The Synthesis of Some New 7-Methyl-3-substituted-1,2,4-triazolo[3,4-b]benzothiazoles

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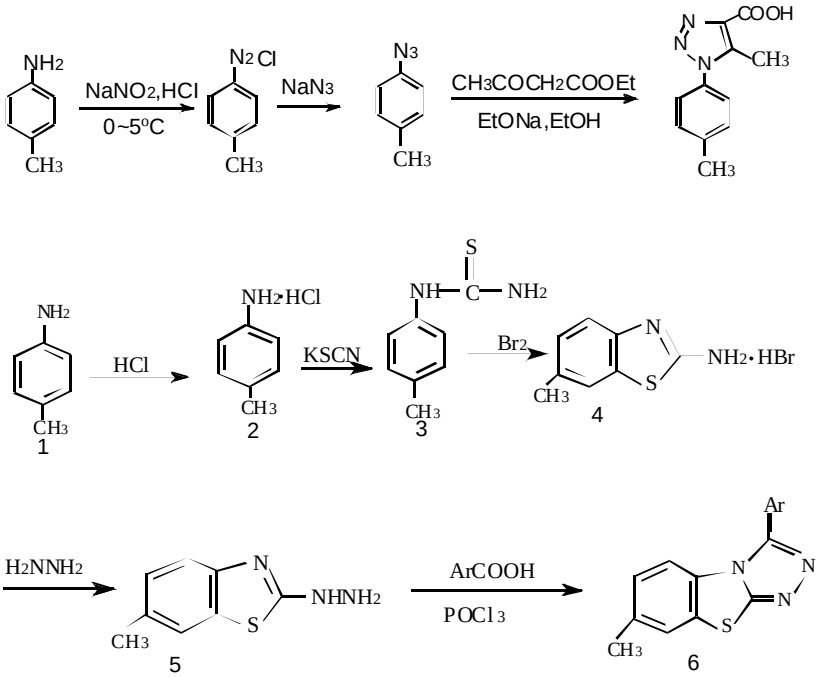
New 7-Methyl-3-substituted-1,2,4-triazolo[3,4-b]benzothiazoles were synthesized from *p*-methylaniline to **5** with various aromatic carbonic acids. The yielded product **6a-j** was investigated with Elemental analyses, NMR, MS and IR techniques.

INTRODUCTION

Tricyclazole is one of the benzothiazole derivatives, which are well known for developing this synthesis as many compounds with this ring system are associated with diverse biological activities such as application as potent antibacterials[1,2] and as fungicides for the control of *Piricularia oryzae* in the prevention of rice blast.[3] In particular, *s*-triazolo[3,4-b]benzothiazole derivatives are of interest because of their broad spectra of biological activities. Therefore, it was planned to investigate a system which combines these three biologic components in a molecule to give a compact system for screening their biologic activities. Recently, we have synthesized some new 7-methyl-3-substituted-1,2,4- triazolo [3,4-b]benzothiazoles from *p*-methylaniline to **5** with various aromatic carboxylic acids in the presence of phosphorus oxy-

Scheme I



Ar = **6a** 5-methyl-1-(4-chlorophenyl)-1,2,3-triazol-4-yl; **6b** 2,4-dichlorophoxymethylene; **6c** 2-phenylquinolino-4-yl; **6d** 5-methyl-1-(4-methylphenyl)-1,2,3-triazol-4-yl; **6e** 5-methyl-1-(2-methylphenyl)-1,2,3-triazol-4-yl; **6f** 2-furyl; **6g** 1-$C_{10}H_7CH_2$-; **6h** 1-$C_{10}H_7OCH_2$-; **6i** 2-$C_{10}H_7OCH_2$-; **6j** 3-bromopyridyl.

chloride. The structures of these compounds were established by elemental analysis, NMR, MS and IR techniques. The synthesis pathway of compound **6a-j** is shown in Scheme I.

RESULTS AND DISCUSSION

The new 7-methyl-3-substituted-1,2,4-triazolo[3,4-b]-benzothiazoles were synthesized from *p*-methylaniline to **5** with various aromatic carboxylic acids in the presence of phosphorus oxychloride. The 2-Hydrazino-6-methyl benzothiazole **5** (mp 225-226 °C) was prepared in 93% yield from **4**, the latter being prepared from **1** to **2** (mp 195-196°C) and **3** (mp 254-255 °C). Compound **5** on treatment with aromatic carboxylic acid in the presence of phosphorus oxychloride gave the triazolo[3,4-b]benzothiadiazole **6a-j** (Table 1). The spectral data of **6a-j** are presented in Tables 2-4. IR absorption peaks of **5** at 3167, 3203 cm^{-1} are assigned to its $NHNH_2$ group ings. When **5** is converted **6**, the $NHNH_2$ peak disappears but a new peak characteristic of $\nu_{C=N}$ appears at 1588-1626 cm^{-1}. Like the allied system,[4] compound **6a-j** shows absorption peaks for ν_{C-S-C} in the region of 693-702 cm^{-1}.

In ^1H NMR spectra of **5** with **6a-j**, we found that after cyclization the evident change is that the signals of -$NHNH_2$ protons are at δ3.11 ppm. The chemical shifts of the aromatic methyl group show in the range of δ 2.36-2.52 ppm.[5,6]

In the mass spectra of **6a-j**, the molecular ion peaks of **6b** are weak (their relative intensities were about 1%) and the others are strong. All the members of **6a-j** exhibit some important ion peaks at *m/z* 190, 189, 163, 162, 121, 110, 91, 77,

Table 1. Structures, Yields and Melting Points of the Compounds **6a-j**

Compound	Yield (%)	M.p. (°C)	Formula	Found (required) (%)		
				C	H	N
6a	39	289-290	$C_{18}H_{13}ClN_6S$	56.54 (56.77)	3.40 (3.44)	22.14 (22.07)
6b	53	278-279	$C_{16}H_{11}Cl_2N_3OS$	52.80 (52.76)	3.01 (3.04)	11.40 (11.54)
6c	58	253-254	$C_{24}H_{16}N_4S$	73.39 (73.45)	4.08 (4.11)	13.40 (13.26)
6d	50	195-196	$C_{19}H_{16}N_6S$	63.41 (63.31)	4.45 (4.47)	23.55 (23.32)
6e	45	175-176	$C_{19}H_{16}N_6S$	63.30 (63.31)	4.45 (4.47)	23.30 (23.32)
6f	39	155-156	$C_{13}H_9N_3OS$	61.05 (61.16)	3.49 (3.55)	16.60 (16.46)
6g	41	203-204	$C_{20}H_{15}N_3S$	73.01 (72.92)	4.55 (4.59)	12.85 (12.76)
6h	41	194-195	$C_{20}H_{15}N_3OS$	69.48 (69.54)	4.36 (4.38)	12.33 (12.17)
6I	33	190-191	$C_{20}H_{15}N_3OS$	69.55 (69.54)	4.39 (4.38)	12.08 (12.17)
6j	65	228-229	$C_{14}H_9BrN_4S$	49.28 (49.28)	2.58 (2.66)	15.30 (15.25)
7i	52	226-227	$C_{20}H_{17}N_3O_2S$	66.22 (66.10)	4.85 (4.71)	11.67 (11.56)

Table 2. IR Spectral Data for Compounds **6a-j**

Compound	IR (cm^{-1}) (KBr disc)						
6a	3058,	2915,	1610,	1593, 1492, 1461,	972.3,	861, 823,	693.5
6b	3099, 3031,	2957, 2922, 2855,	1614,	1605, 1582, 1492, 1375, 1262, 1240,		862, 798,	710.4
6c	3027,	2915,	1600,	1600, 1492, 1446, 1377,		861, 807, 764,	696.1
6d	3104, 3003,	2920, 2852,	1610,	1593, 1492, 1456, 1372,	972.6,	860, 815,	692.9
6e	3044,	2921,	1610,	1593, 1492, 1456, 1368,	972.9,	824, 762,	698.1
6f	3112,	2917,	1597,	1593, 1493, 1458, 1368, 1256, 1188,		888, 808, 759,	701.5
6g	3046,	2918,	1597,	1586, 1495, 1461, 1377,		807, 788, 768,	697.2
6h	3055, 3003,	2968, 2896,	1610,	1578, 1491, 1462, 1399, 1261, 1100,		811, 789, 768,	705.7
6i	3098, 3058,	2952, 2920, 2852,	1629,	1600, 1499, 1462, 1394, 1254, 1217, 1181,		839, 801, 740,	693.5
6j	3037,	2952, 2924, 2861,	1588, 1546,	1504, 1482, 1429, 1370,		807, 781,	703.3
7i	3203, 3058, 3023,	2980, 2911, 2844,	1686, 1666, 1627,	1602, 1546, 1511, 1467, 1393, 1257, 1216, 1179,		836, 812,	695,

Table 3. ^{1}H NMR Spectral Data for Compounds **6a-j**

Compound	^{1}H NMR ($CDCl_3$-*d*) δ (ppm), *J* (Hz)
6a	8.96-9.06 (d, 2H, *J* = 8.5, Bti-4,7H), 7.28-7.37 (d, 2H, *J* = 8.5, p-ClC_6H_4-), 7.37-7.60 (m, 3H, Bti-5H, p-ClC_6H_4-), 2.51 (s, 3H, Ph-CH_3), 2.79 (s, 3H, Tazo-CH_3)
6b	7.99-8.09 (d, 1H, *J* = 8.4, Bti-4H), 7.26-7.52 (m, 5H, Bti-5, 7H, 2,4-di ClC_6H_3), 5.74 (s, 2H, -OCH_2-), 2.52 (s, 3H, Ph-CH_3)
6c	6.72-8.43 (m, 13H, Bti-H, Ar-H), 2.42 (s, 3H, Ph-CH_3)
6d	9.10-9.14 (d, 1H, *J* = 8.4, Bti-4H), 7.54 (m, 1H, Bti-7H), 7.33-7.37 (m, 1H, *J* = 8.4, Bti-5H), 7.44 (s, 4H, Ph-CH_3), 2.74 (s, 3H, Tazo-CH_3), 2.51 (s, 3H, Ph-CH_3)
6e	9.10-9.15 (d, 1H, *J* = 8.4, Bti-4H), 7.31-7.36 (m, 2H, *J* = 8.4, Bti-5,7H), 7.44-7.54 (m, 4H, Ph-H), 2.59 (s, 3H, Tazo-CH_3), 2.50 (s,3H, Ph-CH_3), 2.15 (s, 3H, o-Ph-CH_3)
6f	8.06-8.10 (d, 1H, *J* = 8.4, Bti-4H), 7.49-7.50 (d, 1H, *J* = 1.0, Bti-7H), 7.24-7.29 (q or 2d, 1H, *J* = 8.4, *J* = 1.0, Bti-5H), 7.75-7.76 (2d, 1H, *J* = 1.8, *J* = 0.8, F-5H), 7.22-7.24 (2d, 1H, *J* = 3.5, *J* = 0.8, F-3H), 6.68-6.71 (2d, 1H, *J* = 3.5, *J* = 1.8, F-4H), 2.50 (s, 3H, CH_3), 2.49 (s, 3H, Ph-CH_3)
6g	8.22-8.18 (d, 1H, *J* = 8.4, Bti-4H), 7.58-7.66, (m, 2H, Bti-5, 7H), 7.76-7.95, 7.29-7.44, 6.95-7.02 (m, 7H, α-$C_{10}H_7$), 5.04 (s, 2H, -CH_2-), 2.36 (s, 3H, Ph-CH_3)
6h	8.11-8.15 (d, 1H, *J* = 8.2, Bti-4H), 7.16-7.21 (m, 2H, Bti-5, 7H), 7.36-7.86 (m, 7H, α-$C_{10}H_7$), 5.79 (s, 2H, -OCH_2-), 2.44 (s, 3H, Ph-CH_3)
6i	7.82-7.92 (d, 1H, *J* = 8.2, Bti-4H), 7.16-7.21 (m, 2H, Bti-5, 7H), 7.23-7.92 (m, 7H, β-$C_{10}H_7$), 5.77 (s, 2H, -OCH_2-), 2.46 (s, 3H, Ph-CH_3)
6j	9.00-8.92 (t, 1H, *J* = 8.4, Bti-4H), 7.38-7.42 (d, 1H, Bti-7H), 7.19-7.22 (m, 2H, Bti-5H), 9.00 (s, 1H, Py-2H), 8.33-8.35 (t, 1H, *J* = 2, Py-4H), 7.55 (s, 1H, Py-6H), 2.48 (s, 3H, Ph-CH_3)
7i	7.06-8.92 (m, 10H, Bti-H, α-$C_{10}H_7$-H), 4.87 (s, 2H, -CH_2-), 3.09 (b, 2H, -NHNH-), 2.35 (s, 3H, Ph-CH_3)

Bti = benzothiazole; Tazo = 1,2,3-triazol; F = 2-furyl; Py = 3-bromopyridyl

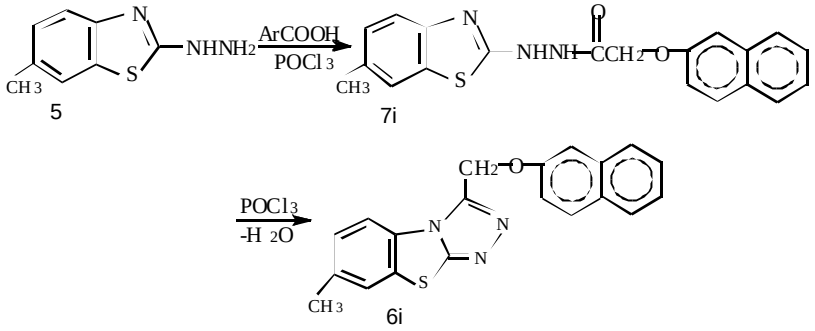
Table 4. MS Spectral Data for Compounds **6a-j**

No	M^+	*m/z* (%)
6a	380(19)	353(15) 352(51) 323(20) 317(18) 289(7) 274(3) 219(2) 197(10) 190(22) 189(20) 163(100) 162(26) 161(17) 144(8) 136(12) 121(28) 111(8) 89(15) 77(28) 75(77) 65(10) 51(24)
6b	363(1)	330(8) 329(3) 328(17) 237(2) 203(12) 202(100) 174(7) 173(6) 163(4) 159(24) 135(11) 133(16) 130(18) 121(8) 111(7) 103(6) 89(6) 77(11) 63(18) 51(6)
6c	392(52)	391(100) 376(1) 362(1) 334(2) 315(2) 289(2) 261(3) 230(36) 229(59) 203(8) 190(1) 189(1) 163(7) 162(48) 161(25) 134(17) 121(21) 111(4) 110(21) 77(27) 65(10)
6d	360(49)	333(24) 332(100) 317(6) 303(25) 289(4) 214(3) 198(5) 197(5) 190(1) 170(34) 169(39) 163(72) 143(21) 121(13) 110(6) 102(8) 91(36) 77(15) 65(33) 51(7)
6e	360(41)	333(21) 332(93) 317(6) 303(22) 289(4) 262(3) 247(2) 214(3) 198(3) 197(4) 190(4) 170(38) 169(100) 163(64) 143(33) 121(18) 110(10) 91(41) 77(18) 65(46) 51(10)
6f	255(100)	218(1) 202(1) 198(1) 190(1) 163(8) 162(62) 147(5) 136(4) 135(3) 121(5) 111(3) 110(6) 95(4) 77(5) 65(3)
6g	329(69)	328(100) 301(2) 300(2) 287(3) 256(1) 202(2) 181(4) 167(28) 166(53) 152(11) 141(13) 140(11) 139(140) 127(3) 121(3) 115(12) 91(2) 77(6) 65(3)
6h	345(12)	203(14) 202(100) 174(4) 173(3) 163(1) 162(2) 159(12) 147(3) 143(3) 130(9) 127(2) 115(15) 110(2) 89(4) 77(3) 65(2)
6i	345(17)	317(1) 220(1) 203(14) 202(100) 192(1) 174(4) 173(3) 163(1) 162(2) 159(10) 143(1) 130(8) 127(3) 115(12) 110(2) 89(3) 77(3) 65(2)
6j	346(37)	344(38) 265(8) 238(3) 202(1) 184(2) 182(2) 163(12) 162(100) 147(8) 143(1) 136(8) 135(50) 121(6) 111(2) 110(13) 103(12) 91(6) 77(9) 65(6)
7i	363(35)	221(13) 220(100) 206(13) 201(1) 193(11) 192(93) 185(1) 178(15) 177(17) 170(10) 164(55) 163(32) 157(7) 150(38) 144(47) 128(15) 127(73) 115(35) 111(2) 77(19)

65, 45. Compound **6a** had *m/z* 219 (2%), 192 (8%), 111 (81%). **6b** has *m/z* 202 (100%). **6d** and **6e** had *m/z* 197, 170, 143, 91. **6g-i** had *m/z* 141, 127.

We isolated one uncyclized product **7i** when most of these reactions yield the cyclized products under neutral reaction conditions. We claim that the reaction mechanism is the following formation under the neutral reaction conditions.

Scheme II



EXPERIMENTAL

Melting points were de ter mined on a Kofler melt ing point ap pa ra tus and are un cor rected. The mass spec trum was per formed on a HP-5988A spec trom e ter (EI at 70 eV). IR spec tra were ob tained in KBr discs us ing a Nicolet 170SX FT-IR spec trom e ter. ^{1}H NMR spec tros copy were re corded at room tem per a ture at 200.13 MHz on a Avorce DRX 200 in-stru ment. El e men tal anal y ses were car ried out on a Yanaco CHN Corder MT-3 an a lyzer.

Phos pho rus oxychloride was redistilled (bp 105 °C).

5-Methyl-1-(4-methylphenyl)-1,2,3-triazol-4-carbox-ylic acid, 5-Methyl-1-(2-methylphenyl)-1,2,3-triazol-4- car-boxylic acid and 5-Methyl-1-(4-cholophenyl)-1,2,3-triazol-4- carboxylic acid were pre pared by the method re ported in the lit er a ture.[5]

p-tolylthiourea **3**, mp 195-196 °C (**Lit**. 188-9 °C[7,8]).

2-amino-6-methylbenzothiazole hydro bro mide **4**, mp 254-255 °C, ^{1}H NMR (DMSO-d_6) δ = 14.27 (s, 1H), 11.52 (s, 2H), 7.25-7.37 (m, 3H), 2.67 (s, 3H).

2-Hydrazino-6-methylbenzothiazole **5**, mp 169-170 °C. ^{1}H NMR ($CDCl_3$) δ = 7.11-7.46 (m, 3H), 3.11 (broad, 3H), 2.43 (s, 3H).[9]

New 7-methyl-3-substituted-1,2,4-triazolo[3,4-b]-benzothiazole 6

A mix ture of 2-hydrazino-6-methylbenzothiazole **5** (1 mmol), various aromatic carboxylic acids (1 mmol) and $POCl_3$ (5 mL) was heated un der re flux for 12 hours. A por tion of $POCl_3$ was dis tilled out and the re main ing re ac tion mix ture poured into ice wa ter. The so lu tion was made al ka line by add-ing po tas sium hy drox ide so lu tion; the de pos ited solid was fil-tered off and recrystallized from eth a nol to give the ti tle 7-methyl-3-substituted-1,2,4-triazolo[3,4-b]benzothiazole **6a-j**. The re sults are given in Table 1.

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Key Words

Synthesis; 1,2,4-Triazolo[3,4-b]benzothiazole; Benzothiazole derivative.

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