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SPECTRAL AND STRUCTURAL ASSIGNMENTS WITH VARIOUS N-SUBSTITUTED 1,2,4-TRIAZOLES: NOE DIFFERENCE SPECTROSCOPY AS A POWERFUL TOOL

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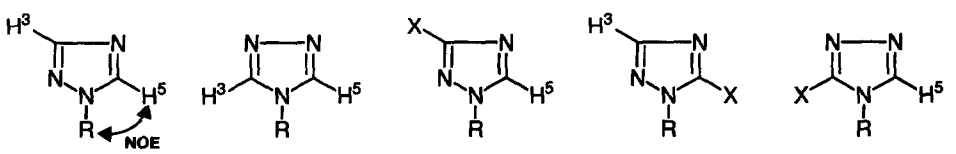
Abstract *- The unambiguous discrimination between signals due to H-3 and H-5 in various 1-substituted 1H-1,2,4-triazoles as well as the differentiation between isomeric 1,3-, 1,5- and 3,4-disubstituted 1,2,4-triazoles by means of NOE difference spectroscopy is described. The assignments based on NOE difference experiments are shown to agree with those resting on triazole-$^{13}C,^{1}H$ spin-coupling constants.*

INTRODUCTION

The (1-substituted) 1*H*-1,2,4-triazole unit represents an important structural element of numerous biologically active compounds,[1] especially of antimycotic[2] and antifungal[3] agents. The alkylation of 1*H*-1,2,4-triazole - the most frequently used method for the synthesis of N-substituted 1,2,4-triazoles - not only leads to N-1 substitution products of type **A**, but more or less also to N-4-alkylated compounds of type **B**.[4-7] When an 1*H*-1,2,4-triazole substituted at C-3(5) serves as the educt, three isomeric N-substitution products (**C**, **D**, **E**) may result upon alkylation.[4,5,8,9] The distinction between such triazole regioisomers by spectroscopic techniques thus provides an interesting challenge.

The differentiation between monosubstituted isomeric 1,2,4-triazoles of type **A** and **B** can be easily achieved by means of ^{1}H-NMR spectroscopy. With the latter type of compounds the two heteroaromatic protons are equivalent giving rise to one two-proton signal,[1,7] whereas in the ^{1}H-NMR spectra of 1-substituted 1*H*-1,2,4-triazoles of type **A** the signals of the triazole protons H-3 and H-5 usually appear as two separated singlets. A comparison of literature data[10] reveals that for compounds **A** assignment of lines due to H-3 and H-5 is easy when the N-1 substituent is electron-withdrawing, as in this case the H-5 proton resonates at markedly higher frequencies (lower field) than the corresponding H-3 proton. On the other hand, if R is electron-releasing, the two signals come close and correct assignment can become a difficult task.

A closely related problem, which also can be tricky in some cases, is the differentiation between isomeric triazoles of type **C**, **D** and **E**. There are several reports in the literature dealing with various



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

possibilities for the discrimination between isomeric N-methyl-1,2,4-triazoles.[8,9,11-17] Amongst them, mass spectrometry[15] and NMR spectroscopy[8,9,11-14] turned out to be suitable methods for this purpose. However, also these methods suffer from certain limitations. Thus, for instance, discrimination via ^{1}H-NMR spectroscopy seems to be problematic in cases when only one isomeric form is at hand, since this approach is mainly based on comparison of chemical shifts (e.g. of the NCH_3 protons) of the individual isomers. Additionally, this method is less suitable for triazoles with N-substituents other than methyl (e.g. phenyl). For all these reasons, the need for a more general approach for unambiguous spectral assignments with this aza-aromatic system arises.

In this study, homonuclear NOE (Nuclear Overhauser Enhancement) difference spectroscopy utilizing a through-space connection between suitable protons of R and the triazole H-5 proton (as indicated in formula **A**) is shown to be a simple and rapid method for the assignment of triazole-H resonances in 1-substituted 1*H*-1,2,4-triazoles of type **A**.[18] In a similar manner, the discrimination of isomeric triazoles of type **C** and **E** (NOE between R and H-5) from compounds of type **D** (no NOE between R and triazole protons) can be accomplished. Moreover, methods for the differentiation between isomers **C**, **D** and **E** employing ^{13}C,^{1}H spin coupling arguments are presented.

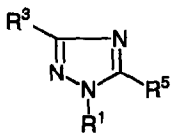
In the following, the application of the present approach shall be exemplified using a variety of representative substituted 1,2,4-triazoles as given in Tables 1 and 2.

RESULTS AND DISCUSSION

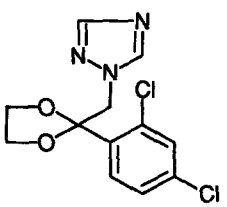
Upon irradiation of the methyl-H resonance of 1-methyl-1*H*-1,2,4-triazole (**1**) a marked enhancement of the triazole-H signal at lower field (higher frequencies) was observed (in $CDCl_3$-, DMSO-d_6-, or acetone-d_6-solution), whereas the high-field triazole-H signal remained nearly unaffected. Thus, the signal of the low-field proton has to be attributed to the triazole H-5 due to the spatial closeness of H-5 to the methyl protons. This assignment is in full agreement with literature data.[8,11,23,34] Similarly, based on the observation of a significant through-space connection between the triazole H-5 and suitable protons of the N-1 substituent, an unambiguous assignment for the heteroaromatic protons H-3 and H-5 could be achieved with a number of other 1-substituted 1,2,4-triazoles,[38] such as 1-benzyl- (**4**, see Figure 1a,b), 1-SEM- (**7**),[39] 1-aryl- (**11**), 1-trityl- (**12**), and 1-silyltriazoles (**13** - **15**), the antifungal agents azaconazole (**23**) and vibunazole (**24**), as well as the anti-epileptic compound loreclezole (**25**) (the results of the NOE-experiments are summarized in Table 3). For compound **12** and 1-tert.butyldiphenylsilyl-1,2,4-triazole (**15**) in $CDCl_3$-solution, the triazole H-3 turned out to resonate at lower field than the corresponding triazole H-5. Thus, the (sometimes carelessly used) "thumb-rule" for the assignment of triazole protons δ(H-5)>δ(H-3) is violated in these cases indicating this relationship not to be a safe criterion.

Whereas with 1-benzoyl-1,2,4-triazole (**17**) the lack of a through-space connection between phenyl-H and triazole protons was observed, investigation of 1,2,4-triazoles bearing an acetyl- or substituted sulfonyl group at N-1 revealed the NOE-method also suitable for the latter type of compounds (except for **16** and **17** in $CDCl_3$-solution). However, due to a larger distance between the spins involved, in these cases the observed effects are smaller than those found with N-alkyl-, N-aryl-, and N-silyltriazoles discussed above. Additionally, also other phenomena have to be taken into consideration. Thus, for instance, 1-acetyl-1,2,4-triazole (**16**) is

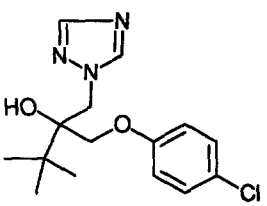
Table 1. 1*H*-1,2,4-Triazoles Investigated



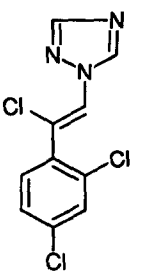
Comp. No.	R^1	R^3	R^5	Ref. prep.
1	Me	H	H	23
2	Me	Br	H	8
3	Me	H	Br	8
4	CH_2Ph	H	H	24
5	CH_2Ph	NO_2	H	[a]
6	CH_2Ph	H	NO_2	[a]
7	SEM [b]	H	H	25
8	SEM [b]	H	Cl	25
9	SEM [b]	H	SPh	25
10	CH_2COOEt	H	H	6
11	p-OH-C_6H_4	H	H	[c]
12	CPh_3	H	H	7
13	SiMe	H	H	[c]
14	$SiBu^tMe_2$	H	H	26
15	$SiBu^tPh_2$	H	H	[a]
16	COMe	H	H	27
17	COPh	H	H	28
18	SO_2Ph	H	H	29
19	Tosyl	H	H	29
20	Tosyl	NO_2	H	30, [c]
21	SO_2Mesityl	H	H	30, [c]
22	SO_2Me_2	H	H	[a]
23	formula below	H	H	31
24	formula below	H	H	32
25	formula below	H	H	33



Azaconazole (**23**)

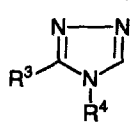


Vibunazole (**24**)



Loreclezole (**25**)

Table 2. 4*H*-1,2,4-Triazoles Investigated



Comp. No.	R^3	R^4	Ref. prep.
26	Br	Me	8
27	NO_2	CH_2Ph	[a]

[a] see Experimental Part [b] SEM = $-CH_2OCH_2CH_2Si(CH_3)_3$ [c] commercially available

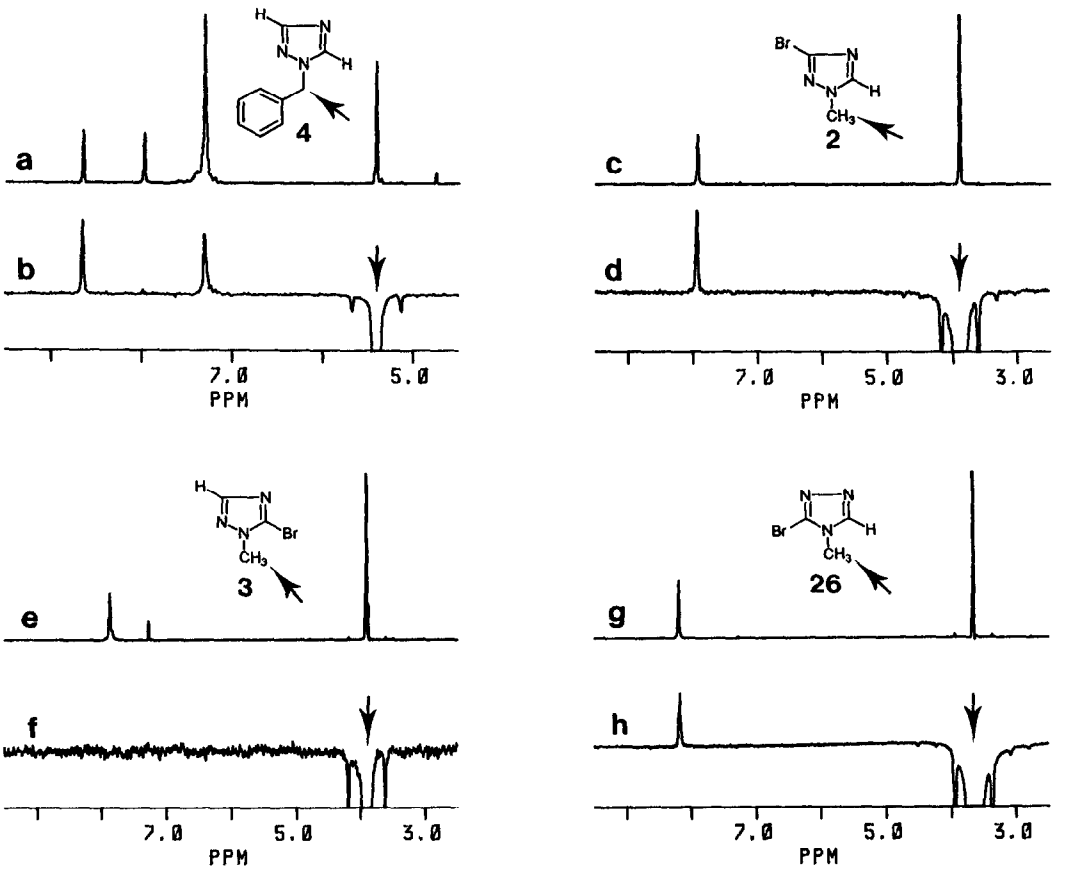


Figure 1. a) ^{1}H-NMR spectrum of **4** (DMSO-d_6) b) NOE difference spectrum of **4** resulting from irradiation of NCH_2
c) ^{1}H-NMR spectrum of **2** ($CDCl_3$) d) NOE difference spectrum of **2** resulting from irradiation of NCH_3
e) ^{1}H-NMR spectrum of **3** ($CDCl_3$) f) NOE difference spectrum of **3** resulting from irradiation of NCH_3
g) ^{1}H-NMR spectrum of **26** ($CDCl_3$) h) NOE difference spectrum of **26** resulting from irradiation of NCH_3

reported to exist predominantly in a conformation with the N-2 and the carbonyl-O in trans-position,[37,40] which is less favourable for the observation of an NOE on H-5 upon perturbation of the methyl-H resonance. On the other hand, this finding also provides a possible explanation for the observation of a (smaller) NOE also on H-3.

The NOE-approach proposed above not only permits to discriminate between azole H-3 and H-5 signals with various 1-substituted 1,2,4-triazoles, but also to differentiate between isomeric disubstituted congeners as demonstrated in Figure 1c-h for isomers **2**, **3**, and **26**.[8] 3-Bromo-1-methyl-1,2,4-triazole (**2**) and 5-bromo-1-methyl-1,2,4-triazole (**3**), the ^{1}H-NMR spectra of which differ only slightly, can be easily

distinguished, as in the case of compound **2** a marked NOE on the azole proton is observed upon irradiation of the methyl-H resonance (Figure 1c), whereas in an analogous experiment with **3** no NOE on an azole-H is induced (Figure 1f). The third isomer, 3-bromo-4-methyl-1,2,4-triazole (**26**), also exhibits a pronounced through-space connection between the methyl-protons and the adjacent triazole H-5 (Figure 1h). It can be distinguished from **2/3** by comparison of the ^{1}H-chemical shifts according to ref.[8] or, more reliable, on basis of its ^{13}C-NMR data, particularly the ^{13}C,^{1}H-spin coupling constants: in compound **26** both azole carbon atoms are coupled to the methyl protons ($^3J \sim 3$ Hz), whereas in the spectra of **2** and **3** only one triazole-C signal shows an appropriate quartet multiplicity [**2**: the signal of the methyl-coupled azole-C shows an additional splitting due to an $^1J(^{13}C,^1H)$ coupling; **3**: methyl-coupled azole-C signal is additionally split due to a vicinal coupling ($J = 10.3$ Hz)].[41]

Similarly, based on homonuclear NOE-difference experiments supported by selected ^{13}C-NMR data, an unambiguous assignment for isomeric N-benzyl-C-nitro-1,2,4-triazoles **5**, **6**, and **27** could be achieved. A further example for the potential of the NOE-method is the determination of the substitution pattern in compounds **8** and **9**, which were obtained from **7** via lithiation and subsequent reaction with appropriate electrophiles.[25] Although it is well known that 1-substituted 1,2,4-triazoles undergo lithiation exclusively in 5-position,[42] according to a recent report[43] also 3-substitution products can be obtained in the course of such reactions due to isomerisation of the initially formed species. In view of this finding, NOE-experiments were carried out with **8** and **9** which clearly revealed an 1,5-substitution pattern with these compounds (**8**: no relevant NOEs observed;[44] **9**: NOE on the signal of the S-phenyl protons and no NOE on the azole-H line upon irradiation of the -NCH_2O- resonance).

A survey of literature data[45,46,47] concerning azole-^{13}C,^{1}H spin-coupling constants of various 1-substituted 1,2,4-triazoles proved that for all compounds specified the relationship ^1J(C-5,H-5)>^1J(C-3,H-3) (within one species) is met. In view of this finding, from the ^{1}H-NMR spectra of the 1-substituted 1,2,4-triazoles investigated throughout this study (compounds **1**, **4**, **7**, **10**, **11-19**, **21-25**), the mentioned two coupling constants were extracted from the ^{13}C-satellites of the triazole-H singlets (compare Table 3) in order to confirm the assignments resting on the NOE difference experiments. It turned out, that in all cases the above relationship was fulfilled. Thus, this criterion has to be considered as a further possibility for the discrimination between H-3 and H-5 in 1,2,4-triazoles substituted at N-1. On the other hand, from the C,H-coupling constants given in Table 3 it emerges, that an unequivocal discrimination between isomeric disubstituted 1,2,4-triazoles (e.g.between **2**, **3**, and **26**; or **5**, **6**, and **27**) on basis of these data is not possible.

In summary, the presented NOE-approach permits the convenient and unambiguous assignment of triazole-H resonances with a variety of 1-substituted 1,2,4-triazoles as well as the differentiation between disubstituted 1,2,4-triazole regioisomers. In particular with derivatives bearing a (substituted) N-alkyl-, N-aryl-, or N-silyl group, excellent results were obtained indicating this approach to be the method of choice for assignments with this type of compounds.

Table 3. ^{1}H-NMR Data (δ, ppm), NOE Data and Selected ^{13}C,^{1}H Spin Coupling Constants (Hz) of Compounds Investigated

No.	Solvent[a]	R^1 (R^4)	R^3	R^5	irrad. reson.	NOE on	^1J [b] (C3,H3)	^1J [b] (C5,H5)	Ref. NMR
1	A	3.89 (CH_3)	7.88	8.00	CH_3	H-5	207.0	208.6	8,11,23
	B	3.85 (CH_3)	7.92	8.43	CH_3	H-5	206.0	211.4	8,11
	C	3.91 (CH_3)	7.81	8.25	CH_3	H-5	204.9	210.0	--
2	A	3.88 (CH_3)	---	7.91	CH_3	H-5	---	211.5	8
	B	3.85 (CH_3)	---	8.47	CH_3	H-5	---	215.3	--
3	A	3.90 (CH_3)	7 86	---	CH_3	---	210.6	---	8,34
	B	3.83 (CH_3)	8.00	---	CH_3	---	210.4	---	--
4	A	7.42-7.26 (Ph), 5.33 (CH_2)	7.96	8.04	CH_2	H-5 (Ph)	207.4	209.5	7
	B	7.31 (Ph), 5.41 (CH_2)	7.97	8.64	CH_2[c]	H-5[c] (Ph)	206.1	211.8	--
5	A	7.40 (Ph), 5.43 (CH_2)	---	8 06	CH_2	H-5 (Ph)	---	216.4	--
	B	7.38 (Ph), 5.56 (CH_2)	---	9.00	CH_2[c]	H-5[c] (Ph)	---	220.1	--
6	A	7.36 (Ph), 5.79 (CH_2)	7.98	---	CH_2	-- (Ph)	214.7	---	--
	B	7.33 (Ph), 5.74 (CH_2)	8.30	---	CH_2	-- (Ph)	215.0	---	--
7	A	5.49 (NCH_2), 3.62 (OCH_2C), 0.90 ($SiCH_2$), -0.03 (CH_3)	7.96	8.24	NCH_2	H-5 (OCH_2)	207.6	210.2	25
	B	5.50 (NCH_2), 3.56 (OCH_2C), 0.82 ($SiCH_2$), -0.06 (CH_3)	8.02	8.70	NCH_2	H-5 (OCH_2)	206.5	213.2	25
8	A	5.47 (NCH_2), 3.66 (OCH_2C), 0.91 ($SiCH_2$), -0.02 (CH_3)	7.86	---	NCH_2	-- (OCH_2)	211.1	---	25
9	B	5.54 (NCH_2), 3.54 (OCH_2C), 0.78 ($SiCH_2$), -0.08 (CH_3)	8.11	7.41	NCH_2[c]	Ph[c] (OCH_2)	209.1	---	25
10	A	4.94 (NCH_2), 4 23 (OCH_2), 1.26 (CH_3)	7.94	8.17	NCH_2	H-5	208.1	211.0	--
	B	5.18 (NCH_2), 4.16 (OCH_2), 1.20 (CH_3)	7.99	8 51	NCH_2[c]	H-5[c]	207.0	215.1	--
11	B	9.83 (OH), 7.70-7.51 (Ph-2,6), 6.99-6.80 (Ph-3,5)	8.13	9.06	H-5[c]	Ph[c] (α to N)	207.3	213.1	35
					H-3	---			
12	A	7.40-7.07 (Ph)	8.08	8.03	Ph[c]	H-5[c]	207.0	212.0	7
	C	7.42-7.06 (Ph)	8.02	8.03	Ph	H-5	-[d]	-[d]	--
13	A	0.51 ($SiCH_3$)	8.10	8.21	$SiCH_3$	H-5	205.1	205.6	--
14	A	0.93 (CCH_3), 0.51 ($SiCH_3$)	8.11	8.22	$SiCH_3$	H-5	204.9	206.0	--
15	A	7.76-7.33 (Ph), 1.23 (CCH_3)	8.25	7.92	Ph[c]	H-5[c]	205.7	208 8	--
16	A	2.72 (CH_3)	8.01	8.89	CH_3	H-5, H-3[e]	210.4	217.9	36,37
	B	2.66 (CH_3)	8.26	9 27	CH_3	H-5[f]	210 5	219 1	37
	C	2.69 (CH_3)	8.09	9.01	CH_3	H-5[f]	209.7	218.1	37
17	A	8.29-8.17 (Ph-2,6), 7.70-7.26 (Ph-3,4,5)	8.11	9.08	H-5	---	210.5	218.3	--
	B	8.14-8.02 (Ph-2,6), 7.77-7 47 (Ph-3,4,5)	8.37	9.41	H-5	---	-[d]	-[d]	--
	C	8.27-8.15 (Ph-2,6), 7.86-7.48 (Ph-3,4,5)	8.20	9.21	H-5	---	-[d]	-[d]	--
18	A	8.15-8.08 (Ph-2,6), 7.74-7.58 (Ph-3,4,5)	8 02	8.75	H-5	---	211.8	220.9	29
	C	8.20-8.08 (Ph-2,6), 7.89-7.60 (Ph-3,4,5)	8.17	9.10	Ph	H-5	-[d]	-[d]	--
19	A	8.01-7.91 (Ph-2,6), 7.43-7.32 (Ph-3,5), 2.45 (CH_3)	8.01	8 73	H-5[c]	Ph-2,6[c,g]	211.6	220.4	29
	C	8.05-7.94 (Ph-2,6), 7.57-7.47 (Ph-3,5), 2.45 (CH_3)	8.14	9.06	Ph-2,6[c]	H-5[c,g]	-[d]	-[d]	--
20	A	8.08-8.97 (Ph-2,6), 7.51-7.40 (Ph-3,5), 2.49 (CH_3)	---	8.78	H-5[c]	Ph-2,6[c]	---	224.4	30
21	A	7.02 (Ar-3,5), 2 66 (2,6-CH_3), 2.32 (4-CH_3)	7.99	8.79	α-CH_3	H-5	211.2	219.8	29
22	A	3.00 (NCH_3)	8 06	8.58	NCH_3	H-5[f]	211 0	219.7	--
	C	3.00 (NCH_3)	8.17	8.83	NCH_3	H-5[f]	210.5	220 6	--
23	A	7.59-7 15 (Ar), 4.78 (NCH_2), 3.81 (OCH_2)	7.89	8 16	NCH_2[c]	H-5[c]	207.6	211.4	--
	B	7.64-7.38 (Ar), 4.76 (NCH_2), 3.81 (OCH_2)	7.83	8.40	NCH_2	H-5	206 0	212.8	--
24	A	7.25-7 14 (Ph-3,5), 6.71-6.60 (Ph-2,6), 4 71/4.37 (NCH_2)[h]	7.94	8 18	NCH_2[c]	H-5[c] (OH, Me)	208.6	212.0	--
		3.99 (OH), 3.95/3 30 (OCH_2)[i], 1.12 (CH_3)			H-3	---			
	B	7.40-7.20 (Ph-3,5), 6.97-6.77 (Ph-2,6), 4.82 (OH), 4.56/	7 87	8 38	H-5[c]	NCH_2[c] (OH)[c]	206.1	212.5	--
		4.36 (NCH_2)[h], 3 86/3.54 (OCH_2)[i], 1 01 (CH_3)			H-3	---			
25	B	7.83 (alkene-H), 7.81-7.50 (Ar)	8.26	9.13	H-5[c]	alkene-H[c]	209 5	217 2	--
26	A	3.67 (CH_3)	---	8.18	CH_3	H-5	---	211.8	8,34
	B	3.60 (CH_3)	---	8 62	CH_3	H-5	---	214 2	8
27	A	7.48-7.18 (Ph), 5.55 (CH_2)	---	8.17	CH_2[c]	H-5[c] (Ph)	---	214.2	--
	B	7 34 (Ph), 5 57 (CH_2)	---	9.00	CH_2[c]	H-5[c] (Ph)	---	216.5	--

[a] A. $CDCl_3$, B. $(CD_3)_2SO$, C $(CD_3)_2CO$

[b] Derived from the ^{13}C-satellites of the triazole H-3/H-5 signals.

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

[d] Not (unequivocally) determined.

[e] Equal enhancement of the signals due to H-3 and H-5

[f] A markedly smaller, but detectable NOE was also observed on H-3

[g] Weak enhancement.

[h] Diastereotopic protons, AB spin-system: $^2J(NCH_2) = 14.0$ Hz.

[i] Diastereotopic protons, AB spin-system: $^2J(OCH_2) = 9.8$ Hz

EXPERIMENTAL PART

General

Melting points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Hewlett-Packard 5890A/5970B-GC/MSD instrument, high-resolution mass spectra were recorded on a Finnigan MAT 8230 spectrometer (both EI, 70 eV).

NMR Measurements

Homonuclear NOE-difference spectra were recorded at 30°C from approximately 0.2 M solutions (non degassed) on a Bruker AC 80 spectrometer (spectrometer frequency for ^{1}H: 80.13 MHz) equipped with an Aspect 3000 computer and standard software. Generally used acquisition parameters: 8 K data points; spectral width: 1441 Hz; acquisition time: 2.84 s; digital resolution: 0.35 Hz/point; pulse width: 3 µs (90°); relaxation delay: 0.5 - 1 s; number of scans: 128 - 800; pre-irradiation time: 3 - 5 s; irradiation power: 46 - 50 dB below 0.2 W. In cases when multiplet signals had to be irradiated or when maximum frequency selectivity was required in crowded regions of the spectrum, the frequency cycling method of Kinns[48] was employed (irradiation power 55 - 58 dB). All NOE-difference spectra displayed were processed with 0.5 - 1.0 Hz line broadening to reduce subtraction artifacts. Heteronuclear NOE experiments were performed on a Bruker AM 400 WB spectrometer (spectrometer frequency for ^{13}C: 100.61 MHz).

Materials

Compounds **11**, **13**, **20**, and **21** are commercially available. Azaconazole (**23**), Loreclezole (**25**), and Vibunazole (**24**) were gifts from the Janssen Research Foundation and from Bayer AG, respectively. All other compounds were prepared according to the references given in Tables 1 and 2. Deuteriochloroform was filtered through aluminia (activity I, basic) before use, DMSO-d_6 and acetone-d_6 were dried over molecular sieve (4 Å).

3-Bromo-1-methyl-1H-1,2,4-triazole (**2**)[8]

^{13}C-NMR ($CDCl_3$): δ (ppm) 144.98 [triazole C-5, ^1J(C5,H5) = 212.5 Hz, ^3J(C5,CH_3) = 3.0 Hz), 139.74 [triazole C-3, ^3J(C3,H5) = 15.3 Hz], 36.65 (CH_3, ^1J = 142.0 Hz).

5-Bromo-1-methyl-1H-1,2,4-triazole (**3**)[8]

^{13}C-NMR ($CDCl_3$): δ (ppm) 152.29 [triazole C-3, ^1J(C3,H3) = 210.3 Hz], 129.32 [triazole C-5, ^3J(C5,H3) = 10.3 Hz, ^3J(C5,CH_3) = 3.2 Hz], 36.40 (CH_3, ^1J = 142.3 Hz).

3-Bromo-4-methyl-4H-1,2,4-triazole (**26**)[8]

^{13}C-NMR ($CDCl_3$): δ (ppm) 145.75 [triazole C-5, ^1J(C5,H5) = 212.5 Hz, ^3J(C-5,CH_3) = 2.9 Hz], 129.87 [triazole C-3, ^3J(C3,H5) = 6.4 Hz, ^3J(C3,CH_3) = 3.4 Hz], 32.25 (CH_3, ^1J = 142.7 Hz).

Reaction of 3-Nitro-1H-1,2,4-triazole with Benzyl Chloride

3-Nitro-1*H*-1,2,4-triazole (456 mg, 4 mmoles) was added to a solution of sodium ethoxide prepared from 104 mg (4.5 mmoles) of sodium and 6 ml of dry ethanol. After 30 minutes of stirring, 633 mg (5 mmoles) of benzyl chloride were added and the resulting mixture was heated to reflux for 20 hours. After cooling, the precipitated material was removed by filtration, the filtrate was evaporated in vacuo and the residue was subjected to column chromatography (silica gel, eluent: dichloromethane - ethyl acetate, 9:1) to afford 85 mg (10%) of **6** (first fraction), 526 mg (64%) of **5** (middle fraction), and 34 mg (4%) of **27** (most retarded component).

1-Benzyl-3-nitro-1H-1,2,4-triazole (**5**): colorless crystals, mp 61°C (from diisopropyl ether); ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 162.55 (broad,[49] triazole C-3), 144.71 [triazole C-5, ^1J(C5,H5) = 217.1 Hz, ^3J(C5,CH_2) = 3.1 Hz], 132.40 (Ph C-1), 129.07 (Ph C-3,4,5), 128.25 (Ph C-2,6), 55.01 (CH_2, ^1J = 143.7 Hz); MS: m/z (%) 204 (M^+, 27), 158 (19), 91 (100), 65 (21). Anal. calcd. for $C_9H_8N_4O_2$: C, 52.94; H, 3.95; N, 27.44. Found: C, 53.20; H, 4.12; N, 27.60.

1-Benzyl-5-nitro-1H-1,2,4-triazole (**6**): pale yellow oil; ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) ~151.5 (broad,[49] triazole C-5), 149.61 [triazole C-3, ^1J(C3,H3) = 214.7 Hz], 133.37 (Ph C-1), 129.05 (Ph C-3,4,5), 128.22 (Ph C-2,6), 56.00 (CH_2, ^1J = 144.6 Hz); MS: m/z (%) 204 (M^+, 2), 158 (65), 131 (16), 107 (32), 105 (34), 104 (18), 103 (27), 91 (100), 77 (20), 65 (37). Anal. calcd. for $C_9H_8N_4O_2$: C, 52.94; H, 3.95; N, 27.44. Found: C, 53.15; H, 3.86; N, 27.59.

4-Benzyl-3-nitro-4H-1,2,4-triazole (**27**): colorless crystals, mp 111-112°C; ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) ~153 (broad,[49] triazole C-3), 146.14 [triazole C-5, ^1J(C5,H5) = 214.2 Hz, ^3J(C5,CH_2) = 3.1 Hz], 132.27 (Ph C-1), 129.70 (Ph C-4), 129.65 (Ph C-3,5), 128.16 (Ph C-2,6), 51.77 (CH_2, ^1J = 145.3 Hz); MS: m/z (%) 204 (M^+, 6), 203 (36), 174 (18), 91 (100). Anal. calcd. for $C_9H_8N_4O_2$: C, 52.94; H, 3.95; N, 27.44. Found: C, 53.22; H, 3.95; N, 27.22.

1-(tert.Butyldiphenylsilyl)-1H-1,2,4-triazole (**15**)

A mixture of 691 mg (10 mmoles) of 1*H*-1,2,4-triazole and 2.749 g (10 mmoles) of tert.butyldiphenylsilylchloride in 30 ml of dry triethylamine was heated to reflux for 20 h. After cooling, the precipitated triethylamine hydrochloride was filtered off, the remaining solution was evaporated under reduced pressure and the residue was subjected to Kugelrohr-distillation. The product came over at 150°C/0.05 mm. Yield: 2.37 g (77%) of a viscous oil, which solidified on standing. The compound turned out to be extremely sensitive to hydrolysis.
^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 154.31 [triazole C-3, ^1J(C3,H3) = 205.7 Hz, ^3J(C3,H5) = 11.7 Hz], 151.37 [triazole C-5, ^1J(C5,H5) = 208.8 Hz, ^3J(C5,H3) = 8.2 Hz], 135.69 (Ph C-2,6), 130.81 (Ph C-4), 129.82 (Ph C-1), 128.16 (Ph C-3,5), 27.07 (CH_3, ^1J = 126.4 Hz, ^3J = 5.4 Hz), 19.15 (C-CH_3, ^2J = 3.4 Hz); MS: m/z (%) 307 (M^+, 1), 251 (23), 250 (100), 181 (10); high-resolution MS: calculated for $C_{18}H_{21}N_3Si$: 307.1505; found: 307.1508 ± 0.0015

1-(N,N-Dimethylsulfamoyl)-1H-1,2,4-triazole (**22**)

A mixture of 691 mg (10 mmoles) of 1*H*-1,2,4-triazole, 1.436 g (10 mmoles) of N,N-dimethylsulfamoyl chloride and 1.012 g (10 mmoles) of triethylamine in 15 ml of dry benzene was stirred at room temperature for 2 days. After the precipitated triethylamine hydrochloride was filtered off, the filtrate was evaporated under reduced pressure. The residue (1.483 g) was subjected to Kugelrohr-distillation. A colorless oil, which solidified on standing, came over at 80°C/0.05 mm. Recrystallisation from diisopropyl ether afforded 487 mg (28%) of colorless, volatile crystals, mp 57°C; ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 153.17 [triazole C-3, ^1J(C3,H3) = 210.8 Hz, ^3J(C3,H5) = 12.7 Hz], 144.91 [triazole C-5, ^1J(C5,H5) = 219.8 Hz, ^3J(C5,H3) = 7.6 Hz], 38.46 (CH_3, ^1J = 141.6 Hz, ^3J = 3.2 Hz); MS: m/z (%) 108 (70), 70 (100). Anal. calcd. for $C_4H_8N_4O_2S$: C, 27.27; H, 4.58; N, 31.80. Found: C, 27.51; H, 4.45; N, 31 99

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