Imidomethylation of benzothiazole and its derivatives

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Imidomethylation of benzothiazole and its derivatives with *N*-hydroxymethylphthalimide in sulfuric acid was investigated and the structure of compounds obtained was adduced from IR spectra.

Исследовано имидометилирование бензотиазола и его производных *N*-гидроксиметилфталимидом в серной кислоте. Строение полученных фталимидов было определено с помощью ИК-спектроскопии.

As known [1] imidomethylation can take place at carbon or nitrogen atoms. This paper was aimed to ascertain, which position is preferred with benzothiazole and its derivatives and therefore, some model substances were suggested. The reactions were carried out in 93 % sulfuric acid at room temperature with the exception of 6-nitro-2-benzothiazolinethione; higher temperature or concentration of sulfuric acid make sulfonation a concurrent reaction [2].

Benzothiazole, 2-alkylthiobenzothiazoles, bis(2-benzothiazolyl) disulfide, 2-benzothiazolinethione (2-mercaptobenzothiazole), 6-nitro-2-benzothiazolinethione, and 3-(2-carbamoylethyl)-2-benzothiazolinone were the starting substances.

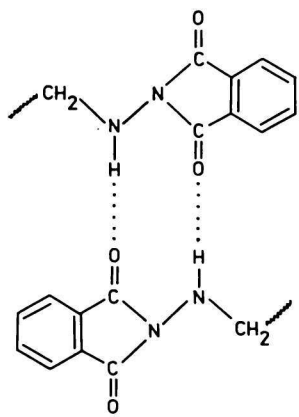
Compounds with a hydrogen atom attached to the nitrogen of the heterocyclic ring can react either in position 3 of the heterocycle or in position 6 of the aromatic ring. Position isomers were distinguished by IR spectrometry.

An attempt to obtain 3-methylamino-2-benzothiazolinethione, *i.e.* to free the amine from phthalimide by heating with hydrazine hydrate failed. Compound *VI* liberated during the reaction the starting 2-benzothiazolinethione, compound *V* generated a derivative of *N*-methylaminophthalimide *VIII* the structure of which was deduced from IR spectral data.

The IR spectra of compounds *I*—*IV* revealed absorption at $\tilde{\nu} = 760$—$730\ cm^{-1}$ and a pair of absorption bands at $\tilde{\nu} = 905$—$800\ cm^{-1}$ in the out-of-plane bending vibration ω(CH) region of the benzene ring; this is an evidence that the imidomethylation took place in position 6 of the benzothiazole ring of the starting

compound. An analogous spectrum in the afore-mentioned region also showed compounds *V* and *VIII* both having position 6 of the 2-thiobenzothiazole ring occupied by a nitro group. Compound *IX* is a product of a double imidomethylation taking place at the nitrogen atom, *i.e.* in position 3, and simultaneously in position 6 of the 2-oxobenzothiazole ring; as a result, also a pair of bands appeared at $\tilde{\nu} = 900—800\ cm^{-1}$. On the other hand, compounds *VI* and *VII*, which are the imidomethylation products in position 3 of 2-thio- or 2-oxobenzothiazole ring displayed in their spectra only a band of an out-of-plane bending vibration ω(CH) in the $\tilde{\nu} = 760—730\ cm^{-1}$ range characterizing the substitution in positions 1 and 2 of the benzene ring, whereas absorption in the $\tilde{\nu} = 900—800\ cm^{-1}$ range, evidencing the substitution in positions 1, 2, and 4, is lacking.

The IR spectra of compounds *I*—*VII*, *IX* revealed in the $\tilde{\nu} = 1800—1700\ cm^{-1}$ range two characteristic absorption bands of the stretching C=O vibration of the phthalimide residue. The more intense band at lower wavenumber belongs to an antisymmetric vibration $\nu_{as}(C=O)$, the less intense one at the higher wavenumber to a symmetric vibration $\nu_s(C=O)$ in a CO—N—CO arrangement [3—5]. The position of bands is solvent effect sensitive and rises from the suspension of the solid in nujol through solutions in chloroform to tetrachloromethane. Compounds *I*—*IV*, which are the products of imidomethylation at benzene ring, have the wavenumbers of stretching C=O vibration by approximately $10\ cm^{-1}$ lower than compounds *V* and *VI*, bearing the imidomethyl substitution at nitrogen of the heterocyclic ring. This fact can be rationalized by a stronger electron-accepting effect of the five-membered heterocyclic ring, when contrasted with the electron-accepting effect of the benzene ring. This analogy makes it possible to ascribe the bands at $\tilde{\nu} = 1722.5\ cm^{-1}$ and $1776\ cm^{-1}$ in the spectrum of tetrachloromethane solution of *IX* to stretching vibration $\nu(C=O)$ of the

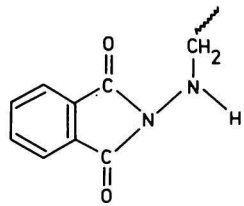


VIIIa

phthalimidomethyl group bound in position 6, whereas those at 1730.5 cm^{-1} and 1784 cm^{-1} to C=O stretching vibration of this group attached in position 3 to 2-oxobenzothiazole skeleton.

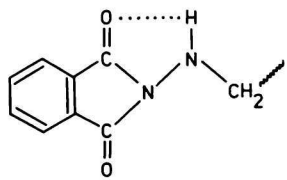
The IR spectrum of solid *VIII* showed two absorption bands of ν(C=O) stretching vibration at $\tilde{\nu} = 1640\ cm^{-1}$ and 1700 cm^{-1} and another one associated with the N—H group vibration at $\tilde{\nu} = 3150\ cm^{-1}$; this finding might be in favour of structure *VIIIa*.

The band at lower wavenumber was assigned to C=O groups linked by intermolecular hydrogen bonds, that at higher wavenumber to absorption of free C=O groups of the phthalimide ring. A change for $CHCl_3$ and CCl_4 solutions caused the intermolecular hydrogen bond to disappear, and consequently, spectra of compound *VIII* displayed in the $\tilde{\nu} = 1790$—1740 cm^{-1} region two characteristic bands due to symmetric and antisymmetric stretching C=O vibrations of the CO—N—CO grouping (*VIIIb*)



VIIIb

Wavenumbers of these bands are shifted by 10—30 cm^{-1} towards higher values with respect to those of analogous vibration of compounds *I*—*IV*, having an arylmethyl group bound to nitrogen atom of the phthalimide ring. Such a shift is in a good agreement with the effect of substituent on the wavenumber of symmetric and antisymmetric C=O stretching vibration, which was observed with analogous saturated cyclic imides [6]. Moreover, spectra of even relatively diluted solutions in $CHCl_3$ and CCl_4 contained two more weaker bands at lower wavenumbers (1732 cm^{-1} and 1666 cm^{-1} in CCl_4); these are probably associated with an absorption of "cyclic dimers" *VIIIa* or caused by conformation *VIIIc* showing a possibility to form intramolecular hydrogen bond between C=O and N—H groups



VIIIc

Solid compound *VII* revealed in nujol, in addition to bands of phthalimide ring, a band at $\tilde{\nu} = 1648\ cm^{-1}$ in the C=O stretching vibration region ascribable to vibrations of —NH—CO— group bound by intermolecular hydrogen bonds. The pair of absorption bands of the N—H stretching vibration at $\tilde{\nu} = 3180\ cm^{-1}$ and $3370\ cm^{-1}$ provides evidence for the presence of free molecules in the equilibrium mixture with bound molecules. Bands ν(C=O) at $\tilde{\nu} = 1710$—$1680\ cm^{-1}$ associated both with the free —NH—CO— grouping and the C=O group in the thiazole ring [7] are overlapped with the ν_{as}(C=O) band of the phthalimidyle residue.

It could be concluded that imidomethylation takes preferentially place at the amide nitrogen, either in the heterocycle or at other place bearing a suitable hydrogen atom, and substitution at the aromatic moiety of the molecule occurs with the second equivalent of the reagent.

Experimental

Yields, melting points, elemental analyses, and crystallization conditions are listed in Table 1 for benzothiazoles *I*—*IV* and in Table 2 for benzothiazolinones and benzothiazolinethiones *V*—*X*. The melting points were determined with a Kofler micro hot-stage. Spectral data of phthalimidomethyl derivatives *I*—*IX* are presented in Table 3. The IR spectra were recorded with a Specord 75 IR (Zeiss, Jena) spectrophotometer in the $\tilde{\nu} = 4000$—$700\ cm^{-1}$ range in nujol suspension, and in the $\tilde{\nu} = 1840$—$1560\ cm^{-1}$ region in $CHCl_3$ and CCl_4 solutions. The respective solutions were measured in 0.1 cm and 1.0 cm cells and the concentration fitted the 70—75 % absorption of C=O bands.

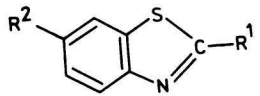
Imidomethylation with N-hydroxymethylphthalimide

Compounds I—VII and IX

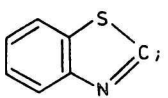
The benzothiazole derivative (50 mmol) was homogenized with *N*-hydroxymethylphthalimide (50 mmol for compounds *I*—*VII*, 0.1 mol for compound *IX*), dissolved in 93 % sulfuric acid (50 cm^3) with stirring and left to stand at room temperature for 48 h. The benzothiazole for preparation of compound *I* was reacted as sulfate; compound *V* was prepared by heating the mixture to 105—110 °C for 5 min and standing for 10 min. The mixture was then poured onto crushed ice (1000 g) and the product was after solidifying washed with cold and afterwards with 60 °C water to neutral reaction. The crude product was crystallized with addition of charcoal from solvents specified in Tables 1 and 2.

Table 1

Benzothiazole derivatives *I*—*IV*



Compound	R^1	R^2	Formula M_r	w_i(calc.)/% w_i(found)/%				Yield/%	M.p./°C	Solvent
				C	H	N	S			
I	H	CH_2Y	$C_{16}H_{10}N_2O_2S$ 294.3	65.29 65.54	3.42 3.43	9.52 9.41	10.89 10.82	71.4	231.5—232.5	Toluene—ethyl acetate (volume ratio = 1 : 1)
II	SCH_3	CH_2Y	$C_{17}H_{12}N_2O_2S_2$ 340.4	59.98 59.95	3.55 3.65	8.30 8.30	18.97 18.97	89.0	175.0—176.5	Acetone
III	SC_2H_5	CH_2Y	$C_{18}H_{14}N_2O_2S_2$ 354.4	60.99 61.10	3.98 4.05	7.90 7.74	18.09 18.30	78.5	156.0—157.5	Acetone
IV	SS-2-(6-CH_2Y)X	CH_2Y	$C_{32}H_{18}N_4O_4S_4$ 650.8	59.06 58.96	2.79 2.85	8.61 8.62	19.71 19.67	84.6	229—232	Dimethylformamide washed with ethanol

X = 

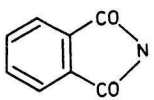
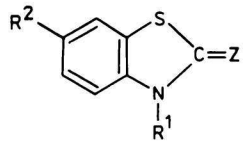
Y = 

Table 2

Benzothiazolinones and benzothiazolinethiones *V*—*X*



Compound	Z	R^1	R^2	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	N	S	Yield/%	M.p./°C	Solvent
V	S	CH_2Y	NO_2	$C_{16}H_9N_3O_4S_2$	51.74	2.44	11.31	17.27	64.2	207—208	Toluene–ethyl acetate
				371.4	51.44	2.31	11.52	17.47			(volume ratio = 1 : 3)
VI	S	CH_2Y	H	$C_{16}H_{10}N_2O_2S_2$	58.88	3.09	8.58	19.65	88.8	140—142.5	Toluene—ethyl acetate
				326.4	58.87	3.13	8.58	19.92			(volume ratio = 1 : 1)
VII	O	CH_2CH_2CONHY	H	$C_{19}H_{15}N_3O_4S$	59.83	3.96	11.02	8.41	90.2	231—234	Toluene
				381.4	60.01	3.98	10.91	8.66			
VIII	S	CH_2NHY	NO_2	$C_{16}H_{10}N_4O_4S_2$	49.73	2.61	14.50	16.60	60.0	258—261	Acetone
				386.4	49.68	2.71	14.45	16.30		decomp.	
IX	S	CH_2Y	CH_2Y	$C_{25}H_{15}N_3O_4S_2$	61.84	3.11	8.65	13.21	97.5	194—196	Toluene—ethyl acetate
				485.5	61.95	3.15	8.67	13.14			(volume ratio = 3 : 2)
X	O	$CH_2CH_2CONH_2$	H	$C_{10}H_{10}N_2O_2S$	54.04	4.54	12.60	14.43	71.2	189—190.5	Ethanol
				222.3	54.17	4.45	12.55	14.50			

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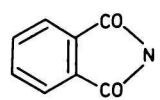

Table 3

Wavenumbers of some infrared bands of substituted phthalimides

Compound	$\tilde{\nu}/cm^{-1}$					
	ν(C=O)			ω(CH)[a]		ν(NH)[a]
	a	in $CHCl_3$	in CCl_4	4H	2H + 1H	
I	1682, 1755	1715.5, 1765	1724.5, 1778	738	800, 870	—
II	1680, 1755	1716, 1762	1721.5, 1774	735	820, 880	—
III	1680, 1755	1716, 1761.5	1721.5, 1773.5	735	820, 890	—
IV	1698, 1750	1716, 1761	1723, 1775.5	743	815, 880	—
V	1700, 1755	1728, 1761.5	1732.5, 1783.5	730	820, 905	—
VI	1705, 1758	1727, 1761	1732, 1784.5	760	—	—
VII	1700, 1758	1715.5, 1761.5	1715, 1767.5	730	—	3180, 3370
	1648	1681.5	1661			
VIII	1640, 1710	1743, 1779.5	1748, 1783.5	733	810, 890	3150
		1728, (1665)	1732 (1666)			
	1700, 1750	1718, 1774	1722.5, 1776	735	810, 880	—
IX		1722, 1778	1730.5, 1784			

a) In nujol.

3-(Phthalimidoaminomethyl)-6-nitro-2-benzothiazolinethione (VIII)

3-(Phthalimidomethyl)-6-nitro-2-benzothiazolinethione (14.8 g; 40 mmol) and 25 % hydrazine hydrate (10.3 g; 80 mmol) in ethanol (150 cm^3) were refluxed for 45 min. After removing phthalic acid hydrazide cold water (300 cm^3) was added and the precipitated product was filtered off.

3-(2-Carbamoylethyl)-2-benzothiazolinone (X)

3-(2-Cyanoethyl)-2-benzothiazolinone (10.2 g; 20 mmol) was dissolved in 96 % sulfuric acid (50 cm^3) with stirring and cooling keeping the temperature up to 20 °C. The mixture was left to stand for 2 h, poured on ice (1000 g) and then kept at 5 °C for 16 h. The separated product was washed with water to neutral reaction and crystallized from ethanol using charcoal.

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References

1. Zaugg, H. E. and Martin, W. B., in *Organic Reactions*, Vol. *14*, p. 52. J. Wiley, New York, 1965.
2. Sidóová, E., unpublished results.
3. Kellie, A. E., O'Sulivan, D. G., and Sadler, P. W., *J. Chem. Soc. 1956*, 3809.
4. Mirone, P. and Chiorboli, P., *Spectrochim. Acta 18*, 1425 (1962).
5. Matsuo, T., *Bull. Chem. Soc. Jap. 37*, 1844 (1964).
6. Fayart, C. and Foucand, A., *Bull. Soc. Chim. Fr. 1970*, 4491.
7. Perjéssy, A. and Sutoris, V., *Chem. Zvesti 38*, 119 (1984).

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