymmetric diols gave excellent selectivity for the indole isomer where the large substituent is placed in the 2-position (Table 4, entries 1–4). With the iridium catalyst pentane-2,3-diol and heptane-2,3-diol gave the two indoles in ratios of 5 : 1 and 7 : 1, respectively (entry 1 and 2). More unsymmetrical diols afforded exclusively the isomer with the aryl or large alkyl group in the 2-position (entries 3 and 4). A cyclic diol and a diol with two aryl groups also reacted with aniline although the latter gave a lower yield due to the instability of the diol under the reaction conditions (entries 5 and 6). With the ruthenium catalyst cyclohexane-1,2-diol reacted quite sluggishly with aniline and only afforded the tetrahydrocarbazole in low yield. However, by co-catalysing the reaction with methanesulfonic acid the yield increased to the same level as with the iridium catalyst (entry 5). Ethylene glycol and diols containing a primary alcohol gave complex mixtures with both the iridium and the ruthenium catalyst. The reason may be the poor stability of the products under the reaction conditions. Control experiments with the iridium catalyst showed that indole, 2-methylindole and 3-methylindole all underwent further reactions when exposed to the diol and methanesulfonic acid.

The mechanism for the condensation presumably involves initial formation of the α-hydroxyketone which then reacts with the aniline to furnish the imine **C** (Scheme 2). The α-hydroxyimine can either isomerise to the corresponding α-aminoketone **D** or react with the catalyst and hydrogen to generate the α-aminoalcohol **E**. Since α-hydroxyimines are known to isomerise readily in refluxing benzene[18] the former reaction is the most likely pathway. This was further confirmed by preparing α-aminoalcohol **E** (with R,R′ = $-(CH_2)_4-$) from aniline and cyclohexene oxide. When this compound was treated with $[Cp^*IrCl_2]_2$ and methanesulfonic acid, a complex mixture was observed with only little indole formation indicating that the α-aminoalcohol **E** is not part of the main reaction pathway. The same experiment was carried out with α-aminoalcohol **E** (with R = R′ = Me) and $RuCl_3 \cdot xH_2O/PPh_3$. In this case, the reaction did not go to completion in 24 h and afforded an equal mixture of aniline and 2,3-dimethylindole, which again



Scheme 2 Suggested mechanism for indole formation.

indicates that **E** is not part of the main pathway. When the reactions in Table 1–3 were monitored by GC-MS, the α-aminoalcohol **E** was observed, but mainly in cases where a weak acid or an electron-withdrawing group on the aniline made the cyclisation difficult. This suggests that α-aminoalcohol **E** is formed in a side reaction by reduction of α-aminoketone **D** and the success of the overall reaction depends on the ability of **D** to undergo electrophilic ring-closure under the acidic conditions. α-Aminoketone **D** (with R = R′ = Me) can be prepared by reacting aniline with acetoin in the absence of an acid.[19] When this aminoketone was heated with 5% methanesulfonic acid at 170 °C, the conversion into the indole was complete in 15 min while the reaction at 100 °C took about 2 h. When α-aminoketone **D** (with R = R′ = Me) was treated with 1% $RuCl_3 \cdot xH_2O/PPh_3$ at 170 °C complete conversion into the indole was observed in less than 2 h. It is unlikely, that the reaction goes through an indoline followed by dehydrogenation to the indole. Control experiments have shown that the iridium catalyst is rather slow at dehydrogenating indoline to indole (2 days at 170 °C) and since indolines are not observed by GC-MS during the course of the reaction they are most likely not intermediates in the cyclocondensation.

The excellent regioselectivity with the unsymmetrical diols in Table 4 is most likely determined in the last cyclisation step. Aminoketone **D** is also formed as an intermediate in the Bischler indole synthesis[7,8] and related transformations[20] and in these cases the cyclisation to the indole is not regiospecific, but occurs in such a way that the aryl or large alkyl group is placed in the 2-position

of the indole. For example, 2-phenylindole is formed exclusively when aniline is reacted with phenacyl bromide[21] indicating a complete rearrangement of the initially formed aminoketone. Therefore, aminoketone **D** will only be prone to cyclisation into the indole when R is a small alkyl group, and if this is not the case isomerisation into the opposite regioisomer and subsequent cyclisation will be more favourable.

Conclusion

In summary, we have developed a simple and atom-economical synthesis of 2,3-disubstituted indoles by cyclocondensation of equimolar amounts of anilines and 1,2-diols in the presence of catalytic amounts of $[Cp^*IrCl_2]_2$/MsOH or $RuCl_3$/phosphine. The reaction does not require any solvent or stoichiometric additives and only produces water and dihydrogen as byproducts.

Experimental

GC yields were obtained on a Shimadzu GC2010 instrument equipped with an Equity™ 1 column (15 m × 0.1 mm, 0.1 μm film) using naphthalene as the internal standard. Melting points are uncorrected. Solvents used for chromatography were of HPLC grade. Thin layer chromatography was performed on aluminium plates coated with silica gel 60. Visualisation was done by UV or by dipping in a solution of cerium(IV)sulfate (2.5 g) and ammonium molybdate (6.25 g) in 10% sulfuric acid (250 mL) followed by charring with a heatgun. Flash chromatography was performed with silica gel 60 (35–70 μm). NMR spectra were recorded on a Varian Mercury 300 instrument. Chemical shifts were measured relative to the signals of residual $CHCl_3$ (7.26 ppm)/$CDCl_3$ (77.0 ppm) or DMSO-d_5 (2.50 ppm)/DMSO-d_6 (39.4 ppm). Mass spectrometry was performed by direct inlet on a Shimadzu GCMS-QP5000 instrument. High resolution mass spectra were recorded at the Department of Physics and Chemistry, University of Southern Denmark.

General procedure for iridium-catalysed preparation of indoles. In an oven-dried heavy-walled vial (11 mL) equipped with a screw cap were placed the aniline (1 mmol), the diol (1 mmol), $[Cp^*IrCl_2]_2$ (8 mg, 0.01 mmol) and MsOH (3 μL, 0.05 mmol) under an argon atmosphere. The vial was closed and immediately placed in an aluminium block pre-heated to 170 °C and heated for 2 days. The mixture was quenched with triethylamine (15 μL, 0.1 mmol) and purified by column chromatography on silica gel (hexane–CH_2Cl_2 2 : 1 or heptane/EtOAc 5 : 1) to afford the desired indole.

General procedure for ruthenium-catalysed preparation of indoles. In an oven-dried heavy-walled vial equipped with a screw cap were placed the aniline (2 mmol), the diol (2 mmol), $RuCl_3 \cdot xH_2O$ (4.8 mg, 0.02 mmol) and triphenylphosphine (15.7 mg, 0.06 mmol) (or xantphos (17.4 mg, 0.03 mmol)). The vial was closed and placed in an aluminium block for 1 h at 110 °C and then heated to 170 °C for 24 h. The reaction mixture was worked up as described above.

2,3-Dimethylindole. mp 98–101 °C (lit.[19] 106–108 °C, lit.[22] 107–108 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.22 (s, 3H), 2.35 (s, 3H), 7.05–7.14 (m, 2H), 7.22–7.27 (m, 1H), 7.44–7.49 (m, 1H), 7.60–7.75 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.4, 11.5, 107.0, 110.0, 117.9, 118.9, 120.8, 129.3, 130.6, 135.1. MS: m/z 145 [M]. NMR data are in accordance with literature values.[23,24]

2,3,5-Trimethylindole. mp 115–120 °C (lit.[22] 118–120 °C, lit.[19] 120–122 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.19 (s, 3H), 2.33 (s, 3H), 2.44 (s, 3H), 6.92 (dd, 1H, J = 8.1, 1.5 Hz), 7.13 (d, 1H, J = 8.1 Hz), 7.24 (s, 1H), 7.55 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.4, 11.5, 21.5, 106.5, 109.6, 117.7, 122.3, 128.1, 129.6, 130.7, 133.4. MS: m/z 159 [M]. NMR data are in accordance with literature values.[22]

5-Methoxy-2,3-dimethylindole. mp 105–108 °C (lit.[19] 110–112 °C, lit.[25] 106–108 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.19 (s, 3H), 2.34 (s, 3H), 3.86 (s, 3H), 6.76 (dd, 1H, J = 8.7, 2.4 Hz), 6.92 (d, 1H, J = 2.4 Hz), 7.13 (d, 1H, J = 8.7 Hz), 7.58 (br s, 1H). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.11 (s, 3H), 2.27 (s, 3H), 3.73 (s, 3H), 6.60 (dd, 1H, J = 8.6, 2.4 Hz), 6.83 (d, 1H, J = 2.3 Hz), 7.09 (d, 1H, J = 8.6 Hz), 10.45 (s, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.5, 11.6, 55.9, 100.3, 106.9, 110.4, 110.6, 129.8, 130.2, 131.6, 153.8. ^{13}C NMR (DMSO-d_6, 75 MHz): δ 8.4, 11.3, 55.2, 99.6, 104.8, 109.4, 110.7, 129.2, 130.1, 132.0, 152.8. MS: m/z 175 [M]. ^{1}H NMR data are in accordance with literature values.[25,26]

5-Chloro-2,3-dimethylindole. mp 138–140 °C (lit.[19,24] 142–143 °C, lit.[27] 141–142 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.16 (s, 3H), 2.32 (s, 3H), 7.00–7.14 (m, 2H), 7.40–7.41 (m, 1H), 7.62 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.3, 11.5, 106.9, 110.9, 117.5, 120.9, 125.1, 130.5, 132.3, 133.4. MS: m/z 179 [M]. NMR data are in accordance with literature values.[24]

5-Fluoro-2,3-dimethylindole. mp 98–99 °C (lit.[28] 98 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.17 (s, 3H), 2.33 (s, 3H), 6.83 (td, 1H, J = 11.7, 2.4 Hz), 7.06–7.16 (m, 2H), 7.50–7.70 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.4, 11.6, 102.9 (d, J = 23 Hz), 107.4 (d, J = 4.5 Hz), 108.7 (d, J = 26 Hz), 110.4 (d, J = 9.6 Hz), 129.8 (d, J = 9.5 Hz), 131.5, 132.8, 157.7 (d, J = 233 Hz). MS: m/z 163 [M]. ^{1}H NMR data are in accordance with literature values.[26]

2,3,6-Trimethylindole. mp 98–104 °C (lit.[27] 117–118 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.19 (s, 3H), 2.30 (s, 3H), 2.43 (s, 3H), 6.90 (d, 1H, J = 8.1 Hz), 7.00 (s, 1H), 7.35 (d, 1H, J = 8.1 Hz), 7.43 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.6, 11.5, 21.7, 106.8, 110.2, 117.7, 120.6, 127.3, 129.9, 130.5, 135.7. MS: m/z 159 [M].

6-Methoxy-2,3-dimethylindole. mp 129–132 °C (lit.[29] 130 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.21 (s, 3H), 2.31 (s, 3H), 3.85 (s, 3H), 6.75 (d, 1H, J = 2.2 Hz), 6.78 (dd, 1H, J = 8.5, 2.2 Hz), 7.35 (d, 1H, J = 8.5 Hz), 7.48 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.5, 11.5, 55.7, 94.3, 106.8, 108.2, 118.4, 123.9, 129.2, 135.7, 155.7. MS: m/z 175 [M]. ^{1}H NMR data are in accordance with literature values.[29]

6-Chloro-2,3-dimethylindole. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.21 (s, 3H), 2.34 (s, 3H), 7.06 (dd, 1H, J = 8.4, 1.8 Hz), 7.19 (d, 1H, J = 1.8 Hz), 7.36 (d, 1H, J = 8.4 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.4, 11.5, 107.2, 109.9, 118.7, 119.5, 126.6, 128.0, 131.4, 135.4. HRMS: calcd for $C_{10}H_9ClN$: 178.0428 $[M - H]^-$, found: 178.0426.

6-Fluoro-2,3-dimethylindole. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.15 (s, 3H), 2.23 (s, 3H), 6.78–6.84 (m, 2H), 7.30 (dd, 1H, J = 9.2, 5.3 Hz), 7.55 (s, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.3, 11.3, 96.5 (d, J = 26 Hz), 106.8, 107.1 (d, J = 24 Hz), 118.3 (d,

J = 10 Hz), 125.9, 130.9 (d, J = 3.6 Hz), 134.9 (d, J = 12 Hz), 159.2 (d, J = 235 Hz). HRMS: calcd for $C_{10}H_9FN$: 162.0724 [M − H]$^-$, found: 162.0722.

2,3,7-Trimethylindole. mp 64–65 °C (lit.[19] 79 °C, lit.[24,30] 75–76 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.21 (s, 3H), 2.37 (s, 3H), 2.44 (s, 3H), 6.89–6.93 (m, 1H), 7.00 (dd, 1H, J = 7.8, 6.3 Hz), 7.32 (d, 1H, J = 7.8 Hz), 7.60 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.6, 11.6, 16.5, 107.6, 115.7, 119.1, 119.2, 121.5, 128.8, 130.2, 134.5. MS: m/z 159 [M]. NMR data are in accordance with literature values.[24]

7-Methoxy-2,3-dimethylindole. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.20 (s, 3H), 2.33 (s, 3H), 3.93 (s, 3H), 6.58 (d, 1H, J = 7.5 Hz), 6.99 (t, 1H, J = 7.8 Hz), 7.90 (d, 1H, J = 7.8 Hz), 7.90 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.7, 11.5, 55.3, 101.2, 107.5, 111.0, 119.3, 125.2, 130.2, 130.7, 145.3. HRMS: calcd for $C_{11}H_{12}NO$: 174.0924 [M − H]$^-$, found: 174.0928.

2,3-Dimethyl-1*H*-benzo[*g*]indole. mp 149 °C (lit.[19] 153–155 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.29 (s, 3H), 2.45 (s, 3H), 7.36 (ddd, 1H, J = 7.8, 6.9, 1.2 Hz), 7.45 (ddd, 1H, J = 8.2, 6.9, 1.2 Hz), 7.47 (d, 1H, J = 8.2 Hz), 7.61 (d, 1H, J = 8.4 Hz), 7.87–7.95 (m, 2H), 8.40 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.6, 11.6, 118.6, 119.0, 119.7, 121.2, 123.0, 125.1, 128.8, 129.9. MS: m/z 195 [M]. ^{1}H NMR data are in accordance with literature values.[31]

1,2-Dimethyl-3*H*-benzo[*e*]indole. mp 118–121 °C (lit.[32] 131 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.39 (s, 3H), 2.61 (s, 3H), 7.37 (d, 1H, J = 8.7 Hz), 7.37 (ddd, 1H, J = 8.4, 6.9, 1.5 Hz), 7.50 (d, 1H, J = 8.7 Hz), 7.51 (ddd, 1H, J = 8.4, 6.9, 1.5 Hz), 7.90 (d, 1H, J = 8.8 Hz), 7.94 (br s, 1H), 8.49 (d, 1H, J = 8.4 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 11.5, 12.4, 109.7 (2C), 112.2, 121.8, 122.5, 131.1, 125.2, 128.6, 128.9, 129.1, 129.6, 131.3. MS: m/z 195 [M].

2-Ethyl-3-methylindole (major)[a] and 3-ethyl-2-methylindole (minor)[b]. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.21 (t, 3H, J = 7.8 Hz)[b], 1.26 (t, 3H, J = 7.8 Hz)[a], 2.23 (s, 3H)[a], 2.35 (s, 3H)[b], 2.70 (q, 2H, J = 7.8 Hz)[b], 2.74 (q, 2H, J = 7.5 Hz)[a], 7.04–7.14 (m, 4H)[a,b], 7.22–7.28 (m, 2H)[a,b], 7.46–7.54 (m, 2H)[a,b], 7.68 (br s, 2H)[a,b]. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.3[a], 11.5[b], 14.0[a], 15.4[b], 17.3[b], 19.4[a], 106.2[a], 110.1[a,b], 113.9[b], 118.0[a,b], 119.0[a,b], 120.9[a,b], 128.5[b], 129.4[a], 130.1[b], 135.0[a,b], 136.4[a]. MS: m/z: 159 [M]. NMR data for 2-ethyl-3-methylindole[a] are in accordance with literature values.[33] NMR data for 3-ethyl-2-methylindole[b] are in accordance with literature values.[24]

2-Butyl-3-methylindole. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.92 (t, 3H, J = 7.3 Hz), 1.35 (sextet, 2H, J = 7.3 Hz), 1.57 (p, 2H, J = 7.2 Hz), 2.22 (s, 3H), 2.66 (t, 3H, J = 7.3 Hz), 7.09 (m, 2H), 7.20 (d, 1H, J = 7.1 Hz), 7.50 (d, 1H, J = 7.5 Hz), 7.55 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.4, 13.9, 22.4, 25.8, 31.8, 106.7, 110.1, 118.0, 118.9, 120.8, 129.3, 135.0, 135.3. MS: m/z 187 [M]. NMR data are in accordance with literature values.[34]

2-Isopropyl-3-methylindole. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.31 (d, 6H, J = 7.0 Hz), 2.25 (s, 3H), 3.25 (septet, 1H, J = 7.0 Hz), 7.04–7.14 (m, 2H), 7.26–7.30 (m, 1H), 7.47–7.50 (m, 1H), 7.72 (br s, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.4, 22.3, 25.6, 105.2, 110.2, 118.0, 119.0, 120.8, 129.4, 134.8, 140.2. MS: m/z 173 [M]. NMR data are in accordance with literature values.[35]

3-Methyl-2-phenylindole. mp 87–90 °C (lit.[22] 90–91 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.46 (s, 3H), 7.11–7.24 (m, 2H), 7.32–7.36 (m, 2H), 7.44–7.50 (m, 2H), 7.55–7.62 (m, 3H), 8.00 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 9.6, 108.6, 110.6, 119.0, 119.5, 122.2, 127.2, 127.7, 128.7, 129.9, 133.2, 134.0, 135.7. MS: m/z 207 [M]. NMR data are in accordance with literature values.[20a,23]

1,2,3,4-Tetrahydrocarbazole. mp 111–113 °C (lit.[19] 114 °C, lit.[30] 116–118 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.80–1.94 (m, 4H), 2.64–2.74 (m, 4H), 7.02–7.14 (m, 2H), 7.20–7.26 (m, 1H), 7.42–7.48 (m, 1H), 7.52–7.66 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.4, 23.7, 23.8, 110.6, 110.8, 118.2, 119.5, 121.4, 128.3, 134.5, 136.1. MS: m/z 171 [M]. NMR data are in accordance with literature values.[23,24]

2,3-Diphenylindole. mp 108–109 °C (lit.[36] 109 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.10–7.50 (m, 13H), 7.69 (d, 1H, J = 7.8 Hz), 8.18 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 110.9, 115.0, 119.7, 120.4, 122.7, 126.2, 127.7, 128.1, 128.5, 128.7 (2C), 130.1, 132.6, 134.0, 135.0, 135.8 ppm. MS: m/z 269 [M]. NMR data are in accordance with literature values.[36]

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