

Heterocyclic analogs of xanthonones: 5,6-fused 3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)thiones – synthesis and NMR (^1H , ^{13}C , ^{15}N) data

Valerie Huemer, Gernot A. Eller and Wolfgang Holzer*

Various [5,6]pyrano[2,3-*c*]pyrazol-4(1*H*)-thiones were synthesized in high yields by treatment of the corresponding [5,6]pyrano[2,3-*c*]pyrazol-4(1*H*)-ones with Lawesson's reagent. Detailed NMR spectroscopic studies were undertaken of the title compounds. Complete and unambiguous assignment of chemical shifts (^1H , ^{13}C , ^{15}N) and coupling constants (^1H , ^1H ; ^{13}C , ^1H) was achieved by the combined application of various one- and two-dimensional (1D and 2D) NMR spectroscopic techniques. Unequivocal mapping of most ^{13}C , ^1H spin coupling constants is accomplished by 2D (δ , J) long-range INEPT spectra with selective excitation. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: ^1H NMR; ^{13}C NMR; ^{15}N NMR; [5,6]pyrano[2,3-*c*]pyrazol-4(1*H*)-thiones; Lawesson's reagent

Introduction

In the course of a program devoted to the synthesis of new heterocyclic scaffolds for bioactive compounds,^[1–10] we recently presented the synthesis of various [5,6]pyrano[2,3-*c*]pyrazol-4(1*H*)-ones of type **4** via reaction of 2-pyrazolin-5-ones **1** with *o*-haloheteroarene carbonyl chlorides **2** and the subsequent ring closure of the resulting 4-heteroaroylpyrazol-5-ols **3** (Scheme 1). Following this approach, we have obtained type **4** compounds carrying – among others – a pyridine (all positional isomers),^[1] quinoline,^[1] thiophene (all positional isomers),^[2,3] benzo[*b*]thiophene,^[2] and thieno[2,3-*b*]thiophene system^[3] as the variable heteroaromatic moiety ('Het') condensed to the central γ -pyranone ring.

Thio analogs of flavones, isoflavones, xanthonones, and related systems have received considerable attention due to the importance of such molecules in biology and photochemistry as well as their usefulness as synthetic building blocks.^[11] Considering these facts, in the present paper we report on the synthesis of the thio analogs **5** of the above-mentioned polycycles **4**, in which the pyran-4-one moiety is replaced by the corresponding pyran-4-thione. Moreover, we present the results of extensive NMR (^1H , ^{13}C , ^{15}N) studies undertaken with the title compounds and some related systems, with full and unambiguous assignment of all chemical shifts and most spin coupling constants. The obtained data of these rare condensed heteroaromatic systems can be considered as valuable and reliable reference material for databases used in NMR prediction programs such as CSEARCH^[12]/NMRPREDICT^[12,13] and ACD/C + H predictor.^[14] Such programs have become very popular in the last few years, particularly for predicting ^{13}C -NMR chemical shifts.

Results and Discussion

Chemistry

The transformation of carbonyl compounds into their thio analogs can be achieved by the application of many different

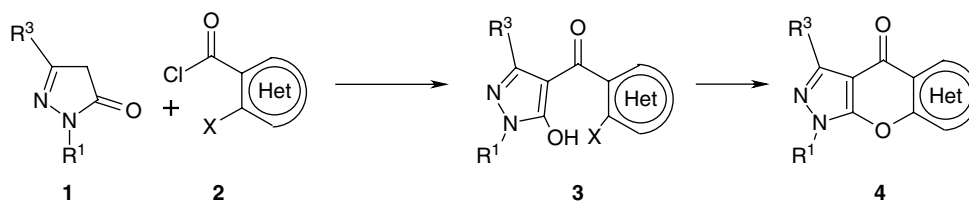
reagents.^[11,15,16] Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide) has been commonly used for this purpose and usually permits efficient conversion of ketones into thioketones.^[17–19] Employing this method, namely by treatment of compounds **4** with 0.5 equivalents of Lawesson's reagent in boiling toluene, we obtained the corresponding target compounds **5** in high yields (Scheme 2). In the same manner, thiones **7** and **9**, required for comparison purposes, were synthesized from oxo compounds **6** and **8**, respectively (Scheme 2). The latter were prepared according to known procedures (**6**,^[2,20] **8**^[21]).

NMR Spectroscopic Investigations

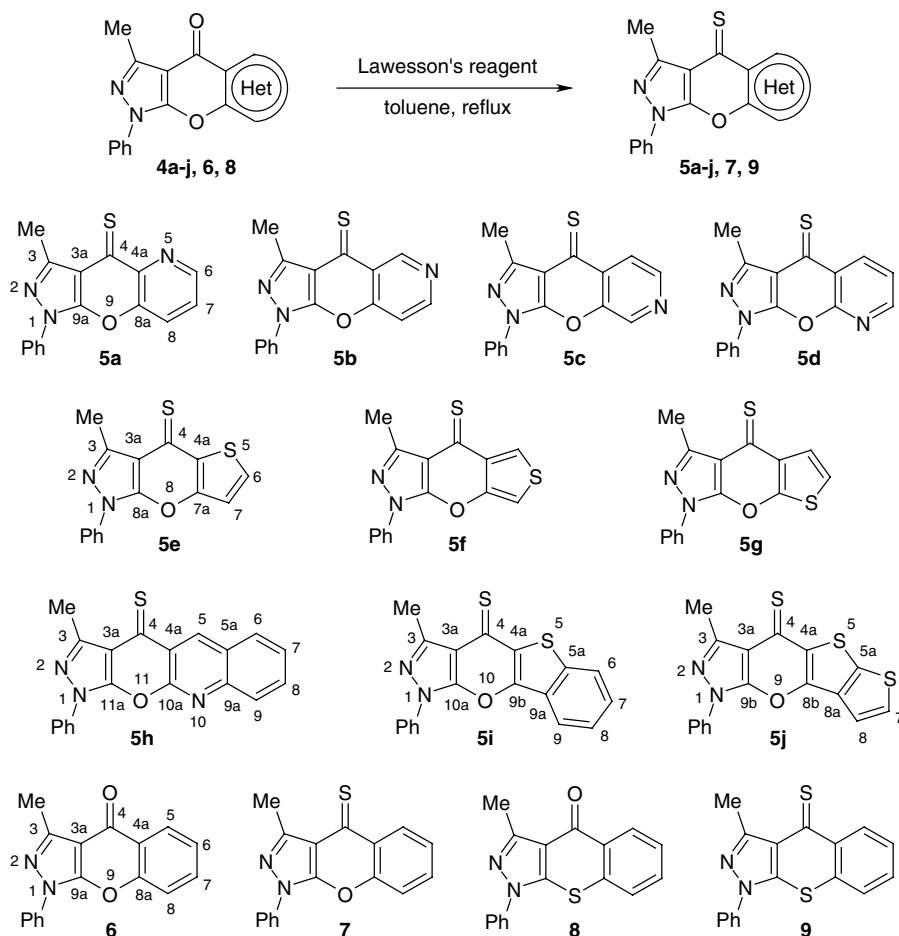
The ^1H NMR data of compounds **4a–j**, **6–9** are collected in Table 1. Assignment of signals due to *N*-phenyl system is easy considering the relative intensities and the coupling patterns (Ph-2,6 resembles a doublet, Ph-3,5 and Ph-4 a triplet). The mapping of signals of protons attached to the variable heterocyclic system ('Het') at the 'east end' of the condensed systems (according to Scheme 2) is mainly based on chemical shift considerations and on COSY, NOE difference and one-dimensional (1D) TOCSY experiments.^[22] Moreover, information from the ^1H -coupled ^{13}C NMR spectra can be employed to achieve unambiguous assignments. Thus, for instance, in thiophene containing systems **5e**, **5g**, and **5j** carbons being in alpha position to the sulfur atom can be distinguished from those in β positions on the basis of their $^1J(^{13}\text{C}, ^1\text{H})$ coupling constants (α -C: $^1J \sim 190$ Hz; β -C: $^1J \sim 175$ Hz)^[23] (Table 3). Via correlations in the HSQC spectra, then, also the corresponding ^1H -signals can be easily assigned. Protons located in position 5 of the anellated ring system receive a downfield shift as a result of the

* Correspondence to: Wolfgang Holzer, Department of Drug and Natural Product Synthesis, Faculty of Life Sciences, University of Vienna, Althanstrasse 14, A-1090 Vienna, Austria. E-mail: wolfgang.holzer@univie.ac.at

Department of Drug and Natural Product Synthesis, University of Vienna, A-1090 Vienna, Austria



Scheme 1. Synthesis of [5,6]pyrano[2,3-c]pyrazol-4(1*H*)-ones **4**.



Scheme 2. Synthesis and atom numbering of the investigated compounds.

magnetic anisotropy of the adjacent C=S bond. Thus, chemical shifts of H-5 in **5b** and **5h** (pyridine 2-H, quinoline 4-H) come close to 10 ppm.

The ^{13}C NMR chemical shifts of the investigated compounds are collected in Table 2. Assignments are based on HSCQ (HMQC), HMBC, and long-range INEPT experiments with selective excitation (INAPT).^[22] In rare cases (for instance, distinction of C-6 vs C-8 in **9**), HMQC-COSY spectra were consulted. Within type **5** compounds, the signals due to the *N*-phenyl ring show a high degree of consistency; this is also the case for δ (3-Me), δ (C-3), and δ (C-3a). The C=S (C-4) resonance is located between 190 and 198 ppm and is, of course, to some degree dependent on the nature of the variable heteroaromatic system. Comparison of the ^{13}C chemical shift data of compounds **5** with those of corresponding type **4** moieties^[1–3] clearly shows the effects of replacing the central pyran-4-one by a pyran-4-thione system. Whereas this replacement has nearly no influence on the chemical shifts of

the *N*-phenyl system or only small impact on those of 3-Me, C-3, and peripheral carbon atoms of the heteroaromatic system, the chemical shifts of the carbon atoms belonging to the central pyrane ring change drastically. Thus, in compounds **4** there is a pronounced 'push–pull situation' leading to a strong polarization of the pyrane C=C bonds – reflected by large chemical shifts of carbons attached to the pyrane O-atom and small ones of those in β -position to the ring oxygen. In contrast, with compounds **5** this polarization effect is much less developed, resulting in an upfield shift for carbons directly bonded to the pyrane O-atoms, whereas those in β -position receive a marked downfield shift compared to the corresponding signals in compounds **4**. Switching from compound **6** to **7** shows the same typical effects (C-3a: 104.9 \rightarrow 116.3 ppm; C-4a: 123.3 \rightarrow 127.9 ppm; C-8a: 154.4 \rightarrow 149.7 ppm; C-9a: 152.9 \rightarrow 146.5 ppm). The chemical shift of C-4 rises between 20 and 25 ppm in the transformation **4** \rightarrow **5** or **6** \rightarrow **7**. The order of magnitude regarding these changes is

Table 1. ^1H NMR chemical shifts of **5a–j**, **6–9** (δ in ppm, CDCl_3)

Compounds	Ph 2,6	Ph 3,5	Ph 4	3-Me	H-5	H-6	H-7	H-8	Other H	Instr. ^j
5a	7.86	7.55	7.41	2.78	–	8.87 ^a	7.64 ^a	7.93 ^a	–	a
5b	7.84	7.56	7.43	2.77	9.83 ^b	–	8.80 ^b	7.39 ^b	–	a
5c	7.89	7.59	7.45	2.79	8.49 ^c	8.66 ^c	–	9.00 ^c	–	a
5d	7.97	7.56	7.41	2.81	9.15 ^d	7.51 ^d	8.69 ^d	–	–	a
5e	7.86	7.55	7.41	2.80	–	7.77 ^e	7.22 ^e	–	–	a
5f	7.85	7.55	7.41	2.77	8.36 ^f	–	7.18 ^f	–	–	b
5g	7.82	7.54	7.40	2.78	7.66 ^g	6.95 ^g	–	–	–	a
5h	8.00	7.58	7.43	2.83	9.64 ^h	8.15	7.65	7.91	8.11 (H-9)	a
5i	7.94	7.61	7.45	2.77	–	7.81	7.55	7.48	8.02 (H-9)	a
5j	7.90	7.59	7.44	2.81	–	–	7.48 ⁱ	7.44 ⁱ	–	b
6	7.87	7.54	7.38	2.69	8.33	7.43	7.68	7.51	–	a
7	7.89	7.55	7.40	2.80	8.76	7.42	7.68	7.49	–	b
8	7.71	7.56	7.45	2.81	8.64	7.53	7.60	7.54	–	b
9	7.71	7.58	7.47	2.90	9.17	7.49	7.56	7.49	–	b

^a $^3J(6,7) = 8.4$ Hz, $^4J(6,8) = 1.4$ Hz, $^3J(7,8) = 4.3$ Hz.

^b $^4J(5,7) < 1$ Hz, $^5J(5,8) < 1$ Hz, $^3J(7,8) = 5.7$ Hz.

^c $^3J(5,6) = 5.3$ Hz, $^5J(5,8) < 1$ Hz, $^4J(6,8) < 1$ Hz.

^d $^3J(5,6) = 7.9$ Hz, $^4J(5,7) = 2.0$ Hz, $^3J(6,7) = 4.6$ Hz.

^e $^3J(6,7) = 5.6$ Hz.

^f $^4J(5,7) = 3.8$ Hz.

^g $^3J(5,6) = 6.0$ Hz.

^h Singlet.

ⁱ $^3J(7,8) = 5.4$ Hz.

^j a: recorded at 300 MHz; b: recorded at 500 MHz.

Table 2. ^{13}C NMR chemical shifts of **5a–j**, **6–9** (δ in ppm, CDCl_3)

Compounds	Ph 1	Ph 2,6	Ph 3,5	Ph 4	3-Me	C-3	C-3a	C-4	C-4a	C-5	C-5a	C-6	C-7	C-8	Other C
5a	136.5	121.4	129.5	127.8	15.9	151.0	118.4	197.3	141.7	–	–	148.5	127.2	127.2	C-8a: 146.9; C-9a: 145.6
5b	136.4	121.6	129.6	128.0	15.8	150.9	117.2	196.6	123.0	152.3	–	–	153.0	112.2	C-8a: 155.1; C-9a: 145.7
5c	136.5	121.5	129.6	128.0	15.8	150.9	117.6	195.9	131.9	120.8	–	146.2	–	141.8	C-8a: 145.0; C-9a: 146.0
5d	136.6	121.4	129.6	127.8	15.7	150.8	116.5	197.3	122.8	139.8	–	122.7	152.2	–	C-8a: 154.4; C-9a: 147.1
5e	136.7	121.4	129.5	127.7	15.3	149.2	114.5	190.9	135.8	–	–	134.8	117.4	–	C-7a: 147.7; C-8a: 148.1
5f	136.7	121.6	129.4	127.7	15.9	150.9	114.8	195.1	135.3	127.4	–	–	105.6	–	C-7a: 146.5; C-8a: 148.3
5g	136.6	121.3	129.5	127.7	15.6	149.9	115.8	193.5	133.2	124.0	–	116.8	–	–	C-7a: 156.8; C-8a: 147.8
5h	136.6	121.8	129.6	127.9	15.9	151.2	115.8	197.9	121.7	141.9	127.3	129.9	127.1	133.2	C-9: 127.8; C-9a: 147.9; C-10a: 152.5; C-11a: 147.5
5i	136.9	121.1	129.6	127.7	15.3	149.0	115.6	191.1	135.0	–	140.8	123.7	128.8	125.5	C-9: 122.2; C-9a: 128.7; C-9b: 141.8; C-10b: 147.7
5j	136.8	121.4	129.6	127.8	15.4	149.0	114.3	190.4	138.8	–	145.0	–	130.1	118.5	C-8a: 134.9; C-8b: 140.3; C-9a: 147.5
6	137.0	121.2	129.4	127.3	14.1	148.1	104.9	173.5	123.3	126.8	–	125.2	133.7	117.6	C-8a: 154.5; C-9a: 152.9
7	136.8	121.2	129.4	127.5	16.0	150.8	116.3	197.9	127.9	129.3	–	125.7	133.6	117.8	C-8a: 149.7; C-9a: 146.5
8	138.5	123.0	129.7	128.4	14.2	152.5	115.5	177.4	131.2	129.2	–	127.0	131.9	126.7	C-8a: 132.9; C-9a: 139.8
9	138.3	123.2	129.7	128.6	17.6	155.0	126.7	202.9	136.4	132.7	–	127.5	131.3	126.7	C-8a: 127.5; C-9a: 134.0

in good agreement with those found by Still and coworkers within the changeover from xanthone (9*H*-xanthen-9-one) to xanthione (9*H*-xanthen-9-thione), with C-8a/C-9a 121.5 \rightarrow 128.7 ppm, C-4a/C-10a 155.7 \rightarrow 150.1 ppm, and C-9 176.6 \rightarrow 204.4 ppm (Fig. 1).^[24]

Comparing the ^{13}C chemical shifts of compounds **6**, **7**, **8**, and **9** explicitly demonstrates the effect of replacing the ring oxygen by sulfur (**6** \rightarrow **8**, **7** \rightarrow **9**) and by changing C=O to C=S (**6** \rightarrow **7**, **8** \rightarrow **9**) on the example of the benzene-fused tricyclic

(Fig. 2, see also Table 2). In Fig. 1, the corresponding changes can be recognized for the transitions xanthone \rightarrow thioxanthone, xanthione \rightarrow thioxanthione as well as for those of xanthone \rightarrow xanthione and thioxanthone \rightarrow thioxanthione.^[24–26]

In Table 3, the ^{13}C , ^1H coupling constants of the investigated compounds are summarized. The data are mainly extracted from the fully ^1H -coupled ^{13}C NMR spectra (gated decoupling). In ambiguous cases, 2D (δ , J) long-range INEPT spectra with selective excitation^[27] were used for the definitive mapping of long-range

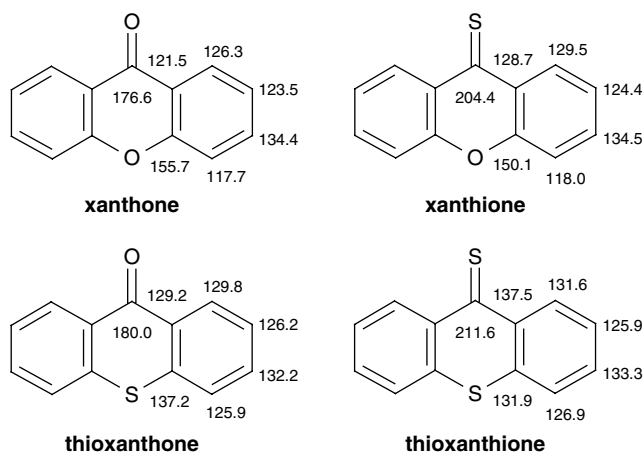


Figure 1. ^{13}C NMR chemical shifts of xanthenone,^[24] xanthenone,^[24] thioxanthenone,^[25] and thioxanthenone^[26] (CDCl_3).

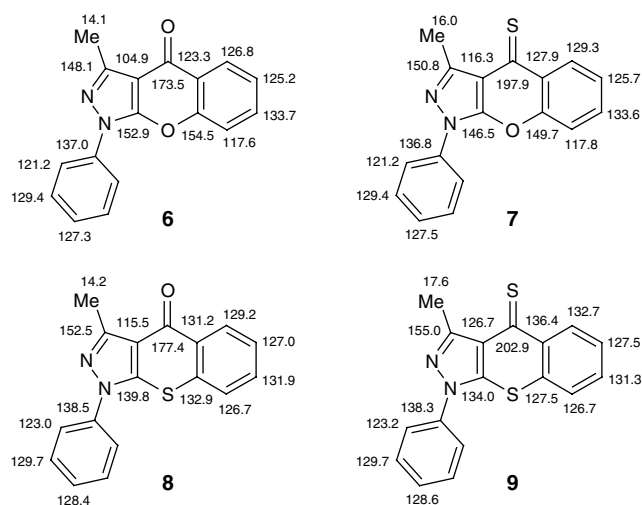


Figure 2. ^{13}C NMR chemical shifts of **6–9** (CDCl_3).

$^{13}\text{C},^1\text{H}$ coupling constants. Thus, for instance, in the ^1H -coupled ^{13}C NMR spectrum of **5b**, the signal due to C-8a (155.1 ppm) is split by 9.7, 7.6, and 3.8 Hz coupling. In the 2D (δ, J) long-range INEPT spectra with selective excitation of H-7, the signal of C-8a is split by 9.7 Hz - thus assigning $^3J(\text{C}8\text{a}, \text{H}7)$ to be 9.7 Hz - whereas in a similar experiment upon selective excitation of H-5, the C-8a signal is split by 7.6 Hz. Hence, the correct assignments $^3J(\text{C}8\text{a}, \text{H}7) = 9.7$ Hz, $^3J(\text{C}8\text{a}, \text{H}5) = 7.6$ Hz, and $^2J(\text{C}8\text{a}, \text{H}8) = 3.8$ Hz (following indirectly) can be unequivocally given. Expectedly, $^{13}\text{C},^1\text{H}$ coupling constants at the pyrazole moiety of compounds **5** are hardly different from the corresponding ones in **4**.^[1–3] In this regard, also the changes of couplings within the variable heteroaromatic systems are not significant.

Finally, Table 4 gives the ^{15}N NMR data of **5a–j** and **6–9**. Within the compound **5** series, the ^{15}N chemical shifts of pyrazole nitrogen atoms N-1 (–196.5 to –194.3 ppm) and N-2 (–93.1 to –90.7 ppm) are very consistent, indicating the marginal influence of the variable heterocyclic system on these resonances. In contrast, the ^{15}N chemical shift of the pyridine N-atom in compounds **5a–d** is strongly influenced by the distinct electron donating resonance (+M) effect of the oxygen atom O-9: in **5d**, O-9 and N-8 are located in the 'ortho' position leading to a considerable

upfield shift of N-8 (–102.3 ppm). In **5b** ('para' position of O-8 and N-6), this effect is less pronounced (δ N-6 –77.4 ppm), whereas in **5a** (δ N-5 –65.7 ppm) and **5c** (δ N-7 –56.3 ppm) it has only very little influence. Comparison of the ^{15}N chemical shifts of N-1 and N-2 in compounds **6–9** clearly indicates the effect of substituting C=O by C=S (**6** \rightarrow **7**, **8** \rightarrow **9**) as well as substitution of the ring oxygen atom by sulfur (**6** \rightarrow **8**, **7** \rightarrow **9**). Whereas the former transformation leads to only small effects (~ 3 ppm upfield shift for N-1, ~ 2.5 ppm downfield shift for N-2), the changeover from pyrane to thiopyrane affects $\delta(\text{N}-1)$ (~ 15 ppm downfield shift) and $\delta(\text{N}-2)$ (~ 20 ppm downfield shift) much more distinctively. Again, the latter effect can be casually explained by the less pronounced electron-releasing mesomeric effect of sulfur compared to oxygen. Comparison of the ^{15}N chemical shift data of compounds **4**^[1–3] with those of **5**, in principle, shows similar effects as found with the transformation **6** \rightarrow **7**, namely 2–3 ppm upfield shift for pyrazole N-1 and 2–2.5 ppm downfield shift for pyrazole N-2. The pyridine ^{15}N atoms in **5a–d** suffer small downfield shifts in relation to the corresponding type **4** compounds.

In conclusion, we have presented an efficient synthesis of various novel [5,6]pyrano[2,3-*c*]pyrazol-4(1*H*)-thiones (**5a–j**) and given full and unambiguous assignments of ^1H , ^{13}C , and ^{15}N NMR chemical shifts. Moreover, an analysis of many spin coupling constants ($^1\text{H},^1\text{H}$: $^{13}\text{C},^1\text{H}$) with the investigated systems was provided.

Experimental

All NMR experiments were performed using standard NMR spectroscopic techniques.^[22] The ^1H NMR and ^{13}C NMR spectra were recorded from CDCl_3 solutions either on a Varian UnityPlus NMR spectrometer (300 MHz for ^1H , 75 MHz for ^{13}C) or on a Bruker Avance 500 instrument (500 MHz for ^1H , 125 MHz for ^{13}C) at 25 °C using 5-mm direct detection broad-band probes and deuterium lock. The center of the solvent signal was used as an internal standard, which was related to tetramethylsilane with δ 7.26 ppm (^1H) and δ 77.0 ppm (^{13}C). The recording conditions were the following: ^1H NMR: pulse angle 30°, acquisition time 5 s, digital resolution 0.2 Hz/data point, spectral width 16 ppm, 16 transients, relaxation delay 5 s; broad-band decoupled ^{13}C NMR spectra: pulse angle 30°, acquisition time 2 s, digital resolution 0.5 Hz/data point, spectral width 220 ppm, 128–1024 transients, relaxation delay 2 s, exponential multiplication with 1.0 Hz line broadening factor before FT; gated decoupled ^{13}C NMR spectra: as above but acquisition time 2.5 s, digital resolution 0.4 Hz/data point, 512–8192 transients, relaxation delay 2.5 s, resolution enhancement by Gaussian weighting (Varian: lb = –0.15, gf = 0.7; Bruker: lb = –0.6, gb = 0.2) before FT. Full and unambiguous assignments were achieved by consequent application of fully ^1H -coupled ^{13}C NMR spectra (gated decoupling), gs-HSQC^[28] (1024 \times 256 data matrix, 10 ppm for ^1H , 160 ppm for ^{13}C , 4 transients accumulated per t_1 increment; optimized for $J = 160$ Hz, qsrine multiplication in both dimensions), and gs-HMBC^[29] (1024 \times 256 data matrix, 10 ppm for ^1H , 180 ppm for ^{13}C , 8 transients accumulated per t_1 increment; optimized for $J = 8$ Hz, sine multiplication in both dimensions) techniques to all compounds. The unequivocal mapping of $^{13}\text{C},^1\text{H}$ coupling constants was performed via 2D long-range INEPT (δ, J) spectra with selective excitation (DANTE)^[27] of unequivocally assigned proton resonances (12–24 Hz excitation width, optimized for $J = 8$ Hz, 32 increments for 20 Hz width in F1, 128 transients

Table 3. Selected ^{13}C , ^1H spin coupling constants of **5a–j**, **6–9** (Hz, CDCl_3)

Compounds	$^1J(3\text{-Me})$	$^2J(3,3\text{-Me})$	$^3J(3\text{a},3\text{-Me})$	$^3J(4,5)$	Other couplings
5a	129.7	7.2	2.4	–	$^3J(4\text{a},6) = 12.3$, $^3J(4\text{a},8) = 3.8$, $^4J(4\text{a},7) = 1.2$; $^1J(6) = 183.7$, $^2J(6,7) = 3.0$, $^3J(6,8) = 7.8$; $^1J(7) = 166.8$, $^2J(7,6) = 9.8$; $^1J(8) = 166.9$, $^2J(8,7) = 1.1$, $^3J(8,6) = 6.5$; $^2J(8\text{a},8) = 3.7$, $^3J(8\text{a},7) = 9.7$, $^4J(8\text{a},6) = 1.7$
5b	129.7	7.2	2.4	–	$^2J(4\text{a},5) = 6.4$, $^3J(4\text{a},8) = 3.8$, $^4J(4\text{a},7) = 1.4$; $^1J(5) = 187.0$, $^3J(5,7) = 12.0$; $^1J(7) = 182.8$, $^2J(7,8) = 1.4$, $^3J(7,5) = 13.8$; $^1J(8) = 168.2$, $^2J(8,7) = 8.9$, $^4J(8,5) = 1.6$; $^2J(8\text{a},8) = 3.8$, $^3J(8\text{a},5) = 7.6$, $^3J(8\text{a},7) = 9.7$
5c	129.7	7.3	2.6	5.0	$^2J(4\text{a},5) = 1.1$, $^3J(4\text{a},6) = 7.4$, $^3J(4\text{a},8) = 4.0$; $^1J(5) = 169.0$, $^2J(5,6) = 9.5$, $^4J(5,8) = 1.6$; $^1J(6) = 183.1$, $^2J(6,5) = 2.4$, $^3J(6,8) = 11.9$; $^1J(8) = 185.0$, $^2J(8,6) = 11.5$, $^4J(8,5) = 1.0$; $^2J(8\text{a},8) = 3.3$, $^3J(8\text{a},5) = 7.6$, $^4J(8\text{a},6) = 1.8$
5d	129.6	7.2	2.7	4.9	$^2J(4\text{a},5) = 0$, $^3J(4\text{a},6) = 7.4$, $^4J(4\text{a},7) = 1.5$; $^1J(5) = 168.2$, $^2J(5,6) = 1.9$, $^3J(5,7) = 6.5$; $^1J(6) = 167.7$, $^2J(6,5) = 0.9$, $^2J(6,7) = 8.1$; $^1J(7) = 182.8$, $^2J(7,6) = 4.3$, $^3J(7,5) = 8.9$; $^3J(8\text{a},5) = 8.5$, $^3J(8\text{a},7) = 13.5$, $^4J(8\text{a},6) = 1.4$
5e	129.5	7.2	2.6	–	$^3J(4\text{a},6) = 5.2$, $^3J(4\text{a},7) = 5.8$; $^1J(6) = 188.0$, $^2J(6,7) = 4.5$; $^1J(7) = 175.2$, $^2J(7,6) = 4.1$; $^2J(7\text{a},7) = 0.9$, $^3J(7\text{a},6) = 12.8$
5f	129.5	7.2	2.4	2.8	$^2J(4\text{a},5) = 2.4$, $^3J(4\text{a},7) = 6.3$; $^1J(5) = 193.2$, $^3J(5,7) = 5.2$; $^1J(7) = 190.2$, $^3J(7,5) = 4.5$; $^2J(7\text{a},7) = 0$, $^3J(7\text{a},5) = 10.8$
5g	129.6	7.2	2.5	0	$^2J(4\text{a},5) = 3.7$, $^3J(4\text{a},6) = 8.5$; $^1J(5) = 176.1$, $^2J(5,6) = 3.5$; $^1J(6) = 191.7$, $^2J(6,5) = 6.8$; $^3J(7\text{a},5) = 11.0$, $^3J(7\text{a},6) = 8.6$
5h	129.5	7.1	2.6	5.5	$^1J(5) = 166.4$, $^3J(5,6) = 4.7$; $^3J(10\text{a},5) = 9.8$
5i	129.5	7.2	2.7	–	$^3J(9\text{b},9) = 3.4$
5j	129.5	7.2	2.8	–	$^3J(5\text{a},7) = 7.8$, $^3J(5\text{a},8) = 9.5$; $^1J(7) = 188.5$, $^2J(7,8) = 6.8$; $^1J(8) = 174.2$, $^2J(8,7) = 4.1$; $^2J(8\text{a},8) = 5.7$, $^3J(8\text{a},7) = 10.5$
6	129.2	7.2	2.7	4.1	–
7	129.6	7.2	2.5	5.2	$^2J(4\text{a},5) = 0$, $^3J(4\text{a},6) = 8.2$, $^3J(4\text{a},8) = 4.4$, $^4J(4\text{a},7) = 1.4$; $^1J(5) = 165.4$, $^3J(5,7) = 8.1$; $^1J(6) = 163.3$, $^3J(6,8) = 8.2$; $^1J(7) = 161.7$, $^3J(7,5) = 9.5$; $^1J(8) = 163.6$, $^3J(8,6) = 7.9$; $^2J(8\text{a},8) = 3.7$, $^3J(8\text{a},5) = 8.8$, $^3J(8\text{a},7) = 11.1$, $^4J(8\text{a},6) = 1.6$
8	129.4	7.1	2.5	4.0	–
9	129.7	7.1	2.2	5.4	$^3J(4\text{a},6) = 6.9$, $^3J(4\text{a},8) = 6.9$

Table 4. ^{15}N NMR chemical shifts of **5a–j**, **6–9** (δ in ppm, CDCl_3)

Compounds	N-1	N-2	Other N	Compounds	N-1	N-2	Other N
5a	–196.1	–91.1	N-5: –65.7	5h	–194.3	–92.3	N-10: –116.4
5b	–194.6	–91.8	N-6: –77.4	5i	–195.2	–91.6	–
5c	–195.3	–90.7	N-7: –56.3	5j	–195.3	–91.4	–
5d	–194.7	–91.8	N-8: –102.3	6	–193.2	–96.2	–
5e	–195.7	–91.8	–	7	–196.2	–93.5	–
5f	–196.5	–93.1	–	8	–178.3	–75.8	–
5g	–196.0	–92.9	–	9	–181.6	–73.5	–

accumulated per t_1 increment; zero-filling to 128 data points in the F1 dimension, shifted sine multiplication in F1). The ^{15}N NMR spectra (CDCl_3) were obtained on a Bruker Avance 500 instrument (50.69 MHz) equipped with a 5-mm broad-band observe probe (BBFO) at 25°C and were referenced against external, neat nitromethane: ^1H , ^{15}N gs-HMBC experiments (Bruker standard program 'inv4gplplrndqr',^[29] 2048 \times 256 data matrix, 10 ppm for ^1H , 200 ppm for ^{15}N , 32 transients accumulated per t_1 increment; 65 ms delay for the evolution of the ^{15}N , ^1H long-range coupling, optimized for $J = 8$ Hz, zero-filling to 1K data points in the F1 dimension, sine multiplication in both dimensions) were undertaken.

Melting points were determined on a Reichert–Kofler hot-stage microscope and are uncorrected. The mass spectra were obtained on a Shimadzu QP 1000 instrument (EI, 70 eV). The elemental analyses (C, H, N) were performed at the Microanalytical Laboratory, University of Vienna.

General procedure for the synthesis of **5a–j**, **7**, and **9**

To a solution of the appropriate oxo compound (**4a–j**,^[1–3] **6**,^[2] **8**^[21]) (1 mmol) in toluene (15 ml) was added Lawesson's reagent (202 mg, 0.5 mmol) and the mixture was heated to reflux overnight (~ 14 h). Then, the solvent was removed under reduced pressure and the residue was subjected to column chromatography (silica gel, eluent: CH_2Cl_2 or CH_2Cl_2 –MeOH, 100:3) to afford the colored thiones **5a–j**, **7**, and **9**. For analytical purposes, the products were recrystallized from an appropriate solvent given below.

3-Methyl-1-phenylpyrazolo[4',3':5,6]pyrano[3,2-b]pyridine-4(1H)-thione (**5a**)

Yield: 88%; mp: 242–244 $^\circ\text{C}$ (toluene); MS: m/z (%) = 294 ($\text{M}^+ + 1$, 20), 293 (M^+ , 100), 292 ($\text{M}^+ - 1$, 41), 260 (22), 157 (34), 146 (22), 77 (42), 51 (27). Anal. calcd. for $\text{C}_{16}\text{H}_{11}\text{N}_3\text{OS}$ (293.34): C, 65.51; H, 3.78; N, 14.32. Found: C, 65.34; H, 3.58; N, 14.25.

3-Methyl-1-phenylpyrazolo[4',3':5,6]pyrano[3,2-c]pyridine-4(1H)-thione (5b)

Yield: 93%; mp: 205–207 °C; MS: m/z (%) = 294 ($M^+ + 1$, 22), 293 (M^+ , 100), 292 ($M^+ - 1$, 33), 77 (28), 51 (17). Anal. calcd. for $C_{16}H_{11}N_3OS$ (293.34): C, 65.51; H, 3.78; N, 14.32. Found: C, 65.49; H, 3.75; N, 13.94.

3-Methyl-1-phenylpyrazolo[4',3':5,6]pyrano[2,3-c]pyridine-4(1H)-thione (5c)

Yield: 94%; mp: 177–179 °C (toluene); MS: m/z (%) = 294 ($M^+ + 1$, 20), 293 (M^+ , 100), 292 ($M^+ - 1$, 31), 91 (19), 77 (33), 51 (20). Anal. calcd. for $C_{16}H_{11}N_3OS \cdot 0.1 H_2O$ (293.34/295.15): C, 65.11; H, 3.82; N, 14.24. Found: C, 65.38; H, 3.80; N, 13.83.

3-Methyl-1-phenylpyrazolo[4',3':5,6]pyrano[2,3-b]pyridine-4(1H)-thione (5d)

Yield: 90%; mp: 224–225 °C (toluene); MS: m/z (%) = 294 ($M^+ + 1$, 19), 293 (M^+ , 100), 292 ($M^+ - 1$, 27), 91 (21), 77 (36), 51 (22). Anal. calcd. for $C_{16}H_{11}N_3OS$ (293.34): C, 65.51; H, 3.78; N, 14.32. Found: C, 65.19; H, 3.61; N, 14.10.

3-Methyl-1-phenylthieno[2',3':5,6]pyrano[2,3-c]pyrazole-4(1H)-thione (5e)

Yield: 95%; mp: 177–178 °C (toluene); MS: m/z (%) = 299 ($M^+ + 1$, 16), 298 (M^+ , 100), 91 (11), 77 (19), 51 (13). Anal. calcd. for $C_{15}H_{10}N_2OS_2$ (298.38): C, 60.38; H, 3.38; N, 9.39. Found: C, 60.37; H, 3.24; N, 9.05.

3-Methyl-1-phenylthieno[3',4':5,6]pyrano[2,3-c]pyrazole-4(1H)-thione (5f)

Yield: 80%; mp: 208–210 °C (toluene); MS: m/z (%) = 299 ($M^+ + 1$, 12), 298 (M^+ , 100), 297 ($M^+ - 1$, 36), 225 (13), 97 (15), 91 (37), 83 (20), 77 (93), 71 (26), 69 (45), 57 (45), 51 (60). Anal. calcd. for $C_{15}H_{10}N_2OS_2$ (298.38): C, 60.38; H, 3.38; N, 9.39. Found: C, 60.38; H, 3.28; N, 9.11.

3-Methyl-1-phenylthieno[3',2':5,6]pyrano[2,3-c]pyrazole-4(1H)-thione (5g)

Yield: 99%; mp: 194–196 °C; MS: m/z (%) = 299 ($M^+ + 1$, 17), 298 (M^+ , 100), 121 (11), 105 (16), 91 (13), 77 (67), 51 (44). Anal. calcd. for $C_{15}H_{10}N_2OS_2$ (298.38): C, 60.38; H, 3.38; N, 9.39. Found: C, 60.58; H, 3.36; N, 9.08.

3-Methyl-1-phenylpyrazolo[4',3':5,6]pyrano[2,3-b]quinoline-4(1H)-thione (5h)

Yield: 71%; mp: 274–276 °C (toluene); MS: m/z (%) = 344 ($M^+ + 1$, 20), 343 (M^+ , 100), 172 (16), 91 (55), 77 (45), 69 (12), 57 (12), 51 (27). Anal. calcd. for $C_{20}H_{13}N_3OS \cdot 0.1H_2O$ (343.40/345.21): C, 69.59; H, 3.85; N, 12.17. Found: C, 59.55; H, 3.69; N, 11.79.

3-Methyl-1-phenyl[1]benzothieno[2',3':5,6]pyrano[2,3-c]pyrazole-4(1H)-thione (5i)

Yield: 93%; mp: 236–237 °C (toluene); MS: m/z (%) = 349 ($M^+ + 1$, 23), 348 (M^+ , 100), 347 ($M^+ - 1$, 15), 174 (11), 104 (11), 77 (25), 76 (11), 51 (16). Anal. calcd. for $C_{19}H_{12}N_2OS_2$ (348.44): C, 60.38; H, 3.38; N, 9.39. Found: C, 65.40; H, 3.29; N, 7.98.

3-Methyl-1-phenylthieno[3'',2'':4',5']thieno[2',3':5,6]pyrano[2,3-c]pyrazole-4(1H)-thione (5j)

Yield: 83%; mp: 245–246 °C (toluene); MS: m/z (%) = 355 ($M^+ + 1$, 20), 354 (M^+ , 100), 177 (12), 77 (22), 51 (15). Anal. calcd. for $C_{17}H_{10}N_2OS_3$ (354.47): C, 67.60; H, 2.84; N, 7.90. Found: C, 57.47; H, 2.65; N, 7.80.

3-Methyl-1-phenylchromeno[2,3-c]pyrazole-4(1H)-thione (7)

Yield: 98%; mp: 185–187 °C (literature^[20] mp: 189–190 °C); MS: m/z (%) = 293 ($M^+ + 1$, 21), 292 (M^+ , 100), 291 ($M^+ - 1$, 33), 146 (11), 91 (18), 77 (23), 51 (15). $C_{17}H_{12}N_2OS$ (292.35).

3-Methyl-1-phenylthiochromeno[2,3-c]pyrazole-4(1H)-thione (9)

Yield: 86%; mp: 183–185 °C (literature^[21] mp: 208–210 °C); MS: m/z (%) = 309 ($M^+ + 1$, 23), 308 (M^+ , 100), 307 ($M^+ - 1$, 48), 263 (26), 172 (19), 146 (11), 138 (12), 120 (11), 83 (10), 77 (51), 69 (27), 57 (22), 55 (17), 51 (44). $C_{17}H_{12}N_2S_2$ (308.42).

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