1-ARYL-5-CARBOXYMETHYLHYDANTOIN DERIVATIVES.

STRUCTURE OF 1-PHENYL-2-THIO-5-CARBOMETHOXYMETHYLHYDANTOIN

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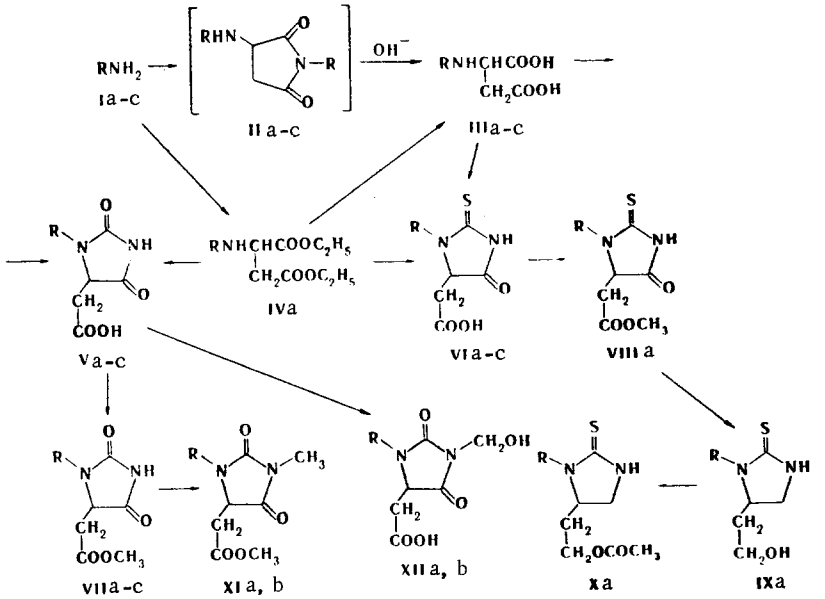
The reaction of aromatic amines with maleic acid or its diethyl ester with subsequent hydrolysis gave N-arylaspartic acids, which were converted to 1-aryl- and 1-aryl-2-thio-5-carboxymethylhydantoins by the action of urea, cyanates, or thiocyanates in an acidic medium. Esterification of the acid products with methanol gave the corresponding carbomethoxymethylhydantoins, which were converted by reduction to tetrahydroimidazole derivatives and by acetylation to acetyl derivatives. Alkylation of the carboxymethylhydantoins with dimethyl sulfate gave 3-methyl derivatives of hydantoins, while alkylation with formaldehyde gave 3-hydroxymethyl derivatives of hydantoins. Data from the x-ray diffraction analysis of 1-phenyl-2-thio-5-carbomethoxymethylhydantoin are presented.

Hydantoin and its derivatives have found application as medicinal preparations and intermediates for their synthesis [1, 2], antibacterial compounds [3], growth regulators [4], and starting compounds in the synthesis of polymers [5].

The aim of the present investigation was to search for new biologically active compounds. The reaction of aromatic amines I with maleic acid with subsequent hydrolysis of the resulting arylimide II gave N-arylaspartic acids III [6], which were also obtained by hydrolysis of diethyl ester IV, which is the product of the reaction of I with diethyl maleate. The reaction of acids III with urea, cyanates, and thiocyanates in acetic acid [7] with subsequent cyclization with hydrochloric acid gave the previously undescribed 1-aryl-5-carboxymethyl- (V) and 1-aryl-2-thio-5-carboxymethylhydantoins (VI). Esterification of V and VI with methanol in the presence of sulfuric acid gave the methyl esters (VII and VIII) of the carboxymethyl derivatives. 1-Phenyl-2-thio-5-carbomethoxymethylhydantoin (VIIIa) was converted by hydrogenation with lithium aluminum hydride to tetrahydroimidazole deriva-



I—XII a R=C_6H_5, b R=p-$CH_3C_6H_4$, c R=p-$CH_3OC_6H_4$

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TABLE 1. Coordinates of the Atoms ($\cdot 10^4$) in the $C_{12}H_{12}N_2O_3S$ (VIIIa) Structure

Atom	x	y	z	Atom	x	y	z
S	3890 (1)	2522 (2)	0615 (1)	C_9	4521 (4)	−2961 (6)	1418 (4)
N_1	3570 (3)	−0936 (5)	0134 (2)	C_{10}	4692 (4)	−3695 (7)	2394 (4)
C_2	3533 (3)	0786 (6)	−0,121 (3)	C_{11}	4120 (5)	−3087 (8)	3095 (4)
N_3	3110 (3)	0869 (5)	−1178 (3)	C_{12}	3379 (4)	−1763 (7)	2848 (4)
C_4	2822 (4)	−0734 (6)	−1609 (3)	C_{13}	3210 (4)	−1018 (7)	1878 (3)
C_5	3158 (4)	−2089 (6)	−0755 (3)	C_{14}	0238 (5)	−2879 (8)	0973 (5)
C_6	2280 (4)	−3339 (6)	−0584 (4)	O_{15}	2408 (3)	−1021 (4)	−2496 (2)
C_7	1468 (3)	−2433 (7)	−0110 (3)	O_{16}	1275 (2)	−0860 (4)	−0181 (2)
C_8	3777 (3)	−1625 (6)	1176 (3)	O_{17}	0994 (3)	−3576 (4)	0409 (2)

TABLE 2. Bond Lengths (d, Å) and Bond Angles (ω, deg) in the VIIIa Structure

Bond	d	Bond	d
N_1—C_2	1,341 (6)	C_6—C_7	1,497 (7)
N_1—C_8	1,446 (5)	C_7—O_{16}	1,213 (6)
N_1—C_5	1,473 (5)	C_7—O_{17}	1,328 (6)
C_2—S	1,642 (5)	C_8—C_9	1,390 (7)
C_2—N_3	1,397 (5)	C_9—C_{10}	1,381 (7)
N_3—C_4	1,358 (6)	C_{10}—C_{11}	1,377 (8)
N_3—H	0,85 (4)	C_{11}—C_{12}	1,382 (8)
C_4—O_{15}	1,208 (6)	C_{12}—C_{13}	1,376 (7)
C_4—C_5	1,521 (6)	C_{13}—C_8	1,374 (7)
C_5—C_6	1,533 (7)	C_{14}—O_{17}	1,447 (7)
Angle	**ω**	**Angle**	**ω**
C_2—N_1—C_5	112,5 (3)	C_6—C_7—O_{16}	124,5 (4)
C_2—N_1—C_8	125,3 (4)	C_6—C_7—O_{17}	111,0 (4)
C_5—N_1—C_8	121,0 (3)	O_{16}—C_7—O_{17}	124,4 (4)
N_1—C_2—N_3	106,4 (4)	N_1—C_8—C_9	117,9 (4)
N_1—C_2—S	129,3 (3)	N_1—C_8—C_{13}	120,0 (4)
N_3—C_2—S	124,3 (3)	C_9—C_8—C_{13}	122,0 (4)
C_2—N_3—C_4	113,5 (4)	C_8—C_9—C_{10}	118,7 (4)
N_3—C_4—C_5	105,9 (4)	C_9—C_{10}—C_{11}	119,1 (5)
N_3—C_4—O_{15}	126,7 (4)	C_{10}—C_{11}—C_{12}	121,8 (5)
C_4—C_5—N_1	101,5 (4)	C_{11}—C_{12}—C_{13}	119,3 (5)
N_1—C_5—C_6	114,1 (4)	C_{12}—C_{13}—C_8	119,0 (5)
C_4—C_5—C_6	114,3 (4)	C_7—O_{17}—C_{14}	117,6 (4)
C_5—C_6—C_7	112,9 (4)		

IXa, which reacts with acetic anhydride to give acetyl derivative Xa. The IR spectrum of IXa does not contain an absorption band at 1700 cm^{-1}; signals of three methylene groups in the form of complex multiplets are observed in the PMR spectrum. At 70°C in d-DMSO the OH group of the compound gives a signal in the form of a triplet at 4.16 ppm, which is absent at room temperature.

3-Methyl derivatives XI were obtained by alkylation of VII with dimethyl sulfate in the presence of alkali, while 3-hydroxymethyl derivatives XII were isolated by refluxing V in 40% formalin.

In order to prove the structure we subjected 1-phenyl-2-thio-5-carbomethoxymethyl-hydantoin (VIIIa) to x-ray diffraction analysis (Fig. 1 and Table 1). The heteroring of the molecule is virtually planar; the maximum deviation of the C_4 atom from the plane is 0.027 Å. The deviations of the S, C_8, and O_{15} atoms from the same plane are, respectively, 0.048, 0.261, and 0.060 Å. Both the bond lengths and the bond angles of the thiohydantoin fragment of the molecule are very close to the corresponding values in the 2-thiohydantoin molecule [8] (the differences do not exceed 0.025 Å and 0.9°). The length of the C=S bond, which is 1.642 Å, is somewhat shorter than the average value of 1.677 Å [9]. The angle between the planes of the phenyl ring and the heteroring is 58.9°. The length of the C_8—N_1 bond is 1.466 Å, which is close to the average value of 1.42 Å [9]. The length of the C—H bonds ranges from 0.83 to 1.06 Å (average value 0.99 Å). The carbomethoxymethyl fragment

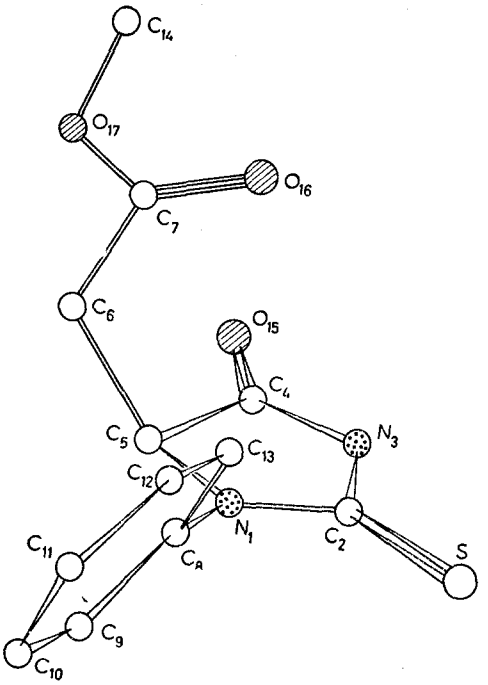

Fig. 1. Geometry of the 1-phenyl-2-thio-5-carbomethoxymethylhydantoin (VIIIa) molecule in the crystalline form.

is close to planar and, as it were, "hangs over" the heteroring. The C_{14}—O_{17}—C_7—C_6 torsion angle is 4.2°. This fragment has the normal geometry.

In the crystal the molecules are connected by hydrogen bonds to form infinite chains oriented along the b axis. The $O_{15}...H(N_3)$ distance (1/2 − x, −1/2 + y, −1/2 − z) is 2.08 Å, while the $O_{15}...N_3$ distance is 2.926 Å, and angle N_3—H...O_{15} is 174°. Some of the shortest intermolecular contacts are as follows:

$S\cdots C_9$ $(x, y+1, z)$ 3,616 Å,
$C_7\cdots C_{11}$ $(x-1/2, -1/2-y, z-1/2)$ 3,494 Å,
$C_6\cdots O_{15}$ $(1/2-x, y-1/2, -1/2-z)$ 3,333 Å,
$C_{11}\cdots O_{16}$ $(3/2-x, y-1/2, 1/2-z)$ 3,335 Å,
$C_{12}\cdots O_{17}$ $(1/2-x, 1/2+y, 1/2-z)$ 3,318 Å,
$C_9\cdots N_3$ $(1-x, -y, -z)$ 3,532 Å.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with Hitachi R-22 (90 MHz) and Tesla BS-487C (80 MHz) spectrometers with hexamethyldisiloxane as the internal standard. The individuality of the substances was verified by thin-layer chromatography (TLC) on plates with a loose layer of aluminum oxide or silica gel and on Silufol UV-254 plates.

The intensities of the reflections were measured with a Syntex-$P2_1$ diffractometer by means of Mo emission, a graphite monochromator, and a 0.30 by 0.35 by 0.55 mm crystal of 1-phenyl-2-thio-5-carbomethoxymethylhydantoin (VIIIa). The crystallographic data are as follows: a = 13.028(2), b = 7.556(1), c = 13.232(2) Å, β = 101.54(1)°, Z = 4, space group $P2_1/n$, d_{meas} = 1.37, and d_{calc} = 1.38 g/cm³. The intensities of 2246 reflections were measured by $2\theta/\omega$ scanning over the range $2\theta \leq 50°$. In the calculations we used 1783 reflections with $I > 2\sigma$, disregarding absorption. The structure was elucidated by the direct method by means of the MULTAN-XTL program. Anisotropic heat factors were used in the final total matrix refinement for the nonhydrogen atoms, while isotropic fixed B values of 4 Å² were used for the hydrogen atoms. Ultimately, R = 0.054 and R_w = 0.059 (R = 0.067 and R_w = 0.060 for all of the measured reflections), where $w = 1/\sigma_{F^2}$. The refined coordinates of the atoms are presented in Table 1.

TABLE 3. PMR Spectra

Compound	Solvent	δ, ppm
IIIa	CD_3OD	2,67 (2H, d CH_2); 4,34 (1H, t, CH); 6,78—7,19 (5H, m, arom.)
IIIb	CD_3OD	2,04 (3H, s CH_3); 2,65 (2H, d, CH_2); 4,22 (1H, t, CH); 6,36—6,9 (4H, arom.)
IIIc	CD_3OD	2,65 (2H, d, CH_2); 3,55 (3H, s, O—CH_3); 4,18 (1H, t, CH); 6,59 (4H, arom.)
IVa	CCl_4	1,08 (6H, t, $2CH_3$); 2,57 (2H, d, CH_2); 3,78—4,25 (5H, m, CH, $2CH_2$); 6,30—7,05 (5H, arom.)
Va	CF_3COOH	2,81 (2H, q, CH_2); 4,9 (1H, t, CH); 7,02—7,39 (5H, arom.)
Vb	CF_3COOH	1,88 (3H, s, CH_3); 2,61 (2H, t, CH_2); 4,57 (1H, t, CH); 6,77 (4H, s, arom.)
Vc	CF_3COOH	2,68 (2H, t, CH_2); 3,48 (3H, s, O—CH_3); 4,62 (1H, t, CH); 6,55—6,95 (4H, arom.)
VIa	CF_3COOH	2,58 (2H, q, CH_2); 4,6 (1H, t, CH); 6,77—7,07 (5H, m, arom.)
VIb	$(CD_3)_2CO$	2,22 (3H s, CH_3); 2,71 (2H, q, CH_2); 4,87 (1H, t, CH); 7,14—7,24 (4H, m, arom.)
VIc	CF_3COOH	2,68 (2H, m, CH_2); 3,49 (3H, s, O—CH_3); 4,60 (1H, t, CH); 6,57—6,97 (4H, m, arom.)
VIIb	$(CD_3)_2CO$	2,17 (3H, s, O—CH_3); 2,74 (2H, d, CH_2); 2,89 (3H, s, $COOCH_3$); 4,85 (1H, t, CH); 6,95—7,30 (4H, m, arom.)
VIIc	$CDCl_3$	2,22 (2H, q, CH_2); 3,46 (3H, s, O—CH_3); 3,67 (3H, s, $COOCH_3$); 4,61 (1H, t, CH); 6,65—7,20 (4H, m, arom.)
VIIIa	$(CD_3)_2CO$	2,76 (2H, q, CH_2); 3,46 (3H, s, $COOCH_3$); 4,98 (5H, s, arom.)
IXa	$(CD_3)_2CO$	1,47—1,72 (2H, m, CH_2); 3,0—3,85 (4H, m, 4-CH_2, CH_2OH); 4,3—4,67 (1H, m, CH); 7,11—7,42 (5H, m, arom.)
Xa	$(CD_3)_2CO$	1,53—1,76 (2H, m, CH_2); 1,86 (3H, s, CH_3); 3,26—4,02 (4H, m, 4-CH_2, CH_2—O); 4,33—4,61 (1H, m, CH); 7,1—7,45 (5H, m, arom.)
XIa	$(CD_3)_2CO$	2,85 (2H, q, CH_2); 2,93 (3H, s, N—CH_3); 3,48 (3H, s, $COOCH_3$); 4,97 (1H, t, CH); 7,08—7,5 (5H, arom.)
XIc	$CDCl_3$	2,57—2,72 (2H, m, CH_2); 2,92 (3H, s, N—CH_3; 3,4 (3H, s, O—CH_3); 3,61 (3H, s, $COOCH_3$); 4,46 (1H, t, CH); 6,61—7,11 (4H, m, arom.)
XIIa	CF_3COOH	2,66 (2H, m, CH_2); 4,56 (1H, t, CH); 4,92 (2H, t, CH_2OH); 6,91 (5H, arom.)
XIIb	CF_3COOH	1,85 (3H, s, CH_3); 2,67 (2H, t, CH_2); 4,54 (1H, t, CH); 4,93 (2H, s, CH_2OH); 6,77 (4H, s, arom.)

N-Phenylaspartic Acid (IIIa). A) A 58-g (0.5 mole) sample of maleic acid was dissolved in 200 ml of water, 93 g (1 mole) of aniline was added, and the mixture was heated with stirring at 100°C for 20 h. It was then cooled and treated with 100 ml of 45% NaOH solution, and the mixture was heated at 100°C for another 12 h. It was then cooled and extracted with ether to remove the liberated aniline. The alkaline solution was treated with hydrochloric acid until it was acidic with respect to Congo, and the liberated acid IIIa was removed by filtration, washed with water and ether, and dried to give 152 g of product (see Tables 3 and 4).

B) A 5.2-g (0.02 mole) sample of diethyl ester IVa was dissolved in 20 ml of ethanol, a solution of 2 g of NaOH in 15 ml of 80% ethanol was added, and the mixture was stirred for 10 min and allowed to stand at 4°C for 2-3 h. The liberated N-phenylaspartic acid salt was removed by filtration and dissolved in 20 ml of water, and the solution was acidified to pH 5 with hydrochloric acid. When the solution was allowed to stand at 4°C, 3 g of IIIa crystallized out.

N-(p-Tolyl)aspartic Acid (IIIb). A) A mixture of 53 g (0.5 mole) of p-toluidine, 29 g (0.25 mole) of maleic acid, and 200 ml of water was heated at 100°C for 20 h, and acid IIIb was isolated as in the preparation of IIIa by method A to give 39 g of product in the form of the monohydrate (see Tables 3 and 4).

B) The reaction of 107 g (1 mole) of toluidine and 49 g (0.5 mole) of maleic anhydride in 100 ml of water as in method A gave 65 g of acid IIIb in the form of the monohydrate.

N-(p-Methoxyphenyl)aspartic Acid (IIIc). The reaction of 123 g (1 mole) of p-anisidine and 58 g (0.5 mole) of maleic acid as in the preparation of IIIa by method A gave 85 g of IIIc (Tables 3 and 4).

Diethyl Ether N-Phenylaspartate (IVa). A mixture of 48 g (0.5 mole) of maleic anhydride mole) of diethyl maleate, and 10 ml of glacial acetic acid was heated at 120°C for 18 h, after which the acetic acid was removed with a rotary evaporator, and the residual viscous mass was distilled *in vacuo* with collection of the fraction with bp 180-190°C (5 mm). The yield was 50 g (see Tables 3 and 4).

TABLE 4. Characteristics of the Synthesized Compounds

Compound	mp, °C	IR spectra, cm^{-1}			N found, %	Empirical formula	N calc., %	Yield, %
		NH, OH	C=O	hydantoin ring				
IIIa	143—145 *	—	—	—	6,8	$C_{10}H_{11}NO_4$	6,7	76[a] 60[b]
IIIb	96—98*	—	—	—	5,6	$C_{11}H_{13}NO_4 \cdot H_2O$	5,8	65
IIIc	157—159*	—	—	—	5,9	$C_{11}H_{13}NO_5$	5,8	71
IVa	47—49†	3408	1745	—	5,4	$C_{14}H_{19}NO_4$	5,3	38
Va	206—207*	3292, 3332	1608, 1662	1160, 1180	12,0	$C_{11}H_{10}N_2O_4$	12,0	54
Vb	223—225 *	3195, 3260	1720, 1754 1795	1161, 1195	11,4	$C_{12}H_{12}N_2O_4$	11,3	62
Vc	180—182	3272, 3460	1730, 1750 1775	1165	10,8	$C_{12}H_{12}N_2O_5$	10,6	65
VIa	264 (dec.)†	3160, 3438	1737, 1759	1195	11,2	$C_{11}H_{10}N_2O_3S$	11,2	57
VIb	226 (dec.)	3140, 3386	1750	1180	10,3	$C_{12}H_{12}N_2O_3S$	10,6	31
VIc	207 (dec.)†	3250, 3430	1732, 1780	1185	9,7	$C_{12}H_{12}N_2O_4S$	10,0	76,5
VIIa	137—138**	3180	1720, 1765	1155, 1180	11,0	$C_{12}H_{12}N_2O_4$	11,3	87
VIIb	135—136**	3182	1734, 1765	1160	10,6	$C_{13}H_{14}N_2O_4$	10,7	76
VIIc	126—128**	3180	1718, 1757	1150, 1175	12,1	$C_{13}H_{14}N_2O_5$	12,3	80
VIIIa	125—126**	—	—	—	10,4	$C_{12}H_{12}N_2O_3S$	10,6	82
IXa	142—144††	—	—	—	12,8	$C_{11}H_{14}N_2OS$	12,6	28
Xa	129—131††	—	—	—	11,9	$C_{13}H_{16}N_2O_2S$	12,1	83
XIa	71—73**	—	1710, 1730 1755	1180, 1200	10,8	$C_{13}H_{14}N_2O_4$	10,7	81
XIb	87—89**	—	1720, 1735 1755	1180	10,2	$C_{14}H_{16}N_2O_4$	10,1	85
XIc	99—101[d]	—	—	—	9,8	$C_{14}H_{16}N_2O_5$	9,6	78
XIIa	186 (dec.)‡‡	—	—	—	10,8	$C_{12}H_{12}N_2O_5$	10,6	73
XIIb	199 (dec.)††	—	—	—	10,2	$C_{13}H_{14}N_2O_5$	10,1	81

*In water.
†In benzene.
In a mixture of dioxane in water.
**In methanol.
††In a mixture of chloroform and hexane.
‡‡In ethanol.

1-Phenyl-5-carboxymethylhydantoin (Va). A mixture of 10 g (0.05 mole) of acid IIIa, 6.5 g (0.1 mole) of sodium cyanate, and 20 ml of glacial acetic acid was heated at 110°C for 3 h, after which 10 ml of concentrated HCl was added, and heating was continued for another 3 h. The mixture was cooled and treated with 100 ml of acetone, and the precipitated sodium chloride was removed by filtration. The filtrate was evaporated *in vacuo*, and the residue was treated with 50 ml of water. The mixture was allowed to stand at 4°C to give 6 g of Va (see Tables 3 and 4).

1-(p-Tolyl)-5-carboxymethylhydantoin (Vb). The reaction of 11 g (0.05 mole) of IIIb and 6.5 g (0.1 mole) of sodium cyanate in 20 ml of glacial acetic acid as in the preparation of Va gave 7.5 g of product (see Tables 3 and 4).

1-(p-Methoxyphenyl)-5-carboxymethylhydantoin (Vc). The reaction of 12 g (0.05 mole) of IIIc and 6.5 g of sodium cyanate in 20 ml of glacial acetic acid as in the preparation of Va gave 8.5 g of Vc (see Tables 3 and 4).

1-Phenyl-2-thio-5-carboxymethylhydantoin (VIa). A mixture of 20 g (0.1 mole) of IIIa, 11.2 g (0.15 mole) of ammonium thiocyanate, and 50 ml of acetic acid was heated at 120°C for 8 h, after which 20 ml of concentrated HCl was added, and heating was continued for 4 h. Water (100 ml) was added, and the mixture was allowed to stand at 4°C for 18 h. It was then filtered to give 14 g of VIa (see Tables 3 and 4).

1-(p-Tolyl)-2-thio-5-carboxymethylhydantoin (VIb). A mixture of 11 g (0.05 mole) of IIIc, 7.6 g (0.1 mole) of ammonium thiocyanate, and 30 ml of glacial acetic acid was heated at 120°C for 8 h, after which 10 ml of concentrated HCl was added, and the mixture was heated for another 4 h. The liquid fractions were removed by vacuum distillation, and the residue was refluxed with 150 ml of water. The mixture was filtered, and 4.3 g of VIb crystallized out from the filtrate (see Tables 3 and 4).

1-(p-Methoxyphenyl)-2-thio-5-carboxymethylhydantoin (VIc). The reaction of 4.8 g (0.02 mole) of IIIc and 3 g (0.04 mole) of ammonium thiocyanate in 20 ml of glacial acetic acid as in the preparation of VIa gave 1.5 g of VIc (see Tables 3 and 4).

1-Phenyl-5-carbomethoxymethylhydantoin (VIIa). A mixture of 4.6 g (0.02 mole) of Va, 20 ml of dry methanol, and three drops of sulfuric acid was refluxed for 5 h, after which the solution was neutralized to pH 7 with sodium carbonate, and the mixture was allowed to stand at 4°C. The precipitated crystals were removed by filtration and crystallized from methanol—ether (1:1) to give 4.2 g of VIIa (see Table 4).

1-(p-Tolyl)-5-carbomethoxymethylhydantoin (VIIb), 1-(p-Methoxyphenyl)-5-carbomethoxymethylhydantoin (VIIc), and 1-Phenyl-2-thio-5-carbomethoxymethylhydantoin (VIIIa). These compounds were obtained by a method similar to that used to prepare VIIa (see Tables 3 and 4).

1-Phenyl-2-thio-5-(β-hydroxyethyl)tetrahydroimidazole (IXa). A solution of 13 g (0.05 mole) of VIIIa in 50 ml of dry dioxane was added dropwise with stirring to a suspension of 3.7 g (0.1 mole) of $LiAlH_4$ in 200 ml of absolute ether, and the reaction mixture was refluxed for 15 h. It was then treated with 50 ml of 95% ethanol, and the solvents were evaporated. The solid mixture was extracted with acetone, the extract was concentrated, and 3.1 g of IXa crystallized out from the concentrate (see Tables 3 and 4).

1-Phenyl-2-thio-5-(β-acetoxyethyl)tetrahydroimidazole (Xa). A mixture of 0.62 g (2.7 mmole) of IXa, 3 ml of acetic anhydride, and 15 ml of acetic acid was heated at 120°C for 1 h, after which the liquid fractions were removed by distillation, and the residue was crystallized from ethanol to give 0.5 g of Xa (see Tables 3 and 4).

1-Phenyl-3-methyl-5-carbomethoxymethylhydantoin (XIa). A mixture of 2.4 g (0.01 mole) of VIIa, 2.5 g (0.02 mole) of dimethyl sulfate, 0.56 g of KOH, 10 ml of water, and 20 ml of methanol was stirred for 1 h, after which it was allowed to stand at 20°C for 18 h. The solvents were removed by distillation, and the residue was washed with water and crystallized from 10 ml of methanol to give 2.1 g of XIa (see Tables 3 and 4).

1-(p-Tolyl)-3-methyl-5-carbomethoxymethylhydantoin (XIb) and 1-(p-Methoxyphenyl)-3-methyl-5-carbomethoxymethylhydantoin (XIc). These compounds were obtained by a method similar to that used to prepare XIa (see Tables 3 and 4).

1-Phenyl-3-hydroxymethyl-5-carboxymethtylhydantoin (XIIa). A mixture of 2.3 g (0.01 mole) of Va and 20 ml of a 40% solution of formalin was heated at 100°C for 5 h, after which it was cooled, as a result of which, 1.9 g of XIIa crystallized out (see Tables 3 and 4).

1-(p-Tolyl)-3-hydroxymethyl-5-carboxymethylhydantoin (XIIb). This compound was obtained by a method similar to that used to prepare XIIa (see Tables 3 and 4).

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