METALATION OF PYRAZINETHIOCARBOXAMIDES
METALATION OF DIAZINES XXVI

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Abstract – Some new pyrazinethiocarboxamides were synthesized and metalated with LTMP in tetrahydrofuran. The reaction of these lithio derivatives with various electrophiles gave access to a large range of 2,5-disubstituted pyrazines. This unexpected regioselectivity was established by application of gradient enhanced HMBC sequence for the observation of long range ^{1}H-^{15}N heteronuclear couplings at natural abundance.

Following our studies on the metalation of π-deficient heterocycles we have recently investigated the use of sulfur derivatives as *ortho*-directing group (O.D.G) in these series.[1,2] It was found that sulfoxides, sulfones and sulfamides were good *ortho*-directing groups.

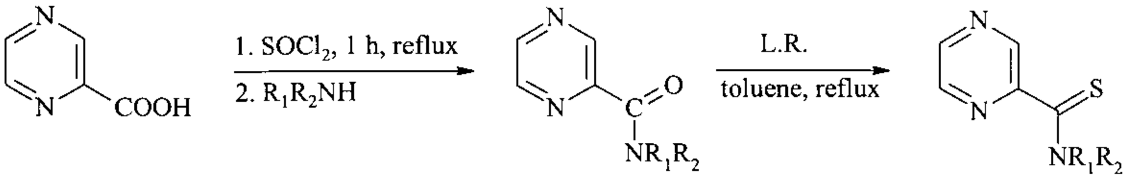
Another type of sulfur derivatives is based on the thiocarbonyl group contained in dithioesters,[3] thiocarboxamides or thioamides. In the benzene series, Gschwend[4] obtained good results with thiocarboxamides so we tested these O.D.G. in the pyrazine series. These thiocarboxamides were, to our knowledge, never tested before as O.D.G. in the diazine series and some were still unknown. Metalation could be a new and versatile way of functionalization of these compounds.

Some pyrazinethiocarboxamides have tuberculostatic and antimycobacterial properties[5-7] and some pyridinylthioacetamides have antiulcer activity.[8,9]

Synthesis of thiocarboxamides was mainly performed following four different ways: thionation of carboxamides with sulfur derivatives of phosphorous (P_2S_5, Lawesson's reagent (L. R.)),[10-13] reaction of an organometallic derivative with an isothiocyanate,[4,14,15] reaction of an amine derivative with sulfur (S_8),[7,15-18] reaction of an amine with a sulfine group.[19] In order to obtain the pyrazinethiocarboxamides, the two first methods were tested.

Synthesis of pyrazinethiocarboxamides

Pyrazinoic acid (**1**) was the starting material for the monosubstituted pyrazinecarboxamides. These amides were then treated with the Lawesson's reagent.[10]

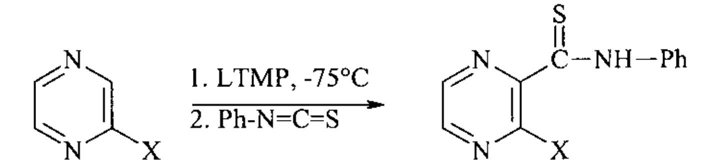


1 R_1 = H, R_2 = *t*Bu **2** 76% **5**
R_1 = H, R_2 = Me **3** 58 % **6**
R_1 = R_2 = *i*Pr **4** 82 % **7**

Table 1. Synthesis of thiocarboxamides

entry	R_1	R_2	x eq. L.R.	time (h)	product	yield %	S.M. %
1	H	*t*Bu	0.6	3	**5**	50	43
2	H	*t*Bu	0.6	40	**5**	81	18
3	H	*t*Bu	1.1	3	**5**	83	16
4	H	*t*Bu	1.1	8	**5**	98	–
5	H	Me	1.1	5	**6**	64	–
6	H	Me	1.1	15	**6**	44	–
7	*i*Pr	*i*Pr	1.1	8	**7**	98	–

Entries **1** and **3** demonstrate that a twofold equivalent of L.R. was effective to obtain a good yield. The same excess was used for the other reactions. In the case of product (**6**) the yield was lower and was not increased by an extension of the reaction time because product (**6**) decomposed. To avoid this, the reaction was performed in THF at room temperature during 87 h but the yield of **6** was still lower (34%) without recovery of the starting material. These reactions allowed us to prepare in two steps three pyrazinethiocarboxamides (**5**), (**6**) and (**7**) with satisfactory yields (75%, 37%, 80%) respectively from pyrazinoic acid (**1**). Another reaction was tested: reaction of a lithio derivative with phenyl isothiocyanate:

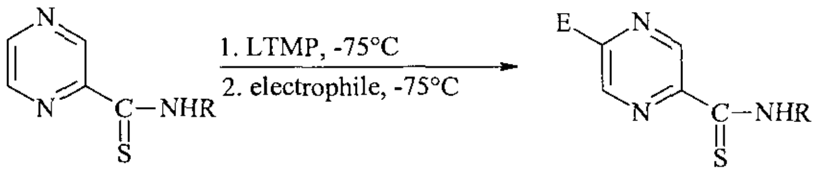


X = H, Cl, OMe X = H **8** 11 %
X = OMe **9** 47 %

With chloropyrazine the reaction failed but was successful with a methoxy group as *ortho*-directing group (product **9**) using the *in situ* trapping method of the lithio derivative.[20] As we highlighted some years ago,[21] it was possible to metalate pyrazine without any *ortho*-directing group with acceptable yields. In our experiments with PhNCS a very low yield of **8** (11%) was obtained starting from the unsubstituted pyrazine. This may be due to the poor stability of the unsubstituted lithiopyrazine.

Metalation of pyrazinethiocarboxamides

Metalation of *N-tert*-butylpyrazinethiocarboxamide was successfully performed at -75°C with an excess of LTMP in THF and some electrophiles were reacted.



R = *t*Bu **5**
Me **6**

R = *t*Bu **10 - 17**
R = Me **18 - 24**

Table 2. Metalation of *N-tert*-butylpyrazinethiocarboxamide (4 eq LTMP, 90 min)

entry	**electrophile**	**–E**	**product**	**yield %**
1	DCl/EtOD	–D	**10**	100
2	MeCHO	–CH(OH)Me	**11**	71
3	Ph_2CO	–C(OH)Ph_2	**12**	94
4	PhCHO	–CH(OH)Ph	**13**	50
5	C_2Cl_6	–Cl	**14**	89
6	Bu_3SnCl	–$SnBu_3$	**15**	100
7	MeI	–Me	**16***	72
8	Me_3SiCl**	–$SiMe_3$	**17**	98

*: *Product (**16**) was the 3,5-disubstituted product*

**: Metalation was performed by the *in situ* trapping method

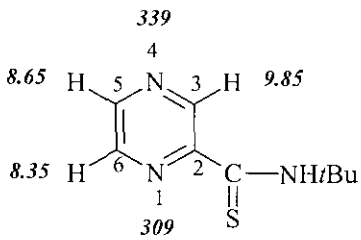
The metalation of compound (**5**) followed by the reaction with various electrophiles led to only one product. This complete regioselectivity must be ensured by an unambiguous attribution of the substitution position. The accurate attribution of the ^1H NMR signals in the pyrazine series has always been a problem due in general to the close vicinity of the signals for H_5 and H_6. In our case a coupling constant of 1.1 Hz was observed and could be attributed to a ^5J coupling constant between H_3 and H_6.

However, in order to determine unambiguously the site of metalation, a structure elucidation of compound (**11**) has been carried out by applying gradient enhanced HMBC sequence, such as a method using long range ^1H-^{15}N heteronuclear coupling at natural abundance. This method has been previously described by Martin to determine the structure of alkaloids,[22,23] and more recently used to determine the structure of quinazoline derivatives.[24]

The unequivocal ^{15}N assignment of **5** was based on ^{2}J (^{1}H-^{15}N) interaction in proton-coupled nitrogen spectrum. The values of ^{2}J (^{1}H-^{15}N) previously established for some azines were given in a range from 9.8 to 14.4 Hz.[25]. The ^{15}N spectrum of **5** exhibited two signals: a doublet at 309 ppm (^{2}J=10 Hz) assigned to N_1 and a triplet at 339 ppm with the same coupling constant for N_4.

The ^{1}H NMR spectrum of **5** showed three signals at 9.85, 8.65 and 8.35 ppm, the first one could be attributed to H_3 deshielded by the thiocarboxamide group at the *ortho* position. The signals at 8.65 and 8.35 ppm have been clearly allocated by applying a gradient HMBC-pulse sequence with a long range delay optimized for a coupling-constant of 10 Hz. Correlations were observed between N_1 at 309 ppm and H_6 (8.35 ppm) and N_4 at 339 ppm and H_5 (8.65 ppm) leading to the accomparing assignment **(Figure 1)**.

Figure 1



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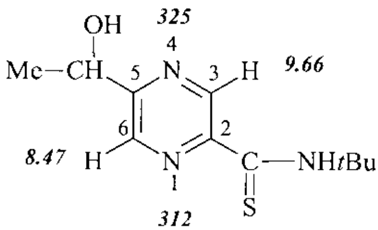
The ^{15}N spectrum of **11** presented two signals at 325 and 312 ppm and the ^{1}H spectrum two signals at 9.66 ppm and 8.47 ppm. The ^{1}H-^{15}N GHMBC spectrum showed correlation between N_4 resonance at 325 ppm and H_3 (9.66 ppm) and between N_1 at 312 ppm and H_6 (8.47 ppm) **(Figure 2)**.

Figure 2



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These results allowed us to determine unambiguously the site of metalation which occurred at the C_5 position. Such an unexpected regioselectivity has been previously highlighted by us when studying the metalation of *N-tert*-butylcarboxamide followed by deuteration.[26] At low temperature (<-80°C) the percentage of 5-deutero compound was greater than the 3-deutero regioisomer.

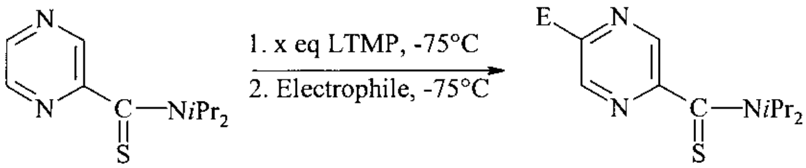
The less hindered *N*-methylthiocarboxamide group was used with good results by Gschwend[4] in the benzene series so we tested *N*-methylpyrazinethiocarboxamide under the same experimental conditions as above.

Table 3. Metalation of *N*-methylpyrazinethiocarboxamide

entry	x eq. LTMP	time (min)	electrophile	-E	product	yield %	S.M. %
1	2.4	60	MeCHO	–CH(OH)Me	**18**	-	28
2	3.1	60	MeCHO	–CH(OH)Me	**18**	43	14
3	3.1	120	MeCHO	–CH(OH)Me	**18**	-	27
4	3.1	10	MeCHO	–CH(OH)Me	**18**	79	3
5	3.1	10	PhCHO	–CH(OH)Ph	**19**	37	-
6	3.1	10	Ph_2CO	$-C(OH)Ph_2$	**20**	8	-
7	3.1	10	I_2	–I	**21**	32	-
8	3.1	10	C_2Cl_6	–Cl	**22**	20	-
9	3.1	10	PhSSPh	–SPh	**23**	34	-
10*	3.1	120	Me_3SiCl	$-SiMe_3$	**24**	17	39

*: performed with the *in situ* trapping method

The yields were much lower than with the *N-tert*-butyl derivative and few starting material was recovered, indicative an important degradation of the reaction mixture. Some authors,[27-29] in the pyridine series, highlighted that *N,N*-di*iso*propylcarboxamide group gave good results as *ortho*-directing group for metalation. So its sulfur analog was tested in the pyrazine series.

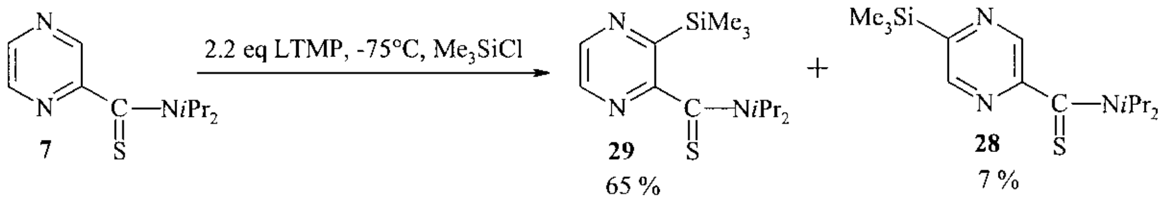


7 **25-27**

Table 4. Metalation of *N,N*-di*iso*propylpyrazinethiocarboxamide

entry	x eq. LTMP	time (min)	electrophile	-E	product	yield %	S.M. %
1	1.1	60	MeCHO	–CH(OH)Me	**25**	-	87
2	2.2	60	MeCHO	–CH(OH)Me	**25**	67	-
3	3.1	60	MeCHO	–CH(OH)Mc	**25**	66	-
4	4.1	60	MeCHO	–CH(OH)Me	**25**	35	-
5	2.2	15	MeCHO	–CH(OH)Me	**25**	-	71
6	2.2	30	MeCHO	–CH(OH)Me	**25**	42	41
7	2.2	120	MeCHO	–CH(OH)Me	**25**	-	-
8	2.2	60	PhCHO	–CH(OH)Ph	**26**	42	-
9	2.2	60	Ph_2CO	$-C(OH)Ph_2$	**27**	45	-
10	2.2	60	C_2Cl_6	–Cl	**-**	-	-
11	2.2	60	I_2	–I	**-**	-	-

A twofold excess of metalating agent was necessary to achieve a 67% yield but a greater excess was useless or deleterious (entries 1-4). The reaction time was also critical (entries 2, 5, 6, 7). The reaction by the *in situ* trapping method with chlorotrimethylsilane afforded mainly the 3-substituted product.



The *in situ* trapping method allows to trap the first lithio derivative in the reaction mixture so it can be supposed that the 3-lithio derivative was the kinetic derivative and that the 5-lithio derivative which gave products (**25** - **28**) was the thermodynamic one.

In summary, we have performed a regioselective metalation of pyrazinethiocarboxamides in position 5 and have highlighted that the *N-tert*-butylthiocarboxamide group gave the best results.

ACKNOWLEDGEMENT

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EXPERIMENTAL

Tetrahydrofuran (THF) was distilled from benzophenone sodium and used immediately (water content <60 ppm). The synthesis of pyrazinecarboxamides from pyrazinoic acid (commercial) was already published.[30-33]. The IR spectra were obtained as potassium bromide pellets with a Perkin-Elmer FMR 1650 spectrophotometer. The NMR spectra were recorded on a Bruker AC 200F (200 MHz) or Bruker ARX (400 MHz) spectrometer. All NMR spectra were carried out with deuteriochloroform solutions and δ are given in ppm. Microanalysis were performed with a Carlo Erba 1106 apparatus. Melting points were determined with a Kofler hot-stage and were uncorrected.

Metalations were performed under an argon atmosphere. Reagents were handled with syringes through septa.

Generals procedures for metalation

Method A

A solution of *n*-butyllithium (*1.6 or 2.5 M* in hexane) was added to cold (-75°C), stirred, anhydrous tetrahydrofuran (15 mL) under an atmosphere of dry argon, then 2,2,6,6-tetramethylpiperidine was added and the mixture was warmed to 0°C and kept at this temperature for 15 min in order to achieve a complete formation of the amide. The solution was cooled to –75°C and a solution of thiocarboxamide (x mmol) in 5 mL of tetrahydrofuran was added and the mixture was stirred for t min at –75°C. Then the electrophile (1.2 eq. mmol) was added dropwise and stirring was continued for t min at –75°C. Hydrolysis was then carried out at –75°C using a mixture of ethanol (1 mL) and tetrahydrofuran (1 mL) or a saturated aqueous solution of NH_4Cl (5 mL) in the case of isothiocyanate as electrophile. The solution was gently warmed to 0°C and the solvent was evaporated under reduced pressure. The residue was extracted with dichloromethane (4 x 25 mL) or ethyl acetate (4 x 25 mL) in the case of using an isothiocyanate. The organic extract was dried with $MgSO_4$ and evaporated. The crude product was purified by column chromatography on neutral alumina.

Method B (*in situ* trapping method)

A solution of *n*-butyllithium (*1.6 or 2.5 M* in hexane) was added to cold (-75°C), stirred, anhydrous tetrahydrofuran (15 mL) under an atmosphere of dry argon, then 2,2,6,6-tetramethylpiperidine was added and the mixture was warmed to 0°C and kept at this temperature for 15 min in order to achieve a complete formation of the amide. The solution was cooled to –75°C and a mixture of the thiocarboxamide (x mmol) and the electrophile (1.2 eq. mmol) in 5 mL of tetrahydrofuran was added slowly and the mixture was stirred for 2 h at –75°C. Hydrolysis was then carried out at –75°C using a mixture of ethanol (1 mL) and tetrahydrofuran (1 mL) or a saturated aqueous solution of NH_4Cl (5 mL) in the case of isothiocyanate as electrophile. The solution was gently warmed to 0°C and the solvent was evaporated under reduced pressure. The residue was extracted with dichloromethane (4 x 25 mL) or ethyl acetate (4 x 25 mL) in the case of using an isothiocyanate. The organic extract was dried with $MgSO_4$ and evaporated. The crude product was purified by column chromatography on neutral alumina.

General procedure for synthesis of pyrazinethiocarboxamides (5-7)

A solution of the appropriate 2-pyrazinecarboxamide (14 mmol) and 6.20 g (15 mmoles) of the Lawesson's reagent in 120 mL toluene was heated 5-8 h at reflux, the reaction progress being controlled by thin-layer chromatography (neutral alumina gel, petroleum ether / ethyl acetate : 14/1). When the reaction was complete, the solvent was evaporated under reduced pressure. The residue was purified on a column packed with neutral alumina gel with petroleum ether / ethyl acetate (14/1) as eluant.

2-*N*-*tert*-Butylpyrazinethiocarboxamide (5)

Synthesis of **5** according to the general procedure with 2-*N*-*tert*-Butylpyrazinecarboxamide (2) (2.510 g, 14 mmol). The thiocarboxamide was isolated as yellow crystals (mp 72°C) in 98% yield (2.646 g); ^{1}H NMR ($CDCl_3$): δ 1.66 (s, 9H, $C(CH_3)_3$), 8.35 (dd, $J_{H5,H6}$= 2.5 Hz, $J_{H3,H6}$= 1.1 Hz, 1H, H_6), 8.65 (d, $J_{H5,H6}$= 2.5 Hz, 1H, H_5), 9.80 (broad, 1H, NH), 9.85 (d, $J_{H3,H6}$= 1.1 Hz, 1H, H_3);^{13}C NMR ($CDCl_3$): δ 28.06 (CH_3), 55.89 ($\underline{C}(CH_3)_3$), 140.84 (C_6), 146.33 (C_3), 146.47 (C_2), 146.67 (C_5), 187.28 (C=S); ^{15}N ($CDCl_3$) : δ 309 (d, *J* = 10.5 Hz, N_1), 339 (t, *J* = 10.5 Hz, N_4); IR (KBr): ν 3266 cm^{-1} (NH), 1015 cm^{-1} (C=S). Anal. Calcd for $C_9H_{13}N_3S$: C, 56.20; H, 6.76; N, 21.85; S, 16.09. Found: C, 56.43; H, 6.92; N, 21.71; S, 15.89.

2-*N*-Methylpyrazinethiocarboxamide (6)

This product was described by Taguchi and Yoshihira[16] without NMR and IR data.

Synthesis of **6** according to the general procedure with 2-*N*-Methylpyrazinecarboxamide (3) (1.920 g, 14 mmol). The thiocarboxamide was isolated as yellow crystals (mp 206°C) in 64% yield (1.373 g); ^{1}H NMR ($CDCl_3$): δ 3.41 (s, 3H, CH_3), 8.45 (dd, $J_{H5,H6}$= 2.4 Hz, $J_{H3,H6}$= 1.2 Hz, 1H, H_6), 8.76 (d, $J_{H5,H6}$= 2.4 Hz, 1H, H_5), 9.87 (br, $J_{H3,H6}$= 1.2 Hz, 2H, NH-H_3); ^{13}C NMR ($CDCl_3$): δ 33.09 (CH_3), 141.54 (C_6), 145.79 (C_3), 146.69 (C_2), 147.33 (C_5), 190.61 (C=S); IR (KBr): ν 3212 cm^{-1} (NH), 1061 cm^{-1} (C=S). Anal. Calcd for $C_6H_7N_3S$: C, 47.00; H, 4.57; N, 27.41; S, 20.89. Found: C, 47.13; H, 4.56; N, 27.34; S, 20.83

2-*N*-Di*iso*propylpyrazinethiocarboxamide (7)

Synthesis of **7** according to the general procedure with 2-*N*-Di*iso*propylpyrazinecarboxamide (4) (2.902 g, 14 mmol). The thiocarboxamide was isolated as yellow crystals (mp 92°C) in 98% yield (3.063 g); ^{1}H NMR ($CDCl_3$): δ 1.07 (d, $J_{CH,CH3}$=6.7 Hz, 6H, $CH(CH_3)_2$), 1.57 (d, 6H, $CH(CH_3)_2$), 3.77 (m, $J_{CH,CH3}$=6.7 Hz, 1H, CH), 4.20 (br, 1H, CH) , 8.25 (m, 2H, H_5-H_6), 8.47 (s, 1H, H_3); ^{13}C NMR ($CDCl_3$): δ 18.79 (CH_3), 20.52 (CH_3), 51.42 (CH), 56.54 (CH), 141.97 (C_6), 142.50 (C_3), 142.94 (C_5), 155.98 (C_2), 193.22 (C=S); IR (KBr): ν 1141 cm^{-1} (C=S). Anal. Calcd for $C_{11}H_{17}N_3S$: C, 59.11; H, 7.61; N, 18.80; S, 14.33. Found: C, 59.14; H, 7.64; N, 18.90; S, 13.98.

2-*N*-Phenylpyrazinethiocarboxamide (8)

Metalation of pyrazine (0.240 g, 3.0 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (7.5 mL, 12 mmol) and 2,2,6,6-tetramethylpiperidine (2.1 mL, 12 mmol), t = 5 min, then reaction with phenyl isothiocyanate (0.36 mL, 3.0 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (9/1) as the eluent, 0.073 g (11%) of an orange oil. ^{1}H NMR ($CDCl_3$) : δ 7.47 (m, 3H, H_{benz}), 8.02 (d, J= 7.8 Hz, 2H, H_{benz}), 8.50 (dd, $J_{H5,H6}$= 2.4 Hz, $J_{H3,H6}$= 1.1 Hz, 1H, H_6), 8.78 (d, $J_{H5,H6}$= 2.4 Hz, 1H, H_5), 9.96 (d, $J_{H3,H6}$= 1.1 Hz, 1H, H_3), 11.35 (br, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 122.65 (C_{benz}), 126.87 (C_{benz}), 128.92 (C_{benz}), 138.20 (C_1), 140.38 (C_3), 145.40 (C_2), 146.49 (C_6), 146.58 (C_5), 185.40 (C=S). Anal. Calcd for $C_{11}H_9N_3S$: C, 61.31; H, 4.18; N, 19.51; S, 14.86. Found: C, 61.07; H, 4.35; N, 19.42; S, 15.16.

2-Methoxy-3-*N*-phenylpyrazinethiocarboxamide (9)

Metalation of 2-methoxypyrazine (0.19 mL, 2.0 mmol) according to the general procedure (method B) with *n*-butyllithium *1.6 M* (2.8 mL, 4.5 mmol) and 2,2,6,6-tetramethylpiperidine (0.78 mL, 4.6 mmol), phenyl isothiocyanate (0.36 mL, 3.0 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (8/2) as the eluent, 0.231 g (47%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 7.25 (m, 3H, H_{benz}), 7.70 (m, 2H, H_{benz}), 8.07 (d, $J_{H5,H6}$= 2.4 Hz, 1H, H_6), 8.22 (d, $J_{H5,H6}$= 2.4 Hz, 1H, H_5), 9.63 (br, 1H, NH); Anal. Calcd for $C_{12}H_{11}N_3OS$: C, 58.70; H, 4.48; N, 17.12; S, 13.04. Found: C, 58.43; H, 4.61; N,16.98; S, 13.38.

5-Deuterio-2-*N*-*tert*-butylpyrazinethiocarboxamide (10)

Metalation of **5** (0.134 g, 0.7 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.8 mL, 2.9 mmol) and 2,2,6,6-tetramethylpiperidine (0.5 mL, 3.0 mmol), t = 90 min, then reaction with a mixture of 0.3 mL of deuterium chloride and 0.5 mL of deuterated ethanol, t = 30 min gave, after purification by filtration on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (14/1) as the eluent, 0.139 g (100%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.64 (s, 9H, $C(CH_3)_3$), 8.37 (d, $J_{H3,H6}$ = 1.1 Hz, 1H, H_6), 9.87 (br, 1H, NH), 9.88 (d, $J_{H3,H6}$ = 1.1 Hz, 1H, H_3); ^{13}C NMR ($CDCl_3$): δ 27.34 (CH_3), 55.14 ($\underline{C}(CH_3)_3$), 140.06 (C_6), 145.57 (C_3), 145.72 (C_5), 146.04 (C_2), 186.56 (C=S); IR (KBr): ν 3266 cm^{-1} (NH), 1519 cm^{-1} (C=S).

5-(1-Hydroxy)ethyl-2-*N*-*tert*-butylpyrazinethiocarboxamide (11)

Metalation of **5** (0.134 g, 0.7 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.8 mL, 2.9 mmol) and 2,2,6,6-tetramethylpiperidine (0.5 mL, 3.0 mmol), t = 90 min, then reaction with acetaldehyde (0.40 mL, 7.0 mmol), t = 45 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (24/1) as the eluent, 0.121 g (71%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.49 (d, $J_{CH,CH3}$ = 6.6 Hz, 3H, $(CH)CH_3$), 1.61 (s, 9H, $C(CH_3)_3$), 3.80 (br, 1H, OH), 5.98 (q, $J_{CH,CH3}$ = 6.6 Hz, 1H, $(\underline{CH})CH_3$), 8.47 (d, $J_{H3,H6}$ = 1.1 Hz, 1H, H_6), 9.66 (d, $J_{H3,H6}$

= 1.1 Hz, 1H, H_3), 9.73 (br, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 23.75 (CH($\underline{C}H_3$)), 27.37 (C($\underline{C}H_3$)$_3$), 55.15 ($\underline{C}(CH_3)_3$), 68.20 ($\underline{C}H(CH_3)$), 137.54 (C_6), 143.85 (C_3), 144.77 (C_5), 160.57 (C_2), 186.48 (C=S); ^{15}N ($CDCl_3$): δ 312 (d, J = 10.5 Hz, N_1), 325 (d, J = 10.5 Hz, N_4). Anal. Calcd for $C_{11}H_{17}N_3OS$: C, 55.88; H, 7.20; N, 17.78; S, 13.55. Found: C, 55.58; H, 7.60; N, 17.58; S, 13.86.

5-Diphenylhydroxymethyl-2-*N*-*tert*-butylpyrazinethiocarboxamide (12)

Metalation of **5** (0.121 g, 0.6 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.6 mL, 2.6 mmol) and 2,2,6,6-tetramethylpiperidine (0.44 mL, 2.6 mmol), t = 90 min, then reaction with benzophenone (0.126 g, 0.7 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (24/1) as the eluent, 0.222 g (94%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.74 (s, 9H, $C(CH_3)_3$), 5.31 (br, 1H, OH), 7.37 (m, 10H, H_{benz}), 8.37 (s, 1H, H_6), 9.85 (br, 1H, NH), 9.94 (s, 1H, H_3); ^{13}C NMR ($CDCl_3$): δ 27.48 (C($\underline{C}H_3$)$_3$), 55.25($\underline{C}(CH_3)_3$), 80.25 ($\underline{C}$(OH)), 127.30 (C_{benz}), 128.02 (C_{benz}), 128.26 (C_{benz}), 139.69 (C_6), 143.63 (C_3), 144.38 (C_5), 160.65 (C_2), 186.26 (C=S). Anal. Calcd for $C_{22}H_{23}N_3OS$: C, 70.51; H, 6.14; N, 11.22; S, 8.55. Found: C, 70.53; H, 6.28; N, 11.53; S, 8.22.

5-Phenylhydroxymethyl-2-*N*-*tert*-butylpyrazinethiocarboxamide (13)

Metalation of **5** (0.140 g, 0.7 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.9 mL, 3.0 mmol) and 2,2,6,6-tetramethylpiperidine (0.53 mL, 3.1 mmol), t = 90 min, then reaction with benzaldehyde (0.09 mL, 0.9 mmol), t = 90 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (24/1) as the eluent, 0.113 g (50%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.64 (s, 9H, $C(CH_3)_3$), 3.91 (br, 1H, OH), 5.90 (s, 1H, CH), 7.34 (m, 5H, H_{benz}), 8.44 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H_6), 9.74 (d, $J_{H3,H6}$ = 1.3 Hz, 2H, NH-H_3). Anal. Calcd for $C_{16}H_{19}N_3OS$: C, 64.36; H, 6.37; N, 14.08; S, 10.73. Found: C, 64.42; H, 6.12; N, 14.33; S, 10.32.

5-Chloro-2-*N*-*tert*-butylpyrazinethiocarboxamide (14)

Metalation of **5** (0.155 g, 0.8 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (2.0 mL, 3.2 mmol) and 2,2,6,6-tetramethylpiperidine (0.55 mL, 3.3 mmol), t = 90 min, then reaction with hexachloroethane (0.230 g, 1.0 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (14/1) as the eluent, 0.160 g (89%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.65 (s, 9H, $C(CH_3)_3$), 8.37 (d, $J_{H3,H6}$ = 1.1 Hz, 1H, H_6), 9.52 (br, 1H, NH), 9.62 (d, $J_{H3,H6}$ = 1.1 Hz, 1H, H_3); ^{13}C NMR ($CDCl_3$): δ 27.39 (CH_3), 55.36 (C(CH$_3$)$_3$), 139.88 (C$_6$), 142.90 (C$_2$), 144.26 (C$_3$), 151.00 (C$_5$), 185.39 (C=S). Anal. Calcd for $C_9H_{12}N_3ClS$: C, 47.08; H, 5.23; N, 18.30; S, 13.95. Found: C, 47.48; H, 5.02; N, 18.51; S, 13.56.

5-Tributylstannyl-2-*N-tert*-butylpyrazinethiocarboxamide (15)

Metalation of **5** (0.135 g, 0.7 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.8 mL, 2.9 mmol) and 2,2,6,6-tetramethylpiperidide (0.51 mL, 3.0 mmol), t = 90 min, then reaction with tributyltin chloride (0.2 mL, 0.8 mmol), *t* = 180 *min* gave, after purification by filtration on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (14/1) as the eluent, 0.337 g (100%) of an orange oil. ^{1}H NMR (CDCl$_3$): δ 1.68 (s, 9H, C(CH$_3$)$_3$), 8.40 (s, 1H, H$_6$), 9.90 (br, 1H, NH), 10.05 (s, 1H, H$_3$).

3,5-Dimethyl-2-*N-tert*-butylpyrazinethiocarboxamide (16)

Metalation of **5** (0.140 g, 0.7 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.9 mL, 3.0 mmol) and 2,2,6,6-tetramethylpiperidine (0.52 mL, 3.1 mmol), t = 90 min, then reaction with methyl iodide (0.1 mL, 1.6 mmol), t = 90 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (24/1) as the eluent, 0.118 g (72%) of an yellow oil. ^{1}H NMR (CDCl$_3$): δ 1.42 (s, 9H, C(CH$_3$)$_3$), 2.10 (s, 3H, CH$_3$), 2.56 (s, 3H, CH$_3$), 8.36 (s, 1H, H$_6$), 8.58 (br, 1H, NH). Anal. Calcd for $C_{11}H_{17}N_3S$: C, 59.40; H, 7.65; N, 18.90; S, 14.40. Found: C, 59.72; H, 7.52; N, 18.61; S, 14.16.

5-Trimethylsilyl-2-*N-tert*-butylpyrazinethiocarboxamide (17)

Metalation of **5** (0.385 g, 2.0 mmol) according to the general procedure (method B) with *n*-butyllithium *1.6 M* (5.1 mL, 8.2 mmol) and 2,2,6,6-tetramethylpiperidine (1.4 mL, 8.4 mmol), chlorotrimethylsilane (0.50 mL, 4.0 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (49/1) as the eluent, 0.517 g (98%) of an orange oil. ^{1}H NMR (CDCl$_3$): δ 0.38 (s, 9H, Si(CH$_3$)$_3$), 1.67 (s, 9H, C(CH$_3$)$_3$), 8.47 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H$_6$), 9.85 (br, 1H, NH), 10.01 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H$_3$); ^{13}C NMR (CDCl$_3$): δ -0.42 (Si(CH$_3$)$_3$), 27.17 (C(CH$_3$)$_3$), 54.80 (C(CH$_3$)$_3$), 143.55 (C$_6$), 144.01 (C$_5$), 145.33 (C$_3$), 165.08 (C$_2$), 188.20 (C=S). Anal. Calcd for $C_{12}H_{21}N_3SSi$: C, 54.47; H, 7.94; N, 15.89; S, 12.10. Found: C, 54.75; H, 8.08; N, 16.17; S, 12.14.

5-(1-Hydroxy)ethyl-2-*N*-methylpyrazinethiocarboxamide (18)

Metalation of **6** (0.145 g, 0.9 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.8 mL, 2.9 mmol) and 2,2,6,6-tetramethylpiperidine (0.51 mL, 3.0 mmol), t = 10 min, then reaction with acetaldehyde (0.40 mL, 7.0 mmol), *t* = 45 *min gave*, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (8/2) as the eluent, 0.148 g (79%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.55 (d, $J_{CH,CH3}$ = 6.6 Hz, 3H, (CH)C$\underline{H}_3$), 3.37 (d, $J_{NH,CH3}$ = 5.1 Hz, 3H, NHC$\underline{H}_3$), 3.57 (br, 1H, OH), 5.02 (q, $J_{CH,CH3}$ = 6.6 Hz, 1H, (C$\underline{H}$)CH_3), 8.52 (s, 1H, H_6), 9.69 (s, 1H, H_3), 9.86 (br, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 23.74 (CH($\underline{C}H_3$)), 32.39 (NH$\underline{C}H_3$), 68.36 ($\underline{C}$H(CH_3)), 138.30 (C_6), 144.16 (C_5), 144.36 (C_3), 160.98 (C_2), 189.28 (C=S). Anal. Calcd for $C_8H_{11}N_3O$: C, 48.68; H, 5.58; N, 21.30; S, 16.23. Found: C, 48.52; H, 5.32; N, 21.30; S, 16.36.

5-Phenylhydroxymethyl-2-*N*-methylpyrazinethiocarboxamide (19)

Metalation of **6** (0.138 g, 0.9 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.7 mL, 2.7 mmol) and 2,2,6,6-tetramethylpiperidine (0.47 mL, 2.8 mmol), t = 10 min, then reaction with benzaldehyde (0.14 mL, 1.3 mmol), t = 90 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (8/2) as the eluent, 0.087 g (37%) of a brown oil. ^{1}H NMR ($CDCl_3$): δ 3.36 (d, $J_{NH,CH3}$ = 4.8 Hz, 3H, CH_3), 5.04 (br, 1H, OH), 5.93 (s, 1H, CH), 7.30 (m, 5H, H_{benz}), 8.48 (s, 1H, H_6), 9.69 (s, 1H, H_3), 9.82 (br, 1H, NH). Anal. Calcd for $C_{13}H_{13}N_3OS$: C, 60.15; H, 5.01; N, 16.20; S, 12.34. Found: C, 59.85; H, 5.24; N, 16.33; S, 11.91.

5-Diphenylhydroxymethyl-2-*N*-methylpyrazinethiocarboxamide (20)

Metalation of **6** (0.138 g, 0.9 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.7 mL, 2.7 mmol) and 2,2,6,6-tetramethylpiperidine (0.47 mL, 2.8 mmol), t = 10 min, then reaction with benzophenone (0.196 g, 1.1 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (8/2) as the eluent, 0.025 g (8%) of a yellow oil. ^{1}H NMR ($CDCl_3$): δ 3.39 (d, $J_{NH,CH3}$ = 5.1 Hz, 3H, CH_3), 5.21 (br, 1H, OH), 7.32 (m, 10H, H_{benz}), 8.31 (d, $J_{H3,H6}$ = 1.4 Hz, 1H, H_6), 9.81 (d, $J_{H3,H6}$ = 1.4 Hz, 2H, H_3+NH). Anal. Calcd for $C_{19}H_{17}N_3OS$: C, 67.97; H, 5.07; N, 12.52; S, 9.54. Found: C, 67.72; H, 5.23; N, 12.92; S, 9.22.

5-Iodo-2-*N*-methylpyrazinethiocarboxamide (21)

Metalation of **6** (0.143 g, 0.9 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.8 mL, 2.9 mmol) and 2,2,6,6-tetramethylpiperidine (0.51 mL, 3.0 mmol), t = 10 min, then reaction with iodine (0.263 g, 1.0 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (8/2) as the eluent, 0.083 g (32%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 3.38 (d, $J_{CH3,NH}$ = 5.2 Hz, 3H, CH_3), 8.69 (d, $J_{H3,H6}$ = 1.4 Hz, 1H, H_6), 9.59 (d, $J_{H3,H6}$ = 1.4 Hz, 1H, H_3), 9.70 (br, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 32.59 (CH_3), 121.00 (C_5), 143.70 (C_2), 147.54 (C_6), 148.96 (C_3), 188.78 (C=S). Anal. Calcd for $C_6H_6N_3IS$: C, 40.20; H, 3.35; N, 23.45; S, 17.87. Found: C, 40.55; H, 3.22; N, 23.82; S, 17.42.

5-Chloro-2-*N*-methylpyrazinethiocarboxamide (22)

Metalation of **6** (0.138 g, 0.9 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.7 mL, 2.7 mmol) and 2,2,6,6-tetramethylpiperidine (0.47 mL, 2.8 mmol), t = 10 min, then reaction with hexachloroethane (0.320 g, 1.3 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (8/2) as the eluent, 0.033 g (20%) of a yellow oil. ^{1}H NMR ($CDCl_3$): δ 3.39 (d, $J_{CH3,NH}$ = 5.2 Hz, 3H, CH_3), 8.44 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H_6), 9.62 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H_3), 9.70 (br, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 32.03 (CH_3), 140.18 (C_6), 142.82 (C_5), 145.29 (C_3), 151.80 (C_2), 188.02 (C=S). Anal. Calcd for $C_6H_6N_3ClS$: C, 38.37; H, 3.20; N, 22.38; S, 17.05. Found: C, 38.58; H, 3.02; N, 22.11; S, 17.38.

5-Thiophenyl-2-*N*-methylpyrazinethiocarboxamide (23)

Metalation of **6** (0.138 g, 0.9 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (1.7 mL, 2.7 mmol) and 2,2,6,6-tetramethylpiperidine (0.47 mL, 2.8 mmol), t = 10 min, then reaction with phenyl disulfide (0.284 g, 1.3 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (24/1) as the eluent, 0.081 g (34%) of a yellow oil. ^{1}H NMR ($CDCl_3$): δ 3.32 (d, $J_{NH,CH3}$ = 5.1 Hz, 3H, CH_3), 7.48 (m, 3H, H_{benz}), 7.57 (m, 2H, H_{benz}) 7.95 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H_6), 9.56 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H_3), 9.64 (br, 1H, NH). Anal. Calcd for $C_{12}H_{11}N_3S$: C, 55.09; H, 4.20; N, 16.07; S, 24.48. Found: C, 54.72; H, 4.51; N, 16.28; S, 24.03.

5-Trimethylsilyl-2-*N*-methylpyrazinethiocarboxamide (24)

Metalation of **6** (0.145 g, 0.9 mmol) according to the general procedure (method B) with *n*-butyllithium *1.6 M* (1.8 mL, 2.9 mmol) and 2,2,6,6-tetramethylpiperidine (0.51 mL, 3.0 mmol), chlorotrimethylsilane (0.18 mL, 1.4 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (8/2) as the eluent, 0.037 g (17%) of a yellow oil. ^{1}H NMR ($CDCl_3$): δ 0.38 (s, 9H, $Si(CH_3)_3$), 3.40 (d, $J_{NH,CH3}$ = 5.1 Hz, 3H, CH_3), 8.50 (d, $J_{H3,H6}$ = 1.5 Hz, 1H, H_6), 9.97 (d, $J_{H3,H6}$ = 1.5 Hz, 2H, H_3+NH); ^{13}C NMR ($CDCl_3$): δ -0.38 ($Si(\underline{C}H_3)_3$), 32.38 (CH_3), 143.54 (C_5), 144.50 (C_6), 146.11 (C_3), 166.37 (C_2), 190.32 (C=S). Anal. Calcd for $C_9H_{15}N_3SSi$: C, 47.92; H, 6.65; N, 18.63; S, 14.20. Found: C, 48.12; H, 6.61; N, 18.88; S, 14.34.

5-(1-Hydroxy)ethyl-2-*N*-di*iso*propylpyrazinethiocarboxamide (25)

Metalation of 7 (0.141 g, 0.6 mmol) according to the general procedure (method A) with *n*-butyllithium *2.5 M* (0.56 mL, 1.4 mmol) and 2,2,6,6-tetramethylpiperidide (0.25 mL, 1.5 mmol), t_1= 60 min, then reaction with acetaldehyde (0.35 mL, 6.0 mmol), t = 45 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (5/1) as an eluant, 0.114 g (67%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.17 (d, $J_{CH,CH3}$ = 6.7 Hz, 6H, CH($\underline{CH_3}$)$_2$), 1.51 (d, $J_{CH,CH3}$ = 6.6 Hz, 3H, (CH)C$\underline{H_3}$), 1.69 (d, $J_{CH,CH3}$ = 6.7 Hz, 6H, CH($\underline{CH_3}$)$_2$), 3.60 (br, 1H, OH), 3.88 (sept, $J_{CH,CH3}$ = 6.7 Hz, 1H, C$\underline{H}$(CH_3)$_2$), 4.91 (q, $J_{CH,CH3}$ = 6.6 Hz, 1H, (C$\underline{H}$)CH_3), 8.45 (d, $J_{H3,H6}$ = 1.1 Hz, 1H, H_6), 8.50 (d, $J_{H3,H6}$ = 1.1 Hz, 1H, H_3); ^{13}C NMR ($CDCl_3$): δ 18.88 (CH($\underline{C}H_3$)$_2$), 20.63 ($\underline{C}$H(CH_3)$_2$), 23.62 (CH($\underline{C}H_3$)$_2$), 29.52 ($\underline{C}$H(CH_3)$_2$), 36.01 ($\underline{C}$H(OH)), 68.04 ((CH)$\underline{C}H_3$), 139.27 (C_6), 141.24 (C_5), 154.63 (C_2), 156.69 (C_3), 194.03 (C=S). Anal.Calcd for $C_{13}H_{21}N_3OS$: C, 53.85; H, 7.85; N, 15.71; S, 11.99. Found: C, 53.55; H, 7.71; N, 15.98; S, 12.38.

5-Phenylhydroxymethyl-2-*N*-di*iso*propylpyrazinethiocarboxamide (26)

Metalation of 7 (0.132 g, 0.6 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (0.82 mL, 1.3 mmol) and 2,2,6,6-tetramethylpiperidine (0.23 mL, 1.4 mmol), t = 10 min, then reaction with benzaldehyde (0.08 mL, 0.8 mmol), t = 90 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (7/3) as the eluent, 0.081 g (42%) of an orange oil. ^{1}H NMR ($CDCl_3$): δ 1.53 (d, $J_{CH,CH3}$ = 6.3 Hz, 6H, CH($\underline{CH_3}$)$_2$), 1.69 (d, $J_{CH,CH3}$ = 6.3 Hz, 6H, CH($\underline{CH_3}$)$_2$), 3.90 (sept, $J_{CH,CH3}$ = 6.3 Hz, 1H, C$\underline{H}$(CH_3)$_2$), 5.84 (s, 1H, C$\underline{H}$(OH)), 6.47 (br, 1H, OH), 7.36 (m, 5H, H_{benz}), 8.48 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H_6), 8.52 (d, $J_{H3,H6}$ = 1.3 Hz, 1H, H_3). Anal. Calcd for $C_{18}H_{23}N_3OS$: C, 65.59; H, 6.98; N, 12.75; S, 9.71. Found: C, 65.73; H, 6.49; N, 13.03; S, 9.85.

5-Diphenylhydroxymethyl-2-*N*-di*iso*propylpyrazinethiocarboxamide (27)

Metalation of 7 (0.132 g, 0.6 mmol) according to the general procedure (method A) with *n*-butyllithium *1.6 M* (0.82 mL, 1.3 mmol) and 2,2,6,6-tetramethylpiperidine (0.23 mL, 1.4 mmol), t = 10 min, then reaction with benzophenone (0.120 g, 0.6 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (14/3) as the eluent, 0.108 g (45%) of a yellow oil. ^{1}H NMR ($CDCl_3$): δ 1.23 (d, $J_{CH,CH3}$ = 6.2 Hz, 6H, CH($\underline{CH_3}$)$_2$), 1.75 (d, $J_{CH,CH3}$ = 6.2 Hz, 6H, CH($\underline{CH_3}$)$_2$), 3.97 (sept, $J_{CH,CH3}$ = 6.2 Hz, 1H, C$\underline{H}$(CH_3)$_2$), 5.17 (br, 1H, OH), 7.33 (m, 10H, H_{benz}), 8.25 (d, $J_{H3,H6}$ = 1.5 Hz, 1H, H_6), 8.68 (d, $J_{H3,H6}$ = 1.5 Hz, 1H, H_3); ^{13}C NMR ($CDCl_3$): δ 18.94 (CH($\underline{C}H_3$)$_2$), 50.12 ($\underline{C}$H(CH_3)$_2$), 80.00 ($\underline{C}$(OH)), 127.67 (C_{benz}), 127.84 (C_{benz}), 128.08

(C_{benz}), 141.23 (C_6), 144.68 (C_3), 154.43 (C_5), 156.79 (C_2), 194.02 (C=S). Anal. Calcd for $C_{24}H_{27}N_3OS$: C, 71.03; H, 6.66; N, 10.36; S, 7.89. Found: C, 70.87; H, 6.73; N, 10.03; S, 8.28.

5-Trimethylsilylpyrazine-2-*N*-di*iso*propylpyrazinethiocarboxamide (28)

Metalation of **7** (0.132 g, 0.6 mmol) according to the general procedure (method B) with *n*-butyllithium *1.6 M* (0.82 mL, 1.3 mmol) and 2,2,6,6-tetramethylpiperidine (0.23 mL, 1.3 mmol), chlorotrimethylsilane (0.30 mL, 2.4 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (49/1) as the eluent, 0.013 g (7%) of a yellow oil. ^{1}H NMR ($CDCl_3$): δ 0.36 (s, 9H, $Si(CH_3)_3$), 1.25 (d, $J_{CH,CH3}$ = 6.7 Hz, 6H, CH($\underline{C}H_3$)$_2$), 1.76 (d, $J_{CH,CH3}$ = 6.7 Hz, 6H, CH($\underline{C}H_3$)$_2$), 3.97 (sept, $J_{CH,CH3}$ = 6.7 Hz, 1H, C$\underline{H}$(CH_3)$_2$), 8.49 (d, $J_{H3,H6}$ = 1.4 Hz, 1H, H_6), 8.76 (d, $J_{H3,H6}$ = 1.4 Hz, 1H, H_3). Anal. Calcd for $C_{14}H_{25}N_3SSi$: C, 56.87; H, 8.46; N, 14.21; S, 10.83. Found: C, 56.61; H, 8.53; N, 14.01; S, 11.30.

3-Trimethylsilylpyrazine-2-*N*-di*iso*propylpyrazinethiocarboxamide (29)

Metalation of **7** (0.132 g, 0.6 mmol) according to the general procedure (method B) with *n*-butyllithium *1.6 M* (0.82 mL, 1.3 mmol) and 2,2,6,6-tetramethylpiperidine (0.23 mL, 1.3 mmol), chlorotrimethylsilane (0.30 mL, 2.4 mmol), t = 120 min gave, after purification by column chromatography on neutral alumina gel with a mixture of ether petroleum / ethyl acetate (49/1) as the eluent, 0.112 g (65%) of a yellow oil. ^{1}H NMR ($CDCl_3$): δ 0.37 (s, 9H, $Si(CH_3)_3$), 1.26 (d, $J_{CH,CH3}$ = 5.6 Hz, 6H, CH($\underline{C}H_3$)$_2$), 1.78 (d, $J_{CH,CH3}$ = 5.6 Hz, 6H, CH($\underline{C}H_3$)$_2$), 3.89 (sept, $J_{CH,CH3}$ = 5.6 Hz, 1H, C$\underline{H}$(CH_3)$_2$), 8.23 (d, $J_{H5,H6}$ = 2.2 Hz, 1H, H_6), 8.55 (d, $J_{H5,H6}$ = 2.2 Hz, 1H, H_5); ^{13}C NMR ($CDCl_3$): δ -0.57 (Si($\underline{C}H_3$)$_3$), 18.47 (CH($\underline{C}H_3$)$_2$), 19.14 (CH($\underline{C}H_3$)$_2$), 51.08 ($\underline{C}$H(CH_3)$_2$), 57.34 ($\underline{C}$H(CH_3)$_2$), 140.48 (C_5), 142.65 (C_6), 159.92 (C_3), 160.18 (C_2), 195.52 (C=S). Anal. Calcd for $C_{14}H_{25}N_3SSi$: C, 56.87; H, 8.46; N, 14.21; S, 10.83. Found: C, 56.48; H, 8.62; N, 14.28; S, 10.98.

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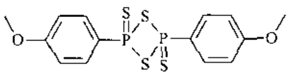

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