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^{1}H and ^{13}C NMR Study of the Structure of Alkylthio Enyne Alcohols and Glycols

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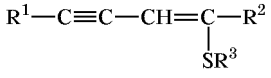
Abstract—Steric structure of some alkylthio enyne alcohols and glycols was determined by ^{1}H and ^{13}C NMR spectroscopy. Analysis of cross peaks in the 2M NOESY spectra showed that the double bond in these compounds has *Z* configuration. Criteria were found which indicate the position of the hydroxy-containing substituent with respect to the triple or double bond.

Our previous studies showed that nucleophilic addition of thiols to diacetylene derivatives is regio- and stereoselective [1–3]. In this connection, reliable determination of steric configuration of the vinylthioacetylene derivatives thus obtained is an important problem. For this purpose, we calculated the chemical shifts of olefinic protons according to the additivity scheme and analyzed long-range coupling constants for the same protons [1–3]. However, additivity schemes for calculation of proton chemical shifts in stereochemically nonrigid systems are insufficiently reliable because of possible conformational heterogeneity of configurational isomers. On the other hand, coupling constants reflect proton–proton interactions which are transmitted through both σ- and π-bond systems (as in the case of olefinic protons) and show a complicated angular dependence; therefore, their use in configurational analysis should be preceded by careful consideration [4].

The up-to-date level of NMR spectroscopy allows routine applications of two-dimensional homo- and heteronuclear techniques, which provide radically new possibilities for configurational and conformational analysis. The goal of the present study was to unambiguously assign signals in the ^{1}H and ^{13}C NMR spectra of some alkylthio-substituted enyne alcohols and glycols (compounds **I**–**VII**) and reliably determine their steric configuration with the aid of two-dimensional NMR techniques.

It was difficult to assign signals from the 1-CH_2OH and 4-CH_2OH groups in glycol **III**, as well as those of the 1-$C_2H_5C(CH_3)OH$ and 4-$C_2H_5C(CH_3)OH$ groups in glycol **IV**. The former showed a cross peak in the 2M NOESY spectrum [5] between the olefinic proton and that appearing at δ 4.26 ppm. Therefore, this signal was assigned to the 4-CH_2OH group. The corresponding signal in the ^{13}C NMR spectrum was identified using ^{1}H–^{13}C heteronuclear 2M HSQC technique [6]. In the 2M NOESY spectrum of glycol **IV** we observed a cross peak between the olefinic proton and the singlet at δ 1.41 ppm, which was attributed to 4-CH_3. The 2M ^{1}H–^{13}C HMBC spectrum [7] contained a cross peak for the above proton and carbon atom (δ_C 33.69 ppm) through three bonds, indicating that the latter belongs to 4-CH_2. The other signals were assigned using a combination of the NOESY and COSY techniques [8]. There were no problems in the assignment of ^{1}H NMR signals of compounds **I** and **V**–**VII**, so that their ^{13}C signals were unambiguously assigned using the HSQC technique. Signals from the β-, γ-, and δ-carbon atoms of the cyclohexane ring in **II** could be identified when the corresponding protons give a cross peak with the



I–**VII**

I, R^1 = $(CH_3)_2COH$, R^2 = H, R^3 = $(CH_3)_2CH$; **II**, R^1 = HOC_6H_{10}-*cyclo*, R^2 = H, R^3 = C_2H_5; **III**, R^1 = R^2 = CH_2OH, R^3 = C_2H_5; **IV**, R^1 = R^2 = $CH_3CH_2C(CH_3)OH$, R^3 = C_2H_5; **V**, R^1 = C_6H_5, R^2 = $(CH_3)_2COH$, R^3 = C_2H_5; **VI**, R^1 = $(CH_3)_2COH$, R^2 = CH_2OH, R^3 = C_2H_5; **VII**, R^1 = CH_2OH, R^2 = $(CH_3)_2COH$, R^3 = C_2H_5.

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^{1}H and ^{13}C NMR spectra of compounds **I**–**VII**[a]

Compound no.	^{1}H NMR spectrum, δ, ppm				
	3-H	4-H	R^1	R^2	R^3
I[b]	5.48	6.55	1.57 (CH_3), 2.00 (OH)		1.33 (CH_3), 3.19 (CH)
II[b]	5.52	6.49	1.60; 1.93 (β-H), 1.62 (γ-H), 1.23; 1.53 (δ-H), 1.95 (OH)		1.32 (CH_2), 2.78 (CH_3)
III[c]	5.87		4.45 (CH_2)	4.26 (CH_2), 2.08 (OH)	1.28 (CH_3), 2.94 (CH_2)
IV[d]	6.19		1.53 (β-CH_3); 1.10 (γ-CH_3); 1.76, 1.77 (CH_2)	1.41 (β-CH_3), 0.88 (γ-CH_3), 1.66; 1.81 (CH_2)	1.28 (CH_3), 3.08; 3.09 (CH_2)
V	6.40		7.32 (*o*-H), 7.47 (*m*-H), 7.32 (*p*-H)	1.44 (CH_3), 2.29 (OH)	1.32 (CH_3), 3.18 (CH_2)
VI	5.83		1.26 (CH_2), 2.14 (OH)	4.21 (CH_2), 1.90 (OH)	1.26 (CH_3), 2.93 (CH_2)
VII	6.24		4.42 (CH_2), 1.84 (OH)	1.40 (CH_3), 2.22 (OH)	1.25 (CH_3), 3.06 (CH_2)

Compound no.	^{13}C NMR spectrum, δ_C, ppm						
	C^1	C^2	C^3	C^4	R^1	R^2	R^3
I	101.88	78.78	104.00	138.90	31.53 (CH_3), 65.84 (C)		23.81 (CH_3), 37.46 (CH)
II	100.94	80.80	104.50	139.80	69.25 (C^{α}), 39.93 (C^{β}), 23.41 (C^{γ}), 25.23 (C^{δ})		15.68 (CH_3), 27.68 (CH_2)
III	95.38	82.12	106.55	148.83	51.81 (CH_2)	65.05 (CH_2)	15.05 (CH_3), 25.03 (CH_2)
IV	100.81	80.66	110.90	154.61	29.21 (β-CH_3), 9.08 (γ-CH_3), 36.53 (CH_2), 69.34 (C)	26.71 (β-CH_3), 8.23 (γ-CH_3), 33.69 (CH_2), 76.90 (C)	14.77 (CH_3), 28.53 (CH_2)
V	97.45	86.89	109.86	156.04	123.39 (C^i), 131.30 (C^o), 128.39 (C^m), 128.42 (C^p)	28.99 (CH_3), 74.35 (C)	14.83 (CH_3), 28.66 (CH_2)
VI	101.87	82.68	106.42	148.13	31.31 (CH_3), 65.65 (C)	64.82 (CH_2)	15.00 (CH_3), 24.92 (CH_2)
VII	95.71	82.68	109.72	156.01	51.39 (CH_2)	32.00 (CH_3), 74.53 (C)	14.71 (CH_3), 28.67 (CH_2)

[a] The indices "α," "β,", "γ," and "δ," refer to the position relative to the C^1 or C^4 carbon atom, and "*i*," "*o*," "*m*," and "*p*" denote the position of carbon atoms in the benzene ring.

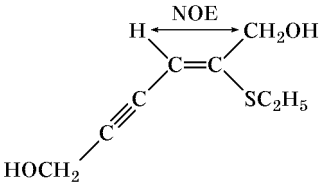
[b] ^3J(3-H, 4-H) = 9.9 Hz (**I**), 9.7 Hz (**II**).

[c] Signals from the hydroxy protons are averaged due to exchange.

[d] Signals from the CH_2 protons, which are neighboring to the chiral center, are nonequivalent.

SCH_2 carbon atom in the HSQC spectrum. By the same method, signals of the above protons in **II** were assigned.

Steric configuration of alcohols **I** and **II** can readily be determined from the coupling constants $^3J_{3\text{-H},4\text{-H}}$ which are equal to 9.9 and 9.7 Hz, respectively. These values correspond to *cis* arrangement of 3-H and 4-H. Hence alcohols **I** and **II** are *Z* isomers. In the NOESY spectrum of compounds **III**–**V** we observed a cross-peak between the olefinic proton and those of the CH_2OH (glycol **III**) or 4-CH_3 group (**III** and **IV**), which indicates that the corresponding fragments are spatially close (see structure **A**).



A

Therefore, compounds **III**–**V** also have *Z* configuration. In the case of isomeric glycols **VI** and **VII**, apart from determination of the position of substituents with respect to the double bond, it was necessary to elucidate whether the CH_2OH [or $(CH_3)COH$] group is located at the double or triple bond. Analysis of the ^{13}C NMR data for compounds **I**, **II**, and **IV** shows that the chemical shift of C^1 falls into the δ_C range from 100 to 102 ppm when a tertiary alcohol fragment is present at the triple bond. In the presence of a primary alcohol moiety, $\delta_C(C^1)$ decreases to 95 ppm (glycol **III**). Likewise, tertiary hydroxy group at the double bond gives rise to $\delta_C(C^4)$ 154–156 ppm (compounds **IV** and **V**), whereas primary hydroxy group reduces the corresponding value to 148 ppm (glycol **III**). These differences are explained by the fact that NMR spectral parameters of a nucleus are influenced mainly by its nearest environment [9].

The above differences in the chemical shifts of C^1 and C^4 led us to conclude that the primary hydroxy group in glycol **VI** is located at the double bond, while tertiary one, at the triple bond. Glycol **VII** is characterized by the reverse arrangement of the alcoholic fragments. This assignment is consistent with the presence of cross-peaks between the olefinic proton and CH_2OH group in the NOESY spectrum of **VI** and between the olefinic proton and 1-CH_3 group in the spectrum of **VII**. In addition, these data indicate *Z* configuration of glycols **VI** and **VII** with respect to the double bond.

It should be noted that our previous analysis of long-range proton coupling constants [1] gave directly opposite results while assigning the configuration of isomeric glycols **VI** and **VII**. Therefore, the use of long-range coupling constants is inappropriate for studying such structural isomerism. The ranges of C^1 and C^4 chemical shifts, determined in the present work for different alcoholic moieties, can be regarded as an efficient tool for analysis of the structure of other alkylthio enyne alcohols and glycols.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-250 spectrometer operating at 250.1 and 62.9 MHz, respectively; $CDCl_3$ was used as solvent, and HMDS, as internal reference; the concentration of samples was 5–10 wt % for ^{13}C NMR spectra and 1 wt % for ^{1}H NMR. Typical parameters of the pulse sequences and detailed description of NOESY, COSY, HSQC, and HMBC experiments were reported in [11]. The ^{1}H and ^{13}C NMR spectra of compounds **I**–**VII** are given in table.

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