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Calcium pangamate (vitamin B_{15}) is one of the natural derivatives of dimethylglycine. The positive influence of calcium pangamate on living organisms is associated primarily with the ability of this vitamin to participate in transmethylation reactions [1] and undergo oxidative demethylation through the dimethylglycine group [2]. On the basis of this, other derivatives of dimethylglycine, mainly its esters, were prepared as possible synthetic analogs of vitamin B_{15} [3]. Sulfur containing derivatives of dimethylglycine are not known; however, S-analogs of unsubstituted amino carboxylic acids (thioglycine, thio- β -alanine, etc. [4]) and also certain of their S-esters [5] are reported.

We have prepared a number of esters of dimethylaminothioacetic acid similar to calcium pangamate in containing the dimethylglycine grouping and of general formula $RSCOCH_2N(CH_3)_2 \cdot HX$ (I-II, IV-XI, see Table 1). These compounds will possibly show the properties of donors of active methyl groups.

The possibility of using dicyclohexylcarbodiimide as dehydrating agent for the preparation of thioesters of dimethylglycine was examined. Carbomethoxymethyl dimethylaminothioacetate (I) and carbethoxymethyl dimethylaminothioacetate (II) were prepared by the condensation of dimethylglycine with methyl and ethyl thioglycolate.

 $\begin{aligned} (CH_3)_2 NCH_2 COOH + HSH_2 COOR \rightarrow (CH_3)_2 NCH_2 COSCH_2 COOR. \\ R = CH_3 \ (I), \qquad C_2 H_5 \ (II) \end{aligned}$

However, on carrying out the reaction with thiophenol and p-chlorothiophenol instead of the expected S-esters, only S-phenyldicyclohexylisothiourea and the corresponding S-(p-chlorophenyl)dicyclohexyliso-thiourea were isolated. Under similar conditions the reaction with n-propylmercaptan proceeds with the addition of the dimethylglycine to the dicyclohexylcarbodiimide to form N-dimethylaminoacetyl-N,N'-dicyclohexylurea.

The other S-esters were prepared from dimethylaminoacetyl chloride hydrochloride (III) by 2 methods: 1) by vigorous stirring and heating of a mixture of compound (III) and the appropriate lead mercaptide in ether and subsequent isolation of the methyl, propyl, or butyl ester of dimethylaminothioacetic acid as the oxalates (IV, V, and VI); bis-O,S-(dimethylaminoacetyl)thioethylene glycol was obtained as the dioxalate (VII) on carrying out the reaction with the lead mercaptide of monothioethylene glycol; 2) the ester hydrochlorides (VIII-XI; see Table 1) were prepared by heating a suspension of III with an excess of mercaptan in benzene until the hydrogen chloride evolution ceased.

EXPERIMENTAL

Carbomethoxymethyl Dimethylaminothioacetate Hydrochloride (I). To a mixture of 0.14 g of dimethylglycine hydrochloride, 0.1 g of triethylamine, and 0.11 g of methyl thioglycolate in 6 ml of anhydrous chloroform was added 0.21 g of dicyclohexylcarbodiimide. After 48 h the precipitate of dicyclohexylurea which had formed was filtered off and 3 ml of water added to the concentrated filtrate. The solution was extracted with ether, the extract was dried, and an ether solution of hydrogen chloride was added. A white

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Calc., 0/0	s	14,36	12,76	12,09	13,04	13,84	12,04		13,35	15,32
	z							10,13	11,66	
	ច				14,42	15,30	26,64			
	Ħ	5,87	6,82	7,22	6,56	6,09	4,93			7,23
	υ	37,66	43,01	45,27	53,74	51,82	45,11			63, 13
Empirical formula		C ₇ H ₁₃ NO ₅	C ₉ H ₁₇ NO ₅ S	C ₁₀ H ₁₉ NO ₅ S	C ₁₁ H ₁₆ CINOS	C ₁₀ H ₁₄ CINOS	C10H13Cl2NOS	C ₁₀ H ₁₃ CIN ₂ O ₃ S	C ₁₀ H ₁₂ N ₂ O ₃ S	C ₁₁ H ₁₆ NOS
Found, η_{o}	S	14,15, 14,79	12,70, 12,57	11,93, 11,98	13,01, 13,07	13,41, 13,29	11,64, 11,82		13,33, 13,38	15,09
	z				,			10,11, 10,15	11,60, 11,97	
	σ				14,39, 14,45	14,83, 14,70	26,38, 26,14			
	Н	5,93, 5,96	6,98, 6,76	7,26, 7,38	6,56, 6,68	6,52, 6,53	5,11, 5,07			7,30
	U	37,35, 38,21	43,49, 43,24	44,91, 44,86	54,03, 54,21	52,42, 52,11	45,08, 45,55			63,48
oļ	₩,blэiY		38	9	86	91	60	12	71	86
mp (in deg)		155—6 (decomp.)	160-2 (decomp.)	139-40 (decomp.)	164—6 (decomb.)	156—8 (decomn.)	158-9 (decomp.)	100-2 (decomp.)	634	I
	ХН		C ₂ H ₂ O ₄	C ₂ H ₃ O ₄	HCI	HCI	HCI	HCI	ł	1
×		CH ₃	n-C ₃ H ₇	n-C4H9	CH ₂ C ₆ H ₅	C ₆ H ₆	C ₆ H ₄ Cl-p	C ₆ H ₄ NO ₂ -p	C ₆ H ₄ NO ₂ -p	CH2C6H6*
. punodutoD		IV	>	IV	VIII	ΙX	×	IX	XII	XIII

TABLE 1. Esters of Dimethylaminoacetic Acid $(\rm CH_3)_2\rm NCH_2\rm COSR \cdot \rm HX$

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 $\frac{1}{20} \frac{1.5515}{1.5515}$, d²⁰ 1.0800 g/cm³.

precipitate of the hydrochloride (0.23 g, 100%) separated. The mp was 129-131°C (decomp., from a mixture of ether and isobutanol, 1:1). Found, %: Cl 15.94; 15.83. $C_7H_{14}CINO_3S$. Calculated, %: Cl 15.57.

Carbethoxymethyl Dimethylaminothioacetate Hydrochloride (II). This was prepared by an analogous route in 62% yield. The mp was 114-116° (decomp., from ethyl acetate). Found, %: Cl 14.74; 14.80; S 13.27; 13.58. C₈H₁₆ClNO₃. Calculated, %: Cl 14.67; S 13.26.

Dimethylaminoacetyl Chloride Hydrochloride (III). Finely ground phosphorus pentachloride (10.4 g) was suspended in 100 ml of acetyl chloride. Well ground dimethylaminoacetic acid (5.15 g) was added to the suspension with ice cooling over 1 h. After 4 h the acetyl chloride was filtered and the precipitate of III washed with several portions of dry petroleum ether or benzene. The washed product was at once all used in acylation reaction.

<u>bis-O,S-(dimethylaminoacetyl)thioethylene Glycol Dioxalate (VII)</u>. The lead mercaptide of monothioethylene glycol (11 g) and III prepared from 1.55 g of dimethylaminoacetic acid was stirred in 100 ml of dry benzene at 60-70° for 2 days. The precipitate was filtered off and treated with alcohol. The alcoholic solution was rapidly neutralized in the cold to pH 9.0 with aqueous sodium hydroxide solution. The mixture was extracted with ether, the ether extracts were dried with anhydrous sodium sulfate and an ether solution of oxalic acid added to the combined extract. This gave 0.15 g (5%) of VII as a white crystalline powder. The mp was 185°. Found, %: C 39.53; H 5.77; S 7.81, $C_{14}H_{24}N_2O_4$. Calculated, %: C 39.30; H 5.66; S 7.49. The oxalates IV, V, and VI (see Table 1) were prepared similarly in an ether medium.

<u>S-Esters of Dimethylaminothioacetic Acid, Hydrochlorides (VIII-XI; see Table 1).</u> Compound (III), prepared from 0.05 mole of dimethylaminoacetic acid, was suspended in 100 ml of dry benzene. To the suspension was added 0.05-0.08 mole of mercaptan dissolved in benzene. The reaction mixture was heated with stirring to 70-75° until the evolution of hydrogen chloride had ceased completely. Compounds VIII-XI were obtained as hydrochlorides contaminated with small amounts of dimethylglycine hydrochloride. In order to prepare the esters as free bases the salt was dissolved in water and neutralized with aqueous alkali solution while cooling strongly. The free base which separated was rapidly extracted with ether. The ether extracts were dried. After distillation of the solvent the pure S-esters (XII-XIII) were obtained. The substances were readily soluble in organic solvents but insoluble in water. They decomposed on distillation in vacuum (3 mm). The analytically pure hydrochlorides were prepared by adding an ether solution of hydrogen chlor-ide to an ether solution of the free base.

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