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A Proton Magnetic Resonance Study of 2-Amino-1,3,4-thiadiazoles, 2-Amino-1,3,4-selenadiazoles, 4,5-Dihydro-1,2,4-triazole-5-thiones, and 4,5-Dihydro-1,2,4-triazole-5-selones

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The ^{1}H NMR spectra of a series of 2-amino-1,3,4-thiadiazoles (I), 2-amino-1,3,4-selenadiazoles (II), 4,5-dihydro-1,2,4-triazole-5-thiones (III), and 4,5-dihydro-1,2,4-triazole-5-selones (IV) have been studied at 60 MHz. Furthermore, the ^{13}C – H satellite spectra of the ring protons (R^2 = H) and the ^{77}Se···H satellite spectra of II have been investigated. The signals from the ring protons (R^2 = H) were found at lower field in the selenium compounds than in the corresponding sulfur compounds. The solvent shifts (CCl_4 to benzene) indicate that a solvent complex of the π-type is formed in benzene. The concentration and temperature dependence of the chemical shifts of the *N*-H protons indicates that these protons are involved in intermolecular hydrogen bonding. The compounds I – IV form complexes with dimethyl sulfoxide but are self-associated in chloroform.

In recent years many studies of the ^{1}H NMR spectra of five-membered heterocycles have been reported, including comparisons among Group VI heterocycles, *e.g.* the furan, thiophene, and selenophene series,[1,2] the benzoxa-, thia-, and selenazole series,[3–5] and the 1,2,5-oxa-, thia-, and selenadiazole series.[6,7] It has been found that the signals of the ring protons are progressively displaced to lower field as the heteroatom is varied from O to S to Se. Recently the ^{1}H NMR spectrum of 1,3,4-selenadiazole has also been reported.[8]

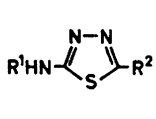
This communication reports the ^{1}H NMR parameters of a series of 2-amino-1,3,4-thiadiazoles (I), 2-amino-1,3,4-selenadiazoles (II), 4,5-dihydro-1,2,4-triazole-5-thiones (III), and 4,5-dihydro-1,2,4-triazole-5-selones (IV), including concentration and solvent dependence and ^{77}Se···H and ^{13}C – H coupling constants. The spectra of the compounds I – IV with $R^1 = CH_3$ and R^2 = H have already been briefly reported.[9]

Both the selenadiazoles (II) and the triazoleselones (IV) were prepared from selenosemicarbazides.[10] The selenadiazoles are unambiguously identified by the observation of ^{77}Se···H coupling constants (56 Hz) when R^2 = H.

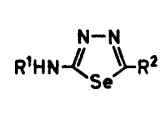
Table 1. The ^{1}H NMR parameters of 2-amino-1,3,4-thiadiazoles (I), 2-amino-1,3,4-selenadiazoles (II), 1,2,4-triazole-5-thiones (III) and 1,2,4-triazole-5-selones (IV).[a]

Compound	Chemical shifts of *N*-H protons				Chemical shifts *b* of protons from R^1				Chemical shifts of protons from R^2			
	I	II	III	IV	I[c]	II[c]	III	IV	I	II[d]	III	IV
a	410–455	415–455	750–810	760–860					512s	552s+d $^2J=55.5$	485s	498s
b	405–425	415–435	750–800	770–830					148s	150s+d $^3J=6.5$	140s	140s
c	430–450	440–460	810–850	810–880					440–470m	440–470m	445–490m	445–490m
d	445–475	450–480	790–830	770–810	174d	174s	207s	213s	517s	556s+d $^2J=57.0$	502s	511s
e	430–455	430–460	770–800	730–810	171d	178s	208s	210s	147s	146s+d $^3J=6.8$	144s	145s
f	450–480	450–480	810–840	840–870	178d	177s	218s	223s	440–475m	440–470m	445–465m	445–465m
g	445–475	450–475	805–840	820–870	229[e]	230[e]	280sep	287sep	516s	552s+d $^2J=55.5$	515s	525s
h	440–460	450–465	780–820	700–900	84s	84s	103s	94s	514s	554s+d $^2J=56.0$	502s	510s
i	430–445	445–460	780–810	810–850	82s	82s	109s	113s	148s	149s+d $^3J=7.0$	148s	151s
j	445–460	455–475	780–820	830–870	190–230m	200–230m	230–270m	240–280m	510s	552s+d $^2J=56.0$	509s	520s
k	430–450	440–460	770–800	810–840	190–230m	195–235m	255–290m	260–300m	147s	150s+d $^3J=7.5$	146s	149s
l	450–475	465–485	815–835	700–900	190–240m	190–235m	245–280m	250–280m	440–475m	440–485m	451s	452s

Notes, see p. 461.



I



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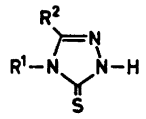
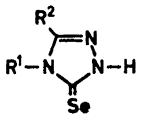


III



IV

I–IV	a	b	c	d	e	f
R^1	H	H	H	CH_3	CH_3	CH_3
R^2	H	CH_3	C_6H_5	H	CH_3	C_6H_5

I–IV	g	h	i	j	k	l
R^1	$(CH_3)_2CH$	$(CH_3)_3C$	$(CH_3)_3C$	C_6H_{11}	C_6H_{11}	C_6H_{11}
R^2	H	H	CH_3	H	CH_3	C_6H_5

Furthermore, the chemical shifts of R^2 (=H), *N*-H, and *N*-CH protons allow differentiation between diazole and triazole structures (*cf.* Table 1). The observation of coupling between the *N*-H protons and the α-protons of R^1 shows that the diazoles, at least at temperatures where the exchange of the *N*-H protons is slow, have the amino structure (I or II) and not the tautomeric iminodiazoline structure. The tautomeric *Se*-H form of IV could not be detected in the IR or NMR spectra (these compounds form Se-methyl derivatives upon treatment with CH_3I; *cf.* Table 4).

RESULTS AND DISCUSSION

The chemical shifts of the compounds I – IV (a – l) and the $^{77}Se\cdots H$ coupling constants of II are given in Table 1. In the diazole series, I and II, the signals of the ring protons (R^2 = H) are found at lower field for the selenadiazoles than

[a] The spectra were recorded with field sweep at 60 MHz using 5– 10 % solutions in DMSO-d_6 at *ca.* 40°C with TMS as internal reference. Chemical shifts and coupling constants are given in Hz.

[b] Only the chemical shifts of the α-protons of R^1 are listed, except for compounds I– IV h and i for which the chemical shifts of the *tert*butyl protons are given. s=singlet, d=doublet, sep=septet and m=unresolved multiplet.

[c] The observed multiplicity, spacing and line width of the signal from R^1 are dependent on temperature and concentration owing to exchange of the *N*-H protons. The values of ^3J(HCNH) without exchange is 4.8 Hz.

[d] The signals from R^2=H and CH_3 appear as a singlet corresponding to the selenium isotopes with $I=0$ and a doublet corresponding to the 7.5 % abundance of ^{77}Se with $I=\frac{1}{2}$. The coupling constants listed in the table are $^2J(^{77}SeCH)$ and $^3J(^{77}SeCCH)$.

[e] The signal appears as a sextet owing to coupling to the methyl protons and the *N*-H proton with nearly the same coupling constants. The outer lines were indistinguishable from the noise.

for the thiadiazoles, a difference opposite to that expected from the electronegativity of the Group VI elements. The deshielding of the ring proton of the selenadiazoles compared to that of the thiadiazoles may be rationalized in terms of mesomeric changes in charge distribution, probably conjoined with increases from S to Se in the deshielding effect of the diamagnetic anisotropy of the ring and in the paramagnetic contribution from the heteroatom.

The ring protons ($R^2 = H$) of the diazoles are less shielded than those of the triazoles, with the selenium compounds (II, IV) exhibiting the greatest chemical shift difference. This fact supports the assumption that one of the main reasons for the low-field displacement of the ring protons of the selenadiazoles is the diamagnetic anisotropy of the ring system.

The *o*-protons (at lowest field) of $R^2 = C_6H_5$ can be distinguished from the *m*- and *p*-protons in the spectra of all diazoles (I, II) and the triazoles with $R^1 = H$ (IIIc, IVc). In the triazoles, the line width of the signal from $R^2 = C_6H_5$ decreases with increasing steric requirement of the R^1 group, probably as a result of a twisting of the phenyl group.

The chemical shifts (at 60 MHz) of the ring protons of selenophene,[1] benzoselenazole,[3] 1,2,5-selenadiazole,[7] and 1,3,4-selenadiazole [8] are listed in Table 5 and show that the introduction of the nitrogen atoms causes a shift towards lower field of *ca.* 130 Hz for protons at both the 2- and the 3-positions. As expected from the mesomeric effect of an amino moiety, the signals from the ring protons of the 2-amino-1,3,4-selenadiazoles are found at *ca.* 40 Hz higher field than those of the unsubstituted compound.

The ^{77}Se (natural abundance 7.5 %, $I = \frac{1}{2}$) satellite spectra could be detected in the ^1H NMR spectra of the selenadiazoles (II) for $R^2 = H$ or CH_3. No long range $^{77}Se \cdots H$ splittings (with the nuclei more than three bonds apart) could be detected for the diazoles (II) or the triazoles (IV). The values of ^2J ($^{77}Se \cdots H$) and ^3J ($^{77}Se \cdots H$) for II ($R^2 = H$ or CH_3) are listed in Table 1 and are of the same magnitude as found for other aromatic selenaheterocycles (*cf.* Table 5).

The values of the $^{13}C - H$ coupling constants of the ring protons are of the same magnitude for all the compounds I – IV (Table 3). The values of the $^{13}C - H$ coupling constants are sensitive to, among other influences, the electronegativity of the substituents and the geometry of the molecules (see, *e.g.*, Ref. 2 and references cited therein). Because of the differences in arrangement of the electronegative elements, the $^{13}C - H$ coupling constants cannot be used as the basis for comparison between the geometry of the diazoles and that of the triazoles. The difference in electronegativity between S and Se is very small, and the similarity of the $^{13}C - H$ coupling constants for the thiadiazoles (I) and the selenadiazoles (II) may indicate that the geometry of the molecules is the same, although a comparison of this type may be hazardous due to, *e.g.*, changes in excitation energies. The ring $^{13}C - H$ coupling constants of the selenadiazoles have, within one Hz, the same value as those of benzoselenazole and 1,3,4-selenadiazole (*cf.* Tables 3 and 5).

The ^1H NMR spectra of the compounds I – IV are solventdependent. Corresponding S and Se compounds exhibit the same dependence (Table 2). As is also observed for, *e.g.*, protons in the 2-positions of oxazoles,[11] the signals from R^2 (= H or CH_3) of the compounds I – IV are shifted towards higher

Table 2. Solvent dependence of the ^1H NMR spectra of 2-cyclohexylamino-1,3,4-thiadiazoles (Ij,k) and 4-cyclohexyl-1,2,4-triazole-5-thiones (IIIj,k).[a]

Compound	Solvent	Chemical shifts in Hz		
		*N*CH protons	=C−H protons	=C−CH$_3$ protons
Ij	DMSO d_6	190−230 m	510 s	
	$CDCl_3$	195−220 m	501 s	
	Benzene	175−205 m	466 s	
	CCl_4	170−200 m	489 s	
IIIj	DMSO d_6	230−270 m	509 s	
	$CDCl_3$	250−290 m	474 s	
	Benzene	240−280 m	420 s	
	CCl_4	250−280 m	462 s	
Ik	DMSO d_6	190−230 m		147 s
	$CDCl_3$	190−220 m		158 s
	Benzene	175−205 m		130 s
	CCl_4	170−200 m		152 s
IIIk	DMSO d_6	255−290 m		146 s
	$CDCl_3$	270−305 m		155 s
	Benzene	270−305 m		119 s
	CCl_4	270−300 m		147 s

[a] The chemical shifts are given in Hz (at 60 MHz) relative to TMS.

field by charging the solvent from CCl_4 to benzene. This probably indicates that a complex, of the π-type, is formed between the azoles and the benzene molecules with R^2 placed in the shielding area of the diamagnetic anisotropy of the benzene molecules.

The signals from the *N*-H protons of the compounds I−IV exhibit a shift towards higher field on dilution of the samples with $CDCl_3$, indicating intermolecular hydrogen bonding (solute−solute), which for the diazoles may tentatively be of the type shown by V.

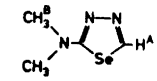
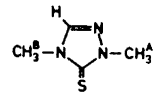
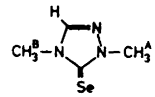
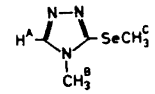
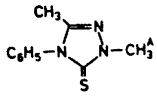
In DMSO the chemical shifts of the *N*-H protons of I−IV are nearly independent of the concentration, which indicates no solute-solute complex

Table 3. $^{13}C-H$ coupling constants for diazoles (I, II) and triazoles (III, IV).[a]

Compound	IIIh	Ii	IIi	IIIi	Ij	IIj	IVj	IIIk	IVk
$^1J(=^{13}C-H)$	213.58				213.51	213.11	215.77		
$^1J(=C-^{13}C-H)$		129.84	129.56	130.89				130.80	131.08

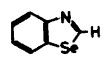
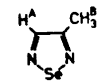
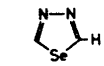
[a] The $^{13}C-H$ coupling constants are given in Hz.

Table 4. ^{1}H NMR parameters for additional *N*- or *Se*-substituted diazoles and triazoles.[a]

Compound	Chemical shift	^{77}Se···H coupling constants
	A: 550 B: 192	A: 58.5
	A: 230 B: 217	
	A: 234 B: 222	
	A: 493 B: 219 C: 157	C: 11.5
	A: 229 [b]	

[a] The chemical shifts are given in Hz (in $CDCl_3$, at 60 MHz) relative to TMS as internal reference. The coupling constants are in Hz.
[b] From Ref. 16.

Table 5. Proton chemical shifts, ^{77}Se···H, and ^{13}C–H coupling constants for aromatic selenaheterocycles.[a]

Compound	Chemical shift	$J(^{77}Se\cdots H)$	$J(^{13}C-H)$	Ref.
	A: 462.0 B: 427.2	A: 48 B: 9.5	A: 187.23 B: 164.62	1, 2
	591.5		214	3
	A: 542.4 B: 151.8	A: 28.8	A: 184.3 B: 129.0	6
	597.6	55.3	214.3	8

[a] The chemical shifts are given in Hz (at 60 MHz) relative to TMS. The coupling constants are in Hz.

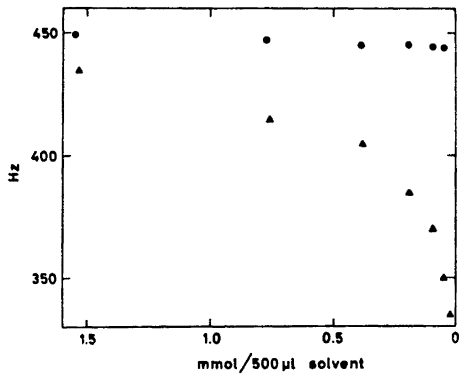


Fig. 1. The dependence of the chemical shift of the *N*-H proton of 2-methylamino-5-methyl-1,3,4-thiadiazole (Ie) on concentration at *ca.* 40°C. ○: In DMSO-d_6. △: In $CDCl_3$.

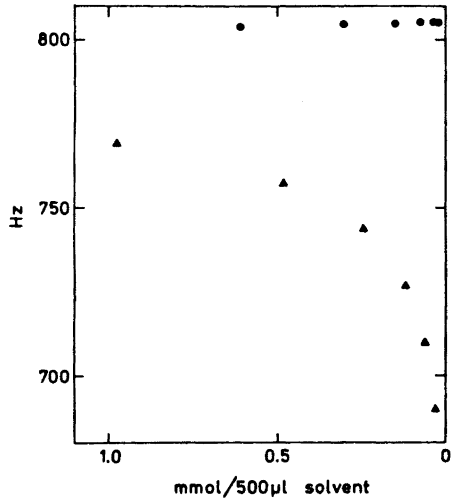
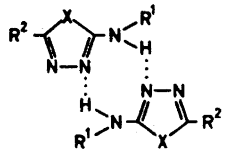
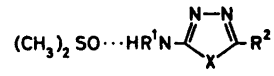


Fig. 2. The dependence of the chemical shift of the *N*-H proton of 3-methyl-4-*cyclo*-hexyl-1,2,4-triazole-5-thione (IIIk) on concentration at *ca.* 40°C. ○: In DMSO-d_6. △: In $CDCl_3$.

formation in this solvent. The *N*-H protons are, however, in view of the low-field chemical shift and the observed broad IR absorption at *ca.* 3250 cm^{-1} (in DMSO-d_6 for the diazoles), undoubtedly involved in hydrogen bonding, probably within a solvent-solute complex (shown in VI for the diazoles). A similar solute-DMSO association has been observed for pyrrole.[12] The typical concentration effects in $CDCl_3$ and in DMSO-d_6 are shown in Fig. 1 for the diazoles and in Fig. 2 for the triazoles.



V X = S, Se



VI

As is usually observed when *N*-H protons are involved in hydrogen bonding, the signals are shifted towards higher field with increasing temperature for both $CDCl_3$ and DMSO-d_6 solutions (*cf.* Fig. 3).

When the exchange rate of the *N*-H protons of the diazoles (I, II) is slow on the NMR scale, the signals from, *e.g.*, the *N*-CH_3 protons are split owing to coupling with the *N*-H protons. The rate constants for the exchange of the

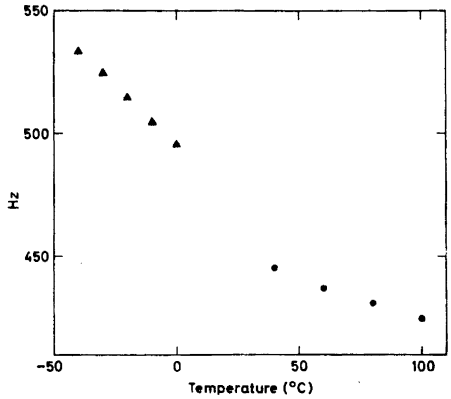


Fig. 3. The dependence of the chemical shift of *N*-H protons on temperature. ○, 2-Methylamino-5-methyl-1,3,4-thiadiazole (Ie) in DMSO-d_6 (0.5 mmol/500 μl). △, 2-Methylamino-1,3,4-thiadiazole (Id) in $CDCl_3$ (0.5 mmol/500 μl).

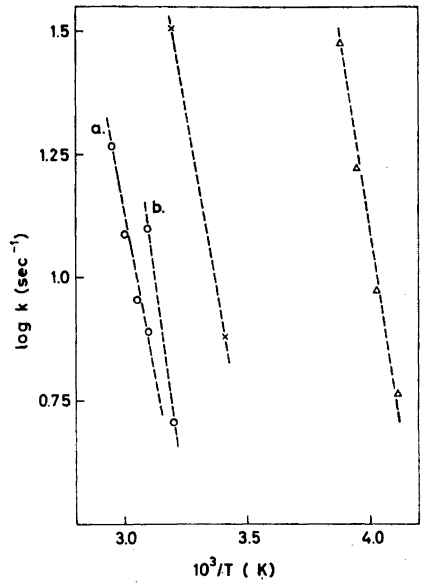


Fig. 4. The dependence of the rate constants (k) for exchange of the *N*-H protons on temperature (T), solvent, and concentration (mmol/500 μl solvent). △, 2-Methylamino-1,3,4-thiadiazole (Id, 0.5 mmol) in $CDCl_3$. ○, 2-Methylamino-1,3,4-thiadiazole (Ie) in DMSO-d_6: a, 0.15 mmol; b, 0.31 mmol. ×, 2-Methylamino-5-methyl-1,3,4-selenadiazole (IIe, 0.08 mmol) in DMSO-d_6.

N-H protons may be found from the line shape of the signals from the *N*-CH_3 protons at temperatures where the signals are exchange-broadened. The exchange rates for the diazoles Id, Ie, and IIe are shown in Fig. 4. As expected, the exchange rates increase with temperature. At a given temperature the exchange rates are much faster in $CDCl_3$ than in DMSO-d_6, in accord with the difference in association in the two solvents. Furthermore, the exchange rate decreases with decreasing concentration and is faster for the selenium compounds than for the sulfur compounds. In order to obtain further information on the association of the compounds in solution, the ^1H NMR spectra of the 2-methylamino-1,3,4-thiadiazoles were also investigated in CCl_4, CD_3CN, CD_3NO_2, $(CD_3)_2CO$, benzene, and pyridine. None of these solvents produced the same effects as DMSO, *e.g.* observable HCNH coupling at room temperature. The presence of a diazole-DMSO was further substantiated by the observation of increasing broadening, due to HCNH coupling, of the signal from the *N*-CH_3 protons when a DMSO-d_6 solution of, *e.g.*, Ie was gradually added to a $CDCl_3$ solution of the same compound at *ca.* 40°C.

No restricted rotation about the C(2)–N bonds of I, II, or 2-dimethylamino-1,3,4-selanadiazole could be detected at low temperature in $CDCl_3$ or in DMSO-d_6.

EXPERIMENTAL

All compounds gave satisfactory analyses as well as IR and ^1H NMR spectra in agreement with the assigned structures. The preparation of the selenium compounds will be reported elsewhere.[10] The 2-amino-1,3,4-thiadiazoles (I) were prepared according to the method of Ohta and Higashijima,[13] and the 4,5-dihydro-1,2,4-triazole-5-thiones (III) according to Kröger, Sattler, and Beyer.[14]

The ^1H NMR spectra were recorded at 60 MHz on a Varian A60A spectrometer equipped with a variable temperature controller (V6040) and a decoupling unit (V6058A). The $^{13}C-H$ coupling constants were determined by matching with sidebands generated by a Wavetek oscillator (VCG116), and the frequency was measured by a Hewlett-Packard frequency counter (5216A). Deuteration and decoupling experiments have been utilized to verify that the splitting of, *e.g.*, the signals from the methyl protons of the 2-methylaminodiazoles in DMSO and in $CDCl_3$ at low temperatures, is caused by coupling with the *N*-H protons and not by differences in structure or conformation.

The rate constants given in Fig. 4 for exchange of the *N*-H protons of the diazoles were estimated from the line widths $\delta\omega_{\frac{1}{2}}$ or the peak separations $\delta\omega_e$ of the signals from the *N*-CH_3 protons by the method of Takeda and Stejskal,[15] *i.e.* from a graph of $\delta\omega_{\frac{1}{2}}/\delta\omega$ or $\delta\omega_e/\delta\omega$ *versus* $\tau\delta\omega$.

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