$NtnOenH_4$ calculated from EA and TGA.

In summary, we can prepare the new layered material containing $NtnOenH_4$. This material is not only interesting as the new layered structure containing macrocyclic ligands, but also of use in the study of the separation chemistry for chromatography. We expect that phyllosilicate compounds similar with these materials will be easily synthesized in other macrocyclic ligand systems. And also, the vast data of free macrocyclic ligand-cation interaction can be applied to new phyllosilicate ones.

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A Facile Method for the Preparation of 2-(N-Pyrimidino)aminothiazoles

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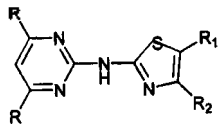
In the course of our studies on the synthesis of novel macrocyclic compounds containing heterocycles such as thiazoles and pyrimidines, we needed a convenient method to prepare α-pyrimidinylthioureas as the synthetic intermediates for obtaining 2-(N-pyrimidino)aminothiazoles **1**.



1

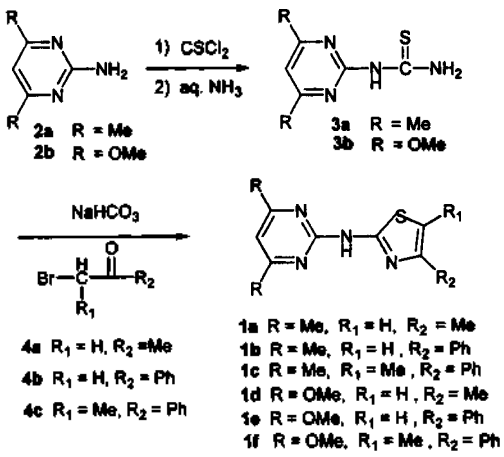
Substituted thiazoles[1] have been frequently made by the reaction of α-substituted thiourea intermediates with α-haloketones known as the Hantzsch thiazole synthesis.[2] Simple α-substituted thioureas have been made in various ways[3]: by treatment of mono-substituted amine with ammonium thiocyanate, thiocyanic acid, thiuram disulfide or silicon thiocyanate, or by the action of ammonia on isothiocyanate. Preparation of α-phenylthiourea described in Organic Syntheses is the classical example where α-phenylthiourea was obtained by the alkaline hydrolysis of α-benzoyl-β-phenylthiourea prepared from the reaction of α-benzoyl-β-phenylisothiocyanate with aniline.[3] However, this method is not generally effective for preparing the α-pyrimidinylthioureas because of poor yield or side products of the reaction are obtained. After various unsuccessful attempts on the convenient transformation of 2-aminopyrimidine derivatives into α-pyrimidinylthioureas, we found a facile procedure of utilizing the isothiocyanate generated by the reaction of thiophosgene[4] with aminopyrimidine for the efficient preparation of α-pyrimidinylthiourea which was readily used for the Hantzsch reaction to follow.

The preparation of 2-(N-pyrimidino)aminothiazoles has been scarcely documented. The only example of the synthesis of 2-(N-pyrimidino)aminothiazoles known to us was the process giving a poor yield. In the process 2'-pyrimidyl-2-thiazoylamine was prepared from the reaction of the sodium salt of 2-aminopyrimidine and 2-chlorothiazole in 9.5% yield.[5] This paper reports a new simple method for the synthesis of 2-(N-pyrimidino)aminothiazoles **1** (Scheme). 2-(N-4,6-disubstituted pyrimidino)aminothioureas **3** were obtained in *ca.* 80% yield by slow addition of thiophosgene to 2-aminopyrimidine **2** during 30 minutes in dichloroethane containing one equivalent of triethylamine at 30 °C and the treatment of the resulting reaction mixture with aqueous ammonia. The reaction of **3** with α-bromoketones **4** in boiling ethanol containing a catalytic amount of sodium bicarbonate gave **1** in a high yield (*ca.* 95%).

Experimental Section

Preparation of α-pyrimidinylthioureas (3)

Typical procedure (3b). To a stirred solution of 2-amino-4,6-dimethoxypyrimidine (310 mg, 2 mmol) in dichloroethane (5 mL) at 30 °C was added slowly thiophosgene (252 mg, 2.2 mmol) in the same solvent (3 mL) during 30 minutes. (Usually 2-aminopyrimidine was dissolved



Scheme

in hot dichloroethane and the solution was cooled to the ambient temperature before use.) After the addition of triethylamine (202 mg, 2 mmol) to the reaction mixture during 30 minutes, solvent was removed under reduced pressure to give an oil. To the crude oil dissolved in ether (5 mL) was added aqueous ammonia (1 mL) and the reaction mixture was stirred for 1 hour. The crude desired product was obtained by extraction with dichloromethane (30 mL) followed by evaporating solvent and drying over anhydrous magnesium sulfate. Flash column chromatography on silica gel (elution solvent: EtOAc/*n*-hexane=3/1) gave the chemically pure **3b** as a pale yellow powder (355 mg).

3a: ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.36 (brs, 1H), 10.26 (brs, 1H), 9.11 (brs, 1H), 6.29 (s, 1H), 2.36 (s, 6H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 23.60, 114.86, 157.53, 167.90, 181.15; MS (EI) m/e 182 (M^+). mp 279 °C. Anal. Calcd for $C_7H_{10}N_4S$: C, 46.13; H, 5.53; N, 30.74. Found; C, 46.53; H, 5.65; N, 31.03; yield (80 %).

3b: ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.32 (brs, 1H), 9.93 (brs, 1H), 9.20 (brs, 1H), 5.93 (s, 1H), 3.85 (s, 6H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 54.34, 156.47, 167.57, 171.85, 181.02; MS (EI) m/e 213 (M^+). mp 215 °C. Anal. Calcd for $C_7H_{10}N_4O_2S$: C, 39.24; H, 4.71; N, 26.17; Found; C, 39.97; H, 4.57; N, 26.17; yield (83 %).

Preparation of 2-(N-pyrimidino)aminothiazoles (1a-f)

Typical procedure (1e). A mixture of **3b** (118 mg, 0.55 mmol) and **4b** (99 mg, 0.5 mmol) in absolute ethanol containing sodium bicarbonate (10 mg) was heated at reflux for 2.5 h. After removal of most of the ethanol under reduced pressure, the residue was taken up in ether (15 mL), washed with a brine solution (5 mL), dried over anhydrous magnesium sulfate and concentrated to give the pure **1e** as a pale yellow solid (147 mg).

1a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.42 (s, 1H), 6.62 (s, 1H), 6.42 (s, 1H), 2.45 (s, 6H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.13, 54.64, 82.59, 106.50, 147.50, 156.15, 159.92, 171.91, MS (EI) m/e (M^+) 220. mp 175 °C. Anal. Calcd for $C_{10}H_{12}N_4S$: C, 54.53; H, 5.50; N, 25.45. Found; C, 54.60; H, 5.64; N, 24.99; yield (96%).

1b: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.38 (s, 1H), 7.85 (d, 2H), 7.40 (dd, 2H), 7.28 (t, 1H), 7.05 (s, 1H), 6.64 (s, 1H), 2.48 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 23.63, 106.44, 113.00, 114.97, 125.97, 128.48, 134.85, 149.85, 156.77, 159.81, 167.87; MS (EI) m/e 282 (M^+). mp 199 °C. Anal. Calcd for $C_{15}H_{14}N_4S$: C, 63.80; H, 5.00; N, 19.84. Found; C, 63.91; H, 5.30; N, 19.59; yield (95%).

1c: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.43 (s, 1H); 7.64 (d, 2H); 7.42 (dd, 2H), 7.31 (t, 1H); 6.61 (s, 1H), 2.51 (s, 3H), 2.44 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.13, 23.64, 112.79, 120.63, 126.97, 128.16, 128.31, 135.51, 144.81, 155.92, 156.72, 167.73; MS (EI) m/e 296 (M^+). mp 199 °C. Anal. Calcd for $C_{16}H_{16}N_4S$: C, 64.84; H, 5.44; N, 18.90. Found; C, 64.86; H, 5.52; N, 19.12; yield (95%).

1d: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.09 (s, 1H), 6.42 (s, 1H), 5.66 (s, 1H), 3.98 (s, 6H), 7.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.21, 23.61, 106.52, 112.77, 147.40, 156.77, 160.02, 167.64; MS (EI) m/e 252 (M^+). mp 156 °C. Anal. Calcd for $C_{10}H_{12}N_4O_2S$: C, 47.61; H, 4.78; N, 22.21. Found; C, 47.70; H, 4.95; N, 21.62; yield (97%).

1e: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.83 (s, 1H); 7.85 (d, 2H), 7.40 (dd, 2H), 7.39 (t, 1H), 7.07 (s, 1H), 5.68 (s, 1H), 3.97 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 54.62, 82.88, 106.33, 126.00, 127.75, 128.55, 134.47, 150.00, 155.98, 159.81, 171.89; MS (EI) m/e 314 (M^+). mp 179 °C. Anal. Calcd for $C_{15}H_{14}N_4O_2S$: C, 57.31; H, 4.49; N, 17.83. Found; C, 57.73; H, 4.45; N, 17.86; yield (94%).

1f: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.32 (s, 1H), 7.63 (d, 2H), 7.43 (dd, 2H), 7.32 (t, 1H), 5.67 (s, 1H), 4.00 (s, 6H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.18, 54.65, 82.55, 120.78, 127.18, 128.25, 128.28, 135.22, 145.08, 155.61, 155.97, 171.94; MS (EI) m/e 220 (M^+- Ph-OMe). mp 176 °C. Anal. Calcd for $C_{16}H_{16}N_4O_2S$: C, 58.52; H, 4.91; N, 17.06. Found; C, 58.57; H, 4.94; N, 17.03; yield (94%).

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