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Synthesis of Some New Series of Hydrazono Derivatives of 2-aminobenzothiazoles

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Some new series of hydrazono derivatives of 2-aminobenzothiazoles were synthesised. 2-aminobenzothiazoles were diazotised and then coupled with reactive methylene compounds viz., 2,4-pentanedione, ethyl-2-cyanoethanoate and 5,5-dimethylcylohexane-1,3-dione in presence of sodium acetate. The three series of compounds are expected to possess remarkable biological activity.

THE sulphur containing organic compounds have been found variegated use in medicine, e.g., antituberculous[1], hypnotics[2], local anaesthetics[3], rodentisides[4] and antispasmodics[5]. Hypoglycemic activity[6] has also been claimed in some derivatives of the series.

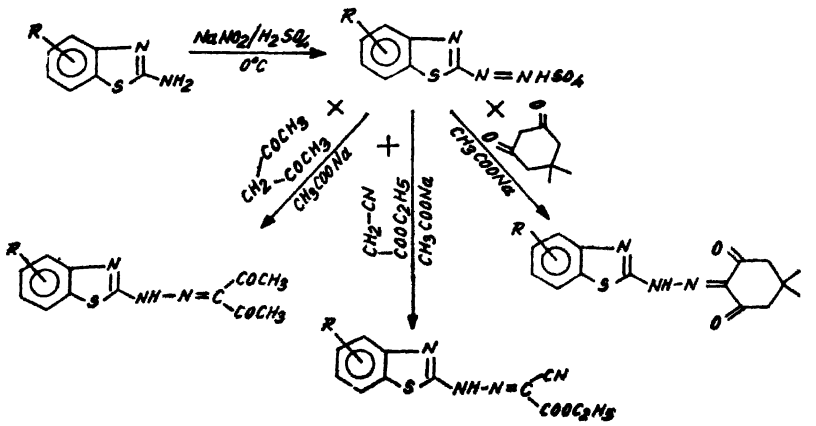
Recently the derivatives of 2-aminobenzothiazoles have been clinically tested for local anaesthetics[7-9]. In this communication, we are reporting the results on the synthesis of some new aminobenzothiazoles in which the arylhydrazono group has been introduced to promote greater biological activity.

Experimental

Several derivatives of 2-aminobenzothiazoles, e.g., 3-benzothiazolylhydrazonopentane-2, 4-diones (I), 2-benzothiazolylhydrazonoethyl-2-cyanoethanoates(II), and 2-benzothiazolylhydrazono-5, 5-dimethylcyclohexane-1, 3-diones(III) with substituents such as methyl, methoxy, ethoxy, chloro and nitro were synthesised.

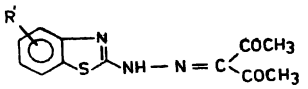
The parent compounds viz., 2-aminobenzothiazoles were synthesised by the method given in literature[10]. These benzothiazoles were diazotised[11,12] and subsequently coupled with reactive methylene compounds e.g., 2, 4-pentanedione, ethyl-2-cyanoethanoate and 5, 5-dimethylcyclohexane-1, 3-dione. Coupling reactions of aromatic diazo compounds with nitroparaffins[13,14] and reactive methylene compounds such as 2, 4-pentanedione, 1-phenyl-1, 3-butanedione-1, 3-diphenyl-1, 3-propanedione, ethylacetoacetate, cyanoacetoacetate[15-20], phenol ethers, polyalkoxybenzene, resorcinol and phloroglucinol[21] etc are known from a long time. The following procedure was adopted for synthesising the above mentioned hydrazono derivatives of 2-aminobenzothiazoles.

The required derivatives of 2-aminobenzothiazoles (3.75 g, 0.025 mol) were dissolved in concentrated sulphuric acid (6.2 ml) and water (6.2 ml). The mixture was cooled to 0° in an ice bath. To this sodium nitrite (1.75 g, 0.025 mol), cooled to 0°, was added in small portions. The diazonium salts so obtained were filtered into cooled mixture of sodium acetate (15.0 gm) (in 40 ml ethyl alcohol) and reactive methylene compound (0.025 mol) : 2, 4-pentanedione (2.5 g, 0.025 mol), ethyl 2-cyanoethanoate (2.8 g, 0.025 mol) and 5, 5-dimethylcyclohexane-1, 3-dione (3.5 g, 0.025 mol) for synthesising the I, II and III series of compounds respectively.



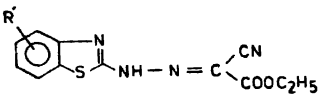
I II III

TABLE 1—CHARACTERISTICS OF SOME 3-BENZOTHIAZOLYLHYDRAZONOPENTANE-2,4-DIONES



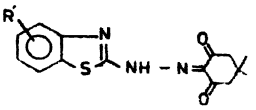
Sl. No.	R	m.p. °C	Yield	Colour	Formula		Analytical data C%	H%	N%
1.	H	187	68	Yellowish Brown	$C_{12}H_{11}N_3SO_2$	Cal.	55.1	4.2	16.0
						Found	55.0	4.0	15.8
2.	4-CH_3	182	66	Brown	$C_{13}H_{13}N_3SO_2$	Cal.	56.7	4.7	15.2
						Found	56.4	4.4	15.1
3.	5-CH_3	165	65	Brown	$C_{13}H_{13}N_3SO_2$	Cal.	56.7	4.7	15.2
						Found	56 5	4.4	15 0
4.	6-CH_3	170	65	Brown	$C_{13}H_{13}N_3SO_2$	Cal.	56.7	4.7	15.2
						Found	56.4	4.6	15.0
5.	4-OCH_3	235	70	Brownish Red	$C_{13}H_{13}N_3SO_3$	Cal.	53.6	4.4	14.4
						Found	53.4	4.0	14.2
6.	6-OCH_3	247	69	Green	$C_{13}H_{13}N_3SO_3$	Cal.	53.6	4.4	14.4
						Found	53.3	4.0	14 0
7.	4-OC_2H_5	125	64	Yellow	$C_{14}H_{15}N_3SO_3$	Cal.	55.0	4.9	13.7
						Found	55.1	4.8	13.5
8.	6-OC_2H_5	160	65	Brown	$C_{14}H_{15}N_3SO_3$	Cal.	55.0	4.9	13.7
						Found	55.1	4.7	13.6
9.	4-Cl	210	68	Yellow	$C_{12}H_{10}ClN_3SO_2$	Cal.	48.7	3.3	14.2
						Found	48.6	3.3	14.0
10.	5-Cl	146	68	Yellow	$C_{12}H_{10}ClN_3SO_2$	Cal.	48.7	3.3	14.2
						Found	48.6	3.2	14.0
11.	6-Cl	180	64	Brown	$C_{12}H_{10}ClN_3SO_2$	Cal.	48.7	3.3	14.2
						Found	48.5	3.3	14 0
12.	4,7-$(Cl)_2$	100	68	Yellow	$C_{12}H_9Cl_2N_3SO_2$	Cal.	43.6	2.7	12.7
						Found	43.5	2.7	12 4
13.	4,5-$(CH_3)_2$	159	68	Yellow	$C_{14}H_{15}N_3SO_2$	Cal.	58.1	5.1	14.5
						Found	58.0	5.2	14.2
14.	6-NO_2	233	69	Yellow	$C_{12}H_{10}N_4SO_4$	Cal.	47.0	3.2	18.3
						Found	47.1	3.1	18.2

TABLE 2—CHARACTERISTICS OF SOME 2-BENZOTHIAZOLYLHYDRAZONOETHYL-2-CYANOETHANOATE



Sl. No.	R	m.p. °C	Yield	Colour	Formula		Analytical data C%	H%	N%
1.	H	190	68	Yellow	$C_{12}H_{10}N_4O_2S$	Cal.	52.5	3.6	20.4
						Found	52.4	3.5	20.4
2.	4-CH_3	132	65	Yellow	$C_{13}H_{12}N_4O_2S$	Cal.	54.1	4.1	19.4
						Found	54.0	4.0	19.2
3.	5-CH_3	210	66	Brown	$C_{13}H_{12}N_4O_2S$	Cal.	54.1	4.1	19.4
						Found	54.0	3.9	19.2
4.	6-CH_3	225	65	Brown	$C_{13}H_{12}N_4O_2S$	Cal.	54.1	4.1	19.4
						Found	54.0	4.0	19.1
5.	4-OCH_3	135	64	Brown	$C_{13}H_{12}N_4O_3S$	Cal.	51.3	3.9	18.4
						Found	51.0	3.8	18.3
6.	6-OCH_3	205	64	Yellow	$C_{13}H_{12}N_4O_3S$	Cal.	51.3	3.9	18.4
						Found	51.2	3.8	18.2
7.	6-OC_2H_5	130	66	Brown	$C_{14}H_{14}N_4O_3S$	Cal.	52.8	4.4	17.6
						Found	51.9	4.2	16.9
8.	5-Cl	118	67	Brown	$C_{12}H_9N_4ClO_2S$	Cal.	46.6	2 9	18.1
						Found	46.5	2.8	18.1
9.	6-Cl	110	67	Brownish Black	$C_{12}H_9N_4ClO_2S$	Cal.	46.6	2.9	18.1
						Found	46.6	2.7	18 0
10.	4,5-$(CH_3)_2$	125	66	Yellow	$C_{14}H_{14}N_4O_2S$	Cal.	55.6	4 6	18.5
						Found	55.5	4.5	18.0
11.	6-NO_2	120	68	Yellow	$C_{12}H_9N_5O_4S$	Cal.	45.1	2.8	21.9
						Found	45.0	2.7	21.4

TABLE 3—CHARACTERISTICS OF SOME 2-BENZOTHIAZOLYLHYDRAZONO-5,5-DIMETHYLCYCLOHEXANE-1,3-DIONES



Sl. No.	R	m.p. °C	Yield %	Formula	Colour		Analytical data C%	H%	N%
1.	H	177	68	$C_{15}H_{15}N_3O_2S$	Yellow	Cal.	59.8	4.9	13.9
						Found	59.7	4.8	13.8
2.	4-CH_3	122	66	$C_{16}H_{17}N_3O_2S$	Brown	Cal.	60.9	5.3	13.3
						Found	60.8	5.3	13.2
3.	5-CH_3	161	65	$C_{16}H_{17}N_3O_2S$	Yellow	Cal.	60.9	5.3	13.2
						Found	60.7	5.2	13.1
4.	6-CH_3	193	65	$C_{16}H_{17}N_3O_2S$	Brown	Cal.	60.9	5.3	13.3
						Found	60.5	5.2	13.0
5.	4-OCH_3	200	64	$C_{16}H_{17}N_3O_3S$	Yellow	Cal.	58.0	5.1	12.6
						Found	58.1	5.0	12.4
6.	6-OCH_3	210	65	$C_{16}H_{17}N_3O_3S$	Yellow	Cal.	58.0	5.1	12.6
						Found	58.2	4.9	12.4
7.	4-Cl	135	66	$C_{15}H_{14}N_3O_2SCl$	Yellow	Cal.	53.6	4.1	12.5
						Found	53.5	4.0	12.2
8.	5-Cl	103	66	$C_{15}H_{14}N_3O_2SCl$	Yellow	Cal.	53.6	4.1	12.5
						Found	53.4	4.0	12.4
9.	4-OC_2H_5	177	64	$C_{17}H_{19}N_3O_3S$	Yellow	Cal.	59.3	5.5	12.1
						Found	58.9	5.0	12.0
10.	6-OC_2H_5	140	65	$C_{17}H_{19}N_3O_3S$	Brown	Cal.	59.3	5.5	12.1
						Found	59.2	5.0	12 0
11.	4,5-$(CH_3)_2$	167	64	$C_{17}H_{19}N_3O_2S$	Yellow	Cal.	62.0	5 7	12.7
						Found	61.8	5.5	12.6

All the melting points (I-III Series) were uncorrected and were determined by Kofler hot stage apparatus.

The products so precipitated were filtered, washed with water and recrystallised from ethyl-alcohol. The characteristics of all these compounds are shown in Tables 1, 2 and 3. The structures were confirmed on the basis of elemental analysis and ir spectra. Though the presence of a nitro group in the 6-position of the benzothiazole ring inhibits diazotisation of 2-amino group[22], the electron withdrawing nature of this group enhances the electrophilic character of the resulting diazonium cation by increasing the positive charge on the diazo group thereby making the coupling easy. Thus yield of the nitro derivative is not low as may be expected due to weakened basic character of amino group in it.

IR spectra :

The ir spectral data provide evidence in support of structures I, II and III for these series of compounds.

Characteristic bands in the region 1600-1630 cm^{-1} and 1480-1550 cm^{-1} due to the presence of $-C=N-$ and $-NH-N=C-$ grouping respectively, were given by all these compounds.

Sharp peaks for $-C=O$ at about 1690 cm^{-1} was obtained in case of 3-benzothiazolylhydrazonopentane-2, 4-diones(I). All the 2-benzothiazolylhydrazonoethyl-2-cyanoethanoates(II) gave characteristic peaks at 2200-2220 cm^{-1} of $-C\equiv N$ group. A peak at about 1680-1700 cm^{-1}, characteristic of cyclic $-C=O$ in case of 2-benzothiazolylhydrazono-$-5,5$-dimethylcyclohexane-1, 3-diones(III) was also distinguishable.

Acknowledgement

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