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On the Discrimination of Tetrazole Regioisomers by NOE Difference Spectroscopy

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Summary. The unambiguous discrimination between 1-substituted and 2-substituted tetrazoles as well as between 1,5- and 2,5-disubstituted tetrazoles by means of homonuclear NOE difference spectroscopy is described.

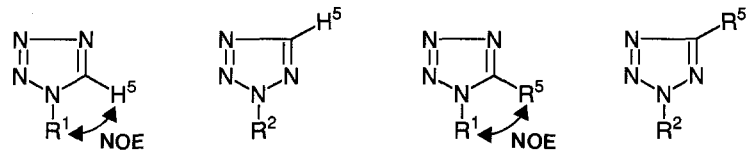
Keywords. N-Substituted tetrazoles; Nuclear Overhauser effect; Difference spectroscopy; ^{13}C-NMR Spectroscopy.

Zur Unterscheidung regioisomerer Tetrazole mittels NOE Differenzspektroskopie

Zusammenfassung. Die Unterscheidung zwischen 1-substituierten und 2-substituierten bzw. zwischen 1,5- und 2,5-disubstituierten Tetrazolen mittels NOE Differenzspektroskopie wird beschrieben.

Introduction

The tetrazole moiety is a substructure of many biologically active compounds. Thus, for instance, a number of antibacterial agents, analeptics, antiinflammatory agents, antilipemics and antiallergics contain this heteroaromatic system [2–4]. Tetrazole derivatives are also used in agriculture and in photography, moreover they are essential components of explosives, rocket propellants and plastics [2]. Some widely used approaches for the synthesis of N-substituted (C,N-disubstituted) tetrazoles, e. g. the cycloaddition of covalent azides with nitriles or the alkylation of NH-tetrazoles [2, 3], can lead either to 1-substituted (**A**) (1,5-disubstituted, **C**) or 2-substituted (**B**) (2,5-disubstituted, **D**) products. In many cases, mixtures of both possible stereoisomers are obtained from such reactions. Thus, simple and reliable spectroscopic methods for the discrimination of tetrazole regioisomers (**A** versus **B**, **C** versus **D**) are required.



A **B** **C** **D**

Apart from mass spectral fragmentation patterns, mainly a number of different proton and ^{13}C-NMR approaches have been employed for this purpose, using chemical shift considerations, long-range spin coupling constants, and solvent effects [2, 3]. However, some of these methods suffer from certain limitations and disadvantages; e. g. all methods based on comparison of chemical shifts are not reliable if only one isomer is at hand.

Recently, we proposed homonuclear NOE difference spectroscopy [5] as a convenient tool for spectral and structural assignments with various N-substituted pyrazoles [6], 1,2,3-triazoles [7] and 1,2,4-triazoles [8]. In continuation of these investigations, this study shall demonstrate the utility of the NOE approach also for the unambiguous discrimination between tetrazole regioisomers as given in Tables 1 and 2, employing through-space connectivities between suitable protons of R^1 and H-5 (**A**) or R^1 and R^5 (**C**), respectively.

Table 1. 1 *H*-Tetrazoles investigated

No.	R^1	R^5	Ref. prep.
1	Me	H	[9]
2	Me	SCH_2Ph	[10]
3	Me	4-pyridyl	[a]
4	CH_2Ph	H	[11]
5	CH_2COOEt	H	[12]
6	CH_2COOEt	4-pyridyl	[a]
7	CH_2COOH	H	[12]
8	$CH_2OCH_2CH_2SiMe_3$[b]	H	[a]
9	CPh_3	H	[13]
10	Ph	H	[14]
11	Ph	SMe	[15]
12	$SiMe_3$	H	[16]
13	COMe	H	[17]
14	SO_2 mesityl	H	[18]

[a] see Experimental
[b] = SEM

Table 2. 2 *H*-Tetrazoles investigated

No.	R^2	R^5	Ref. prep.
15	Me	H	[9]
16	Me	4-pyridyl	[a]
17	Me	[b]	[a]
18	CH_2Ph	H	[11]
19	CH_2COOEt	H	[12]
20	CH_2COOEt	4-pyridyl	[a]
21	$CH_2OCH_2CH_2SiMe_3$[c]	H	[a]

[a] see Experimental
[b] N-methyl-4-pyridylium iodide (see Scheme 1)
[c] = SEM

Table 3. ^{1}H-NMR data (δ, ppm) and NOE data of compounds investigated

No.	Solvent[a]	R^1 (R^2)	R^5	Irrad. reson.	NOE on[b]	Ref. NMR
1	A	4.12 (CH_3)	8.69	NCH_3	H-5	[9, 19]
	B	4.09 (CH_3)	9.30	NCH_3	H-5	–
2	B	3.82 (CH_3)	7.43–7.23 (Ph), 4.50 (CH_2)	CH_2	CH_3	–
3	A	4.25 (CH_3)	8.88 (pyr-2,6), 7.69 (pyr-3,5)	NCH_3	pyr-3,5	–
	B	4.22 (CH_3)	8.84 (pyr-2,6), 7.86 (pyr-3,5)	NCH_3	pyr-3,5	–
4	A	7.40–7.29 (Ph), 5.59 (CH_2)	8.52	NCH_2[c]	H-5 (Ph)	–
	B	7.36 (Ph), 5.71 (CH_2)	9.51	NCH_2[c]	H-5 (Ph)	–
5	A	5.26 (NCH_2), 4.28 (OCH_2), 1.29 (CH_3)	8.82	NCH_2[c]	H-5	[20]
	B	5.54 (NCH_2), 4.19 (OCH_2), 1.22 (CH_3)	9.39	NCH_2[c]	H-5	–
6	A	5.24 (NCH_2), 4.25 (OCH_2). 1.25 (CH_3)	8.84 (pyr-2,6), 7.59 (pyr-3,5)	NCH_2	pyr-3,5	–
	B	5.74 (NCH_2), 4.11 (OCH_2), 1.10 (CH_3)	8.83 (pyr-2,6), 7.77 (pyr-3,5)	NCH_2	pyr-3,5	–
7	B	5.38 (NCH_2)	9.35	NCH_2	H-5	[20]
8	A	5.78 (NCH_2), 3.62 (OCH_2), 0.91 (CH_2Si), −0.02 (CH_3)	8.78	NCH_2	H-5 (OCH_2)	–
	B	5.82 (NCH_2), 3.59 (OCH_2), 0.83 (CH_2Si), −0.07 (CH_3)	9.59	NCH_2	H-5 (OCH_2)	–
9	A	7.50–7.00 (Ph)	8.44	Ph	H-5	[13]
10	A	7.80–7.50 (Ph)	9.02	Ph	H-5	[21]
	B	7.98–7.55 (Ph)	10.08	Ph[c]	H-5	–
11	B	7.65 (Ph)	2.76	Ph	CH_3	[15]
12	A	0.64 ($SiCH_3$)	8.64	$SiCH_3$	H-5	[22]
13	A	2.92 (CH_3)	9.24	CH_3	–	[19, 22]
14	A	7.07 (Bz-3,5), 2.69 (2,6-*Me*), 2.35 (4-*Me*)	9.13	2,6-*Me*	H-5	–
15	A	4.36 (CH_3)	8.46	NCH_3	–	[9]
	B	4.37 (CH_3)	8.91	NCH_3	–	[22]
16	A	4.44 (CH_3)	8.77 (pyr-2,6), 8.00 (pyr-3,5)	NCH_3	–	–
	B	4.46 (CH_3)	8.77 (pyr-2,6), 7.97 (pyr-3,5)	NCH_3	–	–
17	B	4.54 (CH_3)	9.14 (pyr-2,6), 8.67 (pyr-3,5)	NCH_3	–	–
			4.41 (pyr-1-CH_3)	pyr-1-*Me*	pyr-2,6	–

Table 3. *(continued)*

No.	Solvent[a]	R^1 (R^2)	R^5	Irrad. reson.	NOE on[b]	Ref. NMR
18	A	7.37 (Ph), 5.79 (CH_2)	8.50	NCH_2	−(Ph)	[11]
	B	7.36 (Ph), 5.95 (CH_2)	8.97	NCH_2	−(Ph)	−
19	A	5.44 (NCH_2), 4.28 (OCH_2), 1.27 (CH_3)	8.57	NCH_2	−	[20]
	B	5.84 (NCH_2), 4.20 (OCH_2), 1.20 (CH_3)	9.04	NCH_2	−	−
20	A	5.48 (NCH_2), 4.30 (OCH_2), 1.30 (CH_3)	8.77 (pyr-2,6), 8.02 (pyr-3,5)	NCH_2	−	−
	B	5.95 (NCH_2), 4.22 (OCH_2), 1.22 (CH_3)	8.79 (pyr-2,6), 8.00 (pyr-3,5)	NCH_2	−	−
21[d]	A	5.92 (NCH_2), 3.69 (OCH_2), 0.93 (CH_2Si), −0.02 (CH_3)	8.56	NCH_2	−(OCH_2)	−
	B	5.99 (NCH_2), 3.65 (OCH_2), 0.84 (CH_2Si), −0.07 (CH_3)	9.04	NCH_2	−(OCH_2)	−
22[d]	C	−	8.66 (pyr-2,6), 8.33 (pyr-3,5) 4.20 (pyr-1-CH_3)	NCH_3	pyr-2,6	−
	D	−	8.79 (pyr-2,6), 8.40 (pyr-3,5) 4.42 (pyr-1-CH_3)	NCH_3	pyr-2,6	−

[a] A: $CDCl_3$ B: *DMSO-d_6* C: *DMSO-d_6*/D_2O (3 : 1) D: D_2O (standard: trimethylsilylpropionic acid-d_4, sodium salt)

[b] Only strong and medium enhancements considered

[c] Entries in columns "irrad. reson." and "NOE on" can be interchanged (reverse NOE experiment perfomed)

[d] Chemical shifts strongly dependent on solvent and concentration

Results and Discussion

With 1-methyltetrazole (**1**), upon irradiation of the methyl-H resonance a marked enhancement of the tetrazole-H singlet was observed in the NOE difference spectrum (in $CDCl_3$ or *DMSO-d_6* solution), whereas in a similar experiment with 2-methyltetrazole (**15**) only a very slight effect could be detected on the signal of the heteroaromatic proton. Thus, the significant differences in the through-space connections between methyl and heteroaryl protons in methyltetrazoles **1** and **15** can be utilized for an unequivocal assignment of the substitution pattern with these compounds (for ^{1}H-NMR and NOE data compare Table 3).

In an analoguous manner (irradiation of the NCH_2 transition), unambiguous distinctions between 1-substituted and 2-substituted isomers could be performed with benzyltetrazoles **4** and **18** (Fig. 1), ethyl tetrazole acetates **5** and **19**, and *SEM*-tetrazoles **8** and **21**.

Only a sole isomer was at hand with tetrazole-1-acetic acid (**7**), with 1-trityl- (**9**), 1-phenyl- (**10**), 1-trimethylsilyl- (**12**), and 1-mesitylsulfonyltetrazole (**14**). As perturbation of the methylene-H singlet in **7**, the phenyl-H multiplets in compounds **9** and **10** or the methyl-H lines in azoles **12** and **14** always gave the corresponding azole-H singlets distinct NOEs, the 1-substitution pattern of these known compounds could be confirmed.

Expectedly, the NOE method turned out to be not suitable for assignments with N-acetyl compounds, since no clear enhancement of tetrazole H-5 could be observed upon irradiation of the methyl-H resonance of 1-acetyltetrazole (**13**). This can be easily explained by the preferential conformation of **13** with N-2 and the carbonyl-oxygen in *trans*-position [23] being unfavourable for the observation of an NOE between methyl and heteroaryl protons.

The presented NOE approach can also be applied for the discrimination between 1,5- and 2,5-disubstituted tetrazole derivatives, on condition that both substituents contain protons suitable as probes for the NOE experiments. Thus, through-space connectivities between methyl and methylene protons in compound **2**, between methyl and pyridine protons in compound **3** (Fig. 2 b), between methylene and

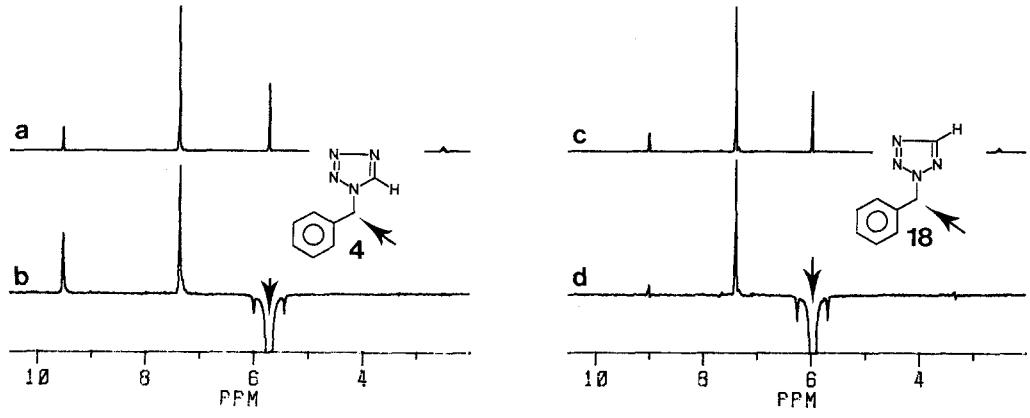


Fig. 1. a: ^{1}H-NMR spectrum of **4** (*DMSO-d_6*), **b**: NOE difference spectrum of **4** resulting from irradiation of NCH_2, **c**: ^{1}H-NMR spectrum of **18** (*DMSO-d_6*), **d**: NOE difference spectrum of **18** resulting from irradiation of NCH_2

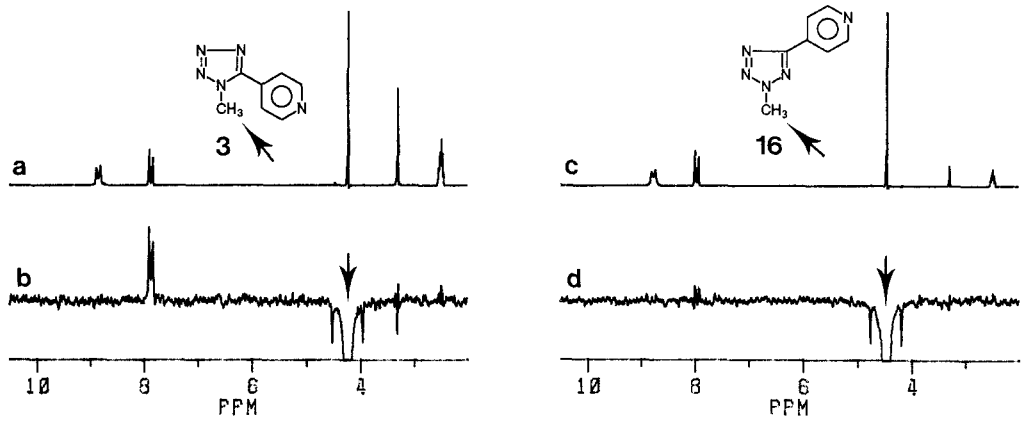
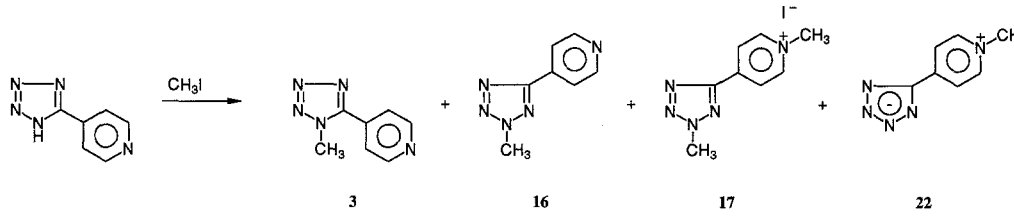


Fig. 2. **a**: ^{1}H-NMR spectrum of **3** (*DMSO-d_6*), **b**: NOE difference spectrum of **3** resulting from irradiation of CH_3, **c**: ^{1}H-NMR spectrum of **16** (*DMSO-d_6*,), **d**: NOE difference spectrum of **16** resulting from irradiation of CH_3

pyridine protons in compound **6** as well as between phenyl-H and methyl-H in azole **11** permit the assignment of an 1,5-disubstitution pattern to these tetrazoles. On the other hand, the lack of an NOE [24] on pyridine protons 3 and 5 upon irradiation of the azole-N-methyl resonances in species **16** and **17** as well as upon perturbation of the NCH_2 resonance in **20** calls for 2,5-disubstitution of **16** (Fig. 2 d), **17**, and **20**. Additionally, NOE difference experiments permit the unequivocal assignment of methyl-H resonances in pyridinium salt **17** and in ylide **22**. These compounds were obtained as main components together with **3** and **16** from reaction of 5-(4-pyridyl)-1 *H*-tetrazole with iodomethane (Scheme 1) [25].



Scheme 1

It should be mentioned that in principle NOE information could have been also obtained via 2D-NOESY spectra, however, this approach is known to be less suitable for small molecules and therefore no attempts were made with the present compounds.

The structures of most compounds (including novel structures **3**, **8**, **16**, **17**, **20**, **21**) were further confirmed by ^{13}C-NMR spectra [26]. Particularly long-range couplings of tetrazole C-5 to protons of the N-1 substituent (derived from fully ^{1}H-coupled ^{13}C-spectra) turned out to be helpful in the independent identification of N-1 substitution patterns.

In conclusion, NOE difference spectroscopy provides a powerful and convenient tool for the determination of the substitution pattern with various tetrazoles. Since assignments can be made within a few minutes and also in cases when only one

isomeric form is at hand, this approach seems to be the method of choice for many N-alkyl and N-aryl tetrazoles.

Experimental Part

The novel tetrazole derivatives **3**, **6**, **8**, **16**, **17**, **20**, and **21** were synthesized as described below. All other compounds were prepared according to known procedures given by the references in Tables 1 and 2. Melting points (uncorrected) were determined on a Reichert-Kofler hot-stage microscope. Elemental analyses were carried out by Mikroanalytisches Laboratorium, Institute of Physical Chemistry, University of Vienna. Column chromatography was carried out using Merck Kieselgel 60 (70 – 230 mesh) as stationary phase. The IR spectra (KBr pellets or dichloromethane solutions) were recorded on a Jasco IRA-1 spectrometer. GLC/MS analyses were carried out on a Hewlett-Packard 5890 A/5970 B-GC/MSD instrument (70 eV), the mass spectra of compounds **17** and **22** were obtained on a Finnigan MAT 8230 (70 eV). For the acquisition of the ^{13}C-NMR spectra of compounds **3**, **16**, and **17** a Bruker AM 400 WB spectrometer was used (spectrometer frequency for ^{13}C: 100.61 MHz), all other NMR spectra described were recorded on a Bruker AC 80 instrument (80.13 MHz for ^{1}H, 20.15 MHz for ^{13}C) equipped with an Aspect 3000 computer and standard software. Chemical shifts are reported in δ-units downfield from *TMS*. Homonuclear NOE difference spectra were recorded at 30°C from approx. 0.2 *M* nondegassed solutions using the frequency cycling method of Kinns and Sanders [27] (NOEMULT); acquisition parameters: 8 K data points; spectral width: 1 441 Hz; acquisition time: 2.84 s; digital resolution: 0.35 Hz/point; pulse width: 3 μs (90°); relaxation delay: 0.5 s; pre-irradiation time: 5 s; irradiation power: 55 – 59 dB below 0.2 W; number of scans: 32 – 400. ^{1}H-coupled ^{13}C-NMR spectra were obtained with the gated decoupling mode (digital resolution 0.28 Hz/point).

5-Benzylthio-1-methyl-1 H-tetrazole (**2**)

^{13}C-NMR ($CDCl_3$): δ 153.3 (tetrazole C-5), 135.5 (*Ph* C-1), 128.8 and 128.6 (*Ph* C-2,3,5,6), 127.9 (*Ph* C-4), 37.6 (CH_2), 33.11 (CH_3).

Reaction of 5-(4-Pyridyl)-1 H-tetrazole with Iodomethane

Iodomethane (4.500 g, 31.7 mmol) was successively added to a solution of 5-(4-pyridyl)-1 *H*-tetrazole [28] (1.471 g, 10 mmol) in a mixture of 10 ml 1 *N* NaOH and 10 ml of ethanol. After refluxing for 20 h, excessive iodomethane and ethanol were removed in vacuo and the remaining solution was extracted with dichloromethane (100 ml). Evaporation of the latter led to a mixture of compounds **3**, **16**, and **17**. After addition of dichloromethane (5 ml), the low soluble pyridinium salt **17** was filtered off, washed with light petroleum and dried to give 37 mg (1%) of yellow crystals. The filtrate was subjected to column chromatography (silica gel, eluent: ethyl acetate) to afford 51 mg (3%) of **16** (first fraction) and 15 mg (1%) of **3**. Evaporation of the water layer led to a residue (3.064 g) consisting mainly of sodium iodide and pyridinium compounds **17** and **22** (ratio **17**:**22** = 1.17:1 according to ^{1}H-NMR). Compound **17** could be extracted from this mixture with *DMSO*, whereas ylide **22** turned out to be nearly unsoluble in this solvent.

1-Methyl-5-(4-pyridyl)-1 H-tetrazole (**3**)

Cream crystals, m. p. 79 – 83°C (after sublimation); MS (*m/z*): 161 (M^+, 100%), 132 (24), 119 (36), 105 (50), 104 (13), 91 (12), 78 (52), 77 (13), 64 (11), 63 (15), 62 (16), 52 (15), 51 (38), 50 (14); ^{13}C-NMR (*DMSO-d*$_6$): δ 152.3 (tetrazole C-5), 150.5 (pyridine C-2,6), 131.4 (pyridine C-4), 122.7 (pyridine C-3,5), 35.3 (CH_3). Anal. calcd. for $C_7H_7N_5$ (161.17): C 52.17, H 4.38, N 43.45. Found: C 52.39, H 4.27, N 43.46.

2-Methyl-5-(4-pyridyl)-2 H-tetrazole (**16**)

Yellowish crystals, m.p. 115–118°C; MS (*m/z*): 161 (M^+, 8%), 133 (100), 132 (26), 105 (53), 104 (11), 78 (27), 77 (11), 51 (17), 50 (10); ^{13}C-NMR (*DMSO-d*$_6$): δ 162.2 (tetrazole C-5), 150.8 (pyridine C-2,6), 134.0 (pyridine C-4), 120.3 (pyridine C-3,5), 39.3 (CH_3). Anal. calcd. for $C_7H_7N_5$ (161.17): C 52.17, H 4.38, N 43.45. Found: C 52.44, H 4.24, N 43.21.

N-Methyl-4-(2-methyl-2 H-tetrazol-5-yl)pyridinium iodide (**17**)

Yellow crystals, m.p. 229–231°C; MS (*m/z*): 176 (5%), 161 (28), 133 (100), 132 (31), 105 (87), 84 (22), 78 (57), 51 (43), 49 (49), 43 (46), 28 (51); ^{13}C-NMR (DMSO-*d*$_6$): δ 159.6 (tetrazole C-5), 146.9 (pyridine C-2,6), 140.8 (pyridine C-4), 123.9 (pyridine C-3,5), 48.0 (pyridine-CH_3), 39.9 (tetrazole-CH_3). Anal. calcd. for $C_8H_{10}N_5I$ (303.11): C 31.70, H 3.33, N 23.11. Found: C 32.00, H 3.08, N 23.01.

N-Methyl-4-pyridinium tetrazolate (**22**)

Yellow crystals, m.p. 229–234°C; MS (*m/z*): 161 (M^+, 18%), 142 (100), 133 (71), 127 (22), 105 (51), 78 (47), 51 (26), 28 (56); high-resolution MS: calcd. for $C_7H_7N_5$ (M^+): 161.070145. Found: 161.0698 ± 0.0016. ^{13}C-NMR (D_2O, reference: trimethylsilylpropionic acid-*d*$_4$, sodium salt): δ 159.3 (tetrazole C-5), 147.8 (pyridine C-2,6), 145.4 (pyridine C-4), 125.5 (pyridine C-3,5), 50.4 (CH_3).

Ethyl 1 H-Tetrazole-1-acetate (**5**)

^{13}C-NMR ($CDCl_3$): δ 165.3 (C=O), 143.8 (tetrazole C-5, ^1J = 218.9 Hz, ^3J = 2.6 Hz), 62.4 (OCH_2, ^1J = 148.9 Hz, ^2J = 4.4 Hz), 48.4 (NCH_2, ^1J = 145.1 Hz), 13.5 (CH_3, ^1J = 127.5 Hz, ^2J = 2.6 Hz).

Ethyl 2 H-Tetrazole-2-acetate (**19**)

^{13}C-NMR ($CDCl_3$): δ 164.7 (C=O), 152.9 (tetrazole C-5, ^1J = 214.7 Hz), 62.3 (OCH_2, ^1J = 148.9 Hz, ^2J = 4.4 Hz), 52.9 (NCH_2, ^1J = 145.0 Hz), 13.6 (CH_3, ^1J = 127.4 Hz, ^2J = 2.6 Hz).

Ethyl 5-(4-Pyridyl)-1 H-tetrazole-1-acetate (**6**) *and Ethyl 5-(4-Pyridyl)-2 H-tetrazole-2-acetate* (**20**)

5-(4-Pyridyl)-1 H-tetrazole [27] (883 mg, 6 mmol) was added to a solution of sodium ethoxide prepared from 138 mg (6 mmol) of sodium and 10 ml of dry ethanol. After stirring for 30 min at 30°C, 1.002 g (6 mmol) of ethyl bromoacetate was added and the mixture was refluxed for 20 h. After filtration, the ethanol was removed in vacuo and the remaining solid was extracted with dichloromethane. The residue obtained upon evaporation of dichloromethane was subjected to column chromatography (silica gel, eluent: ethyl acetate) to afford 308 mg (22%) of **20** (first fraction) and 47 mg (3%) of **6**.

Compound **6**: tan oil, MS (*m/z*): 233 (M^+, 46%), 133 (11), 132 (94), 106 (12), 105 (95), 104 (21), 78 (100), 77 (20), 76 (10), 63 (24), 62 (16), 59 (17), 51 (58), 50 (21). Anal. calcd. for $C_{10}H_{11}N_5O_2$ (233.23): C 51.50, H 4.75, N 30.03. Found: C 51.66, H 4.65, N 29.94.

Compound **20**: yellowish crystals, m.p. 69–70°C. IR (KBr): 2990 (C-H), 1750 cm^{-1} (C=O); MS (*m/z*): 177 (12%), 149 (15), 133 (32), 132 (81), 107 (10), 106 (41), 105 (100), 104 (24), 93 (12), 79 (16), 78 (57), 77 (28), 76 (11), 71 (13), 64 (14), 63 (13), 52 (13), 51 (45), 50 (24); ^{13}C-NMR ($CDCl_3$): δ 164.6 (C=O), 163.3 (tetrazole C-5, $^3J_{pyr\,3,5}$ = 4.1 Hz), 150.4 (pyridine C-2,6, ^1J = 180.5 Hz), 134.1 (pyridine C-4, ^3J = 6.9 Hz), 120.6 (pyridine C-3,5, ^1J = 166.5 Hz), 62.5 (OCH_2, ^1J = 148.9 Hz, ^2J = 4.3 Hz), 53.4 (NCH_2, ^1J = 145.2 Hz), 13.7 (CH_3, ^1J = 127.5 Hz, ^2J = 2.6 Hz). Anal. calcd. for $C_{10}H_{11}N_5O_2$ (233.23): C 51.50, H 4.75, N 30.03. Found: C 51.79, H 4.45, N 29.91.

1-[2-(Trimethylsilyl)ethoxy]methyl-1 H-tetrazole (**8**) *and 2-[2-(Trimethylsilyl)ethoxy]methyl-2 H-tetrazole* (**21**)

Under argon, 900 mg of sodium hydride (80% suspension in mineral oil, 30 mmol) were suspended in 20 ml of dry dioxane. Then 2.102 g (30 mmol) of 1 H-tetrazole in 60 ml dioxane-dimethyl formamide (7 : 1) were added and the mixture was stirred for 1 h. After cooling to 15°C, a solution of 5.002 g (30 mmol) of [2-(trimethylsilyl)ethoxy]methyl chloride in 5 ml of dioxane was added via syringe. Then the cooling bath was removed and the mixture was stirred at room temperature for 1.5 h. After addition of water (40 ml) and ethyl acetate (50 ml) the organic layer was separated and the water phase was exhaustively extracted with ethyl acetate. The combined organic layers were washed with water, the solvents were evaporated in vacuo and the residue was distilled over a short column.

Compound **21** (first fraction): yield 1.601 g (27%), colorless oil, b. p. 57°C/0.2 mbar, $n^{20}{}_D = 1.4536$. IR (CH_2Cl_2): 2920 cm^{-1} (C-$H_{aliph.}$); MS (*m/z*): 172 (1%), 157 (39), 143 (16), 130 (11), 103 (21), 101 (14), 100 (26), 99 (32), 75 (26), 73 (100), 59 (12); ^{13}C-NMR ($CDCl_3$): δ 153.0 (tetrazole C-5, $^1J = 213.9$ Hz), 80.2 (NCH_2O, $^1J = 162.5$ Hz, $^3J = 3.0$ Hz), 68.3 (OCH_2C, $^1J = 143.2$ Hz), 17.4 (CH_2Si, $^1J = 118.9$ Hz), −1.7 ($SiCH_3$, $^1J = 118.8$ Hz). Anal. calcd. for $C_7H_{16}N_4OSi$ (200.32): C 41.97, H 8.05, N 27.97. Found: C 42.41, H 7.97, N 28.21.

Compound **8** (second fraction): yield 2.809 g (47%), colorless oil, bp. 110°C/0.3 mbar, $n^{20}{}_D = 1.4594$. IR (CH_2Cl_2): 2920 cm^{-1} (C-$H_{aliph.}$); MS (*m/z*): 172 (1%), 157 (25), 143 (37), 103 (14), 100 (29), 99 (39), 75 (24), 73 (100), 59 (11); ^{13}C-NMR ($CDCl_3$): δ 142.7 (tetrazole C-5, $^1J = 216.6$ Hz, $^3J = 2.6$ Hz), 76.3 (NCH_2O, $^1J = 162.4$ Hz, $^3J = 3.0$ Hz), 67.8 (OCH_2C, $^1J = 143.0$ Hz), 17.3 (CH_2Si, $^1J = 118.9$ Hz), −1.9 ($SiCH_3$, $^1J = 118.9$ Hz). Anal. calcd. for $C_7H_{16}N_4OSi$ (200.32): C 41.97, H 8.05, N 27.97. Found: C 42.45, H 7.87, N 28.26.

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References and Notes

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[24] Regarding the problem of establishing assignments on the absence of an NOE see Ref. 5, p. 358. Since for compounds **16**, **17**, and **20** causes for the lack of an NOE other than a long distance between the involved spins can be excluded, the assignments can be relied on the absence of an enhancement.
[25] Comparable results were obtained upon reaction of 5- (3-pyridyl) -1 *H*-tetrazole with iodomethane: Butler R. N., Garvin V. C. (1982) J. Chem. Research (S): 122. Assignment of an ylide structure to compound **22** (Scheme 1) was based on the results of Butler and Garvin.
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