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New Syntheses on the Basis of Ethyl 2-Oxotetrahydrofuran-3-carboxylates

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Abstract—Alkylation of 5-substituted ethyl 5-methyl-2-oxotetrahydrofuran-3-carboxylates with alkyl halides in the presence of sodium ethoxide gave the corresponding 3-alkyl derivatives which were converted into 3,5-substituted 5-methyl-*N*-(4-nitrophenyl)-2-oxotetrahydrofuran-3-carboxamides and 5-methyltetrahydrofuran-2-ones. Reactions of the latter with hydrazine hydrate led to the formation of 4-hydroxypentanoic acid hydrazides which were treated with isothiocyanates to obtain the corresponding thiosemicarbazides whose intramolecular cyclization in the presence of aqueous alkali gave previously unknown 1,2,4-triazole-3-thiol derivatives.

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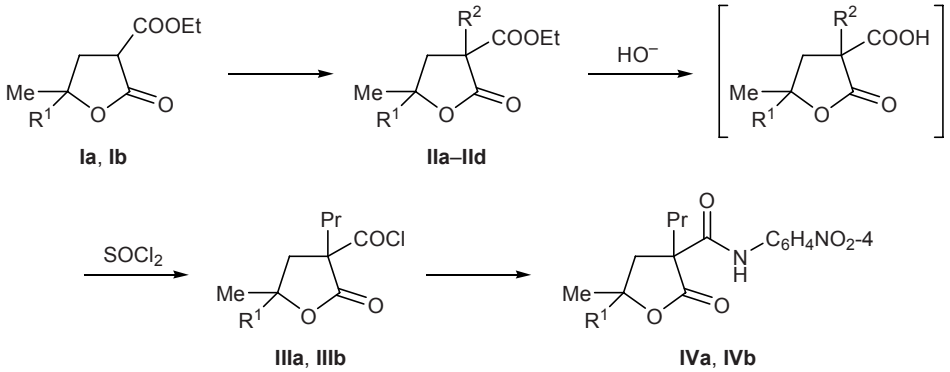
It is known that some carboxy lactone derivatives possess a broad spectrum of useful properties. In particular, various esters derived from carboxy lactones are used as propellant additives [1] and starting compounds for the synthesis of heterocycles [2]. Some carbamoyl-substituted lactones exhibit antitumor activity and inhibit Ehrlich ascites carcinoma and B-16 melanoma [3]. We previously developed procedures for the preparation of carboxy lactones, in which the carboxy group is separated from the lactone ring by one or two methylene units [4–7] and examined their biological properties. The strongest biological effect was found in the series of ethyl 2-oxotetrahydrofuran-3-carboxylates [3]. Obviously, the synthesis of various carboxy lactones is an important problem.

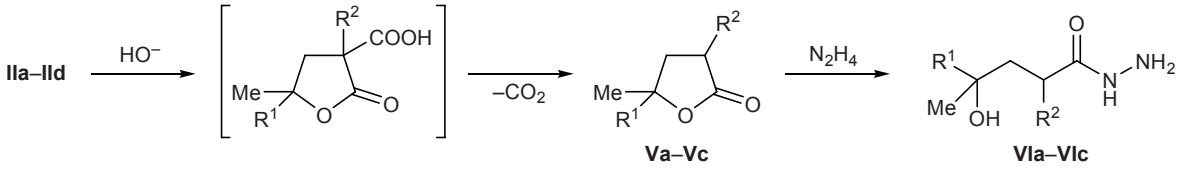
With the goal of obtaining carboxy lactones in which the carboxy group is directly attached to the lactone ring, we performed alkylation of 5-substituted ethyl 2-oxotetrahydrofuran-3-carboxylates **Ia** and **Ib** and subsequent hydrolysis of the corresponding 3,5-substituted derivatives **IIa**–**IId**. The hydrolysis products (carboxy lactones) turned out to be unstable; therefore, they were converted into carbonyl chlorides **IIIa** and **IIIb**, and the latter were treated with 4-nitroaniline to obtain *N*-(4-nitrophenyl)-2-oxotetrahydrofuran-3-carboxamides **IVa** and **IVb** (Scheme 1). Various carboxy lactone derivatives were synthesized according to the above scheme and were analyzed for structure–biologically activity relationships. As shown previously, compounds **Ia** and **Ib** are convenient initial

Scheme 1.



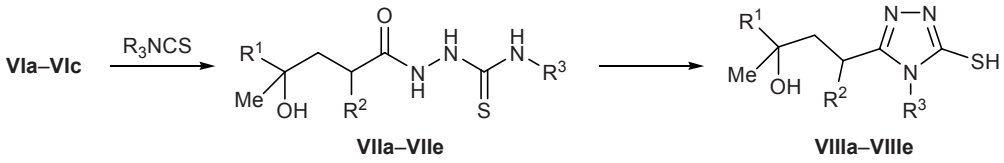
I, R^1 = H (**a**), Me (**b**); **II**, R^1 = Me (**a**, **d**), H (**b**, **c**); R^2 = $PhCH_2$ (**a**, **b**), Pr (**c**, **d**); **III**, **IV**, R^1 = H (**a**), Me (**b**).

Scheme 2.



V, **VI**, R^1 = H (**a**, **c**), Me (**b**); R^2 = $PhCH_2$ (**a**, **b**), Pr (**c**).

Scheme 3.



VII, **VIII**, R^1 = H (**a**, **c**, **d**), Me (**b**, **e**); R^2 = $PhCH_2$ (**a**, **b**, **d**, **e**), Pr (**c**); R^3 = Ph (**a**–**c**); CH_2=$CHCH_2$ (**d**, **e**).

materials for the preparation of heterocyclic lactones [8–10]. While continuing studies in this line, we found that substituted butanolides can be converted into derivatives of γ-hydroxy acids, in particular hydrazides, 1,4-disubstituted thiosemicarbazides, and new heterocyclic compounds. It should be noted that 1,2,4-triazole analogs exhibit antitumor and fungicidal activity [11, 12] and are successfully used for the synthesis of optically active nonprotein amino acids [13, 14].

Hydrolysis of esters **IIa**–**IId**, followed by decarboxylation and treatment of 2,4-disubstituted pentanolides **Va**–**Vc** with hydrazine hydrate gave the corresponding hydrazides **VIa**–**VId** (Scheme 2). This reaction sequence makes it possible to introduce various substituents into the 2-position of γ-hydroxy acid and thus extend the series of such compounds.

1,4-Disubstituted thiosemicarbazides **VIIa**–**VIIe** were synthesized by reaction of hydrazides **VIa**–**VIc** with isothiocyanates. The reaction was complete in a short time, and the products were obtained in high yields. Compounds **VIIa**–**VIIe** underwent intramolecular cyclization by the action of aqueous alkali to give the corresponding 1,2,4-triazole-3-thiols **VIIIa**–**VIIIe** (Scheme 3).

All newly synthesized compounds were characterized by physical constants and IR and ^{1}H NMR spectra, and their purity was checked by TLC.

EXPERIMENTAL

The ^{1}H NMR spectra were measured from solutions in $CDCl_3$ on a Varian Mercury-300 spectrometer (300 MHz). The IR spectra were recorded on a Nicolet FTIR NEXUS instrument from samples prepared as thin films (neat) or dispersed in mineral oil. Thin-layer chromatography was performed on Silufol UV-254 plates using ethanol–benzene–hexane (3 : 3 : 10, A), ethanol–benzene–acetone (2 : 1 : 6, B) or ethanol–benzene (1 : 3, C) as eluent; spots were visualized by treatment with iodine vapor. The melting points were determined on a Boetius hot stage.

Initial ethyl 2-oxotetrahydrofuran-3-carboxylates **Ia** and **Ib** were synthesized according to the procedure reported in [15].

Ethyl 2-oxotetrahydrofuran-3-carboxylates IIa–IId (*general procedure*). Compound **Ia** or **Ib**, 0.1 mol, was added under stirring to a solution of sodium ethoxide prepared by dissolution of 2.3 g (0.1 mol) of metallic sodium in 100 ml of anhydrous ethanol. The mixture was stirred for 1 h, and 0.1 mol of the corresponding alkyl halide was added dropwise. After 30 min, the mixture was heated on a water bath until it showed neutral reaction, and the solvent was distilled off. The residue was cooled, treated with acidified water to pH 3–4, and extracted with diethyl ether. The extract was washed with water and dried over anhydrous magnesium sulfate, the solvent was removed, and the residue was distilled under reduced pressure.

Ethyl 3-benzyl-5,5-dimethyl-2-oxotetrahydrofuran-3-carboxylate (IIa). Yield 80%, mp 37–38°C, bp 133–135°C (1 mm), R_f 0.44 (A), n_D^{20} = 1.5050. IR spectrum, ν, cm^{-1}: 1762 (C=O, lactone); 1734 (C=O, ester); 1130, 1174 (C–O–C); 1600 (C=C_{arom}); 3030 (C–H_{arom}). ^{1}H NMR spectrum, δ, ppm: 0.93 t and 1.35 t (3H each, CH_3), 1.25 t (3H, $CH_2C\mathbf{H}_3$), 2.10 d and 2.40 d (1H each, 4-H), 3.10 d and 3.30 d (1H each, $PhC\mathbf{H}_2$), 4.23 q (2H, OCH_2), 7.15 m (2H, H_{arom}),

7.23 m (2H, H_{arom}). Found, %: C 69.45; H 7.21. $C_{16}H_{20}O_4$. Calculated, %: C 69.56; H 7.25.

Ethyl 3-benzyl-5-methyl-2-oxotetrahydrofuran-3-carboxylate (IIb). Yield 81%, bp 140–140°C (2 mm), n_D^{20} = 1.5085, d_4^{20} = 1.1368, R_f 0.46 (A). The IR spectrum of **IIb** was analogous to that of **IIa**. ^{1}H NMR spectrum, δ, ppm: 0.95 t (3H, CH_3), 1.35 t (3H, CH_2CH_3), 1.80 d (1H, 5-H), 2.20 d and 2.80 d (1H each, 4-H), 3.00 d and 3.40 d (1H each, $PhCH_2$), 4.15 q (2H, OCH_2), 7.15 m (2H, H_{arom}), 7.40 m (1H, H_{arom}), 7.65 m (2H, H_{arom}). Found, %: C 68.56; H 6.85. $C_{15}H_{18}O_4$. Calculated, %: C 68.70; H 6.87.

Ethyl 5-methyl-2-oxo-3-propyltetrahydrofuran-3-carboxylate (IIc). Yield 80%, bp 89–91°C (2 mm), n_D^{20} = 1.4460, d_4^{20} = 1.0547, R_f 0.56 (A). IR spectrum, ν, cm^{-1}: 1750 (C=O, lactone); 1720 (C=O, ester); 1120, 1210 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 0.95 t (3H, CH_2CH_3), 1.10 t (3H, OCH_2CH_3), 1.25 d (3H, 5-CH_3), 1.75 d (1H, 5-H), 2.09 q (2H, $CH_2CH_2CH_3$), 3.05 d and 3.65 d (1H each, 4-H), 4.00 d (2H, OCH_2), 4.20 d (2H, 3-CH_2). Found, %: C 61.80; H 8.20. $C_{11}H_{18}O_4$. Calculated, %: C 61.68; H 8.41.

Ethyl 5,5-dimethyl-2-oxo-3-propyltetrahydrofuran-3-carboxylate (IId). Yield 78%, bp 99°C (2 mm), n_D^{20} = 1.4450, d_4^{20} = 1.0373, R_f 0.59 (A). The IR spectrum of **IId** was analogous to that of **IIc**. ^{1}H NMR spectrum, δ, ppm: 1.00 t (3H, CH_2CH_3), 1.20 t (3H, OCH_2CH_3), 1.35 d (6H, 5-CH_3), 2.05 q (2H, $CH_2CH_2CH_3$), 2.20 d and 2.40 d (1H each, 4-H), 4.10 d (2H, OCH_2), 4.35 d (2H, 3-CH_2). Found, %: C 63.30; H 8.65. $C_{12}H_{20}O_4$. Calculated, %: C 63.16; H 8.77.

5-Methyl-2-oxo-3-propyltetrahydrofuran-3-carbonyl chloride (IIIa). Compound **IId**, 16.5 g (0.073 mol), was added to a 40% aqueous solution of 7.7 g (0.193 mol) of sodium hydroxide, and the mixture was stirred for 30 min at 20–25°C and for 2 h at 70–75°C. The mixture was cooled, acidified to pH 1–2 with hydrochloric acid, and extracted with diethyl ether. The extract was washed with water, dried over anhydrous magnesium sulfate, and evaporated, 50 ml of anhydrous benzene, 9.6 g (0.08 mol) of thionyl chloride, and 0.7 ml of dimethylformamide were added to the residue, and the mixture was left to stand for 1 h at room temperature and was then heated to the boiling point over a period of 3 h. The mixture was maintained boiling for 1 h, the solvent was removed under a residual pressure of 20–30 mm, and the residue was distilled in a vacuum. Yield 12.4 g (83%), bp 113–115°C (3 mm), n_D^{20} = 1.4630, d_4^{20} = 1.1577. IR spectrum, ν, cm^{-1}: 1750 (C=O, lactone); 1730 (ClC=O); 1120, 1210 (C–O–C). Found, %: C 52.95; H 6.45; Cl 17.75. $C_9H_{13}ClO_3$. Calculated, %: C 52.81; H 6.36; Cl 17.85.

5,5-Dimethyl-2-oxo-3-propyltetrahydrofuran-3-carbonyl chloride (IIIb) was synthesized in a similar way. Yield 81%, bp 89–90°C (1 mm), n_D^{20} = 1.4650, d_4^{20} = 1.1359. The IR spectrum of **IIIb** was analogous to that of **IIIa**. Found, %: C 55.05; H 7.00; Cl 16.15. $C_{10}H_{15}ClO_3$. Calculated, %: C 54.92; H 6.87; Cl 16.25.

5,5-Dimethyl-*N*-(*p*-nitrophenyl)-2-oxo-3-propyltetrahydrofuran-3-carboxamide (IVa). A solution of 4.4 g (0.02 mol) of compound **IIIb** in 5 ml of anhydrous acetone was added dropwise on cooling to a mixture of 5.5 g (0.04 mol) of *p*-nitroaniline and 10 ml of anhydrous acetone. The mixture was stirred for 1 h at room temperature and for 2 h on heating so that to maintain it slightly boiling, the solvent was distilled off, and the residue was cooled and treated with water. The precipitate was filtered off, washed with water, and dried. Yield 4.6 g (72%), mp 147–149°C (from water–alcohol, 1:2), R_f 0.54 (A). IR spectrum, ν, cm^{-1}: 1750 (C=O, lactone), 1690 (C=O, amide); 1120, 1210 (C–O–C); 1605 (C=C); 3080 (C–H_{arom}); 3280, 3340 (NH). ^{1}H NMR spectrum, δ, ppm: 1.00 t (3H, CH_2CH_3), 1.25 d (6H, 5-CH_3), 2.10 q (2H, $CH_2CH_2CH_3$), 2.15 d and 2.50 d (1H each, 4-H), 4.40 d (2H, 3-CH_2), 7.25 m (2H, H_{arom}), 7.50 m (2H, H_{arom}), 13.02 (1H, NH). Found, %: C 60.15; H 6.10; N 8.90. $C_{16}H_{20}N_2O_5$. Calculated, %: C 60.00; H 6.25; N 8.75.

5-Methyl-*N*-(*p*-nitrophenyl)-2-oxo-3-propyltetrahydrofuran-3-carboxamide (IVb) was synthesized in a similar way. Yield 67%, mp 123–125°C (from water–alcohol, 1:2), R_f 0.50 (A). The IR spectrum of **IVb** was analogous to that of **IVa**. ^{1}H NMR spectrum, δ, ppm: 0.98 t (3H, CH_2CH_3), 1.10 t (3H, 5-CH_3), 1.80 m (1H, 5-H), 2.05 q (2H, $CH_2CH_2CH_3$), 2.40 d and 3.10 d (1H each, 4-H), 4.35 d (2H, 3-CH_2), 7.00 m (2H, H_{arom}), 7.35 m (2H, H_{arom}), 13.05 (1H, NH). Found, %: C 58.95; H 5.75; N 9.30. $C_{15}H_{18}O_5N_2$. Calculated, %: C 58.82; H 5.88; N 9.15.

3,5-Disubstituted 5-methyl-2-oxotetrahydrofuran-2-ones Va–Vc (*general procedure*). Ester **IIa**–**IId**, 0.066 mol, was added dropwise to a 30% aqueous solution of 6.2 g (0.0.155 mol) of sodium hydroxide, and the mixture was stirred for 30 min at 20–25°C and for 4 h on heating on a boiling water bath. The mixture was cooled, acidified with hydrochloric acid to pH 1–

2, and extracted with diethyl ether. The extract was washed with water and dried over anhydrous magnesium sulfate, the solvent was removed, and the residue was distilled under reduced pressure.

3-Benzyl-5-methyltetrahydrofuran-2-one (Va). Yield 88%, bp 105–106°C (1 mm), R_f 0.43 (A), n_D^{20} = 1.5235, d_4^{20} = 1.0858. IR spectrum, ν, cm^{-1}: 1750 (C=O, lactone); 1121, 1180 (C–O–C); 1600 (C=C$_{arom}$); 3030 (C–H$_{arom}$). ^{1}H NMR spectrum, δ, ppm: 0.93 t (3H, CH$_3$), 1.55 m and 1.80 m (1H each, 3-H, 5-H), 2.15 d and 2.55 d (1H each, 4-H), 3.05 d and 3.35 d (1H each, PhC**H**$_2$), 7.15 m (2H, H$_{arom}$), 7.40 m (1H, H$_{arom}$), 7.55 m (2H, H$_{arom}$). Found, %: C 75.68; H 7.33. $C_{12}H_{14}O_2$. Calculated, %: C 75.79; H 7.37.

3-Benzyl-5,5-dimethyltetrahydrofuran-2-one (Vb). Yield 83%, bp 120–121°C (2 mm), mp 44–46°C, R_f 0.52 (A). The IR spectrum of **Vb** was analogous to that of **Va**. ^{1}H NMR spectrum, δ, ppm: 1.35 d (6H, 5-CH$_3$), 1.75 m (1H, 3-H), 2.05 d and 2.70 d (1H each, 4-H), 3.05 d and 3.18 d (1H each, PhC**H**$_2$), 7.15 m (2H, H$_{arom}$), 7.25 m (2H, H$_{arom}$). Found, %: C 76.38; H 7.88. $C_{13}H_{16}O_2$. Calculated, %: C 76.47; H 7.84.

5-Methyl-3-propyltetrahydrofuran-2-one (Vc). Yield 10.7 g (75%), bp 107–108°C (13 mm). n_D^{20} = 1.4350 [16].

2-Substituted 4-hydroxypentanoic acid hydrazides VIa–VIc (*general procedure***).** 3,5-Substituted 5-methyltetrahydrofuran-2-one **Va**–**Vc**, 0.13 mol, was dissolved in 35 ml of ethanol, 11.2 g of 85% hydrazine hydrate was added, and the mixture was vigorously stirred, left to stand for 0.5 h at 20–25°C, and heated for 2 h on a boiling water bath. After cooling, the precipitate was filtered off, washed with ethanol, and dried.

2-Benzyl-4-hydroxypentanehydrazide (VIa). Yield 69%, mp 157–159°C (from ethanol), R_f 0.54 (B). IR spectrum, ν, cm^{-1}: 1654 (C=O), 1620 (C=C$_{arom}$), 3030 (C–H$_{arom}$), 3100–3400 (NH, NH$_2$, OH). Found, %: C 65.00; H 8.00; N 12.48. $C_{12}H_{18}N_2O_2$. Calculated, %: C 64.87; H 8.11; N 12.61.

2-Benzyl-4-hydroxy-4-methylpentanehydrazide (VIb). Yield 70%, mp 104–106°C (from ethanol), R_f 0.58 (C). The IR spectrum of **VIb** was analogous to that of **VIa**. Found, %: C 65.95; H 8.60; N 11.67. $C_{13}H_{20}N_2O_2$. Calculated, %: C 66.10; H 8.48; N 11.86.

4-Hydroxy-2-propylpentanehydrazide (VIc). Yield 85%, mp 88–89°C (from ethanol), R_f 0.53 (A). IR spectrum, ν, cm^{-1}: 1654 (C=O), 3100–3400 (NH, NH$_2$, OH). Found, %: C 55.05; H 10.45; N 16.15. $C_8H_{18}N_2O_2$. Calculated, %: C 55.17; H 10.34; N 16.09.

Thiosemicarbazides VIIa–VIIe. A mixture of 0.014 mol of hydrazide **VIa**–**VIc** and 0.015 mol of phenyl or allyl isothiocyanate in 25 ml of ethanol was vigorously stirred on heating until it became homogeneous and was then heated for 1 h at 75–80°C. After cooling, the precipitate was filtered off, washed with ethanol, and dried.

2-(2-Benzyl-4-hydroxypentanoyl)-*N*-phenylhydrazinecarbothioamide (VIIa). Yield 80%, mp 150–152°C (from ethanol), R_f 0.63 (C). IR spectrum, ν, cm^{-1}: 1654 (C=O); 1600 (C=C$_{arom}$); 3030 (C–H$_{arom}$); 3144, 3400, 3450 (NH, OH). ^{1}H NMR spectrum, δ, ppm: 1.10 d (3H, CH$_3$), 1.45 d and 1.80 d (1H each, CH$_2$), 2.60 m (1H, CH$_2$C**H**), 2.90 m (C**H**$_2$C$_6$H$_5$), 3.70 m (1H, C**H**OH), 4.75 s (1H, OH), 7.00–7.25 m (2H, H$_{arom}$), 7.45 m (2H, H$_{arom}$), 9.35 s (2H, NH), 9.85 s (1H, NH). Found, %: C 64.00; H 6.30; N 11.86; S 8.82. $C_{19}H_{23}N_3O_2S$. Calculated, %: C 63.87; H 6.44; N 11.76; S 8.96.

2-(2-Benzyl-4-hydroxy-4-methylpentanoyl)-*N*-phenylhydrazinecarbothioamide (VIIb). Yield 90%, mp 142–143.5°C (from water–alcohol, 3:1), R_f 0.68 (C). The IR spectrum of **VIIb** was analogous to that of **VIIa**. ^{1}H NMR spectrum, δ, ppm: 1.15 d (3H, CH$_3$), 2.00 d and 2.50 d (1H each, CH$_2$), 2.70 m (1H, CH$_2$C**H**), 2.90 m (C**H**$_2$C$_6$H$_5$), 4.70 s (1H, OH), 7.00–7.30 m (8H, H$_{arom}$), 7.60 m (2H, H$_{arom}$), 9.35 s (2H, NH), 9.95 s (1H, NH). Found, %: C 64.55; H 6.65; N 11.45; S 8.44. $C_{20}H_{25}N_3O_2S$. Calculated, %: C 64.69; H 6.74; N 11.32; S 8.62.

2-(4-Hydroxy-2-propylpentanoyl)-*N*-phenylhydrazinecarbothioamide (VIIc). Yield 91%, mp 185–186°C (from ethanol), R_f 0.67 (C). The IR spectrum of **VIIc** was analogous to that of **VIIa**. ^{1}H NMR spectrum, δ, ppm: 0.92 d (3H, CH$_3$), 1.15 t (3H, CH$_2$C**H**$_3$), 2.05 q (2H, CH$_2$C**H**$_2$CH$_3$), 2.15 d (2H, CHC**H**$_2$), 2.65 m (1H, CH), 3.40 s (1H, C**H**OH), 3.85 d (2H, C**H**$_2$CH$_2$CH$_3$), 4.20 s (1H, OH), 6.80 m (2H, H$_{arom}$), 7.25 m (3H, H$_{arom}$), 7.70 s (1H, NH), 9.00 s (1H, NH), 9.60 s (1H, NH). Found, %: C 58.35; H 7.56; N 13.67; S 10.17. $C_{15}H_{23}N_3O_2S$. Calculated, %: C 58.25; H 7.44; N 13.59; S 10.37.

***N*-Allyl-2-(2-benzyl-4-hydroxypentanoyl)hydrazinecarbothioamide (VIId).** Yield 92%, mp 144–145°C (from water–alcohol, 3:1), R_f 0.64 (C). IR spectrum, ν, cm^{-1}: 1695 (C=O); 1640 (C=C); 1600 (C=C$_{arom}$); 3030 (C–H$_{arom}$); 3080 (=CH$_2$); 3180, 3290,

3500 (NH, OH). ^{1}H NMR spectrum, δ, ppm: 1.05 d (3H, CH_3), 1.40 d and 1.65 d (1H each, CH_2), 2.60 m (1H, CH_2CH), 2.85 m ($CH_2C_6H_5$), 3.65 m (1H, CHOH), 4.05 m (2H, CH_2N), 4.45 s (1H, OH), 5.05 d and 5.15 d (1H each, $=CH_2$), 5.80 m (1H, CH=), 7.05–7.25 m (5H, H_{arom}), 8.95 s (2H, NH), 9.60 s (1H, NH). Found, %: C 59.95; H 7.05; N 12.98; S 9.83. $C_{16}H_{23}N_3O_2S$. Calculated, %: C 59.81; H 7.17; N 13.08; S 9.97.

***N*-Allyl-2-(2-benzyl-4-hydroxy-4-methylpentanoyl)hydrazinecarbothioamide (VIIe).** Yield 80%, mp 134–135°C (from water–alcohol, 3:1), R_f 0.67 (C). The IR spectrum of **VIIe** was analogous to that of **VIId**. ^{1}H NMR spectrum, δ, ppm: 1.10 d (6H, CH_3), 1.30 d and 1.95 d (1H each, CH_2), 2.65 m (1H, CH_2CH), 2.85 m ($CH_2C_6H_5$), 3.90 d and 4.20 d (1H each, CH_2N), 4.00 s (1H, OH), 5.00 d and 5.15 d (1H each, $=CH_2$), 5.80 m (1H, CH=), 7.10–7.25 m (5H, H_{arom}), 7.75 s (1H, NH), 8.95 s (1H, NH), 9.65 s (1H, NH). Found, %: C 61.00; H 7.35; N 12.64; S 9.36. $C_{17}H_{25}N_3O_2S$. Calculated, %: C 60.90; H 7.46; N 12.54; S 9.55.

4,5-Disubstituted 4*H*-1,2,4-triazole-3-thiols VIIIa–VIIIe (*general procedure*). A mixture of a 10% aqueous solution of sodium hydroxide (0.5 g of NaOH in 4.5 ml of water) and 0.011 mol of thiosemicarbazide **VIIa–VIIe** was heated for 4 h on a boiling water bath. The mixture was cooled and acidified with hydrochloric acid to pH 1–2, and the precipitate was filtered off, washed with water, and dried.

5-(1-Benzyl-3-hydroxybutyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (VIIIa). Yield 83%, mp 207–209°C (from water–alcohol, 1:2), R_f 0.65 (C). IR spectrum, ν, cm^{-1}: 1570 (C=N), 1600 (C=C_{arom}), 3030 (C–H_{arom}), 3100–3300 (OH). ^{1}H NMR spectrum, δ, ppm: 1.00 d (3H, CH_3), 1.63 d and 1.90 d (1H each, CH_2), 2.75 m (1H, CH_2CH), 2.93 m ($CH_2C_6H_5$), 3.60 s (1H, CHOH), 4.10 s (1H, OH), 6.80 m (2H, H_{arom}), 7.18 m (6H, H_{arom}), 7.40 m (2H, H_{arom}), 13.45 s (1H, SH). Found, %: C 67.35; H 6.30; N 12.24; S 9.31. $C_{19}H_{21}N_3OS$. Calculated, %: C 67.26; H 6.19; N 12.39; S 9.44.

5-(1-Benzyl-3-hydroxy-3-methylbutyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (VIIIb). Yield 80%, mp 202–203°C (from water–alcohol, 2:3), R_f 0.67 (C). The IR spectrum of **VIIIb** was analogous to that of **VIIIa**. ^{1}H NMR spectrum, δ, ppm: 0.95 d (6H, CH_3), 1.60 d and 1.90 d (1H each, CH_2), 2.75 m (1H, CH_2CH), 2.93 m (2H, $CH_2C_6H_5$), 4.10 s (1H, OH), 6.80 m (2H, H_{arom}), 7.20 m (6H, H_{arom}), 7.40 m (2H, H_{arom}), 13.43 s (1H, SH). Found, %: C 67.85; H 6.40; N 11.77; S 8.95. $C_{20}H_{23}N_3OS$. Calculated, %: C 67.99; H 6.52; N 11.90; S 9.06.

5-(3-Hydroxy-1-propylbutyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (VIIIc). Yield 80%, mp 141–143°C (from water–alcohol, 1:1), R_f 0.67 (C). IR spectrum, ν, cm^{-1}: 1570 (C=N), 1600 (C=C_{arom}), 3030 (C–H_{arom}), 3100–3300 (OH). ^{1}H NMR spectrum, δ, ppm: 0.97 d (3H, CH_3), 1.15 t (3H, CH_2CH_3), 2.10 q (2H, CH_2CH_3), 2.18 d (2H, $CHCH_2$), 2.95 m (1H, 5-CH), 3.60 s (1H, CHOH), 4.00 d (2H, $CH_2CH_2CH_3$), 4.15 s (1H, OH), 6.80 m (2H, H_{arom}), 7.20 m (1H, H_{arom}), 7.35 m (2H, H_{arom}), 13.25 s (1H, SH). Found, %: C 61.75; H 7.15; N 14.63: S 10.77. $C_{15}H_{21}N_3OS$. Calculated, %: C 61.86; H 7.22; N 14.43; S 10.99.

4-Allyl-5-(1-benzyl-3-hydroxybutyl)-4*H*-1,2,4-triazole-3-thiol (VIIId). Yield 73%, mp 128–129.5°C (from water–alcohol, 1:1), R_f 0.65 (C). IR spectrum, ν, cm^{-1}: 1564 (C=N), 1600 (C=C_{arom}), 1640 (C=C), 3030 (C–H_{arom}), 3080 ($=CH_2$), 3150–3360 (OH). ^{1}H NMR spectrum, δ, ppm: 1.05 d (3H, CH_3), 1.65 d (2H, CH_2), 2.95 m ($CH_2C_6H_5$), 3.20 m (1H, CH_2CH), 3.65 s (1H, CHOH), 4.20 s (1H, OH), 4.30–4.43 m (2H, CH_2N), 4.85 d and 5.00 d (1H each, $=CH_2$), 5.60 m (1H, CH=), 7.00–7.20 m (5H, H_{arom}), 13.30 s (1H, SH). Found, %: C 63.25; H 7.05; N 13.62; S 10.56. $C_{16}H_{21}N_3OS$. Calculated, %: C 63.37; H 6.93; N 13.86; S 10.56.

4-Allyl-5-(1-benzyl-3-hydroxy-3-methylbutyl)-4*H*-1,2,4-triazole-3-thiol (VIIIe). Yield 75%, mp 164–165°C (from water–alcohol, 2:3), R_f 0.62 (C). The IR spectrum of **VIIId** was analogous to that of **VIIIc**. ^{1}H NMR spectrum, δ, ppm: 1.00 d (6H, CH_3), 1.65 d and 2.00 d (1H each, CH_2), 2.15 m (1H, CH_2CH), 2.90 m ($CH_2C_6H_5$), 4.00 br.s (1H, OH), 4.35 d and 4.50 d (2H, CH_2N), 5.00 m (2H, $=CH_2$), 5.60 m (1H, CH=), 7.05 m (2H, H_{arom}), 7.20 m (3H, H_{arom}), 13.43 s (1H, SH). Found, %: C 64.25; H 7.15; N 13.00; S 9.85. $C_{17}H_{23}N_3OS$. Calculated, %: C 64.35; H 7.26; N 13.25; S 10.09.

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