Acyl Iodides in Organic Synthesis.
Reactions of Acetyl Iodide with Urea, Thiourea,
and Their *N,N′*-Disubstituted Derivatives

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Abstract—Acetyl iodide reacted with urea and its derivatives to give the corresponding N-substituted products. The reactions of acetyl iodide with thiourea, *N,N′*-dimethylthiourea, imidazolidine-2-thione, and hexahydropyrimidine-2-thione resulted in the formation of *S*- or *N*-acetyl derivatives, depending on the temperature and structure of the sulfur functionality (thione or thiol). By contrast, in the reaction of acetyl iodide with *N,N′*-bis(3-triethoxysilylpropyl)thiourea one ethoxy group on the silicon atom was replaced by iodine with formation of *N*-{3-[(diethoxy)iodosilyl]propyl}-*N′*-[3-(triethoxysilyl)propyl]thiourea. The latter decomposed on heating to give 3-triethoxysilylpropyl isothiocyanate and silicon-containing polymer with the composition $C_{45}H_{97}IN_6O_{14.5}S_3Si_6$.
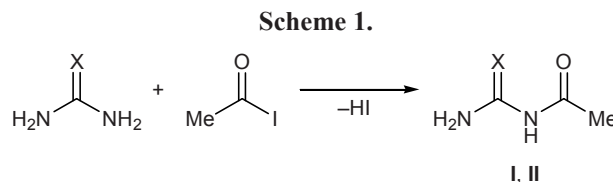
It is known that acyl chlorides react with urea and its derivatives to give the corresponding *N*-acyl-substituted ureas (ureides) [1]. Reactions of acyl chlorides with thiourea and its derivatives lead to the formation of *S*- or *N*-acyl-substituted products, depending on the temperature. *S*-Acyl derivatives are formed at lower temperature, and they usually undergo thermal rearrangement into *N*-acyl isomers (acylation products of thiourea at elevated temperature) [2].

While continuing our systematic studies on the use of the simplest acyl iodides RCOI (R = Me, Ph) as synthons and reagents in organic and organometallic synthesis [3], we were the first to examine reactions of acetyl iodide with urea, thiourea, and some their *N,N′*-disubstituted derivatives such as imidazolidin-2-one, hexahydropyrimidin-2-one, *N,N′*-dimethylthiourea, imidazolidine-2-thione, 3,4,5,6-tetrahydropyrimidine-2-thiol, and *N,N′*-bis(3-triethoxysilylpropyl)-thiourea.
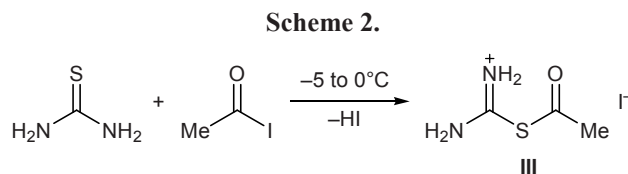
We found that acetyl iodide reacted with urea and thiourea at a molar ratio of 1:1 in a way similar to acyl chloride but, unlike the latter, in the absence of a catalyst (sulfuric acid) [1]. The reactions at room temperature were accompanied by heat evolution, and the

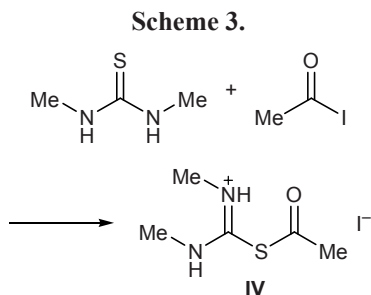products were the corresponding *N*-acetyl derivatives **I** and **II** (yield 85 and 65%, respectively; Scheme 1).

Scheme 1.

I, X = O; **II**, X = S.

Exothermic character of the reaction is responsible for the formation from thiourea of compound **II** rather than of the corresponding isothiuronium salt [4]. When the reaction was performed on cooling (–5 to 0°C), the expected *S*-acetyl derivative, *S*-acetylisothiuronium iodide (**III**), was obtained (Scheme 2).
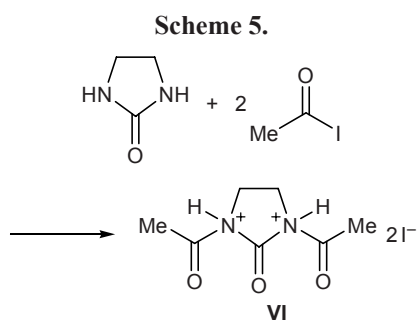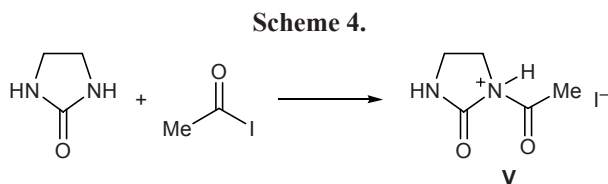
Scheme 2.

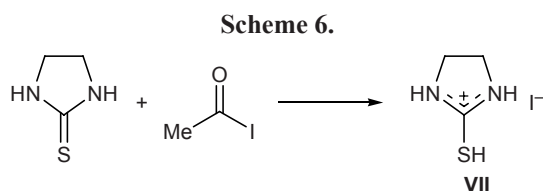Isothiuronium salt, namely *S*-acetyl-*N,N′*-dimethyl-isothiuronium iodide (**IV**), was isolated as the only

product in the reaction of acetyl iodide with *N*,*N'*-di-methylthiourea (Scheme 3).

Scheme 3.

Exothermic reactions of acetyl iodide with imid-azolidin-2-one at ratios of 1:1 and 2:1 afforded crys-talline 1-acetylimidazolidin-2-one hydroiodide (**V**) and 1,3-diacetylimidazolidin-2-one dihydroiodide (**VI**), re-spectively (Schemes 4, 5).

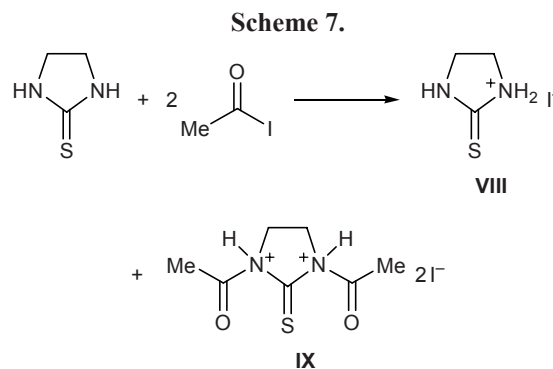**Scheme 4.**

Scheme 5.

Unlike imidazolidin-2-one, the reactions of acetyl iodide with imidazolidine-2-thione were not accom-panied by heat evolution, indicating lower reactivity of the thiourea derivative as compared to its oxygen-con-taining analog. When the reaction of acetyl iodide with imidazolidine-2-thione was carried out in diethyl ether, the product was 2-sulfanyl-4,5-dihydro-1*H*-imidazole hydroiodide (**VII**, yield 86%; Scheme 6). This is the first example of dehydroiodination of acetyl iodide by the action of a base containing a thioxo group.
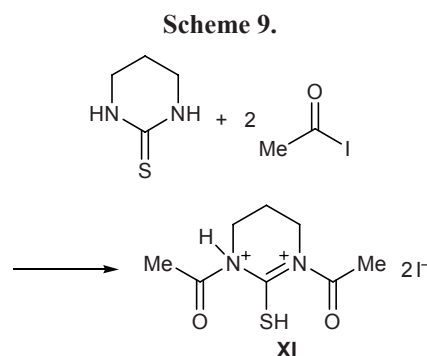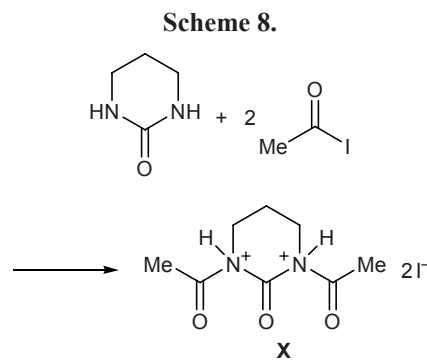
Scheme 6.

The same compound was obtained in 88% yield in the reaction of imidazolidine-2-thione with 2 equiv of acetyl iodide under analogous conditions.

Treatment of imidazolidine-2-thione with 2 equiv of acetyl iodide at 50–60°C resulted in the formation of a mixture of two products, one of which was iso-meric to **VII**. It was assigned the structure of imid-azolidine-2-thione hydroiodide (**VIII**). The second product was 1,3-diacetylimidazolidine-2-thione dihy-droiodide (**IX**) (Scheme 7).

Scheme 7.

The reactions of acetyl iodide with hexahydro-pyrimidin-2-one and 3,4,5,6-tetrahydropyrimidine-2-thione at a molar ratio of 2:1 gave the corresponding 1,3-diacetylpyrimidine dihydroiodides **X** and **XI** (Schemes 8, 9). Dihydroiodide **XI** was formed as the

Scheme 8.

Scheme 9.

Scheme 10.

Scheme 11.

only product in the reactions performed both at 50–60°C under solvent-free conditions and in diethyl ether at 20–24°C. The observed difference in the reactivity of cyclic thiourea derivatives is likely to be determined by the nature of the sulfur functionality (C=S and C–SH groups) [4].
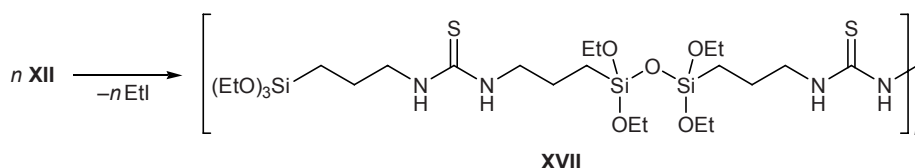
The reaction of acetyl iodide with *N,N′*-bis(3-triethoxysilylpropyl)thiourea followed a quite different path. By analogy with the reaction of MeCOI with alkyl(alkoxy)silanes, studied by us previously [5], in the first step one ethoxy group on the silicon atom is replaced by iodine with formation of *N*-{3-[diethoxy-(iodo)silyl]propyl}-*N′*-[3-(triethoxysilyl)propyl]thiourea (**XII**) and ethyl acetate (Scheme 10). Upon attempted vacuum distillation compound **XII** underwent partial decomposition to produce 3-triethoxysilylpropyl isothiocyanate (**XIII**) which, according to the IR data, contained an impurity of isomeric 3-triethoxysilylpropyl thiocyanate and was converted into rubber-like organosilicon polymer of the composition $C_{45}H_{97}IN_6O_{14.5}S_3Si_6$ (**XVII**) (Scheme 11). Polymer **XVII** is insoluble, but it swells in organic solvents. Its IR spectrum indicated the presence of S=C=N, S–C≡N, and Si–O–Si fragments. Ethyl acetate and ethyl iodide were detected in the reaction mixture by gas chromatography–mass spectrometry. Obviously, polymer **XVII** is formed via polymerization of iodide **XII**, as well as via condensation of iodides **XIV** and

XVI (Scheme 10) resulting from decomposition of **XII**. This process involves cleavage of the C–O bond in the SiOAlk moiety, which is typical of iodosilanes, and formation of Si–O–Si bond [6, 7] and is responsible for the appearance of ethyl iodide in the reaction mixture.

On the other hand, polymer **XVII** contained 9–10% of iodine, while no 3-triethoxysilylpropylamine (**XV**) was detected among decomposition products of compound **XII**. Presumably, the reason is that amine **XV** reacts with ethyl iodide to give quaternary ammonium salt $(EtO)_3Si(CH_2)_3N^+H_2Et\cdot I^-$ (**XVIII**) which is also involved in condensation processes.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer from samples prepared as thin films. Gas chromatographic–mass spectrometric analysis was performed on an HP-5890 gas chromatograph coupled with an HP 5971A mass-selective detector (electron impact, 70 eV; Ultra-2 column, stationary phase 5% of phenylmethylsilicone; injector temperature 250°C, oven temperature programming from 70 to 280°C at a rate of 20 deg/min).

Acetyl iodide was prepared by reaction of anhydrous sodium iodide with acetyl chloride according to the procedure described in [8].

Reaction of acetyl iodide with urea. Acetyl iodide, 8.5 g (50 mmol), was slowly added to 3.0 g (50 mmol) of urea. The mixture warmed up, and evolution of hydrogen iodide was observed. The mixture was kept for 2 h at 55–60°C, and the precipitate was filtered off, recrystallized from ethanol, and sublimed under reduced pressure. We thus isolated 9.8 g (85%) of *N*-acetylurea (**I**) with mp 175–177°C; published data [9]: mp 218–219°C [9]. Found, %: C 35.06; H 6.29; N 27.12. $C_3H_6N_2O_2$. Calculated, %: C 35.29; H 5.88; N 27.45.

Reaction of acetyl iodide with imidazolidin-2-one. *a*. Acetyl iodide, 4.25 g (25 mmol), was added to 2.15 g (25 mmol) of imidazolidin-2-one. The mixture warmed up to 50–60°C and was left to stand for 24 h at room temperature. The resulting crystalline material was kept for 1 h under reduced pressure (2–3 mm) to remove volatile impurities. The residue was 6.1 g (95%) of 1-acetylimidazolidin-2-one hydroiodide (**V**), mp 75–76°C. IR spectrum, ν, cm^{-1}: 1750 (1-C=O), 1650 (C^2=O), 600 (I$^-$). Found, %: C 24.51; H 3.54; I 42.56. $C_5H_9IN_2O_2$. Calculated, %: C 23.46; H 3.54; I 49.56.

b. Imidazolidin-2-one, 4.3 g (50 mmol), was mixed with acetyl iodide, 17.0 g (100 mmol), and the mixture sharply warmed up to 60–65°C. It was left to stand for 24 h and was then evacuated at a residual pressure of 1–2 mm to obtain 20.0 g (94%) of 1,3-diacetylimidazolidin-2-one dihydroiodide (**VI**) as black crystals with mp 104–105°C. IR spectrum, ν, cm^{-1}: 1750 (1-C=O, 3-C=O), 1680 (C^2=O), 600 (I$^-$). Found, %: C 20.09; H 2.84; I 57.88; N 7.37. $C_7H_{12}I_2N_2O_3$. Calculated, %: C 19.74; H 2.84; I 59.58; N 6.58.

Reaction of acetyl iodide with hexahydropyrimidin-2-one. A mixture of 2.5 g (25 mmol) of hexahydropyrimidin-2-one and 8.5 g (50 mmol) of acetyl iodide was heated for 1 h at 50–60°C. The resulting thick black undistillable material was kept at a residual pressure of 1–2 mm at room temperature to remove volatile impurities. We thus obtained 11.0 g (100%) of tarry 1,3-diacetylhexahydropyrimidin-2-one dihydroiodide (**X**). IR spectrum, ν, cm^{-1}: 1740 (1-C=O, 3-C=O), 1620 (C^2=O), 580 (I$^-$). Found, %: C 22.67; H 4.00; I 57.35; N 7.89. $C_8H_{14}I_2N_2O_3$. Calculated, %: C 21.84; H 3.21; I 57.68; N 6.38.

Reaction of acetyl iodide with thiourea. *a*. Acetyl iodide, 8.5 g (50 mmol), was added to 3.8 g (50 mmol) of thiourea, and the mixture was kept for 3 h at 50–60°C. Recrystallization of the precipitate from ethanol gave 7.8 g (64%) of *N*-acetylthiourea (**II**), mp 167°C;

published data [9]: mp 165–166°C. IR spectrum, ν, cm^{-1}: 1700 (C=O); 1600, 1540 (δNH); 1240 (C–N); 1040 (C=S). Found, %: C 30.24; H 5.09; N 22.99; S 25.22. $C_3H_6IN_2OS$. Calculated, %: C 30.50; H 5.08; N 23.72; S 27.11.

b. Acetyl iodide, 8.5 g (50 mmol), was added on cooling to 3.8 g (50 mmol) of thiourea, and the mixture was kept for 3 h at –5 to 0°C. The precipitate was washed with diethyl ether. Yield of *S*-acetylisothiuronium iodide (**III**) 11.3 g (91%), mp 84–85°C. IR spectrum, ν, cm^{-1}: 1700 (C=O); 1600 (δNH); 1580 (δ$^+$NH$_3$). Found, %: C 14.59; H 2.83; I 51.20; N 11.21; S 13.40. $C_3H_7IN_2OS$. Calculated, %: C 14.63; H 2.80; I 51.62; N 11.38; S 13.00.

Reaction of acetyl iodide with *N*,*N*′-dimethylthiourea. Acetyl iodide, 8.5 g (50 mmol), was added to 5.2 g (50 mmol) of *N*,*N*′-dimethylthiourea, and the mixture was kept for 5.5 h at room temperature. Recrystallization from ethanol gave 9.3 g (68%) of *S*-acetyl-*N*,*N*′-dimethylisothiuronium iodide (**IV**) as brown crystals with mp 105°C. IR spectrum, ν, cm^{-1}: 3370 (NH); 1630 (C=N); 1515 (δ$^+$NH); 1490 (δNH); 1230, 1180 (C–N). Found, %: C 21.38; H 2.99; I 56.58; N 8.66; S 10.75. $C_5H_{11}IN_2OS$. Calculated, %: C 21.89; H 4.01; I 46.35; N 10.21; S 11.68.

Reaction of acetyl iodide with imidazolidine-2-thione. *a*. Acetyl iodide, 8.5 g (50 mmol), was added under stirring to a mixture of 5.1 g (50 mmol) of imidazolidine-2-thione and 10 ml of diethyl ether, and the mixture was heated for 6 h under reflux. The precipitate was filtered off, washed with diethyl ether, and kept for 1 h under reduced pressure (3 mm) to remove traces of the solvent. Yield of 4,5-dihydroimidazole-2-thiol hydroiodide (**VII**) 11.7 g (86%), mp 72–73°C. IR spectrum, ν, cm^{-1}: 3330 (CH), 1690 (C=N), 1460 (δNH). Found, %: C 15.55; H 2.95; I 55.07; N 11.86; S 13.11. $C_3H_7IN_2S$. Calculated, %: C 15.65; H 3.04; I 55.21; N 12.17; S 13.91.

b. Under analogous conditions, the reaction of 2.55 g (25 mmol) of imidazolidine-2-thione with 8.5 g (50 mmol) of acetyl iodide gave 9.8 g (88%) of compound **VII**, mp 72–74°C. IR spectrum, ν, cm^{-1}: 3330 (CH), 1690 (C=N), 1460 (δNH). Found, %: C 15.38; H 3.41; I 57.09; N 12.02; S 13.30. $C_3H_7IN_2S$. Calculated, %: C 15.65; H 3.04; I 55.21; N 12.17; S 13.91.

c. Acetyl iodide, 8.5 g (50 mmol), was added under stirring to 2.55 g (25 mmol) of imidazolidine-2-thione, and the mixture was kept for 5.5 h at 55–60°C. When the reaction was complete, crystal deposited on the walls of the flask were collected and washed with

diethyl ether. Yield of imidazolidine-2-thione hydro-iodide (**VIII**) 2.1 g (19%), mp 115–118°C. IR spectrum, ν, cm^{-1}: 3330 (CH); 2650 ($^+$NH), 1690 (C=N$^+$), 1438 (δNH), 1300 (C–N), 1200 (C=S). Found, %: C 16.40; H 3.19; I 56.32; N 11.64; S 12.80. $C_3H_7IN_2S$. Calculated, %: C 15.65; H 3.04; I 55.21; N 12.17; S 13.91. The precipitate was washed with diethyl ether and evacuated to remove traces of diethyl ether and volatile impurities. Yield of 1,3-diacetylimidazolidine-2-thione dihydroiodide (**IX**) 8.7 g (78%), mp 129–130°C. Found, %: C 18.27; H 2.09; I 52.68; N 6.65; S 7.76. $C_5H_9I_2N_2O_2S$. Calculated, %: C 19.00; H 2.71; I 57.46; N 7.24; S 7.24.

Reaction of acetyl iodide with 3,4,5,6-tetrahydro-pyrimidine-2-thione. *a*. Acetyl iodide, 8.5 g (50 mmol), was added to 2.9 g (25 mmol) of 3,4,5,6-tetrahydropyrimidine-2-thione. The mixture slightly warmed up and was kept for 5 h at 50–60°C. The crystalline product was washed with diethyl ether and evacuated at a residual pressure of 2–3 mm to remove traces of diethyl ether and volatile impurities. Yield of 1,3-diacetyl-3,4,5,6-tetrahydropyrimidine-2-thiol dihydroiodide (**XI**) 10.9 g (96%). Brown crystals, mp 115–117°C. IR spectrum, ν, cm^{-1}: 3220 (CH); 2970 ($^+$NH), 2629 (SH), 1744 (C=O), 1652 (C=N$^+$), 1570 (δNH$^+$). Found, %: C 20.37; H 3.19; I 57.74; N 6.24; S 7.28. $C_8H_{14}I_2N_2O_2S$. Calculated, %: C 21.05; H 3.07; I 55.70; N 6.14; S 7.01.

b. A mixture of 2.9 g (25 mmol) of 3,4,5,6-tetra-hydropyrimidine-2-thiol and 8.5 g (50 mmol) of acetyl iodide in 15 ml of diethyl ether was heated for 5.5 h under reflux. The product was compound **XI**, yield 8.5 g (74%), mp 115°C.

Reaction of acetyl iodide with *N,N′*-bis(3-triethoxysilylpropyl)thiourea. Acetyl iodide, 2.3 g (13.5 mmol), was added dropwise to 6.25 g (13.5 mmol) of *N,N′*-bis(3-triethoxysilylpropyl)thiourea. The mixture spontaneously warmed up and was kept for 2 h at 50–55°C. It was then evacuated at a residual pressure of 3 mm to remove volatile substances. Yield of *N*-{3-[(diethoxy)iodosilyl]propyl}-*N′*-[3-(triethoxysilyl)propyl]thiourea (**XII**) 8.3 g (98%). Found, %: C 35.87; H 6.81; I 22.43; N 5.32; S 6.17; Si 9.78. $C_{17}H_{39}IN_2O_5SSi_2$. Calculated, %: C 36.04; H 6.89; I 21.06; N 4.94; S 5.65; Si 9.89.

While attempting to distil thiourea **XII** under reduced pressure we isolated 1.3 g (15%) of 3-triethoxysilylpropyl isothiocyanate (**XIII**) with bp 92°C (0.3 mm), $n_D^{24} = 1.4615$; published data [10]: bp 127–129°C (2 mm), $n_D^{20} = 1.4679$. IR spectrum, ν, cm^{-1}: 2970–2880 (CH), 2160–2070 (SC≡N, N=C=S), 1070 (SiOC). Found, %: C 45.18; H 7.58; N 5.11; S 11.72; Si 8.43. $C_{10}H_{21}NO_3SSi$. Calculated, %: C 45.62; H 7.98; N 5.32; S 12.16; Si 10.64; and 4.7 g (56%) of organosilicon polimer **XVII**. IR spectrum, ν, cm^{-1}: 2180–2050 (N=S=C, SC≡N), 1100–1020 (SiOSi). Found, %: C 40.13; H 6.76; I 9.40; N 7.23; S 7.94; Si 13.79. $C_{45}H_{97}IN_6O_{14.5}S_3Si_6$. Calculated, %: C 40.17; H 7.21; I 9.44; N 6.25; S 7.14; Si 12.54. According to the GC–MS data, volatile fraction, 2.0 g (24%), contained ethyl acetate and ethyl iodide. Mass spectrum, m/z (I_{rel}, %): 156 (38) $[M_1]^+$, 127 (31), 88 (21) $[M_2]^+$, 43 (10).

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