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INVESTIGATION OF ISOMERIC FORMS OF 2-AMINOBENZOTHIAZOLES BY ^{13}C NMR SPECTROSCOPY

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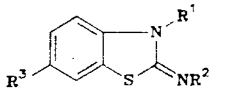
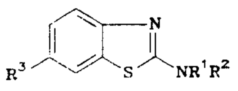
A method is presented for distinguishing the amino and imino isomers in a series of benzothiazoles by ^{13}C NMR. It is shown that this method is suitable for determination of the position of the side chain.

Isomeric 2-aminobenzothiazole derivatives are usually identified by IR, UV, PMR, and mass spectra [1, 2]. However, reliable data are obtained only for relatively simple structures. The presence of branched substituents containing more than one functional group levels the difference between the physicochemical characterizations of the isomers [3], because of which we undertook a study of the ^{13}C NMR spectra of a series of aminobenzothiazoles and iminobenzothiazolines:



I–IX



X–XIV

I $R^1=CH_3$, $R^2=H$; II $R^1=CH_2CH_2OH$, $R^2=H$; III $R^1=CH_2CH_2OH$, $R^2=H$; IV $R^1=CH_2CH(OH)CH_2OC_6H_5$, $R^2=H$; V $R^1=CH_2CH(OH)CH_2OC_6H_5$, $R^2=CH_3$; VI $R^1=CH_3$, $R^2=CH_2CH(OH)CH_2OC_6H_5$; VII $R^1=C_6H_5$, $R^2=CH_2CH(OH)CH_2OC_6H_5$; VIII $R^1=CH_2CH(OH)CH_2OC_6H_5$, $R^2=C_6H_5$; IX $R^1=R^2=CH_2CH(OH)CH_2OC_6H_5$; X $R^1=CH_3$, $R^2=H$; XI $R^1=CH_2CH_2OH$, $R^2=H$; XII $R^1=CH_2CH_2OH$, $R^2=H$; XIII $R^1=CH_2CH(OH) \times CH_2OC_6H_5$, $R^2=H$; XIV $R^1=CH_2CH(OH)CH_2OC_6H_5$, $R^2=CH_3$; I, II, IV—XI, XIII, XIV $R^3=H$, III, XII $R^3=CH_3$

The peaks of the carbon atoms were assigned on the basis of spectral data (see Table 1) obtained with complete and incomplete (off-resonance) suppression of C—H interactions and also by comparison with published data of ^{13}C NMR spectra of structurally close thiazole derivatives [4-6] and by taking into account α, β, and γ contributions of substituents [7].

For substituted aminobenzothiazoles and iminobenzothiazolines, the following order of arrangement of the carbon atoms is accepted:

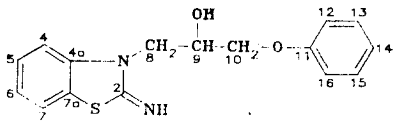


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TABLE 1. Carbon-13 NMR Spectra of Compounds I-XIV (s, singlet; d, doublet; t, triplet; q, quartet)

Compound	Chemical shifts, δ, ppm (in dimethyl-D_6 sulfoxide (DMSO-D_6))											
	$C_{(2)}$, s	$C_{(4)}$ d	$C_{(4a)}$, s	$C_{(5)}$, d	$C_{(6)}$	$C_{(7)}$, d	$C_{(7a)}$, s	$C_{(8)}$, t	$C_{(9)}$	$C_{(10)}$, t	$C_{(11)}$, s	$C_{(12)}$–$C_{(16)}$, d	N–CH_3, q
I	159,4	121,2*	141,0	121,6*	126,2 d	109,3	122,3	—	—	—	—	—	29,4
II	159,9	121,8	141,4	121,8	126,4 d	110,3	122,4	45,2	58,3t	—	—	—	—
III	159,4	121,5	138,7	126,4	130,0 s	109,3	122,0	44,9	58,1t	—	—	—	20,2**
IV	159,1	119,8	140,1	120,7	125,7 d	109,3	121,5	45,3	66,2d	69,3	157,8	128,6; 120,4; 114,0	—
IV	158,7	120,6	141,2	121,5*	126,3 d	110,9	122,2*	46,9	66,8d	70,2	156,6	129,5; 120,6; 114,6	40,4
VI	159,0	120,9	141,0	122,8	126,6 d	110,0	121,6	57,5	69,6d	70,5	155,6	129,6; 120,6; 114,7	30,1
VII	159,0	120,6	141,1	122,8	128,4 d	109,8	123,8	57,8	69,2d	70,5	155,4; 137,1	114,8; 129,9	—
VIII	159,1	120,2	141,0	122,2	127,1 d	111,1	121,9	47,2	66,7d	70,3	156,5; 151,5	129,6; 128,7; 126,8 130,1; 115,3; 121,1	—
IX	159,0	121,0	141,1	122,5	126,7 d	110,3	121,8	47,1; 57,5	67,3 d;59,7d	70,0; 70,5	159,5 156,4	129,8; 121,0; 114,0	—
X	167,7	119,2	153,0	127,1	122,0 d	122,0	130,7	—	—	—	—	—	30,8
XI	166,8	118,2	152,8	125,8	121,1 d	121,1	130,6	47,7	59,9 t	—	—	—	—
XII	165,6	117,3	150,2	126,2	129,6 s	120,5	130,1	46,3	59,3 t	—	—	—	20,4**
XIII	166,7	118,2	152,7	125,7	121,0*d	120,8*	130,7	47,4	67,8 d	70,2	158,8	129,6; 121,0; 114,7	—
XIV	168,3	117,8	153,2	126,7	121,6*d	121,6*	130,8	56,6	67,3 d	70,8	158,8	129,2; 121,6; 114,3	39,6

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*The assignment may be relative.

**CH_3—Ar peaks.

In imino compounds I-IX, the chemical shift of the $C_{(2)}$ atom is manifested in the region of 159.0-160.0 ppm, whereas in amino compounds X-XIV the peak of the $C_{(2)}$ atom resonates in the region of 165.6-168.3 ppm, i.e., the relative difference of the chemical shifts of the $C_{(2)}$ atoms of the amino and imino forms is 6.6-8.3 ppm. The difference of the chemical shifts of the peak of the $C_{(2)}$ atom in 2-aminothiazole and in 2-imino-3-methylthiazoline is 5.5 ppm [4]. Therefore, condensation of thiazole and thiazoline rings with a benzene ring leads to an increase of the difference of the chemical shifts of the $C_{(2)}$ atoms.

In imino compounds I-IX, depending on which nitrogen atom (the endo- or exocyclic one) the side chain is connected to, the chemical shift of the carbon atom that is located in the α position to the nitrogen atom changes significantly ($\Delta C_{(8)}$ = 10-11 ppm). A graphic example is compound IX, in which an identical side chain is connected to both nitrogen atoms, and the difference of the chemical shifts of the $C_{(8)}$ atoms connected to the endocyclic and exocyclic nitrogen atoms is 10.4 ppm.

In going from imino to amino derivatives, the chemical shift of the $C_{(4a)}$, $C_{(7a)}$, and $C_{(7)}$ atoms also changes significantly (Δ = 9-13 ppm), which is probably related to the effect of the bonding, which is more consistent in amino derivatives X-XIV than in the corresponding imino derivatives I-IX.

Thus, with respect to the chemical shifts of the $C_{(2)}$, $C_{(4a)}$, $C_{(7a)}$, and $C_{(7)}$, and $C_{(8)}$ atoms, we can distinguish the amino derivatives of benzothiazole uniquely and reliably from the corresponding imino isomers, and we can also establish which nitrogen atom the side chain is connected to.

EXPERIMENTAL

The ^{13}C NMR spectra of compounds I-XIV were obtained on a Tesla BS-567 A spectrometer (25.142 MHz), and the internal standard was TMS $\delta_{TMS} = \delta_{DMSO\text{-}D_6} + 39.6$ ppm with complete and incomplete suppression of C—H interactions. The PMR spectrum of compound II was recorded on a Jeol C-60 HL instrument, the mass spectrum was recorded on an MKh-1303 instrument (direct sample feed), the inlet-tube temperature was 100-120°C, and the ionizing voltage was 40 eV.

The synthesis of compounds III, XI, and XII is described in [8, 9]. Compounds IV-IX, XIII, and XIV were obtained by the methods of [3].

2-Imino-3-(β-hydroxyethyl)benzothiazoline (II). A solution of 1.5 g (10 mmoles) of 2-aminobenzothiazole in 2.5 ml of ethylene chlorohydrin was heated with stirring on a boiling water bath for 10 h. The precipitate was cooled and filtered, washed with dry acetone (2 × 3 ml), dissolved in the minimum amount of water, filtered to remove impurities, and neutralized with alkali. The precipitate was recrystallized from aqueous alcohol, and compound II, with mp 123-124°C, was obtained in 0.67 g (35%) yield. PMR spectrum (in $CDCl_3$): 3.90 (2H, triplet, CH_2N), 3.95 (2H, triplet, CH_2O), 5.45 (2H, broad singlet, NH, OH), 7.07-7.3 ppm (4H, multiplet, Ar). M^+ 194.

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