A New Synthesis of Pyrrole Derivatives from Tris(isopropylthio)cyclopropenylium Perchlorate and Thioureas

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The reaction of tris(isopropylthio)cyclopropenylium perchlorate (**1**) with sodium thioureides **3a-c**, prepared from thioureas **2a-c** and sodium hydride, in dry acetonitrile gave the pyrrole derivatives **4a-c**, respectively, in high yields.

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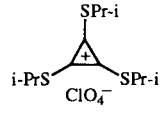
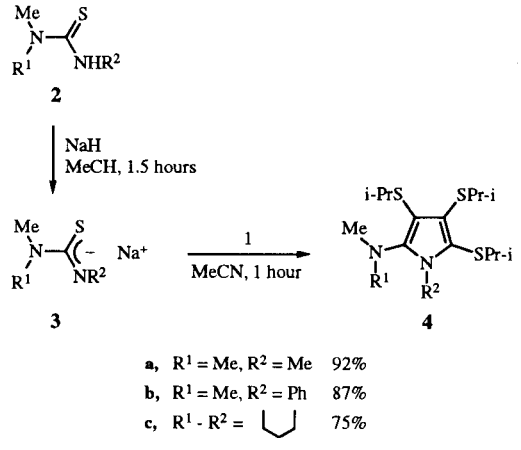
The cyclopropenyl cations are known to undergo ring opening by nucleophiles to form vinylcarbene intermediates which are converted into the cyclic compounds by ring closure [1]. Recently we have established that nitrogen heterocycles such as pyrrolizines [2], indolizines [3], pyrrolo[2,1-*b*]azoles [4], and pyridines [5] are prepared from tris(isopropylthio)cyclopropenylium perchlorate (**1**) and sodium pyrrolide, 2-pyridylmagnesium bromide, 2-lithiated azoles, and α-lithiated isocyanides, respectively. In relation to these reactions, we now report the novel example of the synthesis of pyrrole derivatives **4a-c** using **1** and thioureas **2a-c**, as shown in Scheme 1.



1

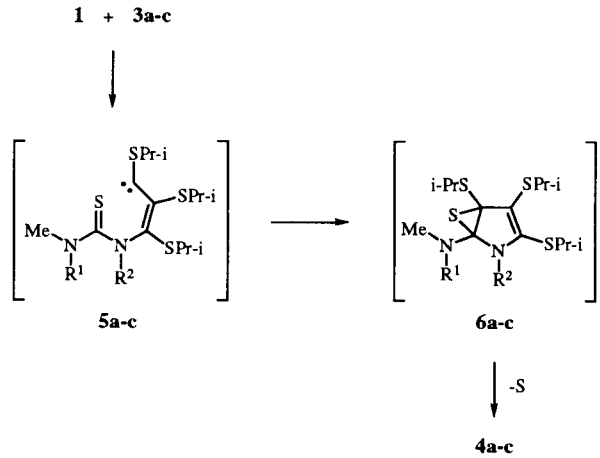
Scheme 1



The reactions were carried out as follows. A solution of **1** in dry acetonitrile was added to a suspended solution of thioureids **3a-c**, prepared from thioureas **2a-c** and sodium hydride, in dry acetonitrile and the mixture was stirred under nitrogen for 1 hour. The reactions with **3a,b** were carried out at room temperature, but that with **3c** at 0° because of being unstable at room temperature. After the removal of acetonitrile *in vacuo*, the chromatography of the residue gave the pyrrole derivatives **4a-c** in high yields. The structures of **4a-c** were determined by their ir, ^{1}H nmr, ^{13}C nmr, and mass spectra and elemental analyses. The ^{1}H nmr spectrum of **4a** showed a singlet (3H, δ 3.54) for the methyl protons at the *N*-position of the pyrrole ring and a singlet (6H, δ 2.85) for the methyl protons of the dimethylamino group. Its ^{13}C nmr spectrum showed four signals (4C, δ 108.5, 122.2, 124.2 and 146.5) for the pyrrole ring carbons. The structures of **4b** and **4c** were elucidated by a similar method described in the case of **4a**.

The reaction is thought to proceed by the pathway shown in Scheme 2. The nucleophilic attack of the nitrogen anion of **3a-c** on **1** forms vinylcarbene intermediates **5a-c**. The intramolecular cyclization of the carbenic carbon of **5a-c** with the >C=S group gives **4a-c** through the intermediary formation of thiiranes **6a-c** followed by desulfurization.

Scheme 2



The above results provide a new route to the pyrrole ring system using **1** as a synthetic reagent.

EXPERIMENTAL

The ir spectra were obtained on a Perkin-Elmer model 1600 spectrophotometer. All ^1H nmr (270 MHz) and ^{13}C nmr (68 MHz) spectra were measured on a JEOL JNM-GX 270 FT nmr spectrometer using deuteriochloroform as a solvent and chemical shifts were reported in parts per million down field from tetramethylsilane as an internal standard. Mass spectra were obtained at 70 eV with a Finnigan mat TSQ 70 spectrometer. Elemental analyses were performed by a Yanaco CHN CORDER MT-3. Column chromatography was performed on silica gel (Wakogel C-300).

General Procedure for the Preparation of Pyrroles **4a,b**.

To a suspended solution of sodium hydride (60% dispersion in mineral oil, 24 mg, 0.6 mmole) in dry acetonitrile (2 ml) was added thioureas **2a,b** (0.5 mmole) and the mixture was stirred under nitrogen at room temperature for 1.5 hour. A solution of the cyclopropenyl cation **1** (180 mg, 0.5 mmole) in dry acetonitrile (2 ml) was added to the solution. After 1 hour, the solvent was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel using hexane-dichloromethane (4:1) as an eluent.

2-(Dimethylamino)-3,4,5-tris(isopropylthio)-1-methylpyrrole (**4a**).

This compound was obtained as a yellow oil, yield 92%; ir (neat): 2959, 2925, 2863, 1520, 1448, 1375, 1364, 1236, 1154, 1050, 953 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.16 (d, 6H, J = 6.7 Hz), 1.20 (d, 12H, J = 6.7 Hz), 2.85 (s, 6H), 3.19 (sep, 1H, J = 6.7 Hz), 3.40-3.62 (m, 2H), 3.54 (s, 3H); ^{13}C nmr (deuteriochloroform): δ 22.8, 22.9, 23.1, 31.0, 38.5, 38.6, 40.5, 44.1, 108.5, 122.2, 124.2, 146.9; ms: m/z 346 (M^+).

Anal. Calcd. for $C_{16}H_{30}N_2S_3$: C, 55.44; H, 8.72; N, 8.08. Found: C, 55.16; H, 9.00; N, 7.80.

2-(Dimethylamino)-3,4,5-tris(isopropylthio)-1-phenylpyrrole (**4b**).

This compound was obtained as a yellow oil, yield 87%; ir (neat): 2960, 2924, 2863, 1522, 1499, 1448, 1423, 1376, 1317, 1236, 1154, 1051, 947 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.97 (d, 6H, J = 6.7 Hz), 1.25 (d, 6H, J = 6.7 Hz), 1.26 (d, 6H, J = 6.7 Hz), 2.66 (s, 6H), 2.78 (sep, 1H, J = 6.7 Hz), 3.50 (sep, 1H, J = 6.7 Hz), 3.67 (sep, 1H, J = 6.7 Hz), 7.19-7.23 (m, 2H), 7.39-7.43 (m, 3H); ^{13}C nmr (deuteriochloroform): δ 22.7, 23.1, 23.2, 38.4, 38.5, 39.9, 43.7, 109.0, 123.3, 125.2, 127.6, 128.2, 129.1, 138.5, 147.7; ms: m/z 408 (M^+).

Anal. Calcd. for $C_{21}H_{32}N_2S_3$: C, 61.72; H, 7.89; N, 6.86. Found: C, 61.42; H, 8.19; N, 6.56.

2,3,4-Trihydro-6,7,8-tris(isopropylthio)-1-methylpyrrolo[1,2-*a*]-pyrimidine (**4c**).

A suspended solution of sodium hydride (60% dispersion in mineral oil, 24 mg, 0.6 mmole) in dry acetonitrile (2 ml) was cooled to 0°. To the solution was added 3,4,5,6-tetrahydro-1-methyl-2-pyrimidinethione (**2c**) (65 mg, 0.5 mmole) and the mixture was stirred under nitrogen at 0° for 1.5 hours to give cyclic thioureide **3c**. A solution of the cyclopropenyl cation **1** (180 mg, 0.5 mmole) in dry acetonitrile (2 ml) was added to the solution. After 1 hour, the solution was allowed to warm to room temperature and acetonitrile was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel using hexane-dichloromethane (4:1) as an eluent to give **4c** as a yellow oil in 75% yield; ir (neat): 2958, 2924, 2861, 1538, 1463, 1428, 1379, 1363, 1327, 1284, 1236, 1192, 1153, 1098, 1049, 999, 929 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.16 (d, 6H, J = 6.7 Hz), 1.17 (d, 6H, J = 6.7 Hz), 1.21 (d, 6H, J = 6.7 Hz), 1.98-2.07 (m, 2H), 3.05-3.24 (m, 4H), 3.28 (s, 3H), 3.52 (sep, 1H, J = 6.7 Hz), 3.98 (t, 2H, J = 6.1 Hz); ^{13}C nmr (deuteriochloroform): δ 22.7, 22.8, 23.1, 29.7, 38.9, 39.5, 40.9, 41.1, 42.6, 50.6, 95.9, 117.4, 126.5, 144.1; ms: m/z 358 (M^+).

Anal. Calcd. for $C_{17}H_{30}N_2S_3$: C, 56.93; H, 8.43; N, 7.81. Found: C, 57.07; H, 8.70; N, 7.53.

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