

Synthesis of 1,2,4-Triazolin-5-ones from S-Allyl N-Acylmonothiocarbamates

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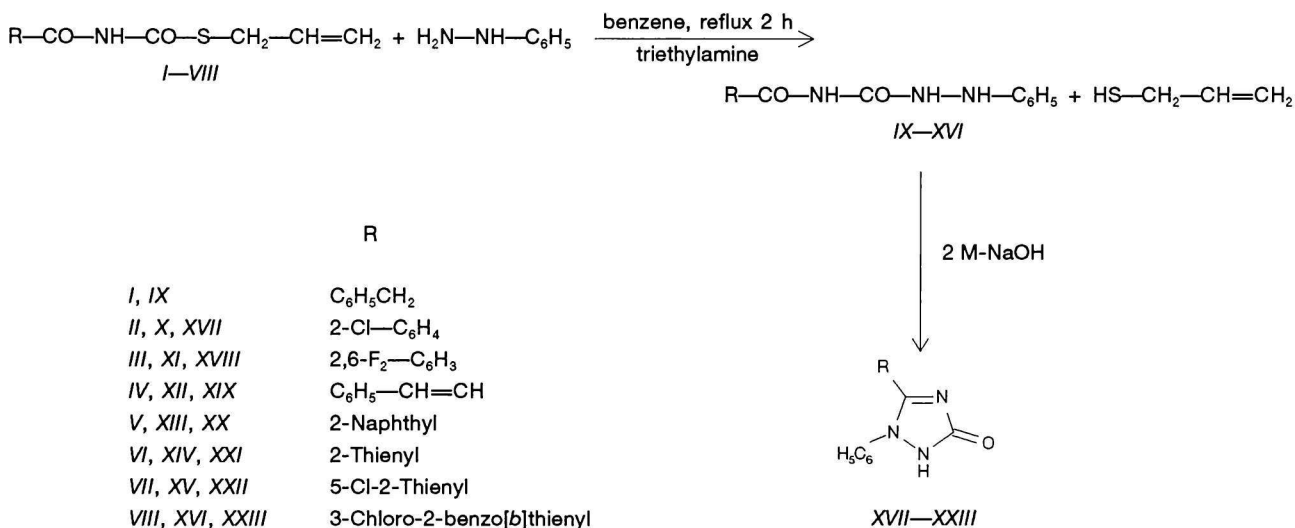
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Reaction of S-allyl N-acylmonothiocarbamates with phenylhydrazine in boiling benzene in the presence of catalytic amount of triethylamine afforded 1-substituted 4-acylsemicarbazides in good yields (40–80 %). These compounds cyclized by the action of 2 M-NaOH solution to 3-substituted 2-phenyl-1,2,4-triazolin-5-ones. The structure of the prepared compounds was confirmed by elemental analysis, IR, ¹H NMR, and mass spectroscopy.

In our previous paper [1] we have studied the synthesis of acyl urea derivatives from S-allyl N-acylmonothiocarbamates. The present paper describes the utilization of S-allyl N-acylmonothiocarbamates in the synthesis of 1,2,4-triazolin-5-one derivatives (XVII–XXIII, Scheme 1). S-Allyl esters

carbazides IX–XVI prepared by our method cyclize in aqueous solution of 2 M-NaOH to triazoline derivatives XVII–XXIII in good yields (70–90 %). The only exception is 1-phenyl-4-phenylacetylsemicarbazide (IX), which does not cyclize in NaOH, by the action of sodium alcoholate in ethanol or



Scheme 1

I–VIII readily react with phenylhydrazine on heating in boiling benzene in the presence of triethylamine with the formation of 1-phenyl-4-acylsemicarbazides IX–XVI (yields 40–80 %). Analogous acylsemicarbazides are usually prepared by the reaction of unstable and toxic acyl isocyanates [2, 3], N-acylcarbamoyl chlorides [3], or N-acylcarbamates [4] with substituted hydrazines. Cyclization of several acylsemicarbazides to triazolines in basic medium was described [5], however higher attention was paid to corresponding acylthiosemicarbazides [6, 7]. We have found that acylsemi-

even by treatment with lithium and sodium hydride in dimethylformamide. This is probably caused by lowered reactivity of acyl carbonyl group of compound IX with possible enolization of CH₂CO group.

The structure of the prepared compounds was confirmed by elemental analysis, IR, ¹H NMR, and mass spectroscopy. In IR spectra of acylsemicarbazides IX–XVI there are present absorption bands due to ν(CO–NH–CO, in-phase) vibrations at $\tilde{\nu} = 1630\text{--}1660\text{ cm}^{-1}$ and ν(CO–NH–CO, out-of-phase) ones at $\tilde{\nu} = 1660\text{--}1720\text{ cm}^{-1}$, whereas the triazoline derivatives XVII–XXIII exhibit absorp-

tion bands of $\nu(\text{C}=\text{O})$ at $\tilde{\nu} = 1630\text{--}1690\text{ cm}^{-1}$ and $\nu(\text{C}=\text{N})$ at $\tilde{\nu} = 1550\text{--}1580\text{ cm}^{-1}$. Unequivocal evidence of triazoline structure was afforded by mass spectra of compounds *XVII*, *XVIII*, and *XXIII*. The m/z values of molecular peaks are in agreement with expected molecular masses. The main direction of molecular ions cleavage leads to the fragment peaks $[\text{R}-\text{CNH}]^+$ at $m/z = 138$ (*XVII*), 141 (*XVIII*), and 194 (*XXIII*), respectively.

EXPERIMENTAL

Infrared absorption spectra were recorded on an IR 75 spectrometer (Zeiss, Jena) in KBr pellets. ^1H NMR spectra were recorded on a Tesla BS 487 A (80 MHz) instrument in deuteriochloroform (*I*, *VI*, *IX*) or in a mixture deuteriochloroform—hexadeuterodimethyl sulfoxide. Mass spectra were taken on a JMS-100 D spectrometer (Jeol), ionization energy 70 eV. The reaction course was monitored by thin-layer chromatography on Silufol plates (Kavalier). *S*-Allyl esters of *N*-(2-chlorobenzoyl)- (*II*) [8], *N*-(2,6-difluorobenzoyl)- (*III*) [1], *N*-(3-phenylpropenoyl)- (*IV*) [8], *N*-(2-naphthoyl)- (*V*) [8], *N*-(5-chloro-2-thenoyl)- (*VII*) [1], and *N*-(3-chloro-2-benzo[*b*]thenoyl)- (*VIII*) [8] monothiocarbamic acids were prepared according to the literature.

S-Allyl *N*-Acylmonothiocarbamates *I*, *VI*

Allyl alcohol (3.48 g, 4.08 cm³, 60 mmol) was added to a solution of phenylacetyl isothiocyanate or 2-thenoyl isothiocyanate (50 mmol) in benzene (50 cm³). Reaction mixture was left to stand at room temperature for 3 d and then refluxed for 12 h. The crystals separated after cooling were filtered off and recrystallized from tetrachloromethane.

S-Allyl *N*-phenylacetylmonothiocarbamate (*I*), yield 52 %, m.p. = 110—111 °C. For C₁₂H₁₃NO₂S ($M_r = 235.3$) $w_i(\text{calc.})$: 61.25 % C, 5.57 % H, 5.95 % N; $w_i(\text{found})$: 61.40 % C, 5.32 % H, 6.08 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1720 $\nu(\text{CONHCO})$. ^1H NMR spectrum (CDCl₃), δ : 3.55 (m, 2H, CH₂S), 3.78 (s, 2H, CH₂), 5.20 (m, 2H, =CH₂), 5.78 (m, 1H, =CH), 7.33 (m, 5H, C₆H₅), 9.08 (s, 1H, NH).

S-Allyl *N*-(2-thenoyl)monothiocarbamate (*VI*), yield 72 %, m.p. = 125—128 °C. For C₉H₉NO₂S₂ ($M_r = 227.3$) $w_i(\text{calc.})$: 47.56 % C, 3.99 % H, 6.16 % N; $w_i(\text{found})$: 47.31 % C, 4.05 % H, 6.28 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1690 and 1655 $\nu(\text{CONHCO})$. ^1H NMR spectrum (CDCl₃), δ : 3.61 (m, 2H, CH₂S), 5.22 (m, 2H, =CH₂), 5.86 (m, 1H, =CH), 7.20, 7.70, 8.00 (m, m, m, 3 × 1H, 2-thienyl), 10.20 (s, 1H, NH).

1-Phenyl-4-acylsemicarbazides *IX—XVI*

Phenylhydrazine (0.11 g, 0.1 cm³, 1 mmol) was added to a solution of corresponding *S*-allyl monothiocarbamate (*I—VIII*) (1 mmol) in benzene (8 cm³) followed by triethylamine (0.01 g, 0.014 cm³, 0.1 mmol) and reaction mixture was refluxed for 2 h. The precipitate separated after cooling was filtered off and crystallized from a suitable solvent.

1-Phenyl-4-phenylacetylsemicarbazide (*IX*), yield 40 %, m.p. = 168—170 °C (methanol). For C₁₅H₁₅N₃O₂ ($M_r = 269.3$) $w_i(\text{calc.})$: 66.90 % C, 5.61 % H, 15.60 % N; $w_i(\text{found})$: 66.72 % C, 5.83 % H, 15.48 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1660 and 1630 $\nu(\text{CONHCO})$. ^1H NMR spectrum (CDCl₃), δ : 3.79 (s, 2H, CH₂), 6.95—7.58 (m, 10H, 2 × C₆H₅), 8.30, 10.13 (s, s, 2 × 1H, 2 × NH).

1-Phenyl-4-(2-chlorobenzoyl)semicarbazide (*X*), yield 62 %, m.p. = 192—193 °C (ethanol). For C₁₄H₁₂ClN₃O₂ ($M_r = 289.7$) $w_i(\text{calc.})$: 58.04 % C, 4.18 % H, 14.51 % N; $w_i(\text{found})$: 58.19 % C, 4.02 % H, 14.63 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1680 $\nu(\text{CONHCO})$.

1-Phenyl-4-(2,6-difluorobenzoyl)semicarbazide (*XI*), yield 73 %, m.p. = 184—185 °C. For C₁₄H₁₁F₂N₃O₂ ($M_r = 291.3$) $w_i(\text{calc.})$: 57.73 % C, 3.81 % H, 14.43 % N; $w_i(\text{found})$: 57.58 % C, 3.62 % H, 14.59 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1675 $\nu(\text{CONHCO})$. ^1H NMR spectrum (CDCl₃/DMSO-*d*₆), δ : 6.90—7.60 (m, 8H, C₆H₅ and C₆H₃), 9.84, 10.80 (s, s, 2 × 1H, 2 × NH).

1-Phenyl-4-(3-phenylpropenoyl)semicarbazide (*XII*), yield 75 %, m.p. = 226—227 °C (acetone). For C₁₆H₁₅N₃O₂ ($M_r = 281.3$) $w_i(\text{calc.})$: 68.31 % C, 5.38 % H, 14.94 % N; $w_i(\text{found})$: 68.12 % C, 5.43 % H, 14.76 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1690 and 1660 $\nu(\text{CONHCO})$, 1620 $\nu(\text{C}=\text{C})$.

1-Phenyl-4-(2-naphthoyl)semicarbazide (*XIII*), yield 80 %, m.p. = 227—229 °C (acetone). For C₁₈H₁₅N₃O₂ ($M_r = 305.3$) $w_i(\text{calc.})$: 70.81 % C, 4.95 % H, 13.76 % N; $w_i(\text{found})$: 70.59 % C, 4.81 % H, 13.83 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1690 and 1660 $\nu(\text{CONHCO})$.

1-Phenyl-4-(2-thenoyl)semicarbazide (*XIV*), yield 78 %, m.p. = 227—229 °C (ethanol). For C₁₂H₁₁N₃O₂S ($M_r = 261.3$) $w_i(\text{calc.})$: 55.16 % C, 4.24 % H, 16.08 % N; $w_i(\text{found})$: 55.28 % C, 4.39 % H, 16.19 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1670 $\nu(\text{CONHCO})$. ^1H NMR spectrum (CDCl₃/DMSO-*d*₆), δ : 7.10—8.50 (m, 8H, C₆H₅ and 2-thienyl), 10.12, 11.20 (s, s, 2 × 1H, 2 × NH).

1-Phenyl-4-(5-chloro-2-thenoyl)semicarbazide (*XV*), yield 76 %, m.p. = 224—226 °C (ethanol). For C₁₂H₁₀ClN₃O₂S ($M_r = 295.8$) $w_i(\text{calc.})$: 48.74 % C, 3.41 % H, 14.21 % N; $w_i(\text{found})$: 48.52 % C, 3.49 % H, 14.35 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1680 and 1640 $\nu(\text{CONHCO})$.

1-Phenyl-4-(3-chloro-2-benzo[*b*]thenoyl)semicarbazide (XVI), yield 76 %, m.p. = 212–214 °C (methanol). For $C_{16}H_{12}ClN_3O_2S$ ($M_r = 345.8$) $w_i(\text{calc.})$: 55.57 % C, 3.50 % H, 12.15 % N; $w_i(\text{found})$: 55.73 % C, 3.39 % H, 12.28 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1680 and 1660 $\nu(\text{CONHCO})$.

3-Substituted 2-Phenyl-1,2,4-triazolin-5-ones XVII–XXIII

1-Phenyl-4-acylsemicarbazide (X–XVI, 1 mmol) was dissolved in 2 M-NaOH (6 cm³, 12 mmol) and the solution was heated until it started to boil. After cooling by cold water the solution was acidified by diluted hydrochloric acid (7 mass %). Separated precipitate was filtered with suction, washed with water, dried and crystallized from a suitable solvent.

2-Phenyl-3-(2-chlorophenyl)-1,2,4-triazolin-5-one (XVII), yield 70 %, m.p. = 245–247 °C (ethanol). For $C_{14}H_{10}ClN_3O$ ($M_r = 271.7$) $w_i(\text{calc.})$: 61.89 % C, 3.71 % H, 15.47 % N; $w_i(\text{found})$: 61.63 % C, 3.48 % H, 15.63 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1690 $\nu(\text{C=O})$, 1580 $\nu(\text{C=N})$. Mass spectrum, m/z ($I_r/\%$): M^+ 271 (39), $[M - Cl]^+$ 236 (32), $[Cl - C_6H_4 - CNH]^+$ 138 (39), $[CO]^+$ 28 (100).

2-Phenyl-3-(2,6-difluorophenyl)-1,2,4-triazolin-5-one (XVIII), yield 90 %, m.p. = 275 °C (ethanol). For $C_{14}H_9F_2N_3O$ ($M_r = 273.3$) $w_i(\text{calc.})$: 61.54 % C, 3.32 % H, 15.38 % N; $w_i(\text{found})$: 61.43 % C, 3.59 % H, 15.12 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1690 $\nu(\text{C=O})$, 1585 $\nu(\text{C=N})$. Mass spectrum, m/z ($I_r/\%$): M^+ 273 (31), $[M - Cl]^+$ 158 (86), $[2,6-F_2 - C_6H_3 - CNH]^+$ 141 (100).

2-Phenyl-3-(2-phenylethenyl)-1,2,4-triazolin-5-one (XIX), yield 92 %, m.p. = 292 °C (acetone). For $C_{16}H_{13}N_3O$ ($M_r = 263.3$) $w_i(\text{calc.})$: 72.99 % C, 4.98 % H, 15.96 % N; $w_i(\text{found})$: 72.81 % C, 5.13 % H, 15.79 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1630 $\nu(\text{C=C})$, 1570 $\nu(\text{O=C-N=C})$.

2-Phenyl-3-(2-naphthyl)-1,2,4-triazolin-5-one (XX), yield 89 %, m.p. = 247–248 °C (acetone). For

$C_{18}H_{13}N_3O$ ($M_r = 287.3$) $w_i(\text{calc.})$: 75.25 % C, 4.56 % H, 14.63 % N; $w_i(\text{found})$: 75.15 % C, 4.42 % H, 14.81 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1580 $\nu(\text{O=C-N=C})$.

2-Phenyl-3-(2-thienyl)-1,2,4-triazolin-5-one (XXI), yield 92 %, m.p. = 253–254 °C (acetone). For $C_{12}H_9N_3OS$ ($M_r = 243.3$) $w_i(\text{calc.})$: 59.24 % C, 3.73 % H, 17.27 % N; $w_i(\text{found})$: 59.18 % C, 3.90 % H, 17.08 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1580 $\nu(\text{O=C-N=C})$.

2-Phenyl-3-(5-chloro-2-thienyl)-1,2,4-triazolin-5-one (XXII), yield 86 %, m.p. = 264–266 °C (ethanol). For $C_{12}H_8ClN_3OS$ ($M_r = 277.7$) $w_i(\text{calc.})$: 51.90 % C, 2.90 % H, 15.13 % N; $w_i(\text{found})$: 51.73 % C, 2.73 % H, 15.29 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1650 $\nu(\text{C=O})$, 1580 $\nu(\text{C=N})$.

2-Phenyl-3-(3-chloro-2-benzo[*b*]thienyl)-1,2,4-triazolin-5-one (XXIII), yield 82 %, m.p. = 259–261 °C (acetone). For $C_{16}H_{10}ClN_3OS$ ($M_r = 327.8$) $w_i(\text{calc.})$: 58.63 % C, 3.08 % H, 12.82 % N; $w_i(\text{found})$: 58.49 % C, 2.93 % H, 12.69 % N. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 1650 $\nu(\text{C=O})$, 1550 $\nu(\text{C=N})$. Mass spectrum, m/z ($I_r/\%$): M^+ 327 (58), $[M - Cl]^+$ 292 (92), $[ClSC_8H_4 - CNH]^+$ 194 (70).

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