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ON THE TAUTOMERISM OF CINNOLIN-4-OL, CINNOLINE-4-THIOL, AND CINNOLIN-4-AMINE

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Abstract – Detailed NMR spectroscopic investigations (^{1}H, ^{13}C, ^{15}N) with cinnolin-4-ol (**1**) reveal this compound to exist exclusively in the cinnolin-4(1*H*)-one form in deuteriodimethyl sulfoxide solution. This finding is confirmed by comparison of the NMR spectroscopic data of **1** with those of the corresponding 'fixed' *O*-methyl and *N*-methyl derivatives, i.e. 4-methoxycinnoline (**3**) and 1-methylcinnolin-4(1*H*)-one (**5**). Similarly, cinnoline-4-thiol (**4**) is present in the thione form in deuteriodimethyl sulfoxide, whereas cinnolin-4-amine (**7**) exists in the amino form. In addition, in-depth analyses of the NMR spectra of some simple 4-substituted cinnolines are provided.

INTRODUCTION

Prototropic tautomerism of heteroaromatic compounds has been extensively studied for a long period and is the subject of several excellent reviews.[1–3] This phenomenon is not only of academic interest but of the highest biological importance as, for instance, the tautomeric form of the nucleic acid bases is crucial for base pairing in the DNA molecule.[4] In particular, prototropic ring chain tautomerism of six-membered heteroaromatic systems such as that in hydroxypyridines or aminopyridines has been investigated by a large variety of experimental and theoretical methods.[5] Also the corresponding benzo-annulated systems show such a behavior.[5] In this respect, hydroxy- or aminocinnolines represent rarely assayed moieties to which relatively little attention has been focused. Thus, from early reports – mainly based on UV, pK_a, and IR investigations – it was concluded that cinnolin-4-ol (**1**) and cinnoline-4-thiol (**4**) predominantly exist as oxo or thioxo tautomers (**1b**) and (**4b**), respectively, whereas for cinnolin-4-amine (**7**) the amino form (**7a**) is preferred (Figure 1).[5–10] Also the role of zwitterionic forms of type (**c**) (Figure 1) has been

discussed.[5,8–11] In this study we report on continuative investigations with cinnolin-4-ol (**1**), cinnoline-4-thiol (**4**), cinnolin-4-amine (**7**), and related compounds employing modern NMR spectroscopic methods including also ^{13}C-NMR and ^{15}N-NMR spectroscopy. Since comparatively little is known concerning the ^{13}C- and ^{15}N-NMR spectra of simple 4-substituted cinnolines[6,12] we here present detailed data in this respect. Moreover, some improvements in the syntheses of the investigated compounds are specified, amongst these also one for the preparation of cinnolin-4-ol (**1**), which represents the central synthon in the construction of 4-substituted cinnolines due to its simple availability from 2-aminoacetophenone *via* Borsche synthesis.[13]

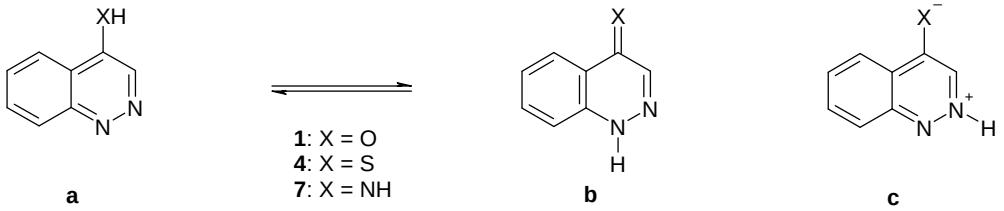


Figure 1

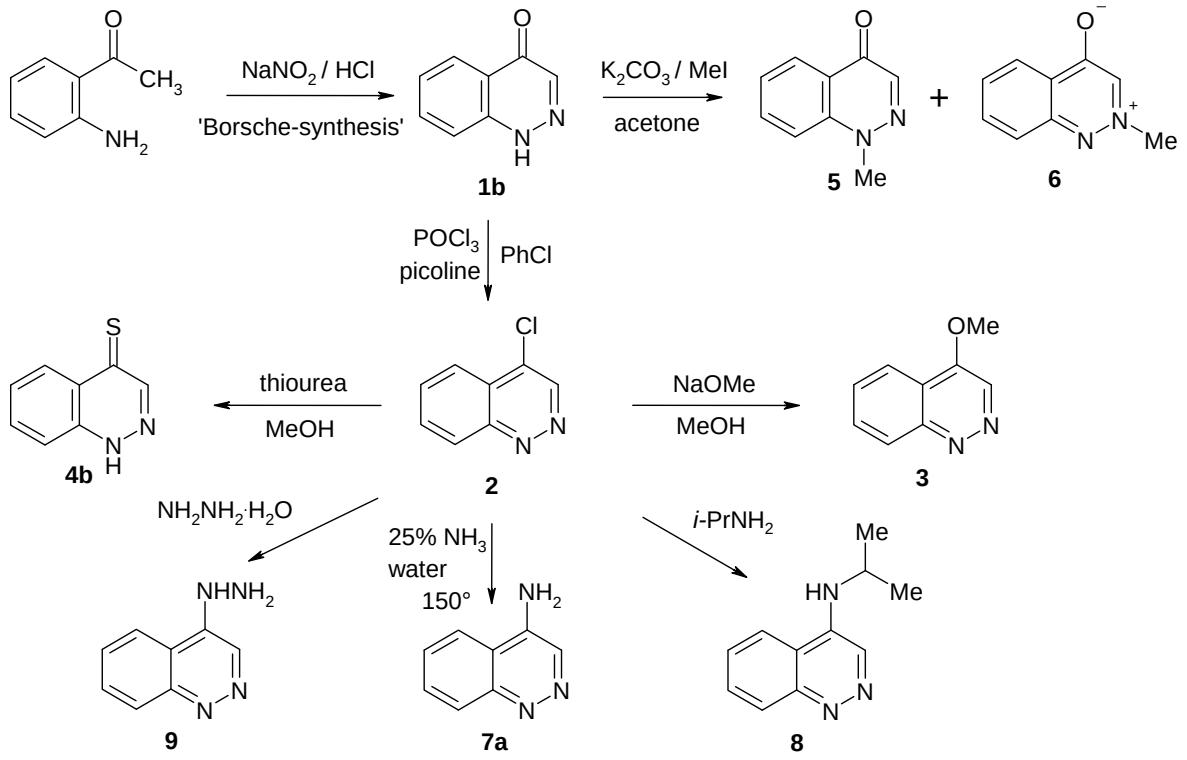
RESULTS AND DISCUSSION

Syntheses

The syntheses of the investigated compounds were largely carried out according to known procedures (Scheme 1). However, in some cases specific modifications emerged to be advantageous compared to the original procedures. Details in this respect are given in the Experimental part. Compound (**8**), which hitherto had not been described in the literature, was obtained by treatment of **2** with isopropylamine.

NMR Spectroscopic Investigations

Detailed NMR spectroscopic analyses for all prepared compounds are reported. Full and unambiguous assignment for all proton, carbon, and nitrogen resonances was achieved by combined application of standard NMR spectral techniques,[14] such as NOE-difference experiments, fully ^{1}H-coupled ^{13}C-NMR spectra, APT, HMQC, and HMBC spectra as well as experiments with selective excitation such as selective long-range INEPT experiments in a 1D[15] and a 2D version.[16] The ^{15}N-NMR spectra were mainly recorded using the gradient selected, sensitivity enhanced HMBC sequence.[17] The obtained data show a high degree of consistency and are summarized in Table 1 (^{1}H-NMR chemical shifts), Table 2 (^{1}H,^{1}H coupling constants), Table 3 (^{13}C-NMR chemical shifts and selected ^{13}C,^{1}H spin coupling constants), and Table 4 (^{15}N-NMR chemical shifts). Coupling constants are given in absolute values (signs not determined).



Scheme 1

Due to the very limited solubility of cinnolin-4-ol (**1**) in non-polar solvents such as $CDCl_3$ the recording of ^{13}C-NMR or ^{15}N-NMR spectra was only possible from DMSO-d_6 solution. Especially the ^{15}N-NMR spectral data – but also the ^{13}C-NMR spectra – unequivocally indicate compound **1** to exist as NH-isomer **1b** [i.e. as cinnolin-4(1*H*)-one]. This assignment is mainly based on the following observations (Figure 2):

- In the ^{13}C-NMR spectrum of **1** the C-4 signal appears at δ 170.3 ppm. This shift is typical for a carbonyl-C atom and not for a =C−OH moiety. In the latter the carbon atom is expected to have a somewhat smaller chemical shift.
- Comparison of the ^{1}H-, ^{13}C- and ^{15}N-NMR data of **1** with those of the corresponding ‚fixed' tautomeric forms, i.e. 4-methoxycinnoline (**3**) (as fixed OH-form) and 1-methylcinnolin-4(1*H*)-one (**5**) (as fixed NH-form) shows a high degree of consistence with the data of **5** (Figure 2).
- The ^{15}N-NMR spectrum of **1** exhibits two essentially different types of N-atoms (δ −42.2 ppm and −206.8 ppm), whereas the ‘aromatic’ 4-methoxycinnoline (**3**) expectedly shows two related ^{15}N resonances with larger chemical shifts (δ 41.3 ppm for N-2 and δ 15.7 ppm for N-1).

On the basis of similar criteria it can be deduced that **4** is present as cinnoline-4(1*H*)-thione (**4b**) in DMSO-d_6 solution (N-1: δ −191.2 ppm, N-2: δ −62.4 ppm, Figure 2). In contrast, **7** exists in the amino form (**7a**), what can be derived not only by the ^{15}N chemical shifts of the cinnoline N-atoms (N-1: δ −20.1 ppm, N-2: δ 26.4 ppm), but also from that of the exocyclic nitrogen atom (δ −312.7 ppm, triplet multiplicity in a DEPT experiment without ^{1}H-decoupling, ^1J = 89.7 Hz) (Figure 2). Similarly, the presence of **8** as secondary amine follows from the ^{15}N-NMR data (N-1: δ −17.2 ppm, N-2: δ 29.9 ppm, *i*-PrNH: δ −288.9 ppm; in DMSO-d_6 solution). The ^{1}H- and ^{13}C-NMR spectra of 4-hydrazinocinnoline (**9**) are characterized by pronounced line broadening indicating a dynamic behavior. This phenomenon (chemical exchange in the range of the NMR timescale) also can explain the fact that ^{15}N-NMR signals could not be found for **9** in HSQC, HMBC, INEPT, or DEPT experiments. Comparison of the ^{1}H- and ^{13}C-NMR chemical shifts of the investigated compounds (in DMSO-d_6) shows that isomers of type (**b**) exhibit smaller chemical shifts for H-3 (7.69–8.47 ppm) and C-8a (136.5–140.9 ppm) compared to 'aromatic' cinnolines of type (**a**), which have 8.64–9.50 ppm for H-3 and 148.2–150.3 ppm for C-8a. Considering these data, the chemical shifts of H-3 (δ 7.71 ppm) and C-8a (δ 138.2 ppm) in **9** suggest a substantial proportion of forms similar to (**b**) in the overall tautomeric composition.

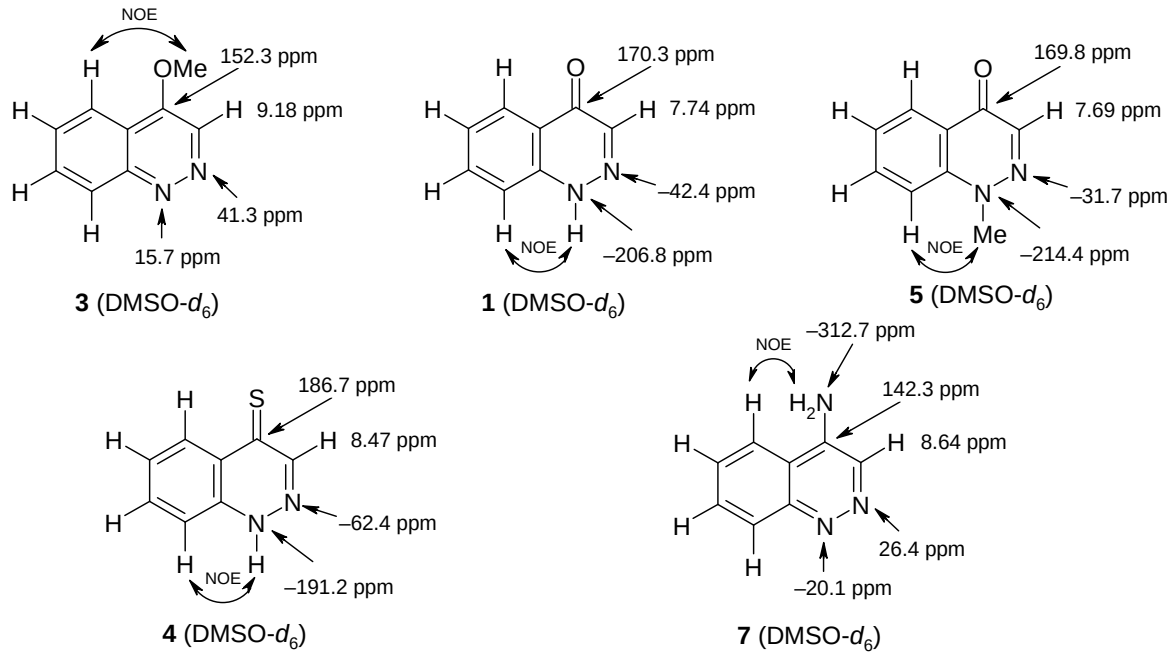


Figure 2. Selected ^{1}H-, ^{13}C- and ^{15}N-NMR Chemical Shifts of Compounds (**1**), (**3**–**5**), and (**7**).

In conclusion, our multinuclear NMR-spectroscopic studies confirm the previous findings that title compounds (**1**) and (**4**) are present as cinnolin-4(1*H*)-one and -4(1*H*)-thione, respectively, in DMSO-d_6 solution, whereas **7** is present in the amino form. (**7a**). Moreover, we have demonstrated the outstanding utility of ^{15}N-NMR spectroscopy in the investigation of cinnolines capable of prototropic tautomerism.

Table 1. ^{1}H-NMR Chemical Shifts (δ, ppm) of Compounds (**1**−**10**)

Comp.	*Solvent*	*H-3*	*H-5*	*H-6*	*H-7*	*H-8*	*Other H*
1	DMSO-d_6	7.74	8.02	7.42	7.79	7.58	13.52 (NH)
2	$CDCl_3$	9.32	8.16	7.84	7.90	8.53	–
	DMSO-d_6	9.50	8.08	7.98	8.01	8.47	–
3	$CDCl_3$	8.91	8.07	7.61	7.74	8.37	4.07 (OMe)
	DMSO-d_6	9.18	8.08	7.76	7.88	8.34	4.14 (OMe)
4	$CDCl_3$	8.51	8.58	7.46	7.75	7.39	10.39 (NH)
	DMSO-d_6	8.47	8.36	7.53	7.84	7.66	14.41 (NH)
5	$CDCl_3$	7.74	8.26	7.38	7.71	7.39	4.05 (NMe)
	DMSO-d_6	7.69	8.07	7.47	7.84	7.71	4.05 (NMe)
6	$CDCl_3$	7.88	8.33	7.53	7.72	7.81	4.32 (NMe)
	DMSO-d_6	8.21	8.08	7.51	7.75	7.78	4.30 (NMe)
7	DMSO-d_6	8.64	8.20	7.56	7.71	8.05	7.27 (NH_2)
8	$CDCl_3$	8.66	7.89	7.57	7.73	8.31	5.39 (NH), 4.02 (CH), 1.42 (Me)
	DMSO-d_6	8.66	8.34	7.59	7.73	8.07	7.12 (NH), 4.02 (CH), 1.27 (Me)
9	DMSO-d_6	7.71	7.69	7.01	7.27	7.00	5–11 (NH, NH_2)[a]

[a] Very broad signal.

Table 2. ^{1}H,^{1}H Spin Coupling Constants (Hz) of Compounds (**1**−**10**)

Comp.	*Solvent*	$^3J(5,6)$	$^4J(5,7)$	$^5J(5,8)$	$^3J(6,7)$	$^4J(6,8)$	$^3J(7,8)$
1	DMSO-d_6	8.2	1.5	0.6	7.0	1.1	8.5
2	$CDCl_3$	8.4	1.5	0.7	6.9	1.3	8.4
	DMSO-d_6	8.2	1.5	0.7	6.9	1.4	8.4
3	$CDCl_3$	8.4	1.5	0.8	6.9	1.3	8.5
	DMSO-d_6	8.3	1.4	0.6	6.8	1.2	8.5
4	$CDCl_3$	8.4	1.4	0.6	7.0	1.1	8.5
	DMSO-d_6	8.4	1.4	0.6	6.9	1.2	8.5
5	$CDCl_3$	8.0	1.6	[a]	7.0	1.0	[a]
	DMSO-d_6	8.1	1.6	0.6	7.0	0.9	8.7
6	$CDCl_3$	8.2	1.5	0.7	6.8	1.3	8.5
	DMSO-d_6	8.1	1.4	0.8	6.5	1.8	8.6
7	DMSO-d_6	8.5	1.3	0.6	6.8	1.2	8.6
8	$CDCl_3$ [b]	8.5	1.1	0.6	6.8	1.1	8.5
	DMSO-d_6 [c]	8.4	1.3	1.0	6.8	1.3	8.5
9	DMSO-d_6	[a]	[a]	[a]	[a]	[a]	[a]

[a] Not unambiguously determined. [b] $^3J(CH_3,CH)$ = 6.3 Hz. [c] $^3J(CH_3,CH)$ = 6.3 Hz, $^3J(CH,NH)$ = 7.9 Hz.

Table 3. ^{13}C-NMR Shifts (δ, ppm) and Selected ^{13}C,^{1}H Coupling Constants (*Hz, in Italics*) of Compounds (**1**–**10**)

Comp.	*Solv.*	*C-3* *^{1}J*	*C-4* *^{2}J(3), ^{3}J(5), ^{4}J(8)*	*C-4a* *^{3}J(3), ^{3}J(6), ^{3}J(8)*	*C-5*	*C-6*	*C-7*	*C-8*	*C-8a* *^{3}J(5), ^{3}J(7)*	*Other C* *J of Other C*
1	b	140.2	170.3	122.8	123.8	124.9	133.8	116.4	140.9	–
		184.1	*5.2, 3.5, 1.7*	*3.7, 8.1, 4.9*					*7.3, 9.7*	
2	a	144.3	134.7	124.7	122.9	132.1	131.4	130.0	150.9	–
		189.0	*2.0, 5.6, 2.0*	*4.6, 8.8, 5.1*					*6.2, 8.5*	
	b[b]	144.1	133.9	123.7	122.5	133.0	132.2	129.3	150.3	–
3	a	128.7	152.8[c]	118.4	120.6	129.6	130.5	128.6	150.3	56.1 (OMe)
		181.4	*2.9, 4.0, 1.6*	*4.6, 8.8, 5.2*					*6.0, 9.3*	*146.1 (^{1}J)*
	b	129.6	152.3[c]	117.6	120.4	130.0	130.9	128.2	149.7	56.7 (OMe)
		183.6	*2.9, 3.8, 1.6*	*4.5, 8.7, 5.1*					*6.0, 9.2*	*146.9 (^{1}J)*
4	a	150.9	190.7	133.4	128.1	127.1	134.9	116.0	135.8	–
	b	149.7	186.7	132.6	126.6	127.4	134.8	117.9	136.5	–
		189.5	*6.8, 4.4, 1.0*	*4.3, 8.5, 5.0*					*7.2, 9.9*	
5	a	139.9	171.0	124.3	125.6	124.8	133.8	114.8	141.0	43.5 (NMe)
		185.5							*6.7, –*	*140.7 (^{1}J)*
	b	139.0	169.8	123.8	124.4	125.1	134.0	116.4	140.7[d]	43.6
		184.9	*4.9, 3.6, 1.7*	*3.6, 7.9, 5.0*					*7.6, 9.6*	*141.2 (^{1}J)*
6	a	132.2	171.1	126.3	123.7	128.2	132.7	126.3	149.4	52.0 (NMe)
		183.7, 3.2 (^{3}J)		*–, 8.5, –*						*143.2 (^{1}J), 3.1 (^{3}J)*
	b	133.2	169.9	125.3	122.8	127.3	132.5	125.9	148.8	51.4 (NMe)
		186.3, 3.1 (^{3}J)	*2.0, 3.5, –*	*3.2, 8.2, 4.0*					*6.6, 7.9*	*143.6 (^{1}J), 3.4 (^{3}J)*
7	b	132.3	142.3	114.9	121.9	127.2	130.4	128.0	148.8	–
		179.4	*5.1, 3.8, 1.4*	*4.3, 8.7, 5.1*					*6.1, 8.9*	
8	a	128.6	139.5	115.5	119.1	128.2	130.2	128.8	148.0	44.4 (CH), 22.5 (Me)
	b	128.4[e]	139.3	115.3	121.5	127.2	129.9	128.2	148.2	43.3 (CH), 21.9 (Me)
		180.0	*5.4, 3.6, 1.7*	*4.7, 8.8, 5.3*					*6.2, 8.9*	
9	b	128.7	133.1	119.2	121.1	123.3	129.1	114.7	138.2	–

[a] a = $CDCl_3$, b = DMSO-d_6. [b] Decomposes rapidly in DMSO-d_6 solution. [c] ^{3}J(C4,OMe) = 4.0 Hz. [d] ^{3}J(C8a,Me) = 2.1 Hz. [e] ^{2}J(C3,NH) = 6.2 Hz.

Table 4. ^{15}N-NMR Chemical Shifts (δ, ppm) of Compounds (**1**−**10**)

Compd.	*Solvent*	*N-1*	*N-2*	*Compd.*	*Solvent*	*N-1*	*N-2*
1	DMSO-d_6	−206.8	–42.4[a]	**6**	$CDCl_3$	−88.8	−137.4
					DMSO-d_6	−91.8	−132.0
2	$CDCl_3$	34.3	34.7	**7**[b]	DMSO-d_6	−20.1[c]	26.4[d]
3	$CDCl_3$	12.5	35.7	**8**	$CDCl_3$[e]	−29.1	20.0
	DMSO-d_6	15.7	41.3		DMSO-d_6[f]	−17.2	29.9
4	DMSO-d_6	−191.2	−62.4	**9**	DMSO-d_6	[g]	[g]
5	$CDCl_3$	−217.3	−33.8				
	DMSO-d_6	−214.4	−31.7				

[a] ^2J(N2,H3) = 14.0 Hz. [b] δ(NH_2) = −312.7 ppm, ^1J = 89.7 Hz. [c] ^3J(N1,H3) = 4.6 Hz.
[d] ^2J(N2,H3) = 11.6 Hz. [e] δ(NH) = −290.6 ppm. [f] δ(NH) = −288.9 ppm. [g] Not found.

EXPERIMENTAL

Melting points were determined on a Reichert–Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Shimadzu QP 1000 instrument (EI, 70 eV) and on a Finnigan MAT 8230 instrument (EI, 70 eV, HRMS). IR spectra were recorded on a Perkin-Elmer FTIR 1605 spectrophotometer or on a Perkin-Elmer FTIR spectrum 1000 spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian UnityPlus 300 spectrometer at 28 °C (299.95 MHz for ^{1}H, 75.43 MHz for ^{13}C) or on a Bruker Avance 500 spectrometer at 293 K (500.13 MHz for ^{1}H, 125.77 MHz for ^{13}C). The centre of the solvent signal was used as an internal standard which was related to TMS with δ = 7.26 ppm (^{1}H in $CDCl_3$), δ = 2.49 ppm (^{1}H in DMSO-d_6), δ = 77.0 ppm (^{13}C in $CDCl_3$), and δ = 39.5 ppm (^{13}C in DMSO-d_6). ^{15}N-NMR spectra were obtained on a Bruker Avance 500 instrument with a 'directly' detecting broadband observe probe at 300K and were referenced against external nitromethane (coaxial capillary). The digital resolutions were as following: 0.25 Hz/point for the ^{1}H-NMR spectra, 0.5 Hz/point for the ^{1}H-broadband decoupled and 0.4 Hz/point for the ^{1}H-coupled ^{13}C-NMR spectra, 1 Hz/point for the 1D ^{15}N-NMR spectra (refocused INEPT) and ≤ 59 Hz/point for the ^{15}N,^{1}H-HMBC spectra. Preparative layer chromatography was carried out on Merck PLC plates, silica gel 60F_{254}, 20×20 cm, layer thickness 2 mm. 2-Aminoacetophenone is commercially available (Aldrich). Yields of products were not optimized.

Cinnolin-4(1*H*)-one (1)

According to lit.,[18] to a solution of 2-aminoacetophenone (5.40 g, 40 mmol) in glacial acetic acid (4 mL) were added 6.8 mL of concd HCl and 15 mL of water and the resulting mixture was cooled to 0 °C. Then an ice-cold solution of $NaNO_2$ (3.04 g, 44 mmol) in 10 mL of water was added dropwise keeping the

temperature between 0 °C and 5 °C. After the addition was complete, the suspension was stirred at 0–5 °C for 1 h, then 0.2 g of urea were added and stirring was continued for another h at this temperature. Then a solution of sodium acetate (41.0 g, 500 mmol), in 100 mL of water, and 50 mL of CH_2Cl_2 were added and the mixture was stirred for 15 h to gradually reach rt. The red-brown precipitate was filtered off with suction, washed with water and CH_2Cl_2, and dried in a desiccator to yield 4.43 g (76%) of a red-brown solid, mp 234–236 °C (lit.,[19] mp: 236 °C), which was pure according to ^{1}H-NMR spectral analysis. MS (*m/z*, %): 146 (M^+, 100), 119 (45), 92 (49).

4-Chlorocinnoline (2)[20]

A mixture of **1** (3.00 g, 20.6 mmol), $POCl_3$ (4.68 g, 30.5 mmol), 2-methylpyridine (606 mg, 6.5 mmol), and chlorobenzene (75 mL) was refluxed for 1 h. After cooling to rt, the mixture was poured onto ice/water and immediately made slightly alkaline with a saturated Na_2CO_3 solution (ca. 10 mL). Then the mixture was extracted with CH_2Cl_2 (3 × 25 mL), the combined organic phases were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The dark, solid residue was treated with boiling light petroleum (50 mL) for 10 minutes and the hot supernatant yellow liquid was rapidly filtered through glass wool. After storing in the refrigerator for some hours the precipitated crystals were filtered off and dried to afford 2.24 g (66%) of fine yellowish needles, mp: 74–76 °C (lit.,[19] mp: 76–77 °C). MS (*m/z*, %): 166 (M^+, 19), 164 (M^+, 55), 136 (20), 101 (100), 75 (35).

4-Methoxycinnoline (3)

Compound (**3**) was prepared in 85% yield from **2** and methanolic NaOMe similarly as described in lit.[22] MS (*m/z*, %): 160 (M^+, 60), 102 (54), 89 (100), 75 (14), 63 (39).

Cinnoline-4(1*H*)-thione (4)

Compound (**4**) was prepared in 78% yield from **2** and thiourea according to lit.[23] MS (*m/z*, %): 162 (M^+, 100), 135 (44), 118 (16), 108 (36), 91 (25), 81 (29), 69 (34), 68 (20).

1-Methylcinnolin-4(1*H*)-one (5) and 2-Methylcinnolin-2-ium-4-olate (6)

On the basis of lit.,[24] a mixture of **1** (438 mg, 3 mmol), K_2CO_3 (9.18 g, 66.4 mmol), and MeI (6.98 g, 49.2 mmol) in acetone (180 mL) was stirred at rt for 10 h. Then the solvent was removed under reduced pressure and the residue was subjected to preparative layer chromatography (eluent: CH_2Cl_2, extraction of the adsorbed materials by repeated treatment with hot EtOAc/MeOH 4:1). From the faster eluted component (**5**) (R_f ~ 0.5) 107 mg (22%) of beige crystals were obtained, mp 110–115 °C (lit.,[24] mp: 113–115 °C), MS (*m/z*, %): 160 (M^+, 100), 132 (44), 105 (41), 104 (79), 78 (37), 77 (31), 64 (17), 63 (24).

The slower eluted compound (**6**) (R_f ~ 0.2) afforded 58 mg (12%) of a light brown solid, mp 163–167 °C (lit.,[25] mp: 162–164 °C). MS (*m/z*, %): 160 (M^+, 100), 132 (62), 131 (41), 104 (18), 63 (18).

Cinnolin-4-amine (7)

In a pressure vessel, a mixture of **2** (823 mg, 5 mmol) and 25% NH_3 in water (30 mL) was heated at 150 °C for 12 h.[26] Immediately after reaching ~ 50 °C the reaction mixture was quickly filtered and the filtrate was kept in a refrigerator overnight. The separated crystals were filtered off, washed with water and dried to afford 375 mg (52%) of **7** as orange-yellow needles, mp 210 °C (lit.,[21] mp 211 °C). MS (*m/z*, %): 145 (M^+, 100), 90 (58), 89 (61), 72 (34), 58 (34).

***N*-Isopropylcinnolin-4-amine (8)**

A mixture of 4-chlorocinnoline (**2**) (164 mg, 1 mmol) and isopropylamine (660 mg, 11.2 mmol) was stirred at rt for 24 h. Then excess isopropylamine was removed under reduced pressure and the red-brown residue was subjected to preparative layer chromatography (eluent: EtOAc/NH_3 100:1, R_f ~ 0.2, extraction of the adsorbed materials by repeated treatment with hot EtOAc/MeOH 4:1) to afford 108 mg (58%) of a light brown solid (pure **8** according to NMR spectral analysis). Subsequent recrystallization from toluene gave 60 mg (32%) of colourless crystals, mp 189−190 °C. IR (KBr): ν (cm^{-1}) 3209 (NH), 1564, 1521, 1291, 1130; MS (*m/z*, %): 187 (M^+, 83), 172 (100), 145 (10), 117 (20), 116 (24), 101 (23), 90 (24), 89 (20), 75 (12), 63 (14). *Anal.* Calcd for $C_{11}H_{13}N_3$: C, 70.56; H, 7.00; N, 22.44. Found: C, 70.45; H, 6.92; N, 22.18. HRMS Calcd for $C_{11}H_{13}N_3$: 187.1109. Found: 187.1112 ± 0.0009.

4-Hydrazinocinnoline (9)

Compound (**9**) was prepared in 82% yield from **2** and hydrazine hydrate according to ref.[27] MS (*m/z*, %): 160 (M^+, 100), 159 (16).130 (19), 102 (18), 90 (14), 77 (15), 76 (15).

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REFERENCES AND NOTES

1. J. Elguero, A. R. Katritzky, and O. V. Denisko, *Adv. Heterocycl. Chem.*, 2000, **76**, 1.
2. J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, *Adv. Heterocycl. Chem., Suppl. 1*, 1976, 1.
3. A. R. Katritzky and J. M. Lagowski, *Adv. Heterocycl. Chem.*, 1963, **1**, 311.
4. A. R. Katritzky, M. Karelson, and P. A. Harris, *Heterocycles,* 1991, **32**, 329.
5. B. Stanovnik, M. Tišler, A. R. Katritzky, and O. V. Denisko, *Adv. Heterocycl. Chem*., 2006, **91**, 1.

6. M. Tišler and B. Stanovnik, 'Comprehensive Heterocyclic Chemistry: Pyridazines and their Benzo Derivatives', Vol. 3, part 2B; ed. by A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, pp. 1–56.
7. D. E. Ames and H. Z. Kucharska, *J. Chem. Soc.*, 1963, 4924.
8. D. E. Ames, R. F. Chapman, H. Z. Kucharska, and D. Waite, *J. Chem. Soc*., 1965, 5391.
9. A. J. Boulton, I. J. Fletcher, and A. R. Katritzky, *J. Chem. Soc. B*, 1971, 2344.
10. A. Albert and G. B. Barlin, *J. Chem. Soc*., 1962, 3129.
11. N. Dennis, A. R. Katritzky, and M. Ramaiah, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1506.
12. N. Haider and W. Holzer, *Science of Synthesis*, 2004, **16**, 251; and references cited therein.
13. W. Borsche and A. Herbert, *Justus Liebigs Ann. Chem*., 1941, **546**, 293.
14. S. Braun, H.-O. Kalinowski, and S. Berger, '150 and More Basic NMR Experiments: A Practical Course – Second Expanded Edition', Wiley-VCH, Weinheim, 1998, (*Chem. Abstr.*, 1999, **131**, 184497).
15. A. Bax, *J. Magn. Reson.*, 1984, **57**, 314.
16. T. Jippo, O. Kamo, and N. Nagayama, *J. Magn. Reson.*, 1986, **66**, 344.
17. W. Willker, D. Leibfritz, R. Kerssebaum, and W. Bermel, *Magn. Reson. Chem.*, 1993, **31**, 287.
18. L. R. Denes, 1986, US 4,620,000 (*Chem. Abstr*., 1987, **106**, 84624).
19. N. J. Leonard and S. N. Boyd, *J. Org. Chem*., 1946, **11**, 419.
20. The following procedure (similar to lit.[21]) gave much better results than the use of $POCl_3$ alone or a mixture of $POCl_3$ and PCl_5.[19] Moreover, we found the presence of picoline to be superior compared to that of pyridine[21] and purification of the raw material by recrystallization from light petroleum to be more convenient than that *via* column chromatography.[21]
21. A. Turck, N. Plé, V. Tallon, and G. Quéguiner, *Tetrahedron*, 1995, **51**, 13045.
22. K. Schofield and J. C. E. Simpson, *J. Chem. Soc.*, 1945, 512.
23. R. N. Castle, H. Ward, N. White, and K. Adachi, *J. Org. Chem*., 1960, **25**, 570.
24. P. A. Marshall, B. A. Mooney, R. H. Prager, and A. D. Ward, *Aust. J. Chem*., 1981, **34**, 2619.
25. D. E. Ames and R. F. Chapman, *J. Chem. Soc*., 1967, 40.
26. We obtained better results when using aqueous NH_3 instead of NH_3 in THF.[21]
27. K. Schofield and T. Swain, *J. Chem. Soc*., 1950, 392.