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UNEXPECTED 5-ACETYL-4-HYDROXY-4,5-DIMETHYL-HEXAHYDROPYRIMIDINE-2-THIONE RING CLEAVAGE BY THE ACTION OF BASES

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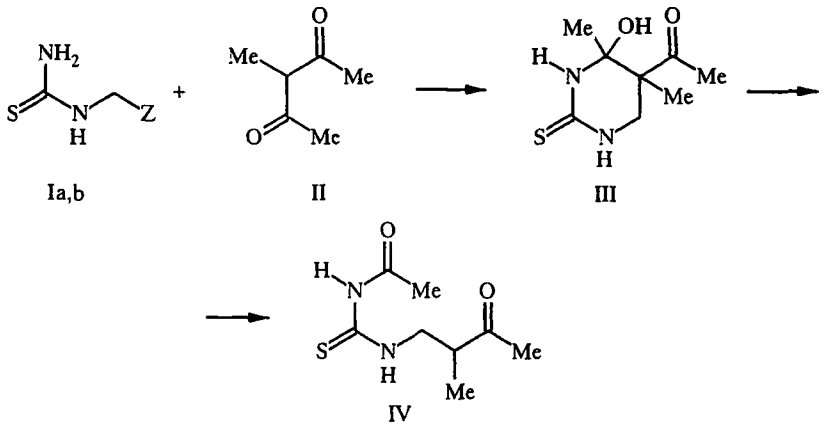
A few years ago [1, 2], we developed a general approach for the synthesis of previously unknown 5-acyl-substituted 4-hydroxyhexahydropyrimidine-2-thiones based on the reaction of the readily available α-azido- or α-tosyl-substituted thioureas with sodium enolates of 1,3-dicarbonyl compounds. In the development of our investigations, the application of α-substituted 1,3-dicarbonyl compounds in these reactions has been studied. The present work gives some results of the investigation into the reaction of N-(azidomethyl)thiourea (Ia) and N-(tosylmethyl)thiourea (Ib) with sodium or potassium enolates of 3-methylpentane-2,4-dione (II).

We showed that azidomethylthiourea (Ia) reacts readily in acetonitrile (at 20°C for 4 h) with the sodium enolate of 3-methylpentane-2,4-dione, obtained by treatment of the corresponding CH-acid with sodium hydride, resulting in the isolation of 5-acetyl-4-hydroxy-4,5-dimethylhexahydropyrimidine-2-thione (III) (yield 84.5%). The last compound is also formed with the yield of 78.4% by the reaction of thiourea Ia with the potassium enolate of 3-methylpentane-2,4-dione (ethanol, at 20°C for 6 h), obtained by the treatment of the CH-acid II with the alcoholic solution of potassium hydroxide.



Ia,b II III IV

I a Z = N_3, b Z = Ts

An unexpected result was obtained in the reaction of tosylmethylthiourea (Ib) with the sodium enolate of compound II in acetonitrile at 20°C. In this case, we isolated N-acetyl-N'-(2-methyl-3-oxobut-1-yl)thiourea (IV) with the yield of 52.0% as the final reaction product. The monitoring of the reaction by TLC showed that the hydroxypyrimidine III formed as an intermediate product is gradually converted into compound IV. We found that

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bases promote the conversion of the hydroxypyrimidine III to the thiourea IV. In fact, according to TLC data, the treatment of compound III with sodium hydride or sodium hydroxide in acetonitrile (20-25 mole % at 20°C) leads to the rapid transformation of this substance into compound IV, which is completed after 1 h. In both cases, the thiourea IV was isolated with the yield of 91.2% after neutralization of the reaction mixtures with acetic acid followed by evaporation, treatment of the resulting residues with water, and filtration of the product.

The unexpected conversion of the 5-acetyl-4-hydroxyhexahydropyrimidine-2-thione (III) to the thiourea IV, can probably be explained by the initial deprotonation of $N_{(3)}$–H or O–H group in compound III under action of the base with subsequent spontaneous cleavage of the $C_{(4)}$–$C_{(5)}$ bond of resulting anion similar to that proceeding in the Claisen retrocondensation.

The described cleavage of the hexahydropyrimidine ring is general and is also characteristic for other substituted 5-acyl-4-hydroxyhexahydropyrimidine-2-thiones, which will be the subject of our further communications.

5-Acetyl-4-hydroxy-4,5-dimethylhexahydropyrimidine-2-thione (III). Mp 210.5-211.5°C (decomp., acetonitrile). IR spectrum: 3320, 3224, 1704, 1580, 1536, 1212, 1096 cm^{-1}. PMR spectrum: 8.42 (1H, br. s, $N_{(3)}$–H); 8.39 (1H, br. d, $J_{NH,6e}$ = 4.8, $J_{NH,6a}$ = 0 Hz, $N_{(1)}$–H); 6.15 (1H, s, OH); 3.87 (1H, d, $J_{6e,6a}$ = 12.4 Hz, 6-H_a); 2.96 (1H, dd, 6-H_e); 2.14 (3H, s, CH_3C=O); 1.29 (3H, s, 4-CH_3); 0.93 ppm (3H, s, 5-CH_3). Found, %: C 47.19; H 6.95; N 13.75. $C_8H_{14}N_2O_2S$. Calculated, %: C 47.50; H 6.98; N 13.85.

N-Acetyl-N'-(2-methyl-3-oxobut-1-yl)thiourea (IV). Mp 110.5-111°C (ethanol). IR spectrum: 3192, 1700, 1560, 1532, 1232, 1164, 752 cm^{-1}. PMR spectrum: 11.22 (1H, s, NHAc); 10.74 (1H, t, NH); 3.67 (2H, dd, $J_{CH,CH}$ = 6.8, $J_{NH,CH}$ = 5.5 Hz, CH_2); 2.98 (1H, m, CH); 2.14 (3H, s, $COCH_3$); 2.05 (3H, s, $NHCOCH_3$); 1.06 ppm (3H, d, J = 7.2 Hz, CH_3). ^{13}C NMR spectrum: 211.18 ($C_{(3)}$=O); 181.24 (C=S); 173.11 (NH–C=O); 46.84 (CH_2); 45.95 (CH); 29.08 ($COCH_3$); 24.52 ($NHCOCH_3$); 14.79 ppm (CH_3). Found, %: C 47.91; H 6.60; N 13.46. $C_8H_{14}N_2O_2S$. Calculated, %: C 47.50; H 6.98; N 13.85.

IR spectra were recorded on the Specord M-80 spectrophotometer in mineral oil. PMR and ^{13}C NMR spectra were registered on the Bruker MSL-200 spectrometer in DMSO-d_6.

REFERENCES

1. A. D. Shutalev and V. A. Kuksa, *Khim. Geterotsikl. Soedin.*, No. 1, 97 (1995).
2. A. D. Shutalev and V. A. Kuksa, *Khim. Geterotsikl. Soedin.*, No. 1, 105 (1997).