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SYNTHESES OF ACRIDINES AND QUINAZOLINE-2,4(1*H*,3*H*)-DITHIONES BY REARRANGEMENTS OF N-HETEROCYCLIC CARBENES OF INDAZOLE

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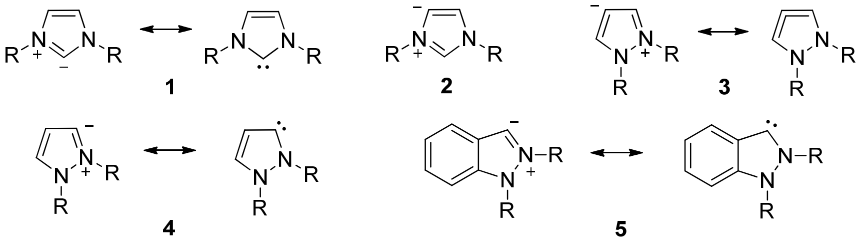
Abstract – N-Heterocyclic carbenes of indazole which are arylated at N1 (1-aryl-indazol-3-ylidenes) have been generated by deprotonation of the corresponding indazolium salts. On deprotonation with potassium carbonate, potassium phosphate or *tert*-butanolat*e* in dioxane or toluene at reflux temperature, a rearrangement to acridines took place. Deprotonation with n-butyllithium in THF at room temperature in the presence of carbon disulfide gave quinazoline-2,4(1*H*,3*H*)-dithiones by a new rearrangement reaction.

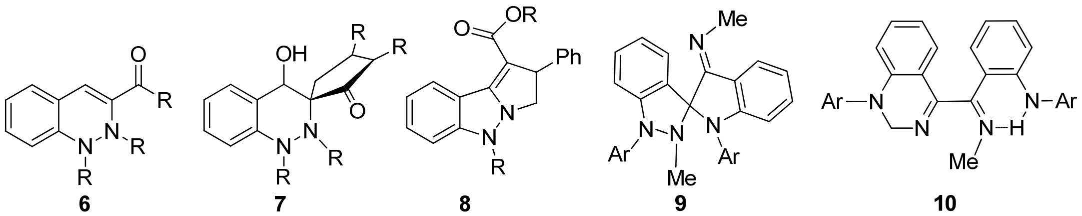
INTRODUCTION

Since the first isolation of a stable N-heterocyclic carbene (NHC) by Arduengo,[1] this class of compounds has developed impressively. Meanwhile a broad variety of different architectures of N-heterocyclic carbenes has been designed, and most of these studies aimed at enhancing the σ-donor capacities at the carbene center for applications in transition metal catalyzed cross-coupling reactions.[2] Scheme 1 presents different types of N-heterocyclic carbenes. Imidazol-2-ylidene **1** belongs to the class of normal N-heterocyclic carbenes (nNHC), whereas its isomer imidazol-4-ylidene **2** is a member of the class of abnormal N-heterocyclic carbenes (aNHC).[3] As it can exclusively be represented by dipolar all-octet resonance forms, aNHC **2** and relatives have also been termed mesoionic carbenes (MIC),[4] although they do not share more than a formal relationship to the class of mesoionic compounds which are well-defined π-conjugated systems.[5] Pyrazol-4-ylidene **3** is a remote N-heterocyclic carbene (rNHC)[6] and has also been described as a cyclic bent allene.[7] Pyrazol-3-ylidene **4** and indazol-3-ylidene **5** belong to the class of normal N-heterocyclic carbenes, however, their chemical properties differ considerably from other NHCs. The chemistry of pyrazol-ylidenes and indazol-ylidenes has been summarized in review articles.[8]



Scheme 1

Indazol-3-ylidenes **5** proved to be versatile starting materials for the synthesis of a broad variety of heterocycles, some of which are shown in Scheme 2. Besides of classical trapping reactions of NHC to indazole-3-thiones with sulfur,[9] to indazolium-3-amidates with isocyanates,[9] and with metals to indazol-3-ylidene complexes,[10] they undergo ring transformations to 1,2-dihydrocinnolines **6**,[11] spiro-cinnolines **7**,[11] 3,5-dihydro-2*H*-pyrrolo[1,2-*b*]indazoles **8**,[12] (1,2-dihydro-spiro-[indazole-3,2′-indolin]-3′-ylidene)methanamines **9**,[13] and the 1,2-dihydroquinazolines **10**.[13]

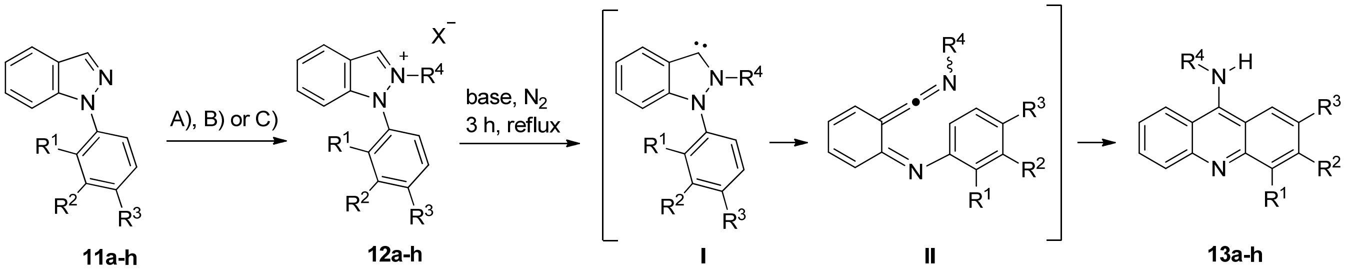


Scheme 2

In continuation of our interest in mesomeric betaines and carbenes derived thereof,[14] polycations in organic synthesis,[15] and N-heterocyclic carbenes in catalysis,[16] we report here on recent examples of indazole → acridine ring transformations via the N-heterocyclic carbene of indazole,[17] and first indazole → quinazoline-2,4(1*H*,3*H*)-dithione rearrangements of indazol-3-ylidenes which surprisingly occur in the presence of carbon disulfide.

RESULTS AND DISCUSSION

The 1-arylindazoles **11a-h**, readily prepared by intramolecular Buchwald-Hartwig reaction or by copper catalyzed coupling reactions of haloaryls with indazole,[17] were methylated or ethylated to form oils which crystallized after anion exchange to hexafluorophosphate or tetraphenylborate as indazolium salts **12a-h** (Scheme 3). In this study, we tested three different methods A) – C). Whereas the methylations to the salts **12a-e** and **12h** were best performed by dimethyl sulfate in boiling toluene, the ethylations to **12f,g** required xylene as solvent to get acceptable yields. Crystallization, isolation and purification of the *ortho*-fluorophenylindazolium hexafluorophosphate rendered with difficulties, so that we prepared the corresponding tetraphenylborate **12h** in very good yields. In the next step, we studied different methods to deprotonate the indazolium salts **12a-h** to the corresponding indazol-3-ylidenes. These rearrange spontaneously in the absence of trapping reagents to the acridines **13a-h** which are slightly fluorescent solids. As shown earlier,[17] the reaction proceeds under ring-cleavage of the indazol-3-ylidene **I**, followed by pericyclic ring-closure of the open-chain intermediate **II**, ring-closure and subsequent tautomerism to the acridines. We applied potassium phosphate and tBuOK in toluene or in dioxane, respectively, and potassium carbonate in toluene and applied identical reactions times (3 h) and reflux temperature in all cases. We found that the rearrangements are not essentially influenced by the reaction conditions, however, they proved to be very sensitive toward substituent effects. Thus, if R^3 = Br (entry 4) very low yields of **13d** were obtained which could not be purified. If R^1 = F and X = BPh_4^- (entry 8) the low yields of **13h** are due to the decomposition of the anion under these conditions. The acridine **13e**, prepared by another method, has been studied before as biologically active compound.[18]



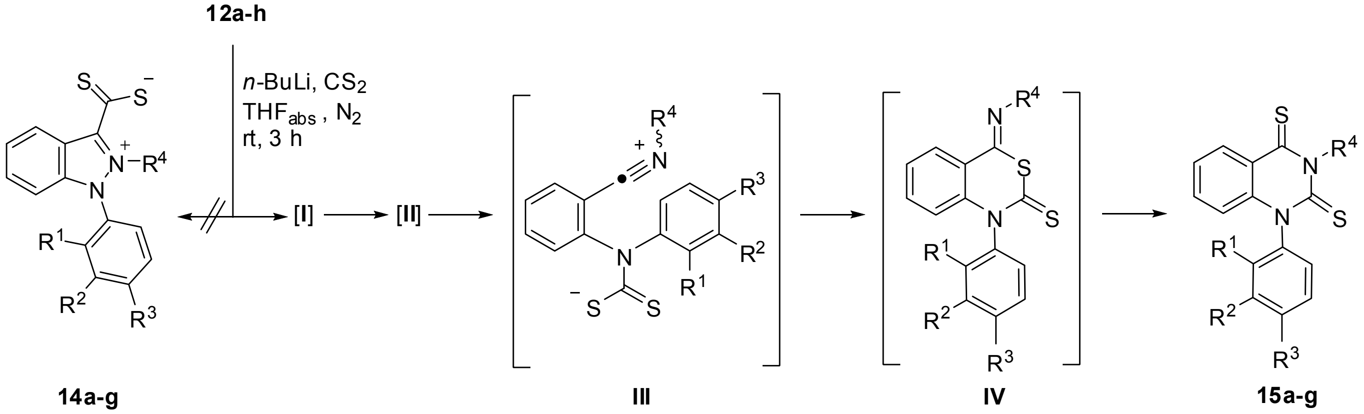
Reaction conditions:
A) 1. Me_2SO_4, toluene, 24 h, reflux. 2. NH_4PF_6, H_2O.
B) 1. Et_2SO_4, xylene, 24 h, reflux. 2. NH_4PF_6, H_2O.
C) 1. Me_2SO_4, toluene, 24 h, reflux. 2. $NaBPh_4$, H_2O.

Scheme 3.

Table 1. Preparation of indazolium salts **12a-h**, acridines **13a-h** and quinazolinedithiones **15a-g**

						Indazolium salts			Acridines				Quinazolinedithiones	
entry	R^1	R^2	R^3	R^4	X	method	product	yield	base	solvent	product	yield	product	yield
1	H	H	H	Me	PF_6^-	A	**12a**	91%	K_3PO_4	dioxane	**13a**	87%	**15a**	62%
2	Cl	H	H	Me	PF_6^-	A	**12b**	91%	K_3PO_4	dioxane	**13b**	83%	**15b**	38%
3	H	Cl	H	Me	PF_6^-	A	**12c**	84%	K_3PO_4	toluene	**13c**	40%	**15c**	40%
4	H	H	Br	Me	PF_6^-	A	**12d**	81%	K_3PO_4	dioxane	**13d**	<10%	**15d**	44%
5	H	H	Me	Me	PF_6^-	A	**12e**	79%	K_2CO_3	toluene	**13e**	50%	**15e**	47%
6	H	H	I	Et	PF_6^-	B	**12f**	87%	tBuOK	dioxane	**13f**	60%	**15f**	35%
7	H	H	Me	Et	PF_6^-	B	**12g**	64%	K_2CO_3	toluene	**13g**	53%	**15g**	36%
8	F	H	H	Me	BPh_4^-	C	**12h**	83%	tBuOK	toluene	**13h**	<10%	**15h**	0%

On trying to intercept the indazol-3-ylidenes **I**, generated *in situ* on treatment with nBuLi in THF from the salts **12a-g**, with carbon disulfide as indazolium-3-dithiocarboxylates **14a-g**, we surprisingly isolated the quinazoline-2,4(1*H*,3*H*)-dithiones **15a-g** (Scheme 4). Attempts to prepare **15h** failed under these conditions. The mechanism can be formulated as ring-cleavage of the indazol-3-ylidene **I**, interception of the resulting intermediate **II** by CS_2 to give **III**, ring closure to 4-(methylimino)-1*H*-benzo[*d*][1,3]thiazine-2(4*H*)-thione **IV**, and final isomerization to **15a-g**. This sequence is a new approach to the class of quinazoline-2,4(1*H*,3*H*)-dithiones. Their syntheses have been described before starting from benzo[*d*][1,3]thiazine-2,4-dithiones and primary aliphatic amines. Anilines, however, gave thioamides.[19] Alternative procedures for the preparation of quinazoline-2,4(1*H*,3*H*)-dithiones are thionations of 2,3-dihydro-1*H*-quinazolinethiones with sulfur at 200 °C[20] or of 2-thioxo-2,3-dihydroquinazolin-4(1*H*)-ones with P_2S_5.[21] The reaction of 2-aminothiobenzamides with thiophosgene[22] or CS_2[23] were described as well. 4-Imino-1*H*-benzo[1,3]thiazine-2-(4*H*)-thiones such as **IV** ($R^1 = R^2 = R^3 = H$, $R^4 =$ i-propyl) were isolated on reaction of benzo[*d*][1,3]thiazine-2,4-dithione with 2-aminopropane for 3 days at rt in MeOH.[24] Depending on the substitution pattern, these heterocycles **IV** are known to be very unstable.[22] On warming of the solid or in solution,[22] or in the presence of bases[25] they rearrange into the quinazoline-2,4(1*H*,3*H*)-dithiones. These earlier observations are in well agreement with the final step of our proposed mechanism.



Scheme 4

Single crystals of **15a**, 3-methyl-1-phenylquinazoline-2,4(1*H*,3*H*)-dithione, were obtained by slow evaporation of a concentrated solution in methanol. The compound crystallized triclinic, space group *P-1*(2). A molecular drawing is shown in Figure 1. The phenyl ring is twisted from the plane of the quinazoline-2,4(1*H*,3*H*)-dithione by 73.828(61)° (torsion angle C10-N1-C11-C16; crystallographic numbering). The C-S bond lengths were determined to be 165.93 (7) pm [C2 and S1; crystallographic numbering] and 164.70 (8) pm [C4 and S2; crystallographic numbering].

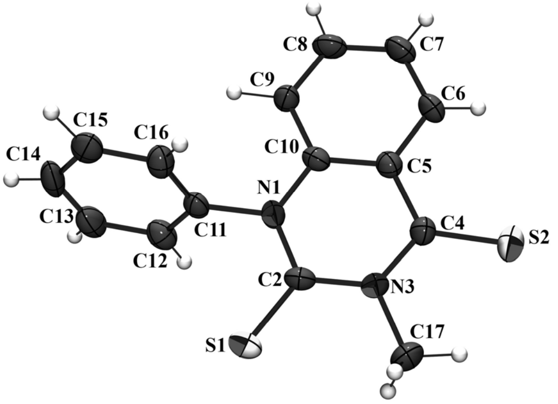


Figure 1. Molecular drawing of **15a**

CONCLUSIONS

The N-heterocyclic carbene of indazole, indazol-3-ylidene, is a suitable starting material for heterocycle synthesis. Its rearrangement yields functionalized acridines, whereas its reaction with carbon disulfide gives quinazoline-2,4(1*H*,3*H*)-dithiones by a new rearrangement reaction.

EXPERIMENTAL

Nuclear magnetic resonance (NMR) spectra were measured 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. 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 (ESIMS) 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. Syntheses of the compounds **12a-c**,[17] **12d**,[13] and **13a-d**[17] were reported in our previous publications. X-Ray structure analysis for $C_{15}H_{12}N_2S_2$, M = 284.39 g mol^{-1}: A suitable single crystal of the title compound was selected under a polarization microscope and mounted in a glass capillary (*d* = 0.3 mm). The crystal structure was determined by X-ray diffraction analysis using graphite monochromated Mo-K$_\alpha$ radiation (0.71073 Å) [T = 223(2) K], whereas the scattering intensities were collected with a single crystal diffractometer (STOE IPDS II). The crystal structure was solved by Direct Methods using SHELXS-97 and refined using alternating cycles of least squares refinements against F^2 (SHELXL-97).[26] All non-H atoms were located in Difference Fourier maps and were refined with anisotropic displacement. The H atoms of the methyl group were refined as riding with C–H = 0.96 A and Uiso(H) = 1.2 Ueq(C). The other H positions were determined by a final Difference Fourier Synthesis.

$C_{15}H_{12}N_2S_2$ crystallized in the triclinic space group $P1$ (no. 2), lattice parameters a = 8.711(6) Å, b = 9.058(4) Å, c = 9.566(4) Å, α = 81.15(4)°, β = 80.31(5)°, γ = 64.17(5)°, V = 666.9(6) Å^3, Z = 2, d$_{calc.}$ = 1.416 g cm^{-3}, F(000) = 296 using 2388 independent reflections and 209 parameters. $R1$ = 0.0963, $wR2$ = 0.1337 [I > 2σ(I)], goodness of fit on $F2$ = 1.135, residual electron density = 0.704 and –0.710 e Å^{-3}. Further details of the crystal structure investigations have been deposited with the Cambridge Crystallographic Data Center, CCDC 1016685. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44(1223)-336 033; e-mail: fileserv@ccdc.ac.uk or http://www.ccdc.cam.ac.uk).

General procedure for the preparation of the 2-alkyl-1-aryl-1*H*-indazolium salts 12a-h:

Solutions of 1.0 mmol of the 1-aryl-1*H*-indazoles **11a-h** in 20 mL of toluene (xylene for **12f**, **12g**) were treated with 4.0 mmol of dimethyl sulfate (diethyl sulfate for **12f**, **12g**) and stirred at reflux temperature for 24 h, during which time an oil formed. After cooling to room temperature the toluene was removed and the remaining dark oil was dissolved in 20 mL of water and filtrated. Then, a solution of 1.0 mmol of ammonium hexafluorophosphat (sodium tetraphenylborate for **12h**) in 1 mL of water was added. Colorless solids formed which were filtered off, recrystallized from water, and dried *in vacuo*.

2-Methyl-1-(*p*-tolyl)-1*H*-indazolium hexafluorophosphate 12e:

Yield: 290 mg (79 %) of colorless crystals, mp 129 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.51 (s, 1H), 8.25 (dt, J = 8.4 / 0.9 Hz, 1H), 7.85 (ddd, J = 8.8 / 7.0 / 0.9 Hz, 1H), 7.72-7.69 (m, 2H), 7.62-7.58 (m, 3H), 7.37 (dd, J = 8.8 / 0.8 Hz, 1H), 4.14 (s, 3H), 2.50 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 142.6, 140.7, 134.7, 133.9, 131.0, 128.8, 128.1, 125.3, 123.3, 119.1, 110.9, 38.4, 21.0 ppm. IR (KBr): 3130, 2928, 1630, 1512, 1453, 1212, 1171, 838, 770, 584, 557, 483 cm^{-1}. ESI-MS: m/z = 223.1 [M]$^+$. HRESIMS: $C_{15}H_{15}N_2$: required 223.1235. Found: 223.1233.

2-Ethyl-1-(4-iodophenyl)-1*H*-indazolium hexafluorophosphate 12f:

Yield 372 mg (75%) of colorless crystals, mp 147 °C. ^{1}H NMR (400 MHz, DMSO-*d$_6$*): δ = 9.61 (d, *J* = 0.4 Hz, 1H), 8.23 (dt, *J* = 8.4 / 1.0 Hz, 1H), 8.19 (d, *J* = 8.6 Hz, 2H), 7.86 (ddd, *J* = 8.8 / 7.0 / 1.0 Hz, 1H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.61 (ddd, *J* = 8.4 / 7.0 / 0.7 Hz, 1H), 7.42 (dd, *J* = 8.8 / 1.0 Hz, 1H), 4.47 (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, 139.7, 134.1, 133.9, 131.1, 130.6, 125.6, 123.3, 119.3, 111.0, 100.4, 50.0, 13.8 ppm. IR (KBr): 3142, 2989, 1628, 1487, 1448, 1396, 1366, 1012, 923, 882, 761, 558 cm^{-1}. ESI-MS: *m/z* = 349 [M]$^+$. HRESIMS: $C_{15}H_{14}N_2I$ required 349.0202. Found: 349.0205.

2-Ethyl-1-(*p*-tolyl)-1*H*-indazolium hexafluorophosphate 12g:

Yield 245 mg (87 %), mp 135 °C. ^{1}H NMR (400 MHz, DMSO-*d$_6$*): δ = 9.59 (s, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 7.86 (ddd, *J* = 8.7 / 7.1 / 1.0 Hz, 1H), 7.74-7.72 (m, 2H), 7.63-7.59 (m, 3H), 7.35 (dd, *J* = 8.7 / 0.7 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 2.51 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-*d$_6$*): δ = 142.7, 141.1, 134.0, 133.4, 131.2, 128.9, 128.2, 125.4, 123.3, 119.2, 110.9, 46.8, 21.0, 13.8 ppm. IR (KBr): 3166, 2992, 1627, 1536, 1513, 1457, 1394, 1238, 1154, 1036, 958, 829, 750, 741, 555, 473 cm^{-1}. ESI-MS: *m/z* = 237.1 [M]$^+$. HRESIMS: $C_{16}H_{17}N_2$ required 237.1392. Found: 237.1392.

1-(2-Fluorophenyl)- 2-methyl-1*H*-indazolium tetraphenylborate 12h:

Yield: 454 mg (83%) of colorless crystals, mp 176 °C. ^{1}H NMR (400 MHz, DMSO-*d$_6$*): δ = 9.60 (s, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 7.98-7.88 (m, 3H), 7.79-7.74 (m, 1H), 7.66-7.61 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.21-7.17 (m, 8H), 6.93 (t, *J* = 7.2 Hz, 8H), 6.79 (t, *J* = 7.2 Hz, 4H), 4.18(s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-*d$_6$*): δ = 163.4 (q, *J* = 49.1 Hz), 157.7 (d, *J* = 254.2 Hz), 141.0, 136.6, 135.5, 134.6, 134.3 (d, *J* = 47.7 Hz), 131.5, 127.4 (d, *J* = 19.4 Hz), 126.6 (d, *J* = 3.8 Hz), 125.8, 125.3 (q, *J* = 3.0 Hz), 123.7, 121.5, 119.2, 117.9 (d, *J* = 18.6 Hz), 110.7, 38.3 ppm. IR (KBr): 3055, 1939, 1887, 1824, 1628, 1507, 849, 744, 734, 704, 613 cm^{-1}. ESI-MS: *m/z* = 227 [M]$^+$. HRESIMS: $C_{14}H_{12}N_2F$ required 227.0985. Found: 227.0982.

General procedure for the rearrangements of indazolium salts into the 9-aminoacridines 13a-g:

A mixture of 1.0 mmol of the 1-aryl-1*H*-indazolium salts **12a-g** and 1.2 mmol of the base in 20 mL of solvent was stirred at reflux temperature for 3 h. After cooling to room temperature the solvent was removed *in vacuo*. The crude product was purified by flash column chromatography ($CHCl_3$: MeOH = 3:1), washed with 20 mL of a 0.1 M solution of NaOH in water, extracted with 10 mL of $CHCl_3$ and dried *in vacuo*.

_N_,2-Dimethylacridin-9-amine 13e:

Yield: 110 mg (50%) of yellow solid, mp 166-168 °C, Lit[18]: 181-183 °C. ^{1}H NMR (600 MHz, MeOH-d_4): δ = 8.32 (ddd, *J* = 8.8 / 1.2 / 0.6 Hz, 1H), 8.06 (s, 1H) 7.83 (ddd, *J* = 8.8 / 1.2 / 0.6 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.61 (ddd, *J* = 8.8 / 6.5/ 1.2 Hz, 1H), 7.50 (dd, *J* = 8.8 / 1.3 Hz, 1H), 7.27 (ddd, *J* = 8.8 / 6.5 / 1.2 Hz, 1H), 3.53 (s, 3H), 2.50 (d, *J* = 1.3 Hz, 1H) ppm. ^{13}C NMR (150 MHz, MeOH-d_4): δ = 152.7, 148.3, 147.0, 132.5, 131.6, 129.7, 129.6, 126.5, 123.8, 121.6, 121.4, 114.9, 114.8, 35.6, 20.4 ppm. IR (ATR): 2957, 2917, 2849, 1557, 1519, 1455, 1376, 1261, 1121, 1008, 850, 826, 819, 758, 663, 635, 550 cm^{-1}; MS (70 eV): *m/z* = 222.1 [M]$^+$. HRESIMS: $C_{15}H_{15}N_2$: required 223.1235. Found: 223.1236.

_N_-Ethyl-2-iodoacridin-9-amine 13f:

Yield: 209 mg (60%) of a yellow solid, mp 201 °C. ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.60 (d, *J* = 1.8 Hz, 1H), 8.25 (d, *J* = 8.8 Hz, 1H), 7.87 (dd, *J* = 9.0 / 1.8 Hz, 1H), 7.73-7.72 (m, 2H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.39-7.35 (m, 1H), 3.92 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 154.9, 146.7, 145.0, 141.5, 134.0, 133.7, 126.5, 126.0, 124.9, 124.2, 117.5, 115.6, 87.1, 45.6, 15.9 ppm; IR (KBr): 3622, 3345, 3140, 2978, 1632, 1586, 1531, 1475, 1273, 882, 842, 761, 557 cm^{-1}; MS (70 eV): *m/z* = 348 [M]$^+$. HRESIMS: $C_{15}H_{14}N_2I$: required 349.0202. Found: 349.0206.

_N_-Ethyl-2-methylacridin-9-amine 13g:

Yield: 126 mg (53%) of a yellow solid, mp 190 °C (dec.). ^{1}H NMR (400 MHz, MeOH-d_4): δ = 8.28 (dd, *J* = 8.8 / 1.0 Hz, 1H), 8.06 (s, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.65 (ddd, *J* = 8.8 / 6.6 / 1.0 Hz, 1H) , 7.54 (dd, *J* = 8.8 / 1.7 Hz, 1H), 7.34 (ddd, *J* = 8.8 / 6.6/ 0.9 Hz, 1H), 3.89 (q, *J* = 7.2 Hz, 2H), 2.53 (d, *J* = 0.6 Hz, 3H), 1.39 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, MeOH-d_4): δ = 153.7, 149.3, 148.2, 134.3, 133.8, 131.4, 128.0, 127.9, 125.2, 123.5, 123.0, 117.4, 117.3, 45.9, 21.9, 16.6 ppm; IR (ATR): 2961, 2922, 2854, 1556, 1517, 1421, 1333, 1260, 1138, 838, 817, 750, 556 cm^{-1}; MS (70 eV): *m/z* = 236.1 [M]$^+$. HRESIMS: $C_{16}H_{17}N_2$ required 237.1392. Found: 237.1391.

General procedure for the preparation of the quinazoline-2,4(1_H_,3_H_)-dithiones 15a-g:

Samples of 38 mg (0.5 mmol) of carbon disulfide were added to a solution of 1.0 mmol of the 1-aryl-1*H*-indazolium salts **12a-g** in 20 mL of anhyd THF. Then, 0.6 mL of a 2M solution of *n*-BuLi in cyclohexane was added dropwise at room temperature. The mixture was stirred for 3 h and the solvent was then removed *in vacuo*. The crude product was finally purified by flash column chromatography (petroleum ether: EtOAc = 3:1) and dried *in vacuo*.

3-Methyl-1-phenylquinazoline-2,4(1*H*,3*H*)-dithione 15a:

Yield: 88 mg (62%) of a yellow solid. mp 195 °C. ^{1}H NMR (400 MHz, $CDCl_3$ + TMS): δ = 8.71 (dd, *J* = 8.1 / 1.5 Hz, 1H), 7.65-7.54 (m, 3H), 7.44 (ddd, *J* = 8.4 / 7.0 / 1.5 Hz, 1H), 7.30-7.25 (m, 3H), 6.41 (d, *J* = 8.3 Hz, 1H), 4.47 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + TMS): δ = 188.6, 175.0, 141.4, 137.5, 134.5, 133.4, 130.6, 129.3, 128.7, 125.4, 124.3, 116.9, 44.8 ppm. IR (ATR): 1582, 1461, 1383, 1346, 1287, 1183, 1153, 1142, 1068, 1038, 762, 745, 695, 617, 504, 443 cm^{-1}. MS (70 eV): *m/z* = 284.1 [M]$^+$. HRESIMS: $C_{15}H_{13}N_2S_2$: required. 285.0520. Found: 285.0509.

1-(2-Chlorophenyl)-3-methylquinazoline-2,4(1*H*,3*H*)-dithione 15b:

Yield: 61 mg (38%) of a yellow solid, mp 160-162 °C. ^{1}H NMR (400 MHz, $CDCl_3$ + TMS): δ = 8.71 (dd, *J* = 8.2 / 1.4 Hz, 1H), 7.66-7.64 (m, 1H), 7.53-7.45 (m, 3H), 7.34-7.28 (m, 2H), 6.34 (d, *J* = 8.2 Hz, 1H), 4.48 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + TMS): δ = 188.5, 174.1, 138.3, 136.4, 134.9, 133.7, 132.9, 131.4, 130.8, 130.4, 129.0, 125.7, 124.2, 115.9, 44.7 ppm. IR (ATR): 2955, 2927, 2869, 1683, 1584, 1518, 1460, 1378, 1294, 1070, 1037, 948, 752, 741, 694, 649, 619, 460 cm^{-1}. MS (70 eV): *m/z* = 318.0 [M]$^+$. HRESIMS: $C_{15}H_{12}N_2S_2Cl$: required 319.0130. Found: 319.0124.

1-(3-Chlorophenyl)-3-methylquinazoline-2,4(1*H*,3*H*)-dithione 15c:

Yield: 64 mg (40%) of a yellow solid, mp 217 °C. ^{1}H NMR (400 MHz, $CDCl_3$ + TMS): δ = 8.71 (dd, *J* = 8.3 / 1.5 Hz, 1H), 7.59-7.53 (m, 2H), 7.47 (ddd, *J* = 8.3 / 7.2 / 1.6 Hz, 1H), 7.32-7.28 (m, 2H), 7.18 (ddd, *J* = 6.9 / 2.2 / 2.0 Hz, 1H), 6.42 (d, *J* = 8.3 Hz, 1H), 4.46 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + TMS): δ = 188.4, 174.8, 142.1, 137.1, 136.1, 134.7, 133.6, 131.5, 129.7, 129.2, 127.2, 125.6, 124.2, 116.6, 44.7 ppm. IR (ATR): 1580, 1460, 1383, 1319, 1290, 1247, 1207, 1037, 1001, 743 687, 620, 456 cm^{-1}. MS (70 eV): *m/z* = 318.1 [M]$^+$. HRESIMS: $C_{15}H_{12}N_2S_2Cl$ required 319.0130. Found: 319.0129.

1-(4-Bromophenyl)-3-methylquinazoline-2,4(1*H*,3*H*)-dithione 15d:

Yield: 80 mg (44%) of a yellow solid, mp 168-170 °C. ^{1}H NMR (400 MHz, $CDCl_3$ + TMS): δ = 8.70 (dd, *J* = 8.0 / 1.5 Hz, 1H), 7.77-7.73 (m, 2H), 7.46 (ddd, *J* = 8.5 / 7.1 / 1.5 Hz, 1H), 7.29 (ddd, *J* = 8.0 / 7.1 / 1.0 Hz, 1H), 7.16-7.13 (m, 2H), 6.42 (d, *J* = 8.5 Hz, 1H), 4.45 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + TMS): δ = 188.4, 174.8, 140.3, 137.2, 134.6, 134.0, 133.6, 130.5, 125.6, 124.3, 123.4, 116.6, 44.8 ppm. IR (ATR): 3049, 1681, 1581, 1485, 1462, 1382, 1292, 1275, 1064, 1036, 1013, 816, 760, 752, 744, 633, 506 cm^{-1}. MS (70 eV): *m/z* = 362 [M]$^+$. HRESIMS: $C_{15}H_{12}N_2S_2Br$: required. 362.9625. Found: 362.9634.

3-Methyl-1-(p-tolyl)quinazoline-2,4(1*H*,3*H*)-dithione 15e:

Yield: 70 mg (47%) of a yellow solid, mp 243-244 °C (decomposition). ^{1}H NMR (600 MHz, $CDCl_3$+TMS): δ = 8.73 (dd, *J* = 8.2 / 1.4 Hz, 1H), 7.46 (ddd, *J* = 8.5 / 7.2 / 1.5 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.30 (ddd, *J* = 8.2 / 7.2 / 1.0 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 2H), 6.49 (d, *J* = 8.5 Hz, 1H), 4.51 (s, 3H), 2.52 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$+TMS): δ =188.6, 175.1, 139.5, 138.9, 137.6, 134.5, 133.3, 131.3, 128.3, 125.4, 124.3, 117.1, 44.9, 21.5 ppm. IR (ATR): 1584, 1465, 1385, 1348, 1293, 1270, 1246, 1193, 1172, 1155, 1143, 1086, 1069, 1036, 1023, 966, 807, 795, 756, 741, 715, 644, 629, 506, 436 cm^{-1}. MS (70 eV): *m/z* = 298.2 $[M]^+$. HRESIMS: $C_{16}H_{15}N_2S_2$: required 299.0677. Found: 299.0675.

3-Ethyl-1-(4-iodophenyl)quinazoline-2,4(1*H*,3*H*)-dithione 15f:

Yield: 74 mg (35%) of a yellow solid, mp 183-186 °C. ^{1}H NMR (600 MHz, $CDCl_3$ + TMS): δ = 8.76 (dd, *J* = 8.3 / 1.4 Hz, 1H), 8.01-7.99 (m, 2H), 7.49 (ddd, *J* = 8.5 / 7.1 / 1.4 Hz, 1H), 7.32 (ddd, *J* = 8.3 / 7.1 / 0.8 Hz, 1H), 7.07-7.05 (m, 2H), 6.44 (dd, *J* = 8.5 / 0.8 Hz, 1H), 5.41(bs, 2H), 1.53 (t, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$ + TMS): δ = 187.3, 174.0, 141.0, 139.9, 137.2, 134.6, 133.7, 130.7, 125.6, 124.3, 116.6, 95.0, 51.4, 10.6 ppm. IR (ATR): 2967, 2925, 2863, 1587, 1483, 1460, 1371, 1349, 1331, 1278, 1258, 1217, 1085, 1070, 1005, 806, 787, 758, 707, 631, 502 cm^{-1}. MS (70 eV): *m/z* = 424.1 $[M]^+$. HRESIMS: $C_{16}H_{14}N_2S_2I$: required 424.9643. Found: 424.9649.

3-Ethyl-1-(p-tolyl)quinazoline-2,4(1*H*,3*H*)-dithione 15g:

Yield: 56 mg (36%) of a yellow solid. mp 148-151 °C. ^{1}H NMR (600 MHz, $CDCl_3$ + TMS): δ = 8.77 (dd, *J* = 8.2 / 1.5 Hz, 1H), 7.48-7.45 (m, 3H), 7.30 (ddd, *J* = 7.6 / 7.0 / 1.0 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 2H), 6.47 (d, *J* = 8.5 Hz, 1H), 5.45(bs, 2H), 2.54 (s, 3H), 1.55 (t, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$ + TMS): δ = 187.4, 174.4, 139.4, 138.8, 137.6, 134.5, 133.5, 131.3, 128.3, 125.3, 124.3, 117.0, 51.5, 21.5, 10.7 ppm. IR (ATR): 2963, 2925, 2868, 1598, 1585, 1507, 1482, 1461, 1381, 1349, 1332, 1278, 1262, 1218, 1180, 1155, 1086, 810, 763, 745, 715, 641, 539 cm^{-1}. MS (70 eV): *m/z* = 312.2 $[M]^+$. HRESIMS: $C_{17}H_{17}N_2S_2$: required 313.0833. Found: 313.0832.

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