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CONVENIENT APPROACH TO THE SYNTHESIS OF ENAMINO-SUBSTITUTED THIAZOLES

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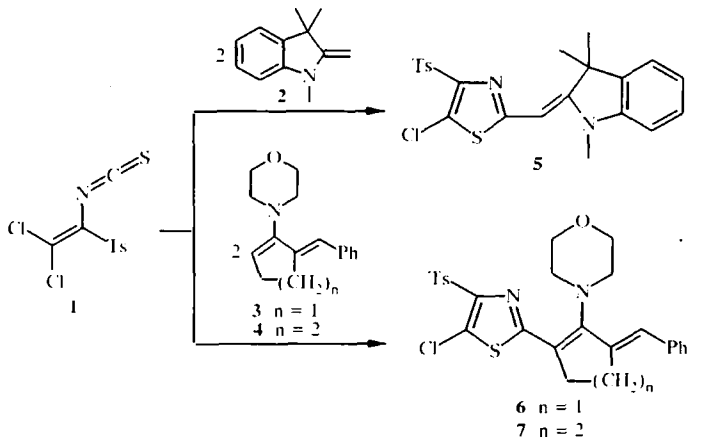
Fairly complex approaches are used to construct substituted thiazoles with an enamine group [1]. It was shown by us that it is convenient for this purpose to use the cyclocondensation of 1-tosyl-2,2-dichloroethenyl isothiocyanate (**1**) with various C_{sp^2}-nucleophiles (**2-4**) containing the enamine fragment.

The structure of the cyclization products (**5-7**) was confirmed by ^{1}H NMR spectra and was in agreement with the fact that the corresponding 2-amino-5-chlorothiazole derivatives are formed on treatment of reactant **1** with primary and secondary amines [2].



EXPERIMENTAL

5-Chloro-4-tosyl-2-(1,3,3-trimethyl-2,3-dihydro-2-indolidenemethyl)-1,3-thiazole (5). Reactant **2** (16 mmol) was added during 10 min with cooling at 10-15°C to a suspension of isothiocyanate **1** (8 mmol) in acetonitrile (16 ml). The reaction mixture was stirred for 18 h at 20-25°C, the precipitate filtered off, and washed with acetonitrile. Yield 82%; mp 169°C (acetonitrile). ^{1}H NMR spectrum: 7.98 (2H, d, J = 9 Hz, Ar); 7.35 (2H, d, J = 9 Hz, Ar); 7.10-7.20 (2H, m, Ar); 6.92 (1H, t, J = 9 Hz, Ar); 6.66 (1H, d, J = 9 Hz, Ar); 5.14, 5.26 (1H, s, C=CH); 3.11 (3H, s, N–CH_3); 2.43 (3H, s, Ar–CH_3); 1.60 ppm (6H, s, C–CH_3). Found, %: C 58.48; H 4.68; N 6.59. $C_{22}H_{21}ClN_2O_2S_2$. Calculated, %: C 59.38; H 4.76; N 6.30.

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General Procedure for Synthesis of Compounds 6 and 7. A mixture of isothiocyanate **1** (3 mmol), compound **3** or **4** (6 mmol), and acetonitrile (6 ml) was stirred for 50 h. The resulting solid was filtered off and washed with water.

2-(3-Benzylidene-2-morpholino-1-cyclopentenyl)-5-chloro-4-tosyl-1,3-thiazole (6). Yield 35%; mp 228-230°C (decomp., from acetonitrile). ^{1}H NMR spectrum (DMSO): 7.88 (2H, d, J_{H-H} = 8 Hz, H_{arom}); 7.47 (4H, d, J_{H-H} = 8 Hz, H_{arom}); 7.38 (2H, t, J_{H-H} = 8 Hz, H_{arom}); 7.25 (1H, t, J_{H-H} = 8 Hz, H_{arom}); 6.82 (1H, s, PhCH=); 3.85 (4H, m, O–CH_2); 3.16 (4H, m, N–CH_2); 2.91 (2H, m, CH_2); 2.83 (2H, m, CH_2); 2.40 ppm (3H, s, Ar–CH_3). Found, %: C 60.70; H 5.02; N 5.27. $C_{26}H_{25}ClN_2O_3S_2$. Calculated, %: C 60.87; H 4.91; N 5.46.

2-(3-Benzylidene-2-morpholino-1-cyclohexenyl)-5-chloro-4-tosyl-1,3-thiazole (7). Yield 22%; mp 226°C (decomp., from 1,2-dichloroethane). ^{1}H NMR spectrum ($CDCl_3$): 8.00 (2H, d, J_{H-H} = 8 Hz, H_{arom}); 7.33-7.39 (4H, m, H_{arom}); 7.25-7.30 (3H, m, H_{arom}); 6.96 (1H, s, PhCH=); 4.02 (4H, m, O–CH_2); 3.1-3.2 (4H, m, N-CH_2); 2.79 (2H, t, J_{H-H} = 4 Hz, CH_2); 2.62 (2H, t, J_{H-H} = 4 Hz, CH_2); 2.43 (3H, s, Ar–CH_3); 1.70 ppm (2H, m, CH_2). Found, %: C 61.71; H 5.03; N 6.45. $C_{27}H_{27}ClN_2O_3S_2$. Calculated, %: C 61.53; H 5.16; N 5.31.

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