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SYNTHETIC APPLICATIONS OF 2-CHLOROOXIRANES: PREPARATION OF THIAZOLES, DIHYDROTHIAZOLES AND SELENAZOLES

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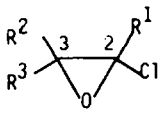
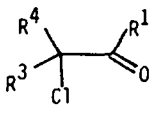
Abstract—The reaction of 2-chlorooxiranes **1** with thioamides and thioureas provides access to thiazoles, 4-hydroxy-4,5-dihydrothiazoles and 2-imino-2,3-dihydrothiazoles under mild conditions and with excellent yields. With **1** and selenourea, near quantitative yields of selenazoles are obtained.

2-Chlorooxiranes **1** are isomeric with α-chlorocarbonyl compounds **2** and have both carbon atoms (2 and 3) in the same oxidation states as the corresponding carbon atoms in **2**.





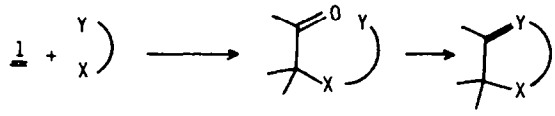
1 **2**

1	R^1	R^2	R^3
a	$-(CH_2)_4-$		H
b	$(CH_3)_2CH$	H	H
c	$ClCH_2$	H	H
d	H	$(CH_3)_3C$	H

Therefore, **1** should function as synthons for the preparation of α-substituted carbonyl compounds. Indeed, nucleophilic attack at **1** occurs in most cases at carbon atom 3 giving rise to the desired products. As in this process the entire strain energy of the three-membered ring is released the α-substituted carbonyl compounds are produced under mild conditions giving high yields.[1] But 2-chlorooxiranes **1** do not only offer a higher reactivity than α-chlorocarbonyl compounds **2**, their reactions might also follow different pathways than those of **2**.

For example, **1a** reacts with sodium methoxide in methanol to afford a quantitative yield of 2-methoxycyclohexanone.[1] 2-Chloro-cyclohexanone **2a**, on the other hand, undergoes the Favorski rearrangement under the same reaction conditions to cyclopentane carboxylic acid methylester and 1-methoxy-7-oxabicyclo[4.1.0]heptane in comparable amounts (both 35–45%).[1,2] Whereas α-chlorocarbonyl compounds give with phosphites variable amounts of Arbusov- and Perkow-product,2-chlorooxiranes only result in β-ketophosphonic acid esters.[3] Thus, 2-chlorooxiranes **1** give clean access to α-substituted carbonyl compounds avoiding side reactions that occur with α-chloro carbonyl compounds **2**.

With bidentate nucleophiles the intermediate α-substituted carbonyl compounds obtained from **1** can close the ring giving access to heterocyclic compounds.

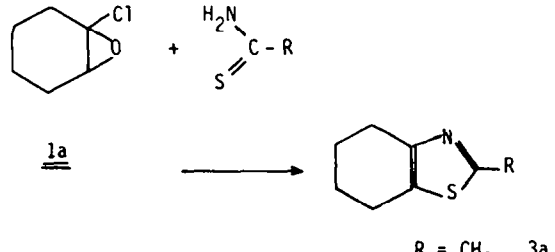


Having improved the synthesis of known 2-chlorooxiranes[4–6] and made available new ones[7] provided the basis for exploring the synthetic capabilities of this class of compounds.

In this paper, access to thiazoles and selenazoles from 2-chlorooxiranes **1a-d** is studied. Instead of performing an exhaustive sequence of reactions we selected only representative examples to demonstrate the scope of the approach.

A cornucopia of syntheses of substituted thiazoles is known.[8] A few systems have already been made available starting from 2-chlorooxiranes.[9] The use of **1** for the synthesis of thiazoles becomes particularly attractive if the higher reactivity of **1** gives better yields and allows the synthesis of labile compounds. This is indeed the case.

Reaction of **1a** with thioacetamide and thiobenzamide gave the thiazoles **3a** and **3b** in 78% and 79% yield, respectively.

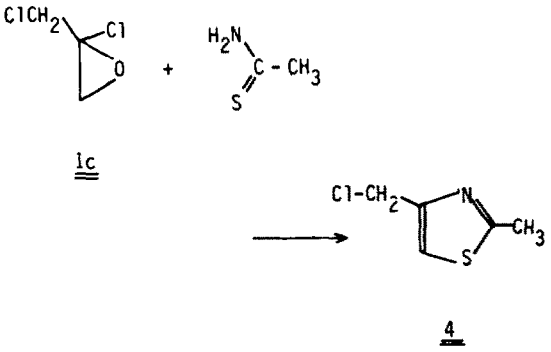


R = CH_3 **3a**

R = C_6H_5 **3b**

3a had been obtained from 2-mercaptocyclohexanone in a two step synthesis in 75% yield, **3b** in 26% yield.[10]

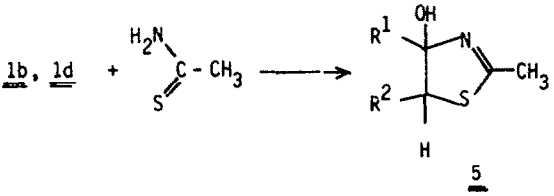
Starting with **2a**, amides and phosphorus pentasulfide **3a** and **3b** can be obtained in about 50%, only.[11] **1c** and thioacetamide gave the corresponding thiazole **4** in 77% yield; distillation resulted in an appreciable loss in yield of this rather unstable compound.[12-14]



4

In **1c** the 2-chlorooxirane system competes with a simple alkylchloride moiety against nucleophilic attack. The rather high yield of **4** where the chloromethylgroup is untouched underlines the higher reactivity of the 2-chlorooxirane group.

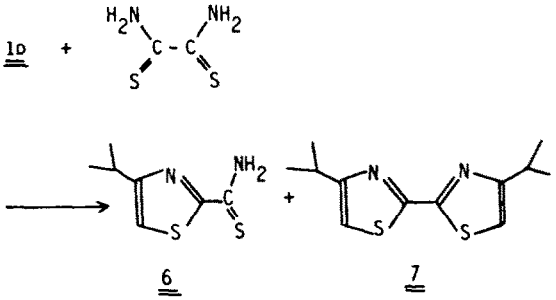
With 2-chlorooxiranes **1b** and **1d** the reaction with thioacetamides could be intercepted at the level of the 4-hydroxy-4,5-dihydro-1,3-thiazole compounds **5a** and **5b**. Whereas **5b** is a new compound, **5a** has already been obtained previously.[15]



5

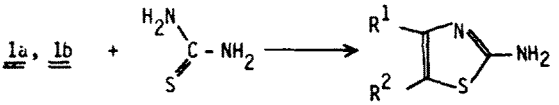
	R^1	R^2
a	$(CH_3)_2CH$	H
b	H	$C(CH_3)_3$

In the reaction of **1b** with dithiooxalic acid diamide, depending on the ratio of starting materials, thiazole-2-thiocarboxylacid amide **6** or 2,2'-bis thiazole **7** can be isolated in good yields.



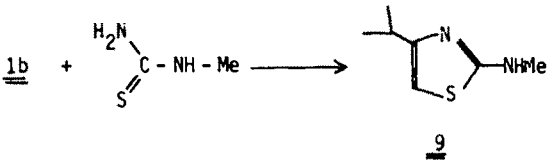
6 **7**

With thiourea 2-aminothiazoles **8** are obtained in excellent yields, far better than in the reported preparations.[16-18]

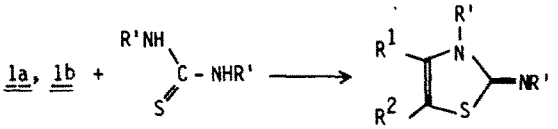


8	R^1	R^2
a	$-(CH_2)_4-$	
b	$(CH_3)_2CH$	H

Reaction of **1b** with N-methylthiourea gave the new compound **9**, again in excellent yield. 2-Imino-2,3-dihydrothiazoles[11] can be obtained from **1** and N,N'-disubstituted thioureas.



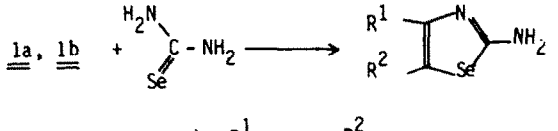
9



10	R^1	R^2	R'
a	$-(CH_2)_4-$		CH_3
b	$(CH_3)_2CH$	H	CH_3
c	$(CH_3)_2CH$	H	C_6H_5

Again, the yields for **10a** and **10c** are much better than the one reported starting from 2-bromoketones.[19-21]

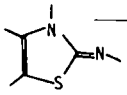
Now that the 2-chlorooxiranes **1** had established their importance in synthesizing thiazole and dihydrothioazole derivatives their potential in giving access to the rather sensitive selenazoles was studied. Reaction of **1a** and **1b** with selenourea resulted in nearly quantitative yields of the corresponding selenazoles **11**. Purification of these rather heat and light sensitive compounds resulted in loss of yields, but the known compound **11a** could still be isolated in a much better yield than by a reported procedure.[22]



11	R^1	R^2
a	$-(CH_2)_4-$	
b	$(CH_3)_2CH$	H

The structure of all compounds can be unambiguously deduced from the spectroscopic data contained in the experimental section. Table 1 contains the collection of ^{13}C-NMR chemical shifts of the ring carbon atom of the various heterocyclic ring systems.

Table 1.

		C-2	C-4	C-5
	3a	164.40	151.35	127.98
	3b	162.20	149.53	129.08
	4	166.93	151.61	116.94
	6	166.29	165.25	121.09
	7	164.92	160.83	112.72
	8a	165.44	145.18	117.52
	8b	168.10	159.01	99.60
	9	171.74	159.66	97.46
	5a	169.14	111.87	39.80
	5b	171.68	99.28	70.45
	10a	160.96	132.07	105.25
	10b	162.59	145.90	89.60
	10c	161.22	152.07	91.29
	11a	167.19	145.51	123.11
	11b	169.73[a]	159.73	103.43[b]

a) This peak has two sidebands resulting from ^{13}C-^{77}Se coupling ^{1}J=124.0 Hz

b) There are two side bands from ^{13}C-^{77}Se coupling ^{1}J=93.8 Hz

The high yields in thiazoles, dihydrothiazoles and selenazoles accessible from **1**, all obtained in single, first runs of reactions without optimization, confirm the synthetic significance of 2-chlorooxiranes **1**. The high reactivity of **1** makes them particularly attractive for the synthesis of sensitive materials.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. The following instruments were used for determining spectral data: IR: Perkin–Elmer 257; ^{1}H-NMR: Varian A 60 and Varian EM 360; ^{13}C-NMR: Jeol JNM-FX 60; MS: AEI MS 9 and Varian MAT CH5.

The synthesis and spectral data of 2-chlorooxiranes **1a-d** have been described elsewhere.[7] The yields of crude material have not been determined as the bulk material but are the actual amount of product as determined by ^{1}H-NMR integration.

2-Methyl-4,5,6,7-tetrahydrobenzothiazole (**3a**)

A soln of 3.04 g (40 mmol) thioacetamide in 20 ml methylene chloride and 5 ml methanol was added to 2.66 g (20 mmol) **1a** in 8 ml methylene chloride and 4.0 g molecular sieves 4Å were added and the mixture heated to 40°C for 24 hr. The solvent was removed and the residue was extracted two times with 25 ml pentane. Distillation (crude yield 86%) gave 2.43 g (78%) **3a**. b.p. 102–103°/11Torr (lit[9] 102°/11Torr) (Found: C, 62.54; H, 7.17; N, 8.68; Calc. for $C_8H_{11}NS$ (153.24) C, 62.70; H, 7.24; N, 9.14%). IR(film): ν = 2935, 2855, 1559, 1491, 1445, 1368 cm^{-1}. ^{1}H-NMR($CDCl_3$): δ = 1.6-2.0 (m, 4H, $-CH_2-CH_2-$), 2.4–2.9 (m, 4H, $-CH_2-C=C-CH_2-$), 2.54 (s, 3H, $-CH_3$) ppm. ^{13}C-NMR ($CDCl_3$): δ = 19.02 (CH_3), 22.99 (C-6), 23.44 (C-7, C-5), 26.69 (C-4), 127.98 (C-8), 149.53 (C-9), 162.20 (C-2) ppm. MS (70 eV): *m/e*(%) = 155 (1, M + 2), 154 (2, M + 1), 153 (76, M^+), 125 (68, M^+-C_2H_4), 112 (14, $C_6H_8S^+$), 71 (10, $C_3H_3S^+$), 45 (10, HCS^+).

2-Phenyl-4,5,6,7-tetrahydrobenzothiazole **3b**

Analogously to the preparation of **3a**, 2.93 g (22 mmol) **1a** in 10 ml methylene chloride was treated with 6.16 g (44 mmol) thiobenzamide in 40 ml methylene chloride and 10 ml methanol, with 3.0 g (30 mmol) triethylamine in 10 ml methanol and with 4.0 g molecular sieves. After evaporation of the solvent the residue was extracted with ether, the product distilled at 0.001 Torr and the main fraction purified by CC (SiO_2/methylene chloride/pentane 1:2). 3.76 g (79%) **3b**. b.p. 95–96°C/0.001 Torr (lit. [10]149°C/2 Torr); m.p. 34.5°C (lit[9] liquid). (Found: C, 72.58; H, 6.14; N, 6.31; calc. for $C_{13}H_{13}NS$ (215.31) C 72.51; H, 6.08; N, 6.51%). IR (KBr): ν 3066, 2942, 2866, 2854, 1670, 1607, 1550, 1509, 1365, 770 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.6–2.1 (m, 4H, $-CH_2-CH_2$), 2.5–3.0 (m, 4H, $-CH_2-C=C-CH_2-$), 7.15–7.55 (m, 3H, m-, p-H), 7.65–8.0 (m, 2H, o-H) ppm. ^{13}C-NMR ($CDCl_3$): δ = 23.05 (C-6), 23.38 (C-5), 23.63 (C-7), 26.96 (C-4), 126.16 (o-C), 128.69 (m-C), 129.08 (C-8), 129.34 (p-C), 134.08 (ipso-C), 151.35 (C-9), 164.40 (C-2) ppm. MS (70 eV): *m/e*(%) = 217 (7, M^+ + 2), 216 (16, M^+ + 1), 125 (100, M^+), 187 (59, M^+-C_2H_4), 182 & 50, M^+-SH), 104 (16, $C_6H_5CNH^+$), 84 (59), 77 (27), 58 (22).

4-Chloromethyl-2-methylthiazole **4**

Similarly to the preparation of **3a**, 1.27 g (10 mmol) **1c** and 0.84 g (11 mmol) of thioacetamide were reacted. Extraction with ether provided crude **4** (77%) which was purified by rapid distillation: 0.70 g (48%) **4**. b.p. 26–27°C/0.002 Torr (lit.[13] 84°C/10 Torr). (Found: C, 40.41; H, 4.39; N, 9.52; Calc. for C_5H_6ClNS (147.63): C, 40.68; H, 4.10; N, 9.49). IR(film): ν = 3110, 2965, 2920, 2845, 1515, 1430 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 2.67 (s, 3H, $-CH_3$), 4.64 (d, ^{4}J(HCC=CH)=0.6 Hz; 2H, $-CH_2Cl$), 7.12 (d, ^{4}J(HC=CCH) = 0.6 Hz; 1H, HC-3) ppm. ^{13}C-NMR ($CDCl_3$): δ = 19.22 (CH_3), 40.84 (CH_2Cl), 116.94 (C-5), 151.61 (C-4), 166.93 (C-2) ppm. MS (70 eV): *m/e*(%) = 149, 147 (8, 22, M^+), 112 (100, M^+-Cl), 71 (83, $C_3H_3S^+$), 59 (10, $C_2H_3S^+$), 45 (32, CHS^+).

2-Methyl-4-hydroxy-4-isopropyl-4,5-dihydrothiazole **5a**

To a soln of 1.21 g (10 mmol) **1b** in 3 ml methylene chloride at −30°C 2.28 g (30 mmol) thioacetamide in 15 ml methylene chloride and 7 ml methanol and then 1.22 g (12 mmol) triethylamine in 3 ml methylene chloride were added. After boiling at reflux for 18 hr the solvent was evaporated, the residue (crude yield 90%) was distilled: 1.22 g (77%). B.p. 51.0–52.5°/0.0003 Torr, m.p. 77° (Pentane/ether 3:1) (lit[15] 72°). (Found: C, 52.95; H, 8.44; N, 8.78; Calc. for $C_7H_{13}NOS$ (159.25): C, 52.79; H, 8.23; N, 8.80%. IR (KBr): ν = 3160, 2935, 2910, 2865, 1628, 1387, 1378, 1180 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 0.86 (d, J = 6.8 Hz, 3H, CH(CH_3)), 1.03 (d, J = 6.8 Hz, 3H, CH(CH_3)), 2.20 (sept, J = 6.8 Hz, 1H, C$\underline{H}$(CH_3)$_2$), 2.24 (s, 3H, –CH_3), 3.24 (AB, J_{AB} = 12.0 Hz, 2H, CH_2S, 5.40 (s, 1H, –OH) ppm. ^{13}C-NMR ($CDCl_3$): δ = 16.69 (CH($\underline{C}H_3$)), 17.60 (CH($\underline{C}H_3$)), 20.06 (CH_3), 37.98 (C$\underline{H}$(CH_3)$_2$), 39.80 (C-5), 111.87 (C-4), 169.14 (C-2) ppm. MS (70 eV): *m/e*(%) = 160 (0.2, M + 1), 141 (5, M^+-H_2O), 126 (18, M^+–H_2O–CH_3), 116 (72, M^+–C_3H_7), 71 (44, $C_3H_3S^+$).

2-Methyl-4-hydroxy-5-tert-butyl-4,5-dihydrothiazole **5b**

As in the preparation of **5a** 1.35 g (10 mmol) **1d** are treated with thioacetamide. From the ether extracts **5b** is obtained as slightly yellow needles: 2.30 g (67%); m.p. 110°. (Found: C, 55.34; H, 8.57; N, 8.17; Calc. for $C_8H_{15}NOS$ (173.27): C, 55.45; H, 8.73; N 8.08%. IR (KBr): ω = 3500–2500, 2955, 2900, 2860, 1620, 1425, 1390, 1370, 1360, 1060 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 0.96 (s, 9H, C(CH_3)$_3$), 2.23 (s, 3H, CH_3), 3.63 (d, J = 3.5 Hz, 1H, HC-5), 5.74 (d, J = 3.5 Hz, 1H, HC-4), 6.4 (s, 1H, –OH) ppm. ^{13}C-NMR ($CDCl_3$): δ = 20.23 (CH_3), 27.08 (C($\underline{C}H_3$)$_3$), 33.37 ($\underline{C}$(CH_3)$_3$, 70.45 (C-5), 99.28 (C-4), 171.68 (C-2) ppm. MS (70eV): *m/e*(%) = 173 (35, M^+) 155 (6, M^+–H_2O), 140 (19), 132 (25%), 117 (21, M^+-C_4H_8), 103 (12%), 100 (18), 76 (82), 71 (99, $C_3H_3S^+$).

4-Isopropyl-thiazol-2-thio-carboxylic acid amide **6**

1.28 g (10.5 mmol) dithiooxalic acid diamide in 70 ml methanol were added to a soln of 1.21 g (10 mmol) **1b** in 3 ml methylene chloride at −15°. After warming to room temp. 3.0 ml (10.5 mmol) triethylamine in 5 ml methanol is added in two portions. After stirring for 20 h the solvent was removed, the residue was extracted with hexane and after addition of ether filtered through silica gel. Crystallization from hexane gives 1.44 g (77%) **6**, m.p. 114–116° (decomp). (Found: C, 45.03; H, 5.51; N, 15.11; Calc. for $C_7H_{10}N_2S_2$ (186.30): C, 45.13; H, 5.41; N, 15.04%). IR (KBr): ν = 3300, 3105, 2980, 2965, 1630, 1505, 1370, 1345, 1131, 782 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.28 (d, J = 7.0 Hz, 6H, CH(C$\underline{H}_3$)$_2$), 3.08 (sept, J = 7.0 Hz, 1H, C$\underline{H}$(CH$_3$)$_2$), 7.16 (s, 1H, HC-5), 8.0 (s, br, 1H, NH), 8.7 (s, br, 1H, NH). ^{13}C-NMR ($CDCl_3$): δ = 22.27 (CH($\underline{C}H_3$)$_2$), 30.97 ($\underline{C}$H(CH_3)$_2$), 121.09 (C-5), 165.25 (C-4), 166.29 (C-2), 188.36 ($CSNH_2$) ppm. MS (70 eV): *m/e*(%) = 188 (10, M + 2), 186 (100, M^+), 159 (58), 154 (22), 153 (33), 144 (19), 137 (52), 127 (32, $C_6H_9NS^+$), 85 (24, $C_3H_3NS^+$).

4,4'-Diisopropyl-2,2'-bisthiazole **7**

As in the preparation of **6**, 1.22 g (10 mmol) dithiooxalic acid bisamide is reacted with 2.92 g (24 mmol) **1b**. After evaporation of the solvent, the residue is extracted with ether, and this material, in turn, with hexane yielding a mixture of 0.43 g **6** and 1.43 g **7**. Chromatography on silica gel with hexane gives 1.14 g (45%) **7** as colorless needles showing turquoise fluorescence, m.p. 89°. (Found: C, 57.02; H, 6.35; N, 11.09; Calc. for $C_{12}H_{16}N_2S_2$ (252.40): C, 57.10; H, 6.39; N, 11.09%). IR (KBr) ν = 3125, 2970, 2940, 2895, 2875, 1510, 1385, 1365, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.34 (d, J = 7.0 Hz, 6H, CH(C$\underline{H}_3$)$_2$), 3.16 (dsept, $^3J_{HH}$ = 7.0 Hz, $^4J_{HH}$ = 0.8 Hz, 1H, C$\underline{H}$(CH$_3$)$_2$), 6.96 (d, $^4J_{HH}$ = 0.8 Hz, 1H, HC-5) ppm. ^{13}C-NMR ($CDCl_3$): δ = 22.40 (CH($\underline{C}H_3$)$_2$), 30.91 ($\underline{C}$H(CH_3)$_2$), 112.72 (C-5), 160.83 (C-4), 164.92 (C-2) ppm. MS (70 eV): *m/e*(%) = 254, (6, M + 2), 252 (57, M^+), 237 (100, M^+–CH_3), 210 (2, M^+–C_3H_6), 195 (5, M^+–CH_3–C_3H_6), 111 (12, $C_5H_5NS^+$), 85 (10, $C_3H_3NS^+$).

2-Amino-4,5,6,7-tetrahydrobenzothiazole **8a**

2.30 g (30 mmol) thiourea in 20 ml methanol and then 1.70 g (17 mmol) triethylamine in 5 ml methylene chloride are added at 0° to 2.00 g (15 mmol) **1a** in 3 ml methylene chloride. After adding 3.0 g molecular sieves 4Å the mixture is heated for 16h to 40°. After evaporation of the solvent the residue is extracted with ether, the crude product (2.47 g containing a 85% yield of **8a**) distilled: 1.42 g (62%); b.p. 100°/0.001 Torr; m.p. 88° (lit[16] 88°). (Found: C, 54.74; H, 6.61; N, 17.79; Calc. for $C_7H_{10}N_2S$ (154.18): C, 54.53: H, 6.54; N, 18.17%). IR (KBr): ν = 3380, 3285, 3095, 2940, 2855, 1589, 1524, 1442 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.5–2.0 (m, 4H, –CH_2–CH_2–), 2.25–2.75 (m, 4H, –CH_2–C=C–CH_2–), 5.5 (s, 2H, NH_2) ppm. ^{13}C-NMR ($CDCl_3$): δ = 22.92 (C-6), 23.12 (C-5), 23.50 (C-7), 26.43 (C-4), 117.52 (C-8), 145.18 (C-3), 165.44 (C-2) ppm. MS (70 eV): *m/e*(%) = 156 (3,M + 2), 155 (7, M + 1), 154 (58, M^+), 126 (100, M^+–C_2H_4), 99 (14), 84 (12, $C_3H_2NS^+$), 77 (12), 71 (7, $C_3H_3S^+$).

2-Amino-4-isopropyl-thiazole **8b**

As in the preparation of **8a**, 2.30 g (30 mmol) thiourea are reacted with 1.83 g (15 mmol) **1b**; the crude product (95% yield of **8b**) is distilled: 1.82 g (85%) **8b**, b.p. 50°/0.004 Torr (lit[16] 105–107°/0.5 Torr). (Found: C, 50.19; H, 7.17; N, 19.60; Calc. for $C_6H_{10}N_2S$ (142.17): C, 50.69; H, 7.09; N, 19.71%). IR (film): ν = 3460, 3305, 1631, 1613, 1532, 1380, 1360 cm^{-1}. ^{1}H-NMR ($CDCL_3$): δ = 1.15 (d, J = 7.0 Hz, 6H, CH(C$\underline{H}_3$)$_2$), 2.78 (sept, J = 7.0 Hz, 1H, C$\underline{H}$ (CH_3)$_3$), 5.93 (s, 1H, HC-5), 6.44 (s, 2H, NH_2) ppm. ^{13}C-NMR ($CDCl_3$): δ = 21.95 (CH ($\underline{C}H_3$)$_2$, 30.71 ($\underline{C}$H (CH_3)$_2$), 99.60 (C-5), 159.01 (C-4), 168.10 (C-2) ppm. MS (70 eV): *m/e*(%) × 144 (5, M + 2), 143 (11, M + 1), 142 (100, M^+), 129 (11), 128 (17), 127 (68, M^+–CH_3), 114 (22), 100 (23, M^+–C_3H_6), 99 (9, M^+–C_3H_7), 86 (9, $C_3H_3NS^+$), 45 (42, HCS^+).

2-Methylamino-4-isopropyl thiazole **9**

As for **8a**, 1.51 g (16.5 mmol) N-methylthiourea are reacted with 1.83 g (15 mmol) **1b**. Crude yield 94%, crystallization from pentane gives 1.93 g (82%) **9**, m.p. 95°. (Found: C, 53.60; H, 8.16; N, 18.28; Calc. for $C_7H_{12}N_2S$ (156, 24): C, 53.80; H, 7.74; N, 17.93%. IR (KBr): ν = 3210, 2120, 2970, 2935, 2808, 1600, 1538, 1388, 1369 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.24 (d, J = 6.8 Hz, 6H, CH(C$\underline{H}_3$)$_2$), 2.83 (dsept, J = 6.8 Hz, $^4J_{HH}$ = 0.7 Hz, 1H, C$\underline{H}$ (CH_3)$_2$), 2.90 (s, 3H, NH–CH_3), 6.02 (d, $^4J_{HH}$ = 0.7 Hz, 1Hz, 1H, HC-5), 7.3 (s, 1H, NH–CH_3) ppm. ^{13}C(NMR ($CDCl_3$): δ = 22.01 (CH($\underline{C}H_3$)$_2$, 30.97 ($\underline{C}$H(CH_3)$_2$), 32.14 (NCH_3), 97.46 (C-5), 159.66 (C-4), 171.74 (C-2) ppm. MS (70 eV): *m/e*(%) = 158 (3, M + 2), 157 (7, M + 1), 156 (55, M^+), 141 (100, M^+–CH_3), 128 (37, M^+–C_2H_4), 126 (16), 100 (28, $C_3H_2NSNH_2^+$), 85 (30, $C_3H_3NS^+$).

2-Methylimino-3-methyl-2,3,4,5,6,7-hexahydrobenzothiazole **10a**

As in the preparation of **8a**, 1.16 g (11 mmol) N,N'-dimethylthiourea are reacted with 1.33 g (10 mmol) **1a**. Crude yield 80%; distillation and crystallization from pentane gives 1.22 g (67%), m.p. 65° (lit[20] 67°) b.p. 72–73°/0.002 Torr. (Found: C, 59.43; H, 8.01; N, 15.52; Calc. for $C_9H_{14}N_2S$ (182.29): C, 59.30; H, 7.74; N, 15.37%. IR (KBr): ν = 2845, 2765, 1650, 1612, 1382, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.78 (m, 4H, –CH_2–CH_2–), 2.35 (m, 4H, –CH_2–C=C–CH_2–), 2.99 (s, 3H, N–CH_3), 3.17 (s, 3H, C=N–CH_3) ppm. ^{13}C-NMR ($CDCl_3$): δ = 21.95 (CH($\underline{C}H_3$)$_2$, 30.71 ($\underline{C}$H C-7), 29.80 (NCH_3), 40.71 (C=NCH_3), 105.25 (C-8), 132.07 (C-9), 160.96 (C-2) ppm. MS (70 eV): *m/e*(%) = 184 (6, M + 2), 183 (14, M + 1), 182 (100, M^+), 167 (86, M^+–CH_3), 153 (22, M^+–C_2H_5), 152 (19, M^+-2 CH_2), 140, (71, $C_7H_{10}NS^+$), 113 (21, $C_6H_9S^+$), 98 (10), 81 (14), 79 (10), 68 (13), 67 (16), 42 (16, $HCNCH_3^+$).

2-Methylimino-3-methyl-4-isopropyl-2,3-dihydrothiazole **10b**

As for **8a**, 1.74 g (16.5 mmol) N,N'-dimethylthiourea were reacted with 2.67 g (15 mmol) **1b**. The crude product (91% yield) was distilled to yield 2.04 g (80%) **10b**. b.p. 46°/0.005 Torr. (Found: C, 56.25; H, 8.44; N, 16.32; Calc. for $C_8H_{14}N_2S$ (170.22): C, 56.44; H, 8.29; N, 16.46%. IR (film) : ν = 2980, 2776, 1630, 1593, 1390, 1360 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.16 (d, $^3J_{HH}$ = 6.6 Hz, 6H, CH (C$\underline{H}_3$)$_2$), 2.69 (dsept, $^3J_{HH}$ = 6.6 Hz, $^4J_{HH}$ = 0.5 Hz, 1H, C$\underline{H}$ (CH_3)$_2$), 2.96 (s, 3H, N–CH_3), 3.24 (s, 3H, C=N–CH_3), 5.49 (d, $^4J_{HH}$ = 0.5 Hz, 1H, HC-5) ppm. ^{13}C-NMR ($CDCl_3$): δ = 21.30 (CH($\underline{C}H_3$)$_2$), 27.14 ($\underline{C}$H(CH_3)$_2$), 30.78 (C=NCH_3), 40.25 (NCH_3), 89.60 (C-5), 145.90 (C-4), 162.59 (C-2) ppm. MS (70 eV): *me*(%) = 172 (2, M + 2), 171 (6, M + 1), 170 (47, M^+), 169 (30), 155

(52, M^+-CH_3), 142 (21), 128 (16, $C_6H_{10}NS^+$), 127 (7, $M^+-C_3H_7$), 86 (7, $C_3H_4NS^+$), 84 (32, $C_3H_2NS^+$), 71 (13, $C_3H_3S^+$), 45 (7, HCS^+).

2-Phenylimino-3-phenyl-4-isopropyl-2,3-dihydrothiazole **10c**

As for **8a**, 2.51 g (11 mmol) N,N'-diphenylthiourea were reacted with 1.22 g (10 mmol) **1b**. The crude product (91% yield) was extracted with ether and crystallized: 2.54 g (75%) **10c**; m.p. 132°. (Found: C, 73.41;; H, 6.38; N, 9.56; Calc. for $C_{18}H_{18}N_2S$ (294.41): C, 73.43; H, 6.16; N, 9.52%. IR (KBr): ν = 2965, 2870, 1613, 1587, 1568, 1490, 1373, 1361 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.01 (d, $^3J_{HH}$ = 6.7 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.47 (dsept, $^3J_{HH}$ = 6.7 Hz, $^4J_{HH}$ = 0.8 Hz, 1H, $C\underline{H}(CH_3)_2$), 5.60 (d, $^4J_{HH}$ = 0.8 Hz, 1H, HC-5), 6.8–7.6 (m, 10 H, 2 C_6H_5) ppm. ^{13}C-NMR ($CDCl_3$): δ = 21.43 ($CH(\underline{C}H_3)_2$), 27.14 ($\underline{C}H(CH_3)_2$), 91.29 (C-5), 121.55, 122.72, 128.30, 129.08, 129.27 (o, m, p-C), 137.72 (C=NC_{ipso}), 145.58 (NC_{ipso}), 152.07 (C-4), 161.22 (C-2) ppm. MS (70 eV): *m/e*(%) = 296 (4), 295 (14), 294 (60, M^+), 293 (49), 279 (13, M^+-CH_3), 203 (16), 146 (85, $C_{10}H_{12}N^+$), 104 (100, $C_6H_5NCH^+$), 77 (86, $C_6H_5^+$), 51 (24), 45 (16, HCS^+).

2-Amino-4,5,6,7-tetrahydrobenzoselenazole **11a**

A soln of 1.00 g (8.7 mmol) selenourea in 20 ml methanol was slowly added to 1.06 g (8.0 mmol) **1a** in 5 ml methylene chloride at 0° and with exclusion of light. Then 1.2 g (12 mmol) triethylamine was added and the mixture stirred at room temp for 1 day. After filtering and evaporation of the solvent the residue was extracted with ether to yield 1.38 g (90%) crude product which was purified by sublimation to give 0.80 g (52%) **11a**; m.p. 125.5° (lit[22] 126°), b.p. 110°/0.001 Torr (subl.). (Found: C, 42.48; H, 5.13; N, 13.94; Calc. for $C_7H_{10}N_2Se$ (201.13): C, 41.80; H, 5.01; N, 13.93%. IR (KBr): ν = 3368, 3282, 2936, 2856, 1638, 1590, 1534, 1442 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.6–2.0 (m, 4H, $-CH_2-CH_2-$), 2.3–2.8 (m, 4H, $-CH_2-C{=}C-CH_2$), 5.72 (s, 2H, $-NH_2$) ppm. ^{13}C-NMR ($CDCl_3$): δ = 22.99, 23.89, 25.45, 27.40 (C-4, C-5, C-6, C-7), 123.11 (C-8), 145.51 (C-9), 167.19 (C-2) ppm. MS (70 eV): *m/e*(%) = 202 (86, M^+), 174 (66, $M^+-C_2H_4$), 121 (100, M^+-SeH), 160 (17, $C_6H_8Se^+$) (masses refer to ^{80}Se).

2-Amino-4-isopropylselenazole **11b**

As for the preparation of **11a**, 1.00 g (8.7 mmol) selenourea are reacted with 0.97 g (8.0 mmol) **1b**. The crude product (1.58 g: contains 96% yield) was distilled to give 1.25 g (83%) **11b**; m.p. 49–54°; b.p. 71–73°/0.003 Torr. (Found: C, 38.18; H, 5.47; N, 15.13; Calc. for $C_6H_{10}N_2Se$ (189.12): C, 38.10; H, 5.53;, N, 14.38%. IR (KBr): ν = 3425, 3240, 3100, 2955, 2920, 2870, 1605, 1515 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.19 (d. $^3J_{HH}$ = 6.8 Hz, 6H, CH ($C\underline{H}_3)_2$), 2.77 (dsept, $^3J_{HH}$ = 6.8 Hz, $^4J_{HH}$ = 0.7 Hz, 1H, $C\underline{H}$ ($CH_3)_2$), 6.0 (s, 2H, $-NH_2$), 6.52 (d, $^4J_{HH}$ = 0.7 Hz, 1H, C=CH). ^{13}C-NMR ($CDCl_3$): δ = 22.08 (s, $CH(\underline{C}H_3)_2$), 31.82 (s, $\underline{C}H$ ($CH_3)_2$), 103.43 (s, d, ^{1}J (^{13}C-^{77}Se) = 93.8 Hz, C-5), 159.73 (s, C-4), 169.73 (s, d, ^{1}J (^{13}C-^{77}Se) = 124.0 Hz, C-2) ppm. MS (70 eV): *m/e*(%) = 190 (62, M^+), 175 (100, M^+-CH_3), 162 (23, $M^+-C_2H_4$), 148 (19, $MH^+-C_3H_7$), 133 (52, $C_3H_3NSe^+$), 93 (26, $HCSe^+$) (masses refer to ^{80}Se).

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