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Pericyclic rearrangements of *N*-heterocyclic carbenes of indazole to substituted 9-aminoacridines†

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On deprotonation, 1-arylindazolium salts form 1-arylindazol-3-ylidenes which rearrange spontaneously *via* ring cleavage, ring closure and subsequent proton transfer to substituted 9-aminoacridines. By contrast, the *N*-heterocyclic carbene of 2-phenylindazolium cannot rearrange similarly and was trapped by sulfur.

Introduction

Acridines display a broad variety of biological activities. Thus the antimalarial Mepacrine[1] (Atebrin) was described nearly 80 years ago.[2] Other medicinal and pharmaceutical applications cover the range from antitumor compounds (Nitracrine,[3] Amsacrine[4]), germicides (Proflavine[5]), to antiseptic agents (Ethacridine[6]). It is well known that acridines are DNA intercalators and so they have been used as building elements in intercalator peptides.[7] Tacrine[8] was approved for the treatment of Alzheimer's disease. Some other acridines have been prepared and used as dyes, fluorescent compounds and structure elements of new materials.[9]

The chemistry of acridines has been the subject of several books[10] and reviews.[11] As substitution reactions often result in mixtures of regioisomers, the most widely applied syntheses of acridines are those involving ring closure reactions, often followed by aromatizations. At least six classes of ring closure reactions to acridines can be recognized[10] which are characterized in Fig. 1.

The condensation of 2-aminophenylcarbonyl compounds with phenols[13] (von Niementowski reaction[12]) belongs to class **I** of ring closure reactions and the same is true for the reaction of isatins and phenols.[14] The reaction of 2-aminobenzaldehyde **1** with phloroglucinol to give 1,3-dihydroxyacridine **7a** is presented as an example[13] (Scheme 1). This reaction, however, seems to be of rather limited applicability as some phenols do not react under these conditions. Often strongly basic conditions have to be applied which cause some substituent incompatibilities.[10] The modified Friedländer reaction gives

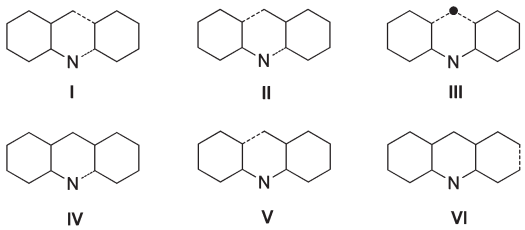

Fig. 1 Six categories of ring closure reactions to form acridines.

di- or tetrahydroacridines which can be oxidized subsequently.[15] Catalysts have been examined in this reaction.[16]

2-Haloacylbenzenes react readily with anilines to afford 9-substituted acridines. This reaction, which represents a ring closure of type **II**, is known as Ullmann synthesis.[10] The treatment of **2** with aniline to give 2-nitro-9-phenylacridine **7b**[17] is shown in Scheme 1. Acridines are also formed on reaction of benzyne with diimines.[18] The Bernthsen reaction belongs to class **III** of acridine syntheses. This reaction starts from diphenylamines and a one-carbon donor such as carboxylic acids or dicarboxylic acids.[19] As shown in Scheme 1, diphenylamine **3** gives **7c**. The Bernthsen reaction, however, proceeds under vigorous conditions which cause considerably diminished yields. Class **IV** is represented by the cyclization of bis(aminoaryl)-methanes such as **4** to **7d**.[20] In the presence of calcium oxide, acridine is formed in 75% yield; however, a temperature of 600 °C over a period of 40 minutes is necessary.[21] The cyclization of 2-(arylamino)benzaldehydes,[22] available by McFayden–Stevens reaction,[23] or (2-arylamino)acetophenones[24] represents class **V** of ring closure reactions to acridines. Indium triflate catalysts have been tested.[25] The reaction of **5** with **7e** is representative of this class of ring closure reactions. Class **VI** is exemplified by the silver-[26] or rhodium-catalyzed[27] cyclisation of 3-oxo-3-(2-ethynylquinolin-3-yl)propanoates (*cf.* **6** to **7f**). A very limited number of acridine syntheses involving ring transformations has been described, among which is the photolysis

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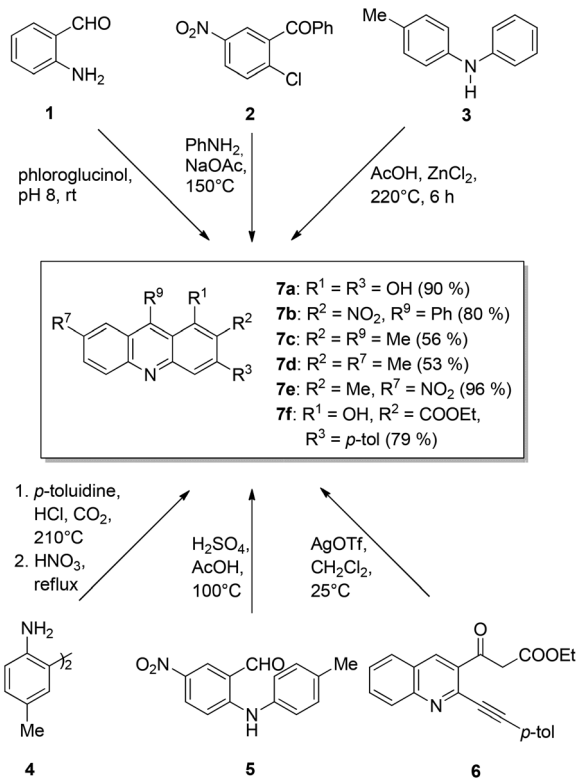
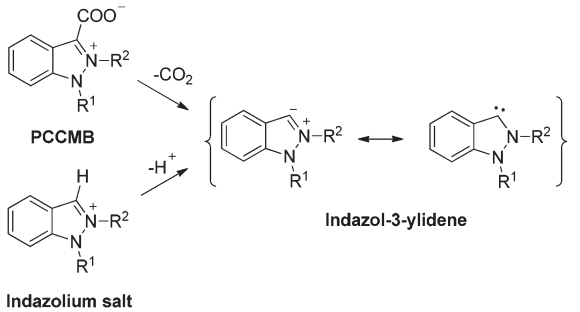


Scheme 1

of suitably substituted benzotriazoles[28] or the ring contraction of dibenzazepines.[29] Either transformation is of limited applicability.

During the last decade, interest in *N*-heterocyclic carbenes (NHC) has been high. New NHC structures,[30] effective NHC ligands in metal-catalyzed reactions,[31] or NHC organocatalysts[32] have been developed and applied very successfully. Less attention has been focused on *N*-heterocyclic carbenes as the starting materials or reactive intermediates in heterocyclic synthesis. Recently, we described a 4-aminoquinoline synthesis *via* pyrazole-3-ylidenes.[33] To the best of our knowledge, the *N*-heterocyclic carbene of indazole has been prepared for the first time by decarboxylation of the pseudo-cross-conjugated heterocyclic mesomeric betaine (PCCMB)[34] indazolium-3-carboxylate[35] (Scheme 2). An alternative approach to indazol-3-ylidene is deprotonation of indazolium salts. In the case where $R^1 \neq Ar$, indazole-3-ylidene can be used as a reagent or as a building block in synthesis,[36] and in coordination chemistry.[37]

We report here a rearrangement reaction for the synthesis of substituted acridines from indazolium salts which possess a phenyl ring in position 1 (R^1 = Ar). This rearrangement proceeds *via* the *N*-heterocyclic carbene of indazole. We examined the scope and limitations of this ring transformation and performed DFT-calculations to gain insight into the mechanism.



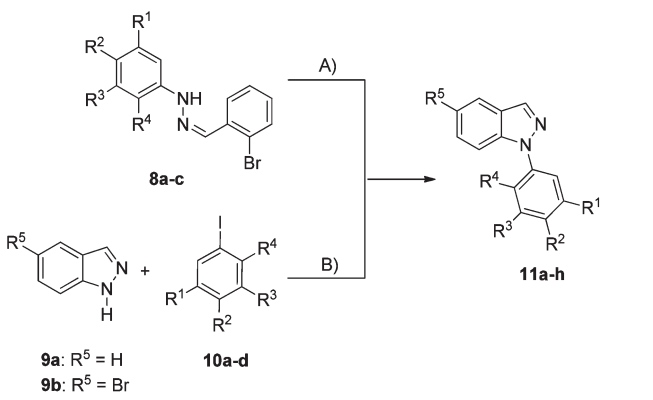
Scheme 2

Results and discussion

Suitable indazole derivatives have been prepared by two different methods (Scheme 3). As method A, a Buchwald–Hartwig coupling of 2-bromobenzaldehyde hydrazones **8** with $Pd(dba)_2$ in the presence of *rac*-BINAP and potassium phosphate according to a modified literature procedure[38] has been applied. Method B, which proved to give slightly better yields in all the compared cases, is a copper(I)-catalyzed coupling of indazoles **9a,b** and iodobenzenes **10a–h** using CuI, 1,2-diaminocyclohexane, and potassium phosphate in dioxane. Thus, method A gave 85% of 1-phenylindazole **11a** (Table 1, entry 1), whereas method B gave 91% (Table 1, entry 4). Method A was employed for the synthesis of the indazoles **11b,c** in good yields, whereas method B was used to prepare **11d–h** in moderate to almost quantitative yields. The indazoles **11c**,[39] **11f**,[38] and **11g**[40] have been described before.

The indazoles **11i** and **11j** were synthesized from **11e**, which was subjected to a Suzuki–Miyaura coupling reaction (Scheme 4 and Table 1, entries 11 and 12, method B + S). The latter mentioned reaction was performed applying a cyclobutene-bis-imidazol-3-ylidene ligand which we described earlier.[41]

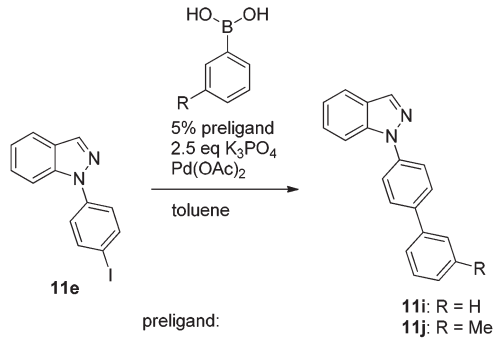
Dimethylsulfate or diethylsulfate in boiling toluene and a subsequent anion exchange converted the 1-arylindazoles into the new indazolium salts **12a–k** as pure crystalline compounds in high yields (Table 1, entries 1–3, 5–12) (Scheme 5).



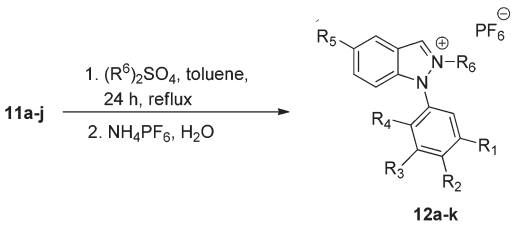
Scheme 3

Table 1 Preparation of indazoles **11a–j** and indazolium salts **12a–k**

Entry	R^1	R^2	R^3	R^4	R^5	R^6	Method	Yield (%)	Yield (%)
1	H	H	H	H	H	Me	A	85 (**11a**)	91 (**12a**)
2	Cl	H	H	H	H	Me	A	67 (**11b**)	84 (**12b**)
3	H	H	H	Cl	H	Me	A	79 (**11c**)	91 (**12c**)
4	H	H	H	H	H	Me	B	91 (**11a**)	/
5	H	I	H	H	Br	Me	B	54 (**11d**)	94 (**12d**)
6	H	I	H	H	H	Me	B	40 (**11e**)	87 (**12e**)
7	H	CF_3	H	H	H	Me	B	82 (**11f**)	83 (**12f**)
8	Me	H	Me	H	H	Me	B	96 (**11g**)	88 (**12g**)
9	H	H	H	H	Br	Me	B	64 (**11h**)	75 (**12h**)
10	H	H	H	H	H	Et	B	/	77 (**12i**)
11	H	Ph	H	H	H	Me	B + S	83 (**11i**)	72 (**12j**)
12	H	3-Tolyl	H	H	H	Me	B + S	95 (**11j**)	58 (**12k**)



Scheme 4



Scheme 5

The indazolium salts **12a–k** were then used to perform the title indazole→acridine rearrangements. Heating 1-phenylindazolium salt **12a** with K_3PO_4 in anhydrous dioxane over a period of three hours gave the *N*-methyl-9-acridinylamine **13a** in 87% isolated yield (Table 2, entry 1). These conditions were also applied to prepare the acridinylamines **13b–k** (Table 2, entries 2–11). As expected, the rearrangement of the indazolium salt **12b** resulted in the formation of two regioisomeric products in 70% overall yield, **13b** and **13c**, which we separated by column chromatography (Table 2, entries 2a,b). The acridinylamines **13ba**, **13c**, **13e**, **13f–h**, **13j,k** are new compounds. The parent compound of the series **13a** has of course been synthesized before by various methods. Among those, the reaction of 9-chloroacridine with methylamine seems to be the most effective one (91% yield[42]). Likewise, **13i** was obtained with ethylamine in 87% yield.[42] The acridines **13bb** and **13c** have been mentioned before; however, experimental details are not available (Scheme 6).[43]

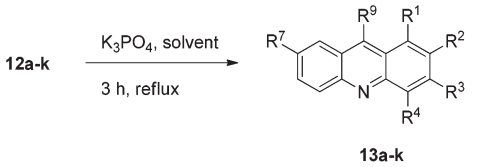
According to a DFT-calculation the rearrangement of **12a** proceeds *via* indazol-3-ylidene **12A**, which is formed on deprotonation of the indazolium salts (Scheme 7). Prominent peaks of the carbene **12A** are visible at m/z = 417.1 [**12a**·**12A**]$^+$ in the ESI mass spectra between 0 and 50 V fragmentor voltage on spraying a sample of **12a** from a methanol solution of Li_2CO_3. The silver adduct [**12A**·Ag·**12A**]$^+$ can be detected at m/z = 523.1 on the addition of AgOAc to the same solution. Ring opening of the pyrazole moiety by cleavage of the N–N bond to **12B** ($\Delta G^{\#}$ = +18.4 kJ mol^{-1}; ΔG = −76.1 kJ mol^{-1}), followed by *trans–cis* isomerisation of the phenylimine group ($\Delta G^{\#}$ = +65.6 kJ mol^{-1}; ΔG = −60.4 kJ mol^{-1}), 6π-electrocyclic ring closure to **12C** ($\Delta G^{\#}$ = +55.1 kJ mol^{-1}; ΔG = −107 kJ mol^{-1}) and subsequent proton transfer yielded the 9-aminoacridine **13a**. The proton transfer must proceed intermolecularly, as an intramolecular process has an activation barrier of $\Delta G^{\#}$ = +165.4 kJ mol^{-1} according to the calculation.

We also calculated bond lengths and partial charges of the intermediate **12B** which is shown in Fig. 2. The calculation predicts a C=C double bond (1.353 Å) as well as a C=N double bond (1.201 Å) in **12B** which are slightly longer and shorter, respectively, in comparison with the calculated values of *N*-vinylidenemethanamine **14** (C=C: 1.316 Å; C=N: 1.224 Å) as model substance. The ketimine resonance structure of **12B** is also reflected in the bond lengths of the former benzene ring and the exocyclic imine moiety (1.298 Å). These data suggest that the ring closure is predominantly pericyclic in nature, similar to the pyrazole-3-ylidene→quinoline rearrangement which we described before.[33]

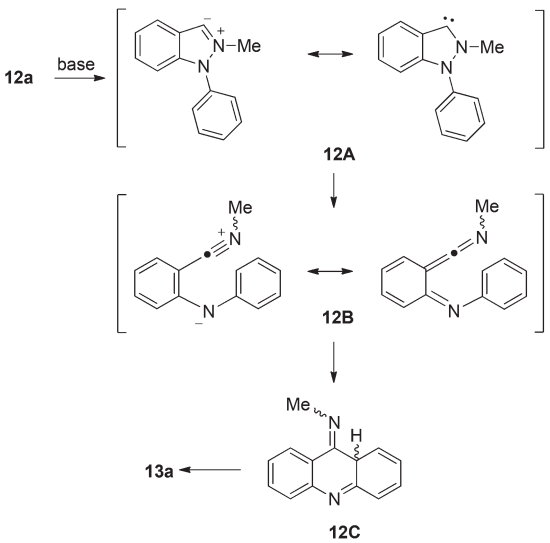
We next prepared the isomer of **12a**, *i.e.* the 1-methyl-2-phenylindazolium salt **17** (Scheme 8). Arylation of indazole with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate **15** in the presence of a mixture of CsF and NaF in MeCN gave 2-phenylindazole **16**.[44] We methylated **16** to **17** which was obtained in 66% yield over two steps after anion exchange with

Table 2 Rearrangement of indazolium salts **12a–k** to acridines **13a–k**

Entry	R^1	R^2	R^3	R^4	R^7	R^9	Starting material	Solvent	Yield (%)
1	H	H	H	H	H	NHMe	**12a**	Dioxane	87 (**13a**)
2a	Cl	H	H	H	H	NHMe	**12b**	Toluene	30 (**13ba**)
2b	H	H	Cl	H	H	NHMe	**12b**	Toluene	40 (**13bb**)
3	H	H	H	Cl	H	NHMe	**12c**	Dioxane	83 (**13c**)
4	H	I	H	H	Br	NHMe	**12d**	Dioxane	35 (**13d**)
5	H	I	H	H	H	NHMe	**12e**	Dioxane	41 (**13e**)
6	H	CF_3	H	H	H	NHMe	**12f**	Dioxane	51 (**13f**)
7	Me	H	Me	H	H	NHMe	**12g**	Dioxane	58 (**13g**)
8	H	H	H	H	Br	NHMe	**12h**	Dioxane	32 (**13h**)
9	H	H	H	H	H	NHEt	**12i**	Toluene	60 (**13i**)
10	H	Ph	H	H	H	NHMe	**12j**	Toluene	83 (**13j**)
11	H	3-Tolyl	H	H	H	NHMe	**12k**	Toluene	37 (**13k**)



Scheme 6



Scheme 7

tetraphenylborate. Deprotonation of **17** with KO*t*Bu in 1,4-dioxane gave the indazolium-3-ylidene **17A**, which cannot rearrange according to the mechanism described above. As a consequence, we were able to trap **17A** with sulfur to the indazole-3-thione **18** in moderate yield.

Conclusions

In summary we present a new synthesis for new acridines *via* a rearrangement of *in situ* generated indazol-3-ylidenes.

Experimental

General considerations

Dioxane was dried over sodium according to standard procedures before usage. All reactions for the palladium-catalyzed intramolecular amination and the rearrangement were carried out under an atmosphere of nitrogen in oven-dried glassware. Flash-chromatography was performed with silica gel 60 (0.040–0.063 mm). Nuclear magnetic resonance (NMR) spectra were obtained with a Bruker Avance 400 MHz and Bruker Avance III 600 MHz. ^{1}H NMR spectra were recorded at 400 MHz or 600 MHz. ^{13}C NMR spectra were recorded at 100 MHz or 150 MHz, with the solvent peak or tetramethylsilane used as the internal reference. Multiplicities are described by using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. FT-IR spectra were obtained on a Bruker Alpha T equipped with a Platinum ATR unit. The mass spectra were measured with a Varian 320 MS Triple Quad GC/MS/MS with a Varian 450-GC. The electrospray ionization mass spectra (ESI-MS) were measured with an Agilent LCMSD series HP 1100 with APIES. Melting points are uncorrected and were determined in an apparatus according to Dr Tottoli (Büchi). Yields are not optimized. Compounds **8a**,[38] **11a**,[38] **11c**,[39] **11f**,[38] and **11g**[40] were prepared as described in the literature.

2-Bromobenzaldehyde 3-chlorophenylhydrazone 8b. A solution of 185 mg (1.0 mmol) of 2-bromobenzaldehyde in 5 mL of methanol was added to a hot solution of 142 mg (1 mmol) of 3-chlorophenylhydrazine in 1 mL of methanol. The mixture was stirred with reflux temperature for 30 minutes. After cooling to −30 °C and keeping this temperature for 12 h, the precipitate was collected by filtration, washed twice with 0.5 mL of cold methanol and dried *in vacuo*. Yield: 209 mg (68%) of a white solid, m.p. 144 °C. ^{1}H NMR (600 MHz, DMSO-d_6): δ = 10.94 (s, 1H), 8.19 (s, 1H), 8.01 (dd, J = 8.0/1.7 Hz, 1H), 7.62 (dd, J = 8.0/1.1 Hz, 1H), 7.42–7.39 (m, 1H), 7.25–7.22 (m, 2H), 7.13 (t, J = 2.0 Hz, 1H), 6.99 (ddd, J = 8.0/2.0/0.8 Hz, 1H), 6.80 (ddd, J = 8.0/2.0/0.8 Hz, 1H) ppm. ^{13}C NMR (150 MHz, DMSO-d_6): δ = 146.3, 135.8, 133.9, 133.8, 132.9, 130.8, 129.9, 127.9, 126.4, 121.9, 118.7, 111.4, 110.9 ppm; IR (KBr): 3316, 2977, 2938, 1590, 1517, 1468, 1436,

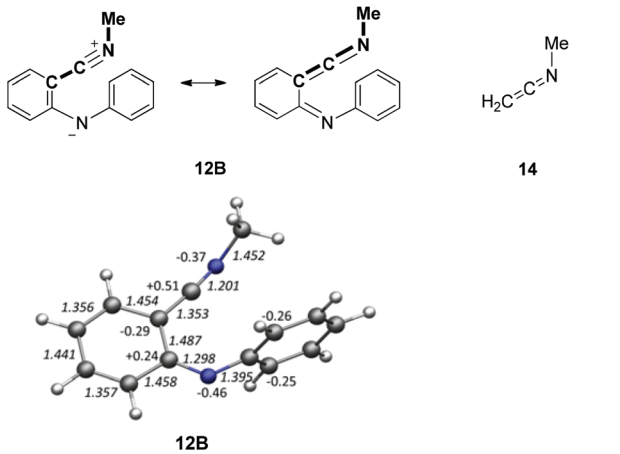
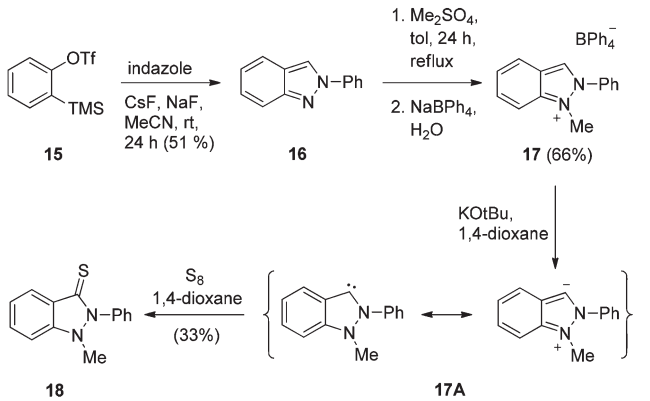


Fig. 2 Results of calculations.



Scheme 8

1261, 1142, 755, 680, 671, 441 cm^{-1}. MS (70 eV): m/z = 308 [M^+]. HR-ESI-MS for $C_{13}H_{11}N_2BrCl$ required 308.9794. Found: 308.9797.

2-Bromobenzaldehyde 2-chlorophenylhydrazone 8c. A solution of 185 mg (1.0 mmol) of 2-bromobenzaldehyde in 5 mL of methanol was added to a hot solution of 142 mg (1 mmol) of 2-chlorophenylhydrazine in 1 mL of methanol. The mixture was stirred with reflux temperature for 30 min. After cooling to −30 °C and keeping this temperature for 12 h, the precipitate was collected by filtration, washed twice with 0.5 mL of cold methanol and dried *in vacuo*. Yield: 262 mg (85%) of a white solid, m.p. 120 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.38 (s, 1H), 8.64 (s, 1H), 8.03 (dd, J = 8.0/1.5 Hz, 1H), 7.64 (dd, J = 8.0/1.1 Hz, 1H), 7.59 (dd, J = 8.3/1.5 Hz, 1H), 7.41 (dd, J = 8.0/7.5 Hz, 1H), 7.34 (dd, J = 8.0/1.5 Hz, 1H), 7.29–7.24 (m, 2H), 6.82 (ddd, J = 8.0/7.5/1.5 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 141.1, 138.3, 134.2, 133.0, 130.0, 129.4, 128.0, 127.9, 126.5, 122.3, 120.1, 116.4, 114.2 ppm; IR (ATR): 3318, 1552, 1455, 1270, 1215, 1047, 1031, 949, 735, 708, 680, 440 cm^{-1}. MS (70 eV): m/z = 308 [M^+]. HR-ESI-MS for $C_{13}H_{11}N_2BrCl$ required 308.9794. Found: 308.9797.

General procedure for the preparation of 1-aryl-1*H*-indazoles by intramolecular palladium-catalysed cross-coupling (method A)

1.0 mmol of the 2-bromobenzaldehyde arylhydrazones, 424 mg (2.0 mmol) of K_3PO_4, 11 mg (0.02 mmol) of *rac*-BINAP, 12 mg (0.02 mmol) of $Pd(dba)_2$ and 10 mL of anhydrous toluene were stirred at reflux temperature under an atmosphere of nitrogen for 12 hours. The resulting mixture was then cooled to room temperature and evaporated to dryness. The crude products were purified by flash column chromatography (petroleum ether–ethyl acetate = 3 : 1).

1-(3-Chlorophenyl)-1*H*-indazole 11b. Yield: 153 mg (67%) of a colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.42 (s, 1H), 7.92–7.87 (m, 2H), 7.82–7.78 (m, 2H), 7.61 (t, J = 8.0 Hz, 1H), 7.52 (dd, J = 8.0/7.2 Hz, 1H), 7.47–7.44 (m, 1H), 7.29 (dd, J = 8.0/7.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.9, 138.0, 136.4, 133.9, 131.3, 127.8, 126.2, 125.2, 122.0, 121.6, 121.5, 120.2, 110.5 ppm; IR (NaCl): 3067, 1594, 1485, 1371, 1259 cm^{-1}. MS (70 eV): m/z = 228 [M^+]. HR-ESI-MS: $C_{13}H_{10}N_2Cl$ required 229.0533. Found: 229.0533.

General procedure for the preparation of 1-aryl-1*H*-indazoles by intermolecular copper(I)-coupling (method B)

A mixture of 1.0 mmol of 1*H*-indazole, 1.2 mmol of aryliodide, 19 mg (0.1 mmol) of copper(I) iodide, 0.01 mL (0.1 mmol) of (*R*,*S*)-1,2-diaminocyclohexane, 424 mg (2.0 mmol) of K_3PO_4 in 10 mL of 1,4-dioxane was stirred at reflux temperature for 24 h. The resulting mixture was then cooled to room temperature and evaporated to dryness. The crude product was purified by flash column chromatography (petroleum ether–ethyl acetate = 2 : 1).

5-Bromo-1-(4-iodophenyl)-1*H*-indazole 11d. Yield: 215 mg (54%) of colorless crystals, m.p. 129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, J = 0.4 Hz, 1H), 7.93 (d, J = 1.8 Hz, 1H), 7.87–7.83 (m, 2H), 7.58 (d, J = 9.0 Hz, 1H), 7.50 (dd, J = 9.0/1.8 Hz, 1H), 7.47–7.44 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.5, 138.6, 137.3, 135.0, 130.5, 127.1, 124.3, 123.9, 114.8, 111.7, 91.4 ppm; IR (KBr): 3061, 2360, 1585, 1494, 1439, 1416, 1183, 1058, 979, 821, 795, 785 cm^{-1}. ESI-MS (100 V, HCl): m/z = 399 [M + H^+]. HR-ESI-MS: $C_{13}H_9N_2BrI$ required 398.8994. Found: 398.8994.

1-(4-Iodophenyl)-1*H*-indazole 11e. Yield: 129 mg (40%) of colorless crystals, m.p. 100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 0.7 Hz, 1H), 7.86–7.83 (m, 2H), 7.80 (dt, J = 8.0/0.9 Hz, 1H), 7.72 (dd, J = 8.6/0.9 Hz, 1H), 7.53–7.49 (m, 2H), 7.46–7.42 (m, 1H), 7.26–7.22 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.0, 138.6, 138.5, 136.0, 127.5, 125.6, 124.3, 121.8, 121.5, 110.3, 90.8 ppm; IR (KBr): 3055, 1612, 1585, 1489, 1418, 1211, 979, 819, 749 cm^{-1}. MS (70 eV): m/z = 320 [M^+]. HR-ESI-MS: $C_{13}H_{10}N_2I$ required 320.9889. Found: 320.9893.

5-Bromo-1-phenyl-1*H*-indazole 11h. Yield: 175 mg (64%) of colorless crystals, m.p. 113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, J = 0.8 Hz, 1H), 7.94 (dd, J = 1.8/0.5 Hz, 1H), 7.70–7.67 (m, 2H), 7.62 (dt, J = 8.9/0.6 Hz, 1H), 7.57–7.53 (m, 2H), 7.49

(dd, J = 8.9/1.8 Hz, 1H), 7.41–7.37 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 137.6, 134.6, 130.3, 129.7, 127.2, 127.0, 123.9, 122.9, 114.6, 112.0 ppm; IR (KBr): 3057, 1599, 1500, 1486, 1183, 980, 908, 811, 784, 760, 727, 695 cm^{-1}. ESI-MS (100 V, HCl): m/z = 273 [M + H$^+$]. HR-ESI-MS for $C_{13}H_{10}N_2Br$ required 273.0027. Found: 273.0027.

General procedure for the preparation of 1-aryl-1*H*-indazoles by Suzuki-coupling

A mixture of 1.0 mmol of 1-(4-iodophenyl)-1*H*-indazole (**11e**), 1.2 mmol of the corresponding boronic acid, 42 mg (0.05 mmol) of a 1 : 1 mixture of $Pd(OAC)_2$ and (cyclobutene-1,2-diyl)bis-imidazolium tetrafluoroborate, and 530 mg (2.5 mmol) of K_3PO_4 in 20 mL of toluene was stirred at reflux temperature for 8 h. The resulting mixture was then cooled to room temperature and evaporated to dryness. The crude product was purified by flash column chromatography (petroleum ether–ethyl acetate = 3 : 1).

1-([1,1′-Biphenyl]-4-yl)-1*H*-indazole 11i. Yield: 223 mg (83%) of a white solid, m.p. 163 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, J = 0.8 Hz, 1H), 7.83–7.80 (m, 4H), 7.78–7.75 (m, 2H), 7.67–7.64 (m, 2H), 7.50–7.43 (m, 3H), 7.40–7.36 (m, 1H), 7.26–7.22 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.3, 139.5, 139.4, 138.8, 135.6, 128.9, 128.1, 127.6, 127.3, 127.1, 125.4, 122.9, 121.6, 121.4, 110.5 ppm. IR (ATR): 3038, 2923, 2363, 2134, 1949, 1656, 1602, 1527, 1463, 1380, 1219, 1185, 1147, 1071, 1017, 948, 837, 753, 690 cm^{-1}. MS (70 eV): m/z = 270.1 [M$^+$]. HR-ESI-MS: $C_{19}H_{15}N_2$ required 271.1235. Found: 271.1233.

1-(3′-Methyl-[1,1′-biphenyl]-4-yl)-1*H*-indazole 11j. Yield: 270 mg (95%) of a white solid, m.p. 85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 0.6 Hz, 1H), 7.79–7.77 (m, 4H), 7.74–7.71 (m, 2H), 7.48–7.40 (m, 3H), 7.36–7.32 (m, 1H), 7.23–7.16 (m, 2H), 2.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.3, 139.7, 139.4, 138.8, 138.6, 135.6, 128.9, 128.3, 128.2, 127.9, 127.3, 125.5, 124.2, 122.9, 121.6, 121.4, 110.6, 21.7 ppm. IR (ATR): 1604, 1520, 1494, 1488, 1464, 1419, 1377, 1353, 1199, 981, 904, 835, 750, 740, 701, 617, 585, 516, 435 cm^{-1}. MS (70 eV): m/z = 284.1 [M$^+$]. HR-ESI-MS: $C_{20}H_{17}N_2$ required 285.1392. Found: 285.1390.

General procedure for the preparation of 2-alkyl-1-aryl-1*H*-indazolium hexafluorophosphates

A solution of 1.0 mmol of 1-aryl-1*H*-indazole in 20 mL of toluene was treated with 4.0 mmol of dimethylsulfate and stirred at reflux temperature for 24 hours, during which time a dark oil formed. After cooling to room temperature the oil was separated from the solvent and dissolved in 20 mL of water and filtrated. Then, a solution of 163 mg (1.0 mmol) of ammonium hexafluorophosphate in 1 mL of water was added. Colorless solids formed which were filtered off, recrystallized from water, and dried *in vacuo*.

2-Methyl-1-phenyl-1*H*-indazolium hexafluorophosphate 12a. Yield: 322 mg (91%) of colorless crystals, m.p. 118 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.53 (s, 1H), 8.26 (d, J = 8.6 Hz, 1H), 7.81–7.89 (m, 6H), 7.59–7.63 (m, 1H), 7.38 (dd, J = 8.6/0.7 Hz, 1H), 4.16 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.7, 134.9, 134.0, 132.5, 130.8, 130.7, 129.1, 125.5, 123.4, 119.2, 110.9, 38.6 ppm. IR (KBr): 3136, 1631, 1541, 1497, 1256, 1209, 1171, 835, 766, 752 cm^{-1}. ESI-MS (20 V): m/z = 209.1 [M$^+$]. HR-ESI-MS: $C_{14}H_{14}N_2$ required: 210.1157. Found: 210.1157.

2-Methyl-1-(3-chlorophenyl)-1*H*-indazolium hexafluorophosphate 12b. Yield: 326 mg (84%) of colorless crystals, m.p. 135 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.55 (s, 1H), 8.26 (d, J = 8.6 Hz, 1H), 8.06–8.05 (m, 1H), 7.95–7.92 (m, 1H), 7.89–7.83 (m, 3H), 7.63–7.59 (m, 1H), 7.46 (dd, J = 8.6/0.7 Hz, 1H), 4.18 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.7, 135.3, 134.5, 134.1, 132.6, 132.2, 131.8, 129.3, 128.2, 125.5, 123.4, 119.2, 110.9, 38.6 ppm. IR (KBr): 3129, 3111, 1631, 1590, 1537, 1504, 1459, 831, 793, 776, 761, 692, 557 cm^{-1}. ESI-MS (0V): 243 [M$^+$]. HR-ESI-MS: $C_{14}H_{13}N_2Cl$ required 244.0767. Found: 244.0767.

1-(2-Chlorophenyl)-2-methyl-1*H*-indazolium hexafluorophosphate 12c. Yield: 354 mg (91%) of colorless crystals, m.p. 145 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.64 (s, 1H), 8.31 (d, J = 8.4 Hz, 1H), 8.07 (dd, J = 7.9/1.6 Hz, 1H), 8.00 (dd, J = 9.1/1.4 Hz, 1H), 7.95–7.89 (m, 2H), 7.82 (ddd, J = 7.9/7.7/1.4 Hz, 1H), 7.65 (ddd, J = 8.6/7.0/0.6 Hz, 1H), 7.40 (dd, J = 8.6/0.8 Hz, 1H), 4.15 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.8, 136.1, 135.0, 134.6, 133.0, 132.3, 131.4, 129.7, 127.8, 125.8, 123.8, 119.1, 110.7, 38.2 ppm. IR (ATR): 3143, 1630, 1540, 1482, 1436, 1381, 1265, 1214, 1158, 998, 817, 757, 553 cm^{-1}. ESI-MS (0 V): m/z = 243.1 [M$^+$]. HR-ESI-MS: $C_{14}H_{12}N_2Cl$ required 243.0689. Found: 243.0692.

5-Bromo-1-(4-iodophenyl)-2-methyl-1*H*-indazolium hexafluorophosphate 12d. Yield: 524 mg (94%) of colorless crystals, m.p. 195 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.50 (s, 1H), 8.58 (dd, J = 1.8/0.5 Hz, 1H), 8.20–8.17 (m, 2H), 7.96 (dd, J = 9.1/1.8 Hz, 1H), 7.63–7.59 (m, 2H), 7.44 (d, J = 9.1 Hz, 1H), 4.16 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 139.6, 139.3, 136.7, 134.5, 131.0, 130.1, 125.5, 120.6, 117.6, 113.3, 100.5, 38.7 ppm. IR (KBr): 3139, 1624, 1536, 1494, 1448, 1246, 1211, 1172, 1052, 1006, 931, 840, 558 cm^{-1}. ESI-MS (0 V): m/z = 413 [M$^+$]. HR-ESI-MS: $C_{14}H_{11}N_2BrI$ required 412.9150. Found: 412.9152.

1-(4-Iodophenyl)-2-methyl-1*H*-indazolium hexafluorophosphate 12e. Yield: 418 mg (87%) of colorless crystals, m.p. 147 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.52 (s, 1H), 8.26 (dd, J = 8.6/0.8 Hz, 1H), 8.20–8.17 (m, 2H), 7.88–7.84 (m, 1H), 7.64–7.58 (m, 3H, 2-H), 7.44 (dd, J = 8.6 Hz/0.8 Hz, 1H), 4.15 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.6, 139.5, 135.1, 134.0, 131.0, 130.4, 125.5, 123.3, 119.2, 110.9, 100.2, 38.5 ppm. IR (KBr): 3143, 1628, 1535, 1487, 1169, 1011, 853, 837, 753, 557 cm^{-1}. ESI-MS (0 V): m/z = 335 [M$^+$]. HR-ESI-MS: $C_{14}H_{12}N_2I$ required: 335.0045. Found: 335.0044.

2-Methyl-1-(4-trifluoromethylphenyl)-1*H*-indazolium hexafluorophosphate 12f. Yield: 351 mg (83%) of colorless crystals, m.p. 120 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.57 (s, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 8.4 Hz, 2H), 8.11 (d, J = 8.4 Hz, 2H), 7.90–7.86 (m, 1H), 7.65–7.61 (m, 1H), 7.49 (dd, J = 8.4/0.6 Hz, 1H), 4.20 (s, 3H) ppm. ^{13}C NMR (100 MHz,

DMSO-d_6): δ = 140.7, 135.7, 134.3, 134.2, 132.2 (q, J = 32.4 Hz), 130.4, 127.9 (q, J = 3.7 Hz), 125.7, 123.6 (q, J = 272.9 Hz), 123.5, 119.3, 111.0, 38.8 ppm. IR (KBr): 3120, 1631, 1614, 1538, 1518, 1454, 1326, 1131, 933, 844, 753 cm^{-1}. ESI-MS (0 V): m/z = 277 [M^+]. HR-ESI-MS: $C_{15}H_{13}N_2F_3$ required 278.1031. Found: 278.1031.

2-Methyl-1-(3,5-dimethylphenyl)-1*H*-indazolium hexafluorophosphate 12g. Yield: 336 mg (88%) of colorless crystals, m.p. 149 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.51 (s, 1H), 8.23 (dt, J = 8.4/0.8 Hz, 1H), 7.87–7.83 (m, 1H), 7.61–7.57 (m, 1H), 7.46 (d, J = 0.5 Hz, 1H), 7.43 (s, 2H), 7.39 (dd, J = 8.8/0.7 Hz, 1H), 4.16 (s, 3H), 2.42 (s, 6H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.6, 140.3, 134.9, 134.0, 133.7, 130.6, 126.3, 125.4, 123.4, 119.2, 111.1, 38.6, 20.8 ppm. IR (KBr): 3145, 1631, 1615, 1594, 1536, 1463, 1245, 1189, 1167, 883, 836, 593, 557 cm^{-1}. ESI-MS (0 V): m/z = 237 [M^+]. HR-ESI-MS: $C_{16}H_{18}N_2$ required 238.1470. Found: 238.1471.

5-Bromo-2-methyl-1-phenyl-1*H*-indazolium hexafluorophosphate 12h. Yield: 161 mg (75%) of colorless crystals, m.p. 170 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.50 (s, 1H), 8.59 (dd, J = 1.8/0.5 Hz, 1H), 7.96 (dd, J = 9.2/1.8 Hz, 1H), 7.85–7.79 (m, 5H), 7.37 (d, J = 9.2 Hz, 1H), 4.16 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 139.4, 136.8, 134.3, 132.7, 130.7, 130.5, 129.1, 125.5, 120.6, 117.5, 113.3, 38.8 ppm. IR (KBr): 3157, 3141, 3109, 3077, 1535, 1500, 1442, 1242, 1142, 1014, 838, 700, 558 cm^{-1}. ESI-MS (0 V): m/z = 287.0 [M^+]. HR-ESI-MS: $C_{14}H_{12}N_2Br$ required 287.0184. Found: 287.0185.

2-Ethyl-1-phenyl-1*H*-indazolium hexafluorophosphate 12i. Yield: 282 mg (77%) of colorless crystals, m.p. 143 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.62 (s, 1H), 8.24 (d, J = 8.3 Hz, 1H), 7.89–7.79 (m, 6H), 7.62 (ddd, J = 8.6/7.0/0.8 Hz, 1H), 7.36 (dd, J = 8.6/0.8 Hz, 1H), 4.48 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 141.0, 134.1, 133.6, 132.5, 130.9, 130.8, 129.1, 125.5, 123.3, 119.2, 110.9, 46.9, 13.7 ppm. IR (KBr): 3148, 3114, 3069, 2991, 2948, 1987, 1632, 1537, 1494, 1447, 1396, 1240, 1158, 883, 835, 759, 691, 558 cm^{-1}. ESI-MS (0 V): m/z = 223.1 [M^+]. HR-ESI-MS: $C_{15}H_{16}N_2$ required 224.1313. Found: 224.1310.

1-([1,1′-Biphenyl]-4-yl)-2-methyl-1*H*-indazolium hexafluorophosphate 12j. Yield: 309 mg (72%) of colorless crystals, m.p. 187 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.55 (s, 1H), 8.28 (d, J = 8.6 Hz, 1H), 7.94–7.92 (m, 2H), 7.90–7.84 (m, 3H), 7.62 (ddd, J = 8.6/7.1/0.6 Hz, 1H), 7.59–7.55 (m, 2H), 7.51–7.46 (m, 2H), 4.21 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 143.8, 140.7, 138.3, 134.9, 134.0, 129.8, 129.6, 129.2, 128.7, 128.6, 127.1, 125.4, 123.3, 119.2, 111.0, 38.6 ppm. IR (ATR): 3126, 1627, 1489, 1449, 1360, 1164, 1010, 822, 778, 753, 728, 582, 555 cm^{-1}. ESI-MS (30 V): m/z = 285.1 [M^+]. HR-ESI-MS: $C_{20}H_{17}N_2$ required 285.1392. Found: 285.1392.

2-Methyl-1-(3′-methyl-[1,1′-biphenyl]-4-yl)-1*H*-indazolium hexafluorophosphate 12k. Yield: 257 mg (58%) of colorless crystals, m.p. 97 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.55 (s, 1H), 8.28 (d, J = 8.5 Hz, 1H), 8.09 (dd, J = 8.5 Hz, 2H), 7.93–7.86 (m, 3H), 7.66–7.60 (m, 3H), 7.47–7.43 (m, 2H), 7.30 (d, J = 7.5 Hz, 1H), 4.21 (s, 3H), 2.43 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 144.0, 140.7, 138.4, 138.2, 134.9, 134.0, 129.7, 129.6, 129.2, 129.1, 128.6, 127.8, 125.4, 124.2, 123.3, 119.2, 111.0, 38.6, 21.1 ppm. IR (ATR): 1629, 1515, 1486, 1360, 1167, 823, 749, 591, 580, 555, 429 cm^{-1}. ESI-MS (30 V): m/z = 299.1 [M^+]. HR-ESI-MS: $C_{21}H_{19}N_2$ required 299.1548. Found: 299.1548.

General procedure for the rearrangements of 2-alkyl-1-aryl-1*H*-indazolium hexafluorophosphates to the acridines 13a–k

A mixture of 1.0 mmol of 2-alkyl-1-aryl-1*H*-indazolium hexafluorophosphate and 2.0 mmol of K_3PO_4 in 20 mL of anhydrous dioxane or toluene was stirred at reflux temperature under a nitrogen atmosphere over a period of 3 hours. Then the resulting mixture was cooled to room temperature and the solvent was removed *in vacuo*. The crude product was purified by flash column chromatography (chloroform–methanol = 3 : 1), dissolved in 20 mL of chloroform, washed with 10 mL of 0.1 M NaOH solution and dried *in vacuo*.

***N*-Methylacridin-9-amine 13a.** Yield: 181 mg (87%) of a yellow solid, m.p. 171 °C (170–171 °C, ref. 45). All spectroscopic data are identical to those reported.

1-Chloro-*N*-methylacridin-9-amine 13ba. Yield: 73 mg (30%) of a yellow solid, m.p. 170 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 7.97 (d, J = 8.3 Hz, 1H), 7.53–7.46 (m, 2H), 7.42–7.35 (m, 2H), 7.18–7.14 (m, 2H), 3.43 (s, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 160.6, 143.6, 142.6, 135.5, 134.5, 131.3, 127.9, 126.6, 123.5, 119.2, 118.6, 114.3, 112.4, 37.8 ppm; IR (ATR): 2913, 2845, 1591, 1547, 1514, 1448, 1393, 1339, 922, 751, 646 cm^{-1}. ESI-MS (0 V): m/z = 243.1 [M + H^+]. HR-ESI-MS: $C_{14}H_{12}N_2Cl$ required 243.0689. Found: 243.0687.

3-Chloro-*N*-methylacridin-9-amine 13bb. Yield: 97 mg (40%) of yellow solid, m.p. 146 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.18 (dd, J = 8.7/0.6 Hz, 1H), 8.17 (d, J = 9.4 Hz, 1H), 7.72 (dd, J = 8.7/0.6 Hz, 1H), 7.69 (d, J = 2.1 Hz, 1H), 7.58 (ddd, J = 8.7/6.6/1.3 Hz, 1H), 7.22 (ddd, J = 8.7/6.6/1.3 Hz, 1H), 7.08 (dd, J = 9.4/2.1 Hz, 1H), 3.46 (s, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 154.5, 150.5, 150.3, 137.4, 131.9, 128.0, 127.2, 126.3, 124.8, 123.2, 123.0, 116.1, 114.1, 36.7 ppm; IR (KBr): 2924, 2853, 1633, 1593, 1465, 1383, 842, 558 cm^{-1}. ESI-MS (0 V): m/z = 243.1 [M + H^+]. HR-ESI-MS: $C_{14}H_{12}N_2Cl$ required 243.0689. Found: 243.0687.

4-Chloro-*N*-methylacridin-9-amine 13c. Yield: 200 mg (83%) of a yellow solid, m.p. 161 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.30 (dd, J = 8.8/0.8 Hz, 1H), 8.23 (dd, J = 8.8/1.2 Hz, 1H), 8.03 (dd, J = 8.8/0.8 Hz, 1H), 7.77 (dd, J = 7.2/1.2 Hz, 1H), 7.65 (ddd, J = 8.8/6.6/0.8 Hz, 1H), 7.31 (ddd, J = 8.8/6.6/0.8 Hz, 1H), δ = 7.18 (dd, J = 8.8/7.2 Hz, 1H), 3.54 (s, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 155.3, 150.2, 146.0, 131.8 (2 carbon signals overlapped), 131.4, 128.6, 125.1, 124.4, 123.5, 121.9, 117.5, 116.5, 37.2 ppm; IR (ATR): 2919, 2849, 1556, 1505, 1456, 1397, 1255, 1118, 882, 859, 760, 731, 660 cm^{-1}. MS (70 eV): m/z = 242.1 [M^+]. HR-ESI-MS: $C_{14}H_{12}N_2Cl$ required 243.0689. Found: 243.0690.

2-Bromo-7-iodo-*N*-methylacridin-9-amine 13d. Yield: 144 mg (35%) of a yellow solid, m.p. 191 °C. ^{1}H NMR (600 MHz,

MeOH-d_4): δ = 8.70 (s, 1H), 8.51 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.77 (d, J = 9.0 Hz, 1H), 7.67 (d, J = 8.9 Hz, 1H), 7.52 (d, J = 9.0 Hz, 1H), 3.56 (s, 3H) ppm. ^{13}C NMR (150 MHz, MeOH-d_4): δ = 153.4, 146.9, 146.7, 141.0, 135.8, 134.2, 128.5, 128.3, 127.7, 117.4, 116.7, 116.6, 87.0, 36.6 ppm; IR (KBr): 3063, 2924, 2854, 2064, 1581, 1559, 1516, 1470, 1398, 1358, 1260, 951, 821, 736 cm^{-1}. ESI-MS (0 V): m/z = 412.7 [M + H$^+$]. HR-ESI-MS: $C_{14}H_{11}N_2BrI$ required 412.9150. Found: 412.9153.

2-Iodo-*N*-methylacridin-9-amine 13e. Yield: 137 mg (41%) of a yellow solid, m.p. 178 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.71 (d, J = 1.8 Hz, 1H), 8.37 (dd, J = 8.8/0.8 Hz, 1H), 7.88 (dd, J = 9.0/1.9 Hz, 1H), 7.86 (dd, J = 9.0/0.6 Hz, 1H), 7.72 (ddd, J = 9.0/6.6/1.3 Hz, 1H), 7.60 (d, J = 9.0 Hz, 1H), 7.36 (ddd, J = 9.0/6.6/1.2 Hz, 1H), 3.59 (s, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 153.7, 149.8, 148.0, 139.9, 133.8, 132.0, 129.4, 127.7, 125.5, 123.3, 117.9, 116.0, 86.1, 36.8 ppm; IR (KBr): 2923, 2852, 1620, 1556, 1521, 1459, 1401, 1384, 1260, 1016, 938, 817, 759, 657 cm^{-1}. MS (70 eV): m/z = 334 [M$^+$]. HR-ESI-MS: $C_{14}H_{12}N_2I$ required 335.0045. Found: 335.0049.

***N*-Methyl-2-(trifluoromethyl)acridin-9-amine 13f.** Yield: 141 mg (51%) of a yellow solid, m.p. 195 °C (dec.). ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.77 (s, 1H), 8.49 (dd, J = 8.8/0.8 Hz, 1H), 8.00 (dd, J = 8.8/1.8 Hz, 1H), 7.89 (ddd, J = 8.8/6.8/1.2 Hz, 1H), 7.85 (d, J = 9.2 Hz, 1H), 7.75 (dd, J = 8.4/0.6 Hz, 1H), 7.49 (ddd, J = 9.4/6.8/1.2 Hz, 1H), 3.71 (s, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 159.4, 144.2, 143.6, 136.2, 130.6 (q, J = 3.0 Hz), 127.1, 125.6 (q, J = 33 Hz), 125.4 (q, J = 271 Hz), 125.0, 124.7 (q, J = 4.5 Hz), 122.6, 121.4, 114.7, 113.5, 36.8 ppm; IR (KBr): 3236, 2947, 2885, 1646, 1594, 1326, 1161, 1127, 1068, 841, 760, 559 cm^{-1}. MS (70 eV): m/z = 276 [M$^+$]. HR-ESI-MS: $C_{15}H_{12}N_2F_3$ required 277.0953. Found: 277.0953.

***N*,1,3-Trimethylacridin-9-amine 13g.** Yield: 137 mg (58%) of a yellow solid, m.p. 120 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 7.95 (dd, J = 8.2/1.1 Hz, 1H), 7.50 (ddd, J = 8.4/6.8/1.4 Hz, 1H), 7.39 (dd, J = 8.2/0.5 Hz, 1H), 7.14 (ddd, J = 8.4/6.8/1.1 Hz, 1H), 7.02 (s, 1H), 6.86 (s, 1H), 3.43 (s, 3H), 2.64 (s, 3H), 2.36 (s, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 160.9, 144.5, 144.1, 142.1, 136.9, 132.4, 132.1, 129.9, 127.7, 127.6, 121.0, 119.0, 116.3, 39.2, 21.7, 21.6 ppm; IR (KBr): 3367, 3144, 2924, 1632, 1595, 1537, 1462, 1154, 839, 759, 557 cm^{-1}; HR-ESI-MS: $C_{16}H_{17}N_2$ required 237.1392. Found: 237.1391.

2-Bromo-*N*-methylacridin-9-amine 13h. Yield: 92 mg (32%) of a yellow solid, m.p. 156 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.54 (d, J = 2.0 Hz, 1H), 8.44 (d, J = 8.8 Hz, 1H), 7.87–7.81 (m, 2H), 7.75 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 9.2 Hz, 1H), 7.45 (ddd, J = 8.8/6.8/1.1 Hz, 1H), 3.66 (s, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 157.0, 144.7, 142.8, 137.4, 134.9, 127.9, 126.6, 124.6, 124.4, 122.8, 116.9, 116.0, 114.6, 36.7 ppm; IR (KBr): 2927, 2899, 2321, 2166, 2108, 2081, 1633, 1589, 1556, 1545, 1471, 1174, 1161, 859, 846, 821, 758 cm^{-1}. ESI-MS (0 V): m/z = 287.0 [M + H$^+$]. HR-ESI-MS: $C_{14}H_{12}N_2Br$ required 287.0184. Found: 287.0182.

***N*-Methyl-2-phenylacridin-9-amine 13j.** Yield: 170 mg (83%) of a yellow solid, m.p. 173 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.46 (d, J = 1.6 Hz, 1H), 8.31 (dd, J = 8.7/0.6 Hz, 1H), 7.93–7.88 (m, 2H), 7.82 (dd, J = 8.7/0.6 Hz, 1H), 7.74–7.72 (m, 2H), 7.62 (ddd, J = 8.7/6.6/1.2 Hz, 1H), 7.48–7.44 (m, 2H), 7.36–7.32 (m, 1H), 7.27 (ddd, J = 8.8/6.6/1.2 Hz, 1H), 3.57 (s, 3H, NHMe-H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 154.9, 149.7, 148.7, 141.9, 135.9, 131.7, 131.2, 130.0, 128.4, 128.3, 128.0, 127.7, 125.4, 123.0, 122.3, 116.2, 116.1, 37.0 ppm; IR (ATR): 3225, 3055, 1612, 1557, 1519, 1499, 1452, 1397, 1381, 1265, 825, 748, 692, 668, 643 cm^{-1}. MS (70 eV): m/z = 284.1 [M$^+$]. HR-ESI-MS: $C_{20}H_{17}N_2$ required 285.1392. Found: 285.1391.

***N*-Methyl-2-(*m*-tolyl)-acridin-9-amine 13k.** Yield: 110 mg (37%) of a yellow solid, m.p. 119 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.52 (d, J = 1.7 Hz, 1H), 8.39 (dd, J = 8.8/0.7 Hz, 1H), 7.97 (dd, J = 9.0/1.9 Hz, 1H), 7.91–7.89 (m, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.66 (ddd, J = 8.6/6.6/1.2 Hz, 1H), 7.60 (s, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.38–7.30 (m, 2H), 7.19 (d, J = 7.4 Hz, 1H), 3.63 (s, 3H, NHMe-H), 2.44 (s, 3H, PhMe-H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 155.0, 149.5, 148.5, 141.8, 139.7, 136.1, 131.7, 131.3, 129.9, 129.1, 128.7, 128.0, 127.6, 125.5, 125.2, 122.9, 122.2, 116.2, 116.1, 37.0, 21.7 ppm; IR (ATR): 2847, 2805, 1637, 1572, 1491, 1475, 1446, 1389, 1356, 1167, 832, 703 cm^{-1}. MS (70 eV): m/z = 298.2 [M$^+$]. HR-ESI-MS: $C_{21}H_{19}N_2$ required 299.1548. Found: 299.1544.

2-Phenyl-2*H*-indazole 16. A mixture of 2.5 mmol of 1*H*-indazole, 2.0 mmol of 2-(trimethylsilyl)phenyl-trifluoromethanesulfonate, 3.0 mmol of NaF and 5.0 mmol of CsF in 15 mL of acetonitrile was stirred at room temperature under a nitrogen atmosphere for 24 hours. The resulting mixture was then evaporated to dryness. The crude product was purified by flash column chromatography (petroleum ether–ethyl acetate = 8 : 1). Yield: 198 mg (51%) of colorless crystals. All spectroscopic data are identical to those reported.[44]

1-Methyl-2-phenyl-2*H*-indazolium tetraphenylborate 17. The methylation was carried out according to the method described above. Sodium tetraphenylborate was used for anion-exchange. Yield: 350 mg (66%) of colorless crystals, m.p. 192 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.53 (s, 1H), 8.17 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.8 Hz, 1H), 7.97–8.01 (m, 1H), 7.87–7.89 (m, 2H), 7.75–7.85 (m, 3H), 7.59–7.63 (m, 1H), 7.17–7.21 (m, 8H), 6.93 (dd, J = 7.8/7.2 Hz, 8H), 6.79 (t, J = 7.2 Hz, 4H), 4.02 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.4 (q, J = 49 Hz), 140.8, 135.5, 134.1 (q, J = 34 Hz), 133.0, 132.6 (q, J = 21 Hz), 130.1, 127.7, 126.6, 125.5, 125.3 (q, J = 3 Hz), 123.2, 121.5, 119.3, 111.7, 34.4 ppm. IR (KBr): 3090, 3053, 1629, 1579, 1526, 1479, 1244, 1190, 741, 707, 613 cm^{-1}. ESI-MS (0 V): m/z = 209.1 [M$^+$]. HR-ESI-MS: $C_{14}H_{13}N_2$ required 209.1079. Found: 209.1081.

1-Methyl-2-phenyl-1*H*-indazole-3(2*H*)-thione 18. A mixture of 1.0 mmol of l-methyl-2-phenyl-2*H*-indazolium tetraphenylborate, 5.0 mmol sulfur and 5.0 mmol of potassium *tert*-butoxide in 20 mL of anhydrous dioxane was stirred at reflux temperature under a nitrogen atmosphere over a period of 2 hours. Then the resulting mixture was cooled to room temperature and the solvent was removed *in vacuo*. The crude product was finally purified by flash column chromatography

(petroleum ether–ethyl acetate = 1 : 1). Yield: 80 mg (33%) of a yellow solid, m.p. 140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, J = 8.0 Hz, 1H), 7.67–7.56 (m, 5H), 7.52–7.48 (m, 1H), 7.32–7.29 (m, 2H), 3.32 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 175.1, 146.5, 134.8, 132.7, 129.5, 129.4, 128.0, 127.9, 125.9, 123.4, 110.8, 37.4 ppm. IR (KBr): 2923, 2361, 1611, 1591, 1487, 1457, 1342, 1322, 1306, 1156, 1126, 1108, 971, 755, 696 cm^{-1}. MS (70 eV): m/z = 240.1 [M$^+$]. HR-ESI-MS: $C_{14}H_{13}N_2S$ required: 241.0799. Found: 241.0802.

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Notes and references

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