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ON THE APPLICATION OF NOE DIFFERENCE SPECTROSCOPY FOR SPECTRAL AND STRUCTURAL ASSIGNMENTS WITH SUBSTITUTED 1,2,3-TRIAZOLES

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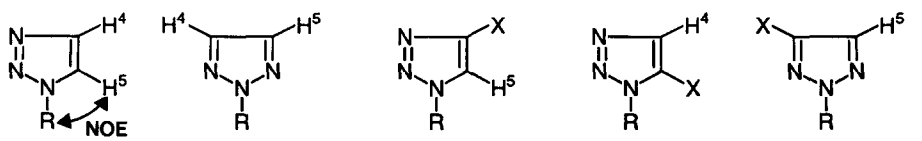
Abstract *- The application of NOE difference spectroscopy for the unambiguous discrimination between signals of H-4 and H-5 in 1-substituted 1H-1,2,3-triazoles as well as for the differentiation between regioisomeric 1,4-, 1,5- and 2,4-disubstituted 1,2,3-triazoles is demonstrated.*

INTRODUCTION

The 1,2,3-triazole moiety is a substructure of a number of biologically active compounds as well as of various agrochemicals, dyestuffs, photostabilizers, corrosion inhibitors and valuable synthetic intermediates.[1] The most important synthesis of 1*H*-1,2,3-triazoles - the 1,3-dipolar cycloaddition of azides to alkynes (or their synthetic equivalents) - can lead to mixtures of regioisomeric 1,2,3-triazoles of type **C** and **D** if unsymmetrically substituted alkynes are employed as educts.[1,2,3] Upon N-alkylation of C-monosubstituted N*H*-1,2,3-triazoles the formation of all three N-monosubstitution products **C**, **D**, and **E** is possible.[3,4,5] Thus, spectroscopic methods for the rapid and unambiguous distinction between such 1,2,3-triazole regioisomers are of special interest.

The discrimination between monosubstituted isomers of type **A** and **B** is trivial by means of ^{1}H-NMR spectroscopy, as **B** is a symmetrical molecule characterized by one two-proton singlet for the heteroaromatic protons, whereas with compounds of type **A** the signals of H-4 and H-5 are not equivalent[1,6] and additionally split due to a characteristically small vicinal coupling (J = 1.0 - 1.5 Hz).[7,8] A survey of literature data[8,9] (compare also Table 3 of this study) indicates that with the latter type of compounds (particularly with 1-alkyl-1,2,3-triazoles) the signals of H-4 and H-5 are close and their relative position is strongly solvent-dependent. Thus, an unambiguous assignment of triazole-H signals calls for additional information, e.g. obtained from the observation of solvent effects[8] or from comparison with literature data of closely related species.



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

A related problem is the discrimination between isomeric disubstituted 1,2,3-triazoles of type **C**, **D**, and **E**. Although ^{1}H-NMR spectroscopy has been successfully employed for assignment of structures in several cases (e.g. refs.[1,3,10,11,12,13]), ^{1}H chemical shifts alone are not always a safe criterion for this purpose. Particularly when no data of closely related congeners (recorded in the same solvent!) are available or when only one isomeric form is at hand, assignments can become difficult since comparison of ^{1}H chemical shifts is required. As shown in several cases, ^{13}C-NMR spectroscopy seems to be superior for the discrimination of 1,2,3-triazole regioisomers,[5,14,15,16] especially when also coupling information (direct and long-range ^{13}C,^{1}H spin coupling constants) is used in addition to chemical shift arguments.[5,16,17]

In contrast to the above mentioned methods based on chemical shift and coupling considerations, this study deals with the application of homonuclear NOE (Nuclear Overhauser Enhancement) difference spectroscopy for the assignment of triazole-H resonances employing a through-space connection between suitable protons of the N-1 substituent and the triazole proton H-5 (as indicated in formula **A**) in 1-substituted 1,2,3-triazoles of type **A**. Similarly, the discrimination of 1,4-disubstituted triazoles **C** from regioisomeric structures **D** and **E** can be realized.[18] Although NOE experiments have been used for structural elucidations with 1,2,3-triazoles in a few individual cases (e.g. refs.[5,19,20]), to the best of our knowledge no systematic study on this approach has been undertaken until now.[21]

In the following, the application of the NOE method shall be demonstrated employing various substituted 1,2,3-triazoles given in Tables 1 and 2.

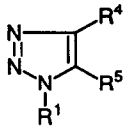
RESULTS AND DISCUSSION

With 1-methyl-1,2,3-triazole (**1**) in $CDCl_3$ solution, irradiation of the methyl-H resonance led to a significant enhancement of the triazole-H signal at higher field (7.52 ppm), whereas the low-field signal (7.66 ppm) was only slightly affected. Thus, the former resonance has to be attributed to the triazole H-5 in order to its spatial closeness to the methyl protons. In contrast, a similar NOE difference experiment with **1** in DMSO-d_6 solution resulted in the enhancement of the low-field triazole-H signal (8.04 ppm), which consequently must be due to H-5. These findings are in full agreement with assignments given in the literature[8,13] reporting δ (H-5) < δ (H-4) for **1** in $CDCl_3$ and δ (H-5) > δ (H-4) in DMSO-d_6.

Similarly, the unambiguous assignment of the heteroaromatic protons in 1-benzyl-1,2,3-triazole (**3**) could be easily achieved (Figure 1a-1d). Again, like with **1**, it was also found with **3** that the signals of H-4 and H-5 change place when switching from $CDCl_3$ to DMSO-d_6 solution.

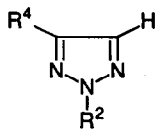
Further examples for the discrimination between triazole H-4 and H-5 signals employing the NOE method with additional 1-substituted 1,2,3-triazoles (**7**, **9**, **10**, and **11**) are given in Table 3. In many cases the NOE experiments could be also performed reversely irradiating the triazole H-5 resonance and observing enhancements on signals of suitable protons of the N-1-substituent (which is advantageous when the H-5 resonance is better separated from other signals than the corresponding R^1-H signal). As an example may serve Figure 1e,f: perturbation of the low-field triazole-H transition of the 1-aryl-1,2,3-triazole **11** leads to a positive NOE on the phenyl H-2,6 signal as well as on the triazole H-4 doublet, clearly indicating the irradiated resonance to be due to the triazole H-5 proton.

Table 1. 1*H*-1,2,3-Triazoles Investigated



Comp. No.	R^1	R^4	R^5	Ref. prep.
1	Me	H	H	28
2	Me	Ph	H	29
3	CH_2Ph	H	H	30
4	CH_2Ph	Br	H	31
5	CH_2Ph	COOEt	H	a
6	CH_2Ph	H	COOEt	a
7	CH_2COOEt	H	H	6
8	CH_2COOEt	Ph	H	a
9	$CHPh_2$	H	H	a, 32
10	CPh_3	H	H	a, 33
11	3,5-dichlorophenyl	H	H	34
12	COMe	H	H	7, 35
13	COPh	H	H	36

Table 2. 2*H*-1,2,3-Triazoles Investigated



Comp. No.	R^2	R^4	Ref. prep.
14	Me	H	28
15	CH_2Ph	COOEt	a
16	CH_2COOEt	H	6
17	CH_2COOEt	Ph	a
18	$CHPh_2$	H	a
19	CPh_3	H	a
20	$SiMe_2Bu^t$	H	a
21	COMe	H	7

a: see Experimental

With 1-acetyl- (**12**) and 1-benzoyl-1,2,3-triazole (**13**) the NOE approach turned out to be less suitable due to the lack of a significant NOE between the triazole H-5 and methyl or phenyl protons, respectively. This finding can be explained by the larger distance of the involved spins (compared to the above mentioned 1-alkyl or 1-aryl-1,2,3-triazoles) taking into consideration that **1**, for instance, is reported to exist preferentially in a conformation with the triazole N-2 and the carbonyl-O in trans-position.[24,25]

The potential of the NOE method for the discrimination between isomeric disubstituted 1,2,3-triazoles of type **C**, **D**, and **E** is demonstrated for regioisomers **5**, **6**, and **15**, obtained upon benzylation of ethyl 1,2,3-triazole-4-carboxylate and subsequent chromatographic separation of the reaction mixture. As the ^{1}H-NMR spectra of compounds **5**, **6**, and **15** (in $CDCl_3$ or DMSO-d_6) differ only slightly (compare data in Table 3), an unequivocal assignment solely on basis of chemical shifts seems to be problematic. In contrast, simple NOE

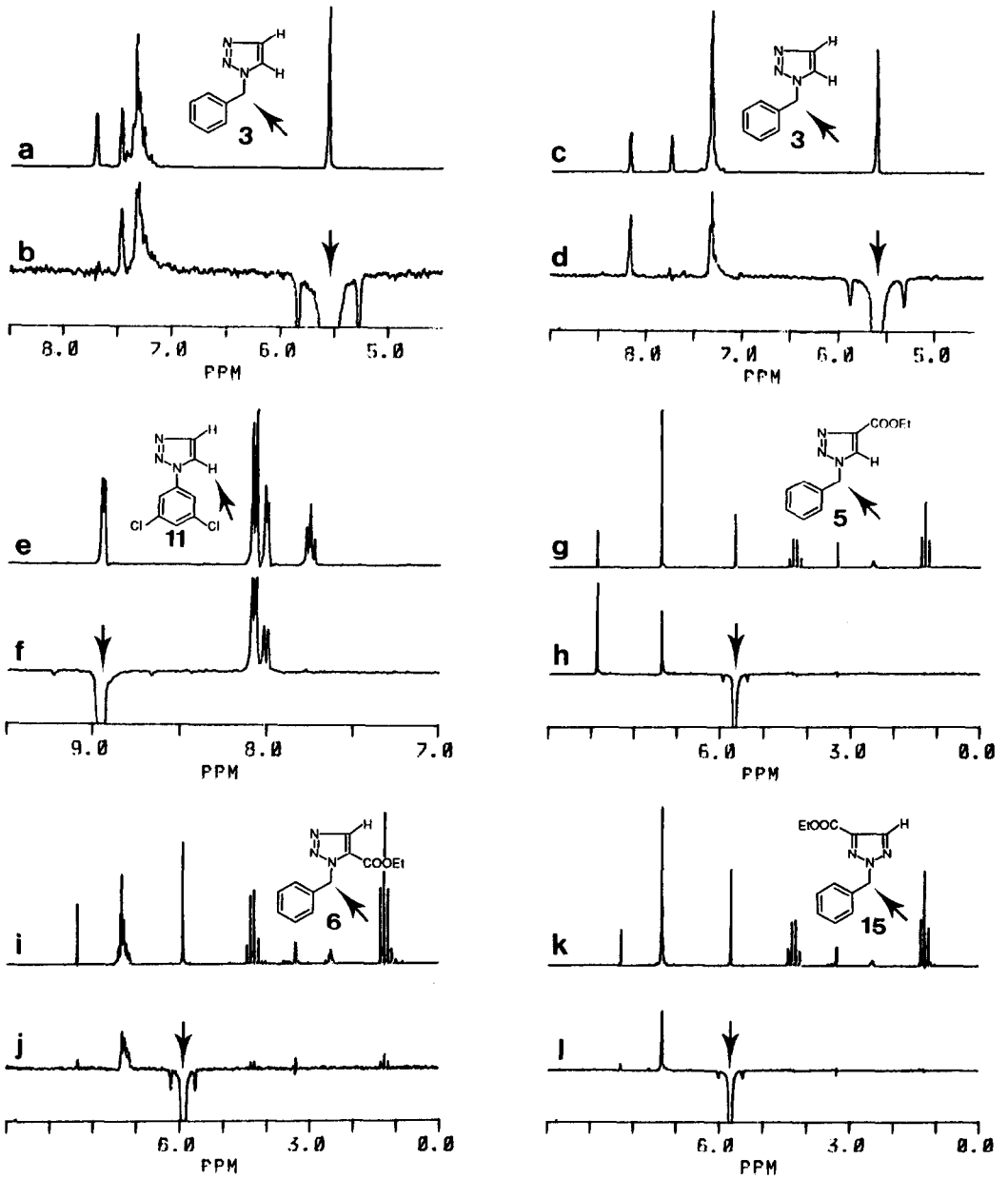


Figure 1. a) ^{1}H-NMR spectrum of **3** ($CDCl_3$) b) NOE difference spectrum of **3** resulting from irradiation of NCH_2
c) ^{1}H-NMR spectrum of **3** (DMSO-d_6) d) NOE difference spectrum of **3** resulting from irradiation of NCH_2
e) ^{1}H-NMR spectrum of **11** (DMSO-d_6) f) NOE difference spectrum of **11** resulting from irradiation of triazole H-5
g) ^{1}H-NMR spectrum of **5** (DMSO-d_6) h) NOE difference spectrum of **5** resulting from irradiation of NCH_2
i) ^{1}H-NMR spectrum of **6** (DMSO-d_6) j) NOE difference spectrum of **6** resulting from irradiation of NCH_2
k) ^{1}H-NMR spectrum of **15** (DMSO-d_6) l) NOE difference spectrum of **15** resulting from irradiation of NCH_2

Table 3. ^{1}H-NMR Data (δ, ppm) and NOE Data of Compounds Investigated

No.	Solvent[a]	R^1 (R^2)	R^4	R^5	Irrad. reson.	NOE on	Ref. NMR
1	A	4.09 (CH_3)	7.66	7.52	CH_3	H-5, H-4[b]	8, 13
	B	4.04 (CH_3)	7.69	8.04	CH_3	H-5, H-4[b]	8
2	A	4.12 (CH_3)	7.88-7.26 (Ph)	7.73[d,e]	CH_3	H-5	37
	B	4.08 (CH_3)	7.88-7.30 (Ph)	8.49	CH_3	H-5	--
3	A	7.42-7.20 (Ph), 5.56 (CH_2)	7.70	7.47	CH_2	H-5 (Ph)	--
	B	7.32 (Ph), 5.61 (CH_2)	7.74	8.16	CH_2[e]	H-5 (Ph)	--
4	A	7.40-7.26 (Ph), 5.52 (CH_2)	---	7.45	CH_2	H-5 (Ph)	--
	B	7.34 (Ph), 5.61 (CH_2)	---	8.46	CH_2	H-5 (Ph)	--
5	A	7.45-7.23 (Ph), 5.57 (CH_2)	4.39 (CH_2), 1.37 (CH_3)	7.96	NCH_2	H-5 (Ph)	38
	B	7.35 (Ph), 5.65 (CH_2)	4.29 (CH_2), 1.28 (CH_3)	8.85	NCH_2	H-5 (Ph)	--
6	A	7.31 (Ph), 5.92 (CH_2)	8.13	4.34 (CH_2), 1.34 (CH_3)	NCH_2	--- (Ph)	--
	B	7.39-7.12 (Ph), 5.90 (CH_2)	8.33	4.30 (CH_2), 1.25 (CH_3)	NCH_2	H-4[b] (Ph,CH_3[b])	--
7	A	5.18 (NCH_2), 4.26 (OCH_2), 1.29 (CH_3)	7.73	7.71	NCH_2	H-5	--
	B	5.39 (NCH_2), 4.16 (OCH_2), 1.21 (CH_3)	7.75	8.11	NCH_2	H-5	--
8	A	5.21 (NCH_2), 4.30 (OCH_2), 1.32 (CH_3)	7.90-7.26 (Ph)	7.91	NCH_2	H-5	39
	B	5.44 (NCH_2), 4.20 (OCH_2), 1.23 (CH_3)	7.92-7.30 (Ph)	8.56	NCH_2	H-5	(40)
9	A	7.44-7.05 (Ph, NCH[d])	7.72	-[d]	H-4	---	--
	B	7.47-7.13 (Ph), 7.32 (NCH)[d,e]	7.78	8.11	NCH[c]	H-5	--
10	A	7.39-7.05 (Ph)	7.70	7.46	Ph	H-5	--
	C	7.43-7.05(Ph)	7.70	7.62	Ph[c]	H-5	--
11	B	8.07 (Ph-2,6), 7.75 (Ph-4)	8.00	8.94	Ph-2,6[c]	H-5	--
	C	7.99 (Ph-2,6), 7.60 (Ph-4)	7.90	8.71	Ph-2,6[c]	H-5	--
12	A	2.88 (CH_3)	7.73	8.26	CH_3	---	(7)
13	A	8.32-8.21 (Ph-2,6), 7.74-7.44 (Ph-3,4,5)	7.83	8.49	Ph-2,6	---	--
					H-5	---	--
14	A	4.18 (CH_3)	7.55	7.55	CH_3	H-4,5[b]	8
	B	4.13 (CH_3)	7.72	7.72	CH_3	H-4,5[b]	8
15	A	7.34 (Ph), 5.64 (CH_2)	8.05	4.42 (CH_2), 1.39 (CH_3)	NCH_2	--- (Ph)	--
	B	7.33 (Ph), 5.74 (CH_2)	8.29	4.31 (CH_2), 1.28 (CH_3)	NCH_2	H-5[b] (Ph)	--
16	A	5.23 (NCH_2), 4.23 (OCH_2), 1.26 (CH_3)	7.67	7.67	NCH_2	---	--
	B	5.42 (NCH_2), 4.15 (OCH_2), 1.19 (CH_3)	7.83	7.83	NCH_2	H-4,5[b]	--
17	A	5.25 (NCH_2), 4.27 (OCH_2), 1.29 (CH_3)	7.92	7.86-7.26 (Ph)	NCH_2	---	--
	B	5.47 (NCH_2), 4.18 (OCH_2), 1.20 (CH_3)	8.32	7.91-7.35 (Ph)	NCH_2	H-5[b]	--
18	A	7.40-7.14 (Ph), 7.10 (NCH)	7.69	7.69	NCH	---	--
					H-4,5	---	--
	B	7.40-7.17 (Ph, NCH[d])	7.87	-[d]	Ph, NCH	H-4,5[b]	--
					H-4,5	---	--
19	A	7.37-7.06 (Ph)	7.74	7.74	Ph	---	--
	C	7.37-7.02 (Ph)	7.78	7.78	Ph	---	--
					H-4,5	---	--
20	A	0.94 (CCH_3), 0.58 ($SiCH_3$)	7.79	7.79	$SiCH_3$	---	--
21	A	2.80 (CH_3)	7.89	7.89	CH_3	---	(7)

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

[b] Weak enhancement.

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

[d] Overlap with signals of phenyl-H.

[e] Emerges clearly in the NOE difference spectrum.

difference experiments (Figure 1g - 1l) allowed the clear identification of the 1,4-disubstituted congener **5**: only with this isomer a pronounced enhancement of the triazole-H singlet was observed upon irradiation of the signal of the benzylic methylene protons (Figure 1g,h). Furthermore, compound **6** could be distinguished from the 2,4-disubstituted isomer **15** considering a (moderate) through-space connection between NCH_2 and the ester ethyl group or, more reliable, on basis of ^{13}C-chemical shifts and $^{13}C,^{1}H$-coupling constants (see Experimental).

In contrast to the latter case, upon reaction of 4-phenyl-1,2,3-triazole with ethyl bromoacetate only two alkylation products (**8**, **17**) were isolated from the reaction mixture (GLC/MS analysis revealed only traces of the third possible isomer to be present), which again could be discriminated by NOE difference spectroscopy: compound **8** was characterized by a strong NOE between NCH_2 and the triazole-H, whereas with the other isomer **17** only a small through-space interaction of these spins could be observed.[26] As ^{13}C-NMR data as well as the complete lack of an NOE between NCH_2 and phenyl protons[27] rule out an 1,5-disubstitution pattern for **17**, this compound then must be the 2,4-isomer. Consequently, 1,5-substitution has to be attributed to the isomeric species being present only in traces in the reaction mixture. This finding is also in full agreement with reactivity considerations as the 1,5-isomer is the congener with the largest sterical hinderance, the formation of which can be assumed to be less favoured upon alkylation.

In summary, the presented NOE method has proven to be a valuable tool for the assignment of triazole-H resonances in various 1-alkyl- and 1-aryl-1,2,3-triazoles. Additionally, it enables a rapid and unambiguous discrimination of 1,4-disubstituted 1,2,3-triazoles from the corresponding 1,5- and 2,4-disubstituted 1,2,3-triazole regioisomers.

EXPERIMENTAL

General

Melting points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. IR spectra were recorded on a Jasco IRA-1 spectrophotometer, mass spectra were obtained on a Hewlett-Packard 5890A/5970B-GC/MSD instrument. Elemental analyses were performed at the Institute of Physical Chemistry, University of Vienna.

NMR Measurements

All NMR spectra were recorded on a Bruker AC 80 spectrometer (spectrometer frequency: 80.13 MHz for ^{1}H, 20.13 MHz for ^{13}C) equipped with an Aspect 3000 computer and standard software. Generally used acquisition parameters for the NOE difference spectra: approximately 0.2 M solutions (non degassed); temperature: 30°C; 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 s; number of scans: 96 - 400; pre-irradiation time: 3 - 5 s; irradiation power: 46 - 51 dB below 0.2 W for single-frequency irradiation (NOEDIFF), 55 - 62 dB below 0.2 W for multiplet irradiation according to the method of Kinns and Sanders[41] (NOEMULT).

Materials

The preparation of compounds investigated was carried out according to the references given in Tables 1 and 2.

*1-Benzyl-4-bromo-1*H*-1,2,3-triazole* (**4**)[31]

^{13}C-NMR ($CDCl_3$): δ (ppm) 133.73 (Ph C-1), 129.11 (Ph C-3,5), 128.94 (Ph C-4), 128.06 (Ph C-2,6), 123.71 (triazole C-5), 120.57 (triazole C-4), 54.72 (NCH_2).

Preparation of Compounds ***5***, ***6***, *and* ***15*** *via Benzylation of Ethyl 1*H*-1,2,3-Triazole-4-carboxylate*

Ethyl 1*H*-1,2,3-triazole-4-carboxylate[42] (1.411 g, 10 mmol) was added to a solution of sodium ethoxide prepared from 241 mg (10.5 mmol) of sodium and 15 ml of dry ethanol. After 30 min of stirring, 1.392 g (11 mmol) of benzyl chloride were added and the mixture was refluxed for 24 h. After cooling, the precipitate was filtered off, the filtrate was evaporated in vacuo and the residue was subjected to column chromatography (silica gel, eluent: dichloromethane - ethyl acetate, 9:1) to afford 492 mg (21%) of **15** (first fraction), 228 mg (10%) of **6** (middle fraction), and 716 mg (31%) of **5** (most retarded component).

*Ethyl 1-Benzyl-1*H*-1,2,3-triazole-4-carboxylate* (**5**): colorless crystals, mp 88-90°C (ref.[38] mp: 82-84°C); ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 160.25 (C=O), 140.02 [triazole C-4, ^2J(C-4,H-5) = 9.1 Hz], 133.71 (Ph C-1), 128.75 (Ph C-3,5), 128.51 (Ph C-4), 127.78 (Ph C-2,6), 127.73 [triazole C-5, ^1J(C-5,H-5) = 198.2 Hz, ^3J(C-5,NCH_2) = 2.8 Hz], 60.72 (OCH_2), 53.89 (NCH_2), 13.85 (CH_3); IR (KBr): 1700 cm^{-1} (C=O); MS: m/z (%) 231 (M^+, 1), 174 (30), 130 (24), 91 (100), 65 (18). Anal. calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.58; H, 5.51; N, 18.33.

*Ethyl 1-Benzyl-1*H*-1,2,3-triazole-5-carboxylate* (**6**): colorless oil; ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 158.10 (C=O), 137.85 [triazole C-4, ^1J(C-4,H-4) = 198.0 Hz], 134.89 (Ph C-1), 128.49 (Ph C-3,5), 128.11 (Ph C-4), 127.75 [Ph C-2,6 and triazole C-5, ^2J(C-5,H-4) = 13.7 Hz, ^3J(C-5,NCH_2) = 2.3 Hz], 61.54 (OCH_2), 53.10 (NCH_2), 13.86 (CH_3); IR (neat): 1710 cm^{-1} (C=O); MS: m/z (%) 231 (M^+, 1), 131 (18), 130 (60), 91 (100), 65 (18). Anal. calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.33; H, 5.54; N, 18.33.

*Ethyl 2-Benzyl-2*H*-1,2,3-triazole-4-carboxylate* (**15**): colorless oil, ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 160.31 (C=O), 140.04 [triazole C-4, ^2J(C-4,H-5) = 10.8 Hz], 137.00 [triazole C-5, ^1J(C-5,H-5) = 197.0 Hz], 134.02 (Ph C-1), 128.55 (Ph C-3,5), 128.34 (Ph C-4), 127.93 (Ph C-2,6), 61.06 (OCH_2), 59.07 (NCH_2), 13.98 (CH_3); IR (neat): 1710 cm^{-1} (C=O); MS: m/z (%) 231 (M^+, 45), 202 (11), 186 (13), 158 (13), 130 (15), 92 (13), 91 (100), 65 (16). Anal. calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.57; H, 5.63; N, 18.36.

*Ethyl 1*H*-1,2,3-Triazole-1-acetate* (**7**)[6]

^{13}C-NMR ($CDCl_3$): δ (ppm) 166.09 (C=O), 133.48 [triazole C-4, ^1J(C-4,H-4) = 195.0 Hz, ^2J(C-4,H-5) = 10.9 Hz], 124.88 [triazole C-5, ^1J(C-5,H-5) = 195.9 Hz, ^2J(C-5,H-4) = 15.7 Hz, ^3J(C-5,NCH_2) = 2.7 Hz], 61.77 (OCH_2), 50.23 (NCH_2), 13.55 (CH_3).

Ethyl 2H-*1,2,3-Triazole-2-acetate* (**16**)[6]

^{13}C-NMR ($CDCl_3$): δ (ppm) 166.51 (C=O), 134.95 [triazole C-4,5 , ^1J(C-4,H-4) = 193.2 Hz, ^2J(C-4,H-5) = 12.8 Hz], 61.77 (OCH_2), 55.19 (NCH_2), 13.81 (CH_3).

*Preparation of Compounds 8 and 17 via Reaction of 4-Phenyl-1*H-*1,2,3-triazole with Ethyl Bromoacetate*

4-Phenyl-1*H*-1,2,3-triazole[43] (435 mg, 3 mmol) was added to a solution of sodium ethoxide prepared from 69 mg (3 mmol) of sodium and 3 ml of dry ethanol. After addition of 501 mg (3 mmol) of ethyl bromoacetate the mixture was heated at reflux for 20 h. 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, 15:1) to afford 217 mg (31%) of **17** (first fraction) and 250 mg (36%) of **8**.

*Ethyl 4-Phenyl-1*H-*1,2,3-triazole-1-acetate* (**8**): colorless crystals, mp 94°C (ref.[40] mp 94-95°C, ref.[39] mp 96-98°C); ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 166.15 (C=O), 147.81 [triazole C-4, ^2J(C-4,H-5) = 9.7 Hz], 130.25 (Ph C-1), 128.59 (Ph C-3,5), 127.97 (Ph C-4), 125.52 (Ph C-2,6), 121.08 [triazole C-5, ^1J(C-5,H-5) = 194.2 Hz, ^3J(C-5,NCH_2) = 2.8 Hz], 62.09 (OCH_2), 50.66 (NCH_2), 13.78 (CH_3); IR (KBr): 1735 cm^{-1} (C=O); MS: m/z (%) 231 (M^+, 51), 203 (17), 175 (11), 174 (12), 160 (18), 147 (10), 146 (20), 131 (39), 130 (53), 118 (42), 116 (100), 105 (32), 103 (52), 102 (41), 91 (31), 89 (24), 77 (36), 63 (15). Anal. calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.50; H, 5.54; N, 18.22.

*Ethyl 4-Phenyl-2*H-*1,2,3-triazole-2-acetate* (**17**): colorless crystals, mp 69°C; ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 166.51 (C=O), 148.43 [triazole C-4, ^2J(C-4,H-5) = 11.1 Hz], 131.85 [triazole C-5, ^1J(C-5,H-5) = 191.6 Hz], 129.85 (Ph C-1), 128.62 (Ph C-3,5), 128.36 (Ph C-4), 125.80 (Ph C-2,6), 61.79 (OCH_2), 55.37 (NCH_2), 13.82 (CH_3); IR (KBr): 1745 cm^{-1} (C=O); MS: m/z (%) 231 (M^+, 89), 158 (100), 131 (33), 104 (35), 103 (16), 77 (17). Anal. calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.48; H, 5.66; N, 18.21.

*1-Diphenylmethyl-1*H-*1,2,3-triazole* (**9**) [32]

^{1}H-NMR: see Table 3; MS: m/z (%) 235 (M^+, 68), 234 (12), 206 (39), 168 (15), 167 (100), 166 (22), 165 (55), 152 (29), 130 (18), 103 (17), 77 (12).

*2-Diphenylmethyl-2*H-*1,2,3-triazole* (**18**)

Following the procedure for the preparation of **9** given in ref.,[32] compound **18** was obtained in 15% yield after column chromatography (silica gel, eluent: dichloromethane - ethyl acetate, 15:1). Colorless crystals, mp 86-88°C; ^{1}H-NMR: see Table 3; MS: m/z (%) 235 (62), 167 (100), 166 (23), 165 (47), 152 (18). Anal. calcd. for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86. Found: C, 76.39; H, 5.68; N, 17.96.

Reaction of 1H-1,2,3-Triazole with Triphenylmethyl Chloride

Following the procedure given in ref.[33] for the preparation of **10**, a mixture of 690 mg (10 mmol) of 1*H*-1,2,3-triazole, 2.788 g (10 mmol) of triphenylmethyl chloride and 1.012 g (10 mmol) of triethylamine in 10 ml of dry acetonitrile was refluxed for 5 h and worked up as described. The crude product was subjected to column chromatography (silica gel, eluent: dichloromethane - ethyl acetate, 15:1) to afford 1.149 g (37%) of **19** (first fraction), 945 mg of **19** containing some triphenylmethanol, and 434 mg (14%) of **10**.[44]

1-Triphenylmethyl-1H-1,2,3-triazole (**10**): colorless crystals, mp 205-207°C (ref.[33] mp 211°C); ^{1}H-NMR: see Table 3; MS: m/z (%) 311 (M^+, 12), 244 (37), 243 (100), 242 (32), 241 (27), 239 (18), 228 (13), 166 (18), 165 (82). Anal. calcd. for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.77; H, 5.64; N, 13.57.

2-Triphenylmethyl-2H-1,2,3-triazole (**19**): colorless crystals, mp 215°C; ^{1}H-NMR: see Table 3; MS: m/z (%) 311 (M^+, 57), 282 (16), 244 (23), 243 (100), 242 (14), 241 (11), 239 (12), 165 (52), 77 (13). Anal. calcd. for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.74; H, 5.53; N, 13.33.

1-Benzoyl-1H-1,2,3-triazole (**13**)[36]

^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 164.40 (C=O), 134.17 (Ph C-4), 133.32 [triazole C-4, ^1J(C-4,H-4) = 197.3 Hz, ^2J(C-4,H-5) = 11.1 Hz], 131.90 (Ph C-2,6), 129.69 (Ph C-1), 128.27 (Ph C-3,5), 123.66 [triazole C-5, ^1J(C-5,H-5) = 200.1 Hz, ^2J(C-5,H-4) = 15.8 Hz].

2-(tert.Butyldimethylsilyl)-2H-1,2,3-triazole (**20**)[45]

A solution of 690 mg (10 mmol) of 1*H*-1,2,3-triazole and 1.507 g (10 mmol) of tert.butyldimethylsilyl chloride in 20 ml of dry triethylamine was heated at reflux for 20 h. After cooling, the precipitated triethylamine hydrochloride was removed by filtration, the remaining solution was evaporated in vacuo and the residue was subjected to Kugelrohr distillation. A colorless oil consisting mainly of **20** accompanied by small amounts (<10%) of isomeric 1-(tert.butyldimethylsilyl)-1*H*-1,2,3-triazole came over at 60°C/0.02 mm. The product turned out to be very sensitive towards hydrolysis. Compound **20**: ^{1}H-NMR: see Table 3; ^{13}C-NMR ($CDCl_3$): δ (ppm) 135.52 [triazole C-4,5 , ^1J(C-4,H-4) = 190.9 Hz, ^2J(C-4,H-5) = 14.0 Hz], 25.32 (C-$\underline{C}H_3$), 17.71 ($\underline{C}$-CH_3), -5.81 ($SiCH_3$); MS: m/z (%) 183 (M^+, 3), 128 (40), 127 (96), 126 (99), 100 (12), 99 (43), 98 (100), 73 (33), 70 (52), 59 (18), 58 (14), 57 (18), 56 (12).

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REFERENCES AND NOTES

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1. Wamhoff, H. "Comprehensive Heterocyclic Chemistry", eds. Katritzky, A. R.; Rees, C. W.; Vol. 5, Pergamon Press, Oxford, 1984, p. 669.
2. Finley, K. T. "The Chemistry of Heterocyclic Compounds", eds. Weissberger, A.; Taylor, E. C.; Vol. 39, Wiley, New York, 1980.

3. Gilchrist, T. L.; Gymer, G. E. *Adv. Heterocyclic Chem.* **1974**, *16*, 33.
4. Pedersen, C. *Acta Chem. Scand.* **1959**, *13*, 888.
5. Mouysset, G,; Grassy, G.; Payard, M.; Commenges, G.; Carpy, A.; Couquelet, J. *J. Heterocylic Chem.* **1988**, *25*, 1167.
6. Gold, H. *Ann. Chem.* **1965**, *688*, 205.
7. Birkofer, L.; Wegner, P. *Chem. Ber.* **1966**, *99*, 2512.
8. Elguero, J.; Gonzalez, E.; Jacquier, R. *Bull. Soc. Chim. Fr.* **1967**, 2998.
9. Schofield, K.; Grimmett, M. R.; Keene, B. R. T. "Heteroaromatic Nitrogen Compounds: The Azoles", Cambridge University Press, Cambridge, 1976, p. 276.
10. L'abbé, G.; Galle, J. E.; Hassner A. *Tetrahedron Lett.* **1970**, 303.
11. Ykman, P.; L'abbé, G.; Smets, G. *Tetrahedron Lett.* **1970**, 5225.
12. Ykman, P.; L'abbé, G.; Smets, G. *Tetrahedron* **1971**, *27*, 5623.
13. Barlin, G. B.; Batterham, T. J. *J. Chem. Soc. B* **1967**, 516.
14. Thurber, T. C.; Pugmire, R. J.; Townsend, L. B. *J. Heterocyclic Chem.* **1974**, *11*, 645.
15. Tsoleridis, C.; Stephanidou-Stephanatou, J.; Alexandrou, N. E. *J. Heterocyclic Chem.* **1980**, *17*, 1127.
16. L'abbé, G.; Bruynseels, M.; Delbeke, P.; Toppet, S. *J. Heterocyclic Chem.* **1990**, *27*, 2021.
17. For a survey of ^{13}C chemical shifts and $^{13}C,^{1}H$ coupling constants of a number of N-substituted 1*H*-1,2,3-triazoles and 2*H*-1,2,3-triazoles see: Begtrup, M.; Elguero, J.; Faure, R.; Camps, P.; Estopá, C.; Ilavsky, D.; Fruchier, A.; Marzin, C.; de Mendoza, J. *Magn. Reson. Chem.* **1988**, *26*, 134.
18. For some representative examples regarding the application of NOE difference spectroscopy for the elucidation of aromatic substitution patterns see: Neuhaus, D.; Williamson, M. P. "The Nuclear Overhauser Effect in Structural and Conformational Analysis", VCH Publishers, New York, 1989, p. 359.
19. Loubinoux, B.; Colin, J.-L.; Tabbache, S. *J. Heterocyclic Chem.* **1984**, *21*, 1669.
20. Yokoyama, M.; Nakao, E.; Sujino, K.; Watanabe, S.; Togo, H. *Heterocycles* **1990**, *31*, 1669.
21. Similar studies have been recently published in the pyrazole (ref. 22) and 1,2,4-triazole series (ref. 23).
22. Holzer, W. *Tetrahedron* **1991**, *47*, 1393.
23. Holzer, W. *Tetrahedron* **1991**, *47*, 5471.
24. (a) Pappalardo, L.; Elguero, J.; Marzin, C. *C. R. Acad.Sci., Ser. C* **1973**, *277*, 1163; (b) Begtrup, M.; Claramunt, R. M.; Elguero, J. *J. Chem. Soc. Perkin Trans. II* **1978**, 99.
25. Benassi, R.; Folli, U.; Schenetti, L.; Taddei, F. *Adv. Heterocyclic Chem.* **1987**, *41*, 75.
26. Analogously, all 2-substituted 1,2,3-triazoles given in Table 3 exhibit only small or no NOEs between protons of R^2 and the triazole H-4,5 protons.
27. In this case causes for the absence of an enhancement other than a large distance between the involved spins can be excluded. Thus, the assignment can be relied on the lack of an NOE. For a discussion of the problem of establishing assignments on the absence of NOEs compare ref. 18, p. 358.
28. Hüttel, R.; Welzel, G. *Ann. Chem.* **1955**, *593*, 207.
29. Hoberg, H. *Ann. Chem.* **1967**, *707*, 147.
30. Wiley, R. H.; Hussung, K. F.; Moffat, J. *J. Org. Chem.* **1956**, *21*, 190.
31. Begtrup, M. *Acta Chem. Scand.* **1971**, *25*, 249.
32. Hirsch, K. S.; Jones, C. D. *Eur. Pat. Appl. EP* 165,778 (27 Dec 1985); *Chem. Abstr.* **1986**, *105*, 49045u.
33. Buechel, K. H.; Draber, W.; Schmidt, R. R.; Regel, E.; Eue, L. *Ger. Offen.* 1,935,292 (14 Jan 1971); *Chem. Abstr.* **1971**, *74*, 75496c.
34. Reisser, F. *Belg. BE* 893,815 (12 Jan 1983); *Chem. Abstr.* **1983**, *99*, 70735m.
35. Hüttel, R.; Kratzer, J. *Chem. Ber.* **1959**, *92*, 2014.
36. (a) Baltzer, O.; von Pechmann, H. *Ann. Chem.* **1891**, *262*, 314; (b) Bladin, J. A. *Chem. Ber.* **1893**, *26*, 2736.
37. Seebach, D.; Enders, D.; Dach, R.; Pieter, R. *Chem. Ber.* **1977**, *110*, 1879.
38. Abu-Orabi, S. T.; Atfah, M. A.; Jibril, I.; Mari'i, F. M.; Al-Sheikh Ali, A. *J. Heterocyclic Chem.* **1989**, *26*, 1461.
39. Biagi, G.; Livi, O.; da Settimo, A.; Lucacchini, A.; Mazzoni, M. R.; Barili, P. L. *Farmacao* **1985**, *40*, 73.
40. Tanaka, Y.; Miller, S. I. *Tetrahedron* **1973**, *29*, 3285.
41. Kinns, M.; Sanders, J. K. M. *J. Magn. Reson.* **1984**, *56*, 518.
42. Buckle, D. R.; Rockell, C. J. M. *J. Chem. Soc. Perkin Trans. I* **1982**, 627.
43. Birkofer, L.; Wegner, P. *Chem. Ber.* **1967**, *100*, 3485.
44. According to ref. 33, compound **10** should result as the sole product upon reaction of 1,2,3-triazole with trityl chloride.
45. Torii, S.; Tanaka, H.; Tanaka, M.; Yamada, S.; Nakai, A. *Eur. Pat. Appl. EP* 331,395 (06 Sep 1989); *Chem. Abstr.* **1990**, *112*, 157959y.