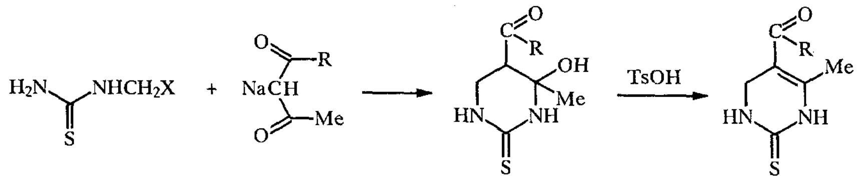
Chemistry of Heterocyclic Compounds, Vol. 29, No. 12, 1993

NEW METHOD FOR THE PREPARATION OF HYDROGENATED PYRIMIDINE-2-THIONES

A. D. Shutalev and V. A. Kuksa

In previous work [1-3], we found that azide or arylsulfonyl groups located in the α-position relative to the nitrogen atom in heterocyclic amides and thioamides display high nucleofugicity in the reactions of these compounds with various nucleophilic reagents. In a continuation of these studies, we investigated the reaction of α-azido and α-arylsulfonyl C—nucleophiles containing an explicit or masked electrophilic site along with the nucleophilic site, which provides the preconditions for the heterocyclization of the initial nucleophilic substitution products. In the present communication, we report preliminary results on the use of this approach in the synthesis of hydrogenated pyrimidines by N–C–N–C + C–C condensation.



IIa,b IIIa,b IVa,b Va,b

II a X = N_3, b X = 4-$CH_3C_6H_4SO_2$; III—V a R = OC_2H_5, b R = Me

Readily available hydroxymethylthiourea I obtained in 96% yield in the reaction of thiourea with formaldehyde was used as the starting reagent. We showed that I readily reacts with HN_3 or *p*-toluenesulfinic acid in water at 20°C to give thiourea IIa or IIb, respectively. The azide or *p*-toluenesulfonyl group in IIa and IIb is readily replaced upon the reaction of these compounds with nucleophilic reagents such as the sodium enolates of ethyl acetoacetate and acetyl acetone obtained from the corresponding C–H acids by reaction with NaH. The reaction of IIa and IIb with C-nucleophiles IIIa and IIIb in acetonitrile at 20°C for 2.5 h gave 4-hydroxyhexahydropyrimidine-2-thiones (IVa and IVb), which are the products of the intramolecular heterocyclization of the intermediate (3-oxobutyl)thioureas. Heating solutions of hydroxypyrimidines IVa and IVb in ethanol using TsOH as the catalyst for 1 h leads to their dehydration and formation of 1,2,3,6-tetrahydropyrimidine-2-thiones (Va and Vb).

Thus, mild reaction conditions, rather high yields, availability of all the starting reagents, and the possibility of using a broad range of starting reagents make this method for the synthesis of hydrogenated pyrimidine-2-thiones extremely promising.

(Azidomethyl)thiourea (IIa, $C_2H_5N_5S$), mp 96-97°C (from 3:2 hexane–ethyl acetate). IR spectrum: 3357, 3263, 3164, 3048 (NH), 2082 (N_3), 1608, 1568 cm^{-1} (thioamide-II). The yield of IIa was 71%.

(*p*-Toluenesulfonylmethyl)thiourea (IIb, $C_9H_{12}N_2O_2S_2$), mp 156.5-157°C (acetone). IR spectrum: 3392, 3291, 3180 (NH), 1608, 1548 (thioamide-II), 1271, 1133 cm^{-1} (SO_2). The yield of IIb was 94%.

4-Hydroxy-4-methyl-5-ethoxycarbonylhexahydropyrimidine-2-thione (IVa, $C_8H_{14}N_2O_3S$), mp 236-237°C (dec., acetone). IR spectrum: 3308, 3288 sh, 3227 (OH, NH), 1738, 1727 (C=O), 1588, 1574, 1529 (thioamide-II), 1196 cm^{-1}. UV spectrum, λ_{max} (log ε): 206 (3.97), 247 nm (4.19). The yield of IVa was 79% (from IIa) and 69% (from IIb).

M. V. Lomonosov Moscow State Academy of Fine Chemical Technology, 117571 Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1698-1699, December, 1993. Original article submitted December 29, 1993.

0009-3122/93/2912-1470$12.50

5-Acetyl-4-hydroxy-4-methylhexahydropyrimidine-2-thione (IVb, $C_7N_{12}N_2O_2S$), mp 221.5-222°C (dec., ethanol). IR spectrum: 3308, 3236 (OH, NH), 1709 (C=O), 1584, 1571, 1527 (thioamide-II), 1220 cm^{-1}. UV spectrum, λ_{max} (log ε): 207 (4.04), 247 nm (4.24). The yield of IVb was 63% (from IIa) and 48% (from IIb).

4-Methyl-5-ethoxycarbonyl-1,2,3,6-tetrahydropyrimidine-2-thione (Va, $C_8H_{12}N_2O_2S$), mp 236-237°C (dec., methanol). IR spectrum: 3194, 3152 (NH), 1716 (C=O), 1662 (C=C), 1615, 1595, 1505 (thioamide-II), 1205 cm^{-1}. UV spectrum, λ_{max} (log ε): 206 (4.11), ~280 sh, 306 nm (4.18). The yield of Va was 86%.

5-Acetyl-4-methyl-1,2,3,6-tetrahydropyrimidine-2-thione (Vb, $C_7H_{10}N_2OS$), mp 230-230.5 (dec., ethanol). IR spectrum: 3274, 3180, 3128 (NH), 1647 sh, 1613 (C=O, C=C), 1592 (thioamide-II), 1189 cm^{-1}. UV spectrum, λ_{max} (log ε):207 (3.99), ~290 sh, 325 nm (4.19). The yield of Vb was 74%.

The IR spectra were taken on a Shimadzu IR-435 spectrometer in Vaseline mull. The UV spectra were taken on a Beckmann DU-6 spectrometer for methanol solutions.

The elemental analysis data for C, H, N, and S for IIa, IIb, IVa, IVb, Va, and Vb corresponded to the calculated values.

REFERENCES

1. A. D. Shutalev, L. A. Ignatova, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 1, 133 (1990).
2. A. D. Shutalev and L. A. Ignatova, Khim. Geterotsikl. Soedin., No. 2, 228 (1991).
3. A. D. Shutalev, Khim. Geterotsikl. Soedin., No. 10, 1389 (1993).