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Novel reactions and mechanism of -HN-N= azole derivatives with DMSO

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The reaction mechanism of –NH-N= azole derivatives and sulfur ketones derivatives is reported. The reaction mechanism is suitable for the synthesis of azole compounds containing thio-functional group. The free-mediated reaction mechanism of –NH-N= azole and DMSO does not agree with Pummerer rearrangement reaction. Some new ethyl 5-(arylamino)-2-[(methylthio)methyl]-2*H*-1,2,3-triazole-4-carboxylate **6a-j** have been synthesized by 5-amino-1-aryl-1,2,3-triazol-4-caroxylic acid ethyl ester **4a-j** and DMSO. The new compounds have been characterized by ^{1}H NMR, MS, IR, HRMS and single-crystal X-ray diffraction.

Keywords: Reaction mechanism, –NH-N= azole derivatives, Sulfur ketones derivatives, (Methylthio)methyl-triazole, Free-mediated, Pummerer rearrangement

Molecules containing 1,2,3-triazole nucleus are important heterocycles and pharmacologically active molecules. Hence, they have been applied extensively to modify and potentiate anticancer[1-6], antibacterial[1,2,5-7], antifungal[1,6], antiviral[1,2,6], anti-inflammatory[1] and analgesic [3] anti-tuberculosis[2,6-7], antidiabetic[1], antimalarial[2] and anti-Alzheimer drugs[2]. Substituted 1,2,3-triazoles are often applied as building blocks in designing drugs to inhibit the growth, invasion, and migration of cancer cells (Scheme 1) [8]. Moreover, some of compounds containing 1,2,3-triazole such as Cefatrizine and Carboxyamidotriazole (Scheme 2) have already been used in clinics or under clinical evaluation for cancer treatment, revealing their potential as putative anticancer drugs[6].

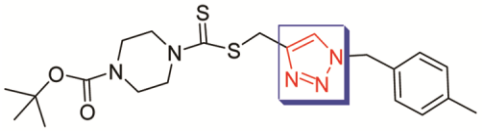
Both 1*H*-1,2,3-triazoles and 2*H*-1,2,3-triazoles series were shown to be active against the *epimastigote* form of *Trypanosoma cruzi*[9]. On the biological activity test, these compounds was founded that they have the medium level of antibacterial activity and good insecticidal activity[10]. 1-(Methylthiomethyl) benzotriazole was synthesis[11-12] and applied in a bifunctional reagent for the coupling of alkyl halides or carbonyl compounds, The successful synthesis of homologated ketones via a 1,2-shift of the diverse heterocyclic groups or a aryl has been investigated[13-17].

Experimental Details

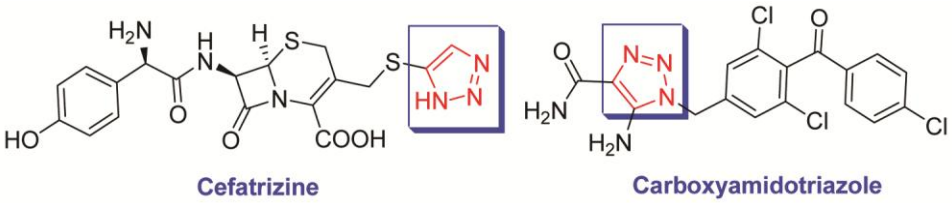
Details of the synthesis of compounds **6a–j** starting with aryl amine **1a-j** through intermediates **4a-j** and **5a-d** were described in our previous report. IR spectra were recorded with a Nicolet NEXUS 670 FT-IR spectrometer as KBr plates or as thin films and peaks are reported in cm^{-1}. ^{1}H NMR spectra were recorded on a Varian Mercury plus-300 type and a Bruker AVANCE III spectra instrument was recorded. Chemical shifts (δ) were measured in ppm relative to TMS δ = 0 ppm for ^{1}H NMR. Mass spectrum were recorded on a Esquire 6000 spectrometer (EI at 70 eV), melting points (mp) were measured on an XT4-100x microscopic melting point apparatus and are uncorrected, high resolution mass spectrometry were measured with MICRO-TOF QII (ESI). 5-Amino-1-aryl-1,2,3-triazol-4-caroxylic acid ethyl ester 4a-j were prepared from aryl amine by the literature method (Supplementary Information)**.**

General preparation procedure of ethyl 5-(arylamino)-2-[(methylthio)methyl]-2*H*- 1,2,3-triazole-4-carboxylate 6a-j following the procedure method[18]

A mixture of 5-amino-1-aryl-1,2,3-triazol-4-caroxylic acid ethyl ester **4a-j** (0.5 g) and dimethyl sulfoxide (DMSO) 6.0 mL was heated under 140-150^{o}C for 10 h with stirring. The cooled reaction mixture was poured into 60 mL water and the thick



Scheme 1 — Anticancer compounds containing 1,2,3-triazole



Scheme 2 — Chemical structures of 1,2,3-triazole-containing anticancer agents

and cloudy liquor was extracted with ethyl ether (20×5 mL) and then the extraction solution was dried with anhydrous sodium sulfate for 4 h. The sodium sulfate was removed by filtration. The extraction solution was concentrated. The solid was purified by chromatography on a column of silica gel, was eluted successively with 1:8 ethyl acetate–petroleum ether to give **5a-d** (Supplementary Information) and **6a-j.**

Ethyl 5-(4-ethoxyphenylamino)-1*H*-1,2,3-triazole-4-carboxylate 5c: The white lamellar crystals, yield 84%, mp 148-149 C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 7.709 (s, 1H, -NH-), 7.400(s, 1H, Triazole ring-H), 7.381-7.410(d, 2H, J=8.7H_Z, Ar- 3,5), 6.884-6.913 (d, 2H, J=8.7H_Z, Ar-2,6), 4.453-4.477 (q, 2H, J=7.2H_Z, -CO_2CH_2 -), 4.008-4.031(q, 2H, J=6.9H_Z, ArOCH_2-), 1.385-1.475 (m, 6H, -$CO_2CH_2CH_3$, Ar-OCH_2CH_3); IR(cm^{-1}) (KBr disc), 3371, 3185, 2979, 2933, 2878, 1692, 1606, 1577, 1537, 1511, 1478, 1417, 1392, 1349, 1328, 1299, 1277, 1236, 1209, 1174, 1153, 1112, 1049, 1020, 985, 922, 820, 785, 617, 536; MS M/Z(%), 276(M^+,100), 247(35), 230(5), 219(7), 201(78), 173(16), 148(21), 134(4), 119(39), 108(11), 90(20), 77(14), 65(52), 53(18), 40(58); HRMS (ESI) m/z calcd for $C_{13}H_{16}N_4O_3$ $(M+H)^+$: 277.1295, found: 277.1298

Ethyl 5-(*p*-tolylamino)-2-[(methylthio)methyl]-2*H*-1,2,3-triazole-4-carboxylate 6a: The white granular crystals, yield 62%, mp 80-81°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 7.949(s, 1H, -NH-), 7.465~7.494(d, 2H, J=8.7H_Z, Ar-3,5), 7.190~7.219(d, 2H, J=8.7H_Z, Ar-2,6), 5.438 (s, 2H, -CH_2S-), 4.496~4.567(q, 2H, J=7.2Hz, -CO_2CH_2-), 2.404 (s, 3H, Ar-CH_3), 2.382(s, 3H, -SCH_3), 1.492~1.540 (t, 3H, J=7.2H_Z, -$CO_2CH_2CH_3$); IR(cm^{-1})(KBr disc), 3356, 3296, 3202, 3097, 3004, 2984, 2919, 2864, 2511, 1882, 1778, 1693, 1608, 1572, 1520, 1474, 1414, 1368, 1349, 1306, 1251, 1138, 1102, 1019, 962, 909, 854, 812, 781, 752, 702, 643, 584, 506; MS M/Z(%),306 (M^+, 100), 292(1), 274(60), 259(43), 246(1), 231(36), 217(13), 203(4), 185(57), 171(10), 157(42), 144(39), 132(62), 118(35), 105(7), 91(68), 77(18), 61(51), 43(6); HRMS (ESI) m/z calcd for $C_{14}H_{18}N_4O_2S$ $(M+H)^+$: 307.1223, found: 307.1220.

Ethyl 5-(4-methoxyphenylamino)-2-[(methylthio) methyl]-2*H*-1,2,3-triazole-4- carboxylate 6b: The white granular crystals, yield 60%, mp 76-77°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 7.783(s, 1H, -NH-), 7.429~7.457(d, 2H, J=8.4H_Z, Ar-3,5), 6.880~6.908 (d, 2H, J=8.4H_Z, Ar-2,6), 5.345 (s, 2H, -CH_2S-), 4.424~4.492(q, 2H, J=6.9Hz, -CO_2CH_2-), 3.787 (s, 3H, Ar-OCH_3), 2.325(s, 3H, -SCH_3), 1.421~1.467(t, 3H, J=6.9H_Z, -$CO_2CH_2CH_3$); IR(cm^{-1}) (KBr disc), 3369, 2962, 2924, 2837, 2483, 2019, 1862, 1689, 1601, 1574, 1514, 1464, 1409, 1371, 1343, 1301, 1251, 1175, 1142, 1109, 1025, 980, 909, 858, 827, 783, 755, 716, 644, 595, 534, 455, 418; MS M/Z(%),322(M^+, 81), 306(1), 275(23), 247(22), 233(7), 219(10), 201(36), 195(13), 179(95), 173(40), 168(13), 149(64), 132(58), 122(4), 104(22), 77(100), 61(48), 51(20), 43(58); HRMS (ESI) m/z calcd for $C_{14}H_{18}N_4O_3S$ $(M+H)^+$: 323.1172, found: 323.1175.

Ethyl 5-(4-ethoxyphenylamino)-2-[(methylthio) methyl]-2*H*-1,2,3-triazole-4- carboxylate 6c: The white granular crystals, yield 48%, mp 65-66°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 7.773(s, 1H, -NH-), 7.410~7.439(d, 2H, J=8.7H_Z, Ar-3,5), 6.869~6.898 (d, 2H, J=8.7H_Z, Ar-2,6), 5.352(s, 2H, -CH_2S-), 4.421~4.490(q, 2H, J=6.9Hz, -CO_2CH_2-), 3.977~4.046(q, 2H, J=6.9H_Z, Ar-OCH_2-), 2.323 (s, 3H, -SCH_3), 1.379~1.465(m, 6H, -$CO_2CH_2CH_3$, ArOCH_2CH_3); IR(cm^{-1})(KBr disc), 3369, 2974, 2929, 1688, 1608, 1577, 1514, 1472, 1392, 1370, 1354, 1306, 1250, 1181, 1142, 1119, 1050, 1019, 951, 927, 910, 862, 825, 807, 786, 752, 710, 646, 614, 575, 544, 517; MS M/Z(%), 336(M^+, 94), 304(55), 289(26), 275(11), 261(31), 247(7), 229(52), 215(42), 201(13), 187(65), 174(15), 162(42), 148(46), 134(53), 119(28), 108(26), 91(22), 81(33), 61(100), 57(15), 43(21); HRMS (ESI) m/z calcd for $C_{15}H_{20}N_4O_3S$ $(M+H)^+$: 337.1329, found: 337.1332.

Ethyl 5-(4-bromophenylamino)-2-[(methylthio) methyl]-2*H*-1,2,3-triazole-4- carboxylate 6d: The white needle crystals, yield 63%, mp 102-103°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 8.084(s, 1H, -NH-), 7.476~7.492(d, 2H, J=4.8H_Z, Ar-3,5), 7.318~7.334

(d, 2H, J=4.8H_Z, Ar-2,6), 5.441(s, 2H, -CH_2S-), 4.500~4.571(q, 2H, J=7.2Hz, -OCH_2-), 2.391(s, 3H, -SCH_3), 1.481~1.529(t, 3H, J=7.2Hz, -OCH_2CH_3); IR(cm^{-1})(KBr disc), 3358, 3192, 3087, 2999, 2938, 2914, 1691, 1603, 1566, 1523, 1471, 1407, 1371, 1349, 1304, 1259, 1144, 1114, 1075, 1024, 998, 964, 908, 811, 783, 745, 693, 668, 646, 588, 502, 429; MS M/Z(%), 372(M^+, 25), 340(53), 325(14), 297(11), 267(1), 251(17), 223(11), 213(100), 196(26), 182(16), 172(46), 157(33), 145(18), 130(26), 117(8), 102(21), 90(13), 76(23), 61(50), 50(8), 43(6); HRMS (ESI) m/z calcd for $C_{13}H_{15}BrN_4O_2S$ $(M+H)^+$: 371.0172, found: 371.0179.

Ethyl 5-(4-chlorophenylamino)-2-[(methylthio) methyl]-2*H*-1,2,3-triazole-4- carboxylate 6e: The white granular crystals, yield 61%, mp 100-101°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 8.004(s, 1H, -NH-), 7.447~7.476(d, 2H, J=8.7H_Z, Ar-3,5), 7.262~7.291 (d , 2H, J=8.7H_Z, Ar-2,6), 5.374 (s, 2H, -CH_2S-), 4.426~4.496(q, 2H, J=6.9Hz, -CO_2CH_2-), 2.323 (s, 3H, -SCH_3), 1.421~1.467(t, 3H, J=6.9Hz, -$CO_2CH_2CH_3$); IR(cm^{-1})(KBr disc), 3358, 3001, 2914, 2362, 1886, 1692, 1606, 1569, 1524, 1494, 1473, 1409, 1370, 1350, 1305, 1260, 1144, 1116, 1090, 1025, 1005, 966, 910, 847, 831, 813, 783, 745, 689, 648, 589, 507, 447; MS M/Z(%), 326(M^+, 59), 294(5), 279(32), 251(20), 237(6), 213(2), 205(34), 191(3), 177(22), 166(7), 152(46), 138(20), 125(6), 111(25), 99(10), 90(6), 75(17), 61(100), 51(4), 45(9); HRMS (ESI) m/z calcd for $C_{13}H_{15}ClN_4O_2S$ $(M+H)^+$: 327.0677, found: 327.0681.

Ethyl 5-(2-ethoxyphenylamino)-2-[(methylthio) methyl]-2*H*-1,2,3-triazole-4- carboxylate 6f: The white flocculent crystals, yield 77%, mp 105-106°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 8.582(s, 1H, -NH-), 8.138~8.186 (m, 1H, Ar-5), 6.900~6.984 (m, 3H, Ar-3,4,6), 5.380(s, 2H, -CH_2S-), 4.432~4.493 (q, 2H J=7.2Hz, -CO_2CH_2-), 4.119~4.189 (q, 2H, J=6.9Hz, -OCH_2-), 2.329(s, 3H, -SCH_3), 1.442~1.542 (m, 6H, -$CO_2CH_2CH_3$, -OCH_2CH_3); IR(cm^{-1}) (KBr disc), 3371, 3047, 2980, 2922, 2879, 1690, 1609, 1577, 1524, 1504, 1465, 1390, 1370, 1350, 1299, 1257, 1208, 1173, 1135, 1045, 928, 906, 845, 812, 787, 744, 705, 650, 633, 604, 537, 490, 456, 422; MS M/Z(%), 336(M^+, 72), 304(18), 289(27), 275(5), 261(15), 243(4), 229(14), 215(31), 201(4), 187(39), 162(11), 145(17), 134(22), 120(28), 105(12), 93(13), 79(9), 61(100), 52(9), 40(8); HRMS (ESI) m/z calcd for $C_{15}H_{20}N_4O_3S$ $(M+H)^+$: 336.1256, found: 336.1260,

Ethyl 2-[(methylthio)methyl]-5-(naphthalen-1-ylamino)-2*H*-1,2,3-triazole-4- carboxylate 6g: The white granular crystals, yield 51%, mp 111-112°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 8.911(s, 1H, -NH-), 8.217~8.244(d, 1H, J=8.1Hz, Ar-8), 8.051~8.080(d, 1H, J=8.7Hz, Ar-5), 7.863~7.889(d, 1H, J=7.8Hz, Ar-4), 7.515~7.578(m, 3H, Ar-3,6,7), 7.478~7.502(d, 1H, J=7.2Hz, Ar-2), 5.426(s, 2H, -CH_2S-), 4.504~4.574(q, 2H, J=7.2Hz, -CO_2CH_2-), 2.361(s,3H,-SCH_3), 1.475~1.528(t, 3H, J=7.2Hz, -$COCH_2CH_3$); IR (cm^{-1}) (KBr disc), 3386, 3053, 3014, 2977, 2928, 2855, 1692, 1626, 1585, 1534, 1479, 1442, 1408, 1369, 1319, 1274, 1244, 1175, 1141, 1109, 1051, 1023, 983, 960, 908, 858, 785, 768, 736, 707, 647, 628, 562, 517, 439; MS M/Z(%), 342(M^+, 64), 334(1), 310(86), 295(18), 277(4), 264(49), 253(7), 234(8), 221(27), 208(11), 193(47), 180(55), 168(67), 154(60), 140(14), 127(78), 115(35), 112(28), 101(8), 77(19), 61(100), 55(54), 41(50); HRMS (ESI) m/z calcd for $C_{17}H_{18}N_4O_2S$ $(M+H)^+$: 343.1223, found: 343.1227.

Ethyl 2-[(methylthio)methyl]-5-(naphthalen-2-ylamino)-2*H*-1,2,3-triazole-4- carboxylate 6h: The pale yellow granular crystals, yield 63%, mp 81-82°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 8.510(s, 1H, -NH-), 8.268~8.297(d, 1H, J=8.7H_Z, Ar-4), 8.043~8.072 (d, 1H, J=8.7H_Z, Ar-3), 7.803~7.831(d, 2H, J=8.4Hz, Ar-5,8), 7.051~7.557(t, 1H, J=8.4H_Z, Ar-7), 7.380~7.436 (t, 1H, J=8.4Hz, Ar-6), 7.319(s, 1H, Ar-1), 5.376(s, 2H, -CH_2S-), 4.486~4.559(q, 2H, J=7.2Hz, -CO_2CH_2), 2.335(s, 3H, -SCH_3), 1.441~1.489(t, 3H, J=7.2Hz, -$CO_2CH_2CH_3$); IR(cm^{-1})(KBr disc), 3309, 2976, 2916, 2360, 1698, 1620, 1599, 1580, 1555, 1514, 1479, 1445, 1402, 1371, 1351, 1316, 1301, 1266, 1241, 1169, 1129, 1015, 992, 957, 891, 857, 806, 785, 747, 701, 653, 572, 530, 487, 453, 424; MS M/Z(%), 342(M^+, 65), 334(1), 310(81), 296(20), 277(9), 261(44), 253(3), 234(6), 220(25), 208(6), 193(42), 180(52), 168(5), 153(38), 140(11), 127(76), 115(29), 112(25), 101(7), 77(13), 61(100), 55(52), 41(43); HRMS (ESI) m/z calcd for $C_{17}H_{18}N_4O_2S$ $(M+H)^+$: 343.1223, found: 343.1229.

Ethyl 5-(3-chlorophenylamino)-2-[(methylthio)-methyl]-2*H*-1,2,3-triazole-4- carboxylate 6i: The white needle crystals, yield 69%, mp 70-71°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 8.043(s, 1H, -NH-), 7.668(s, 1H, Ar-2), 7.205~7.320(m, 2H, Ar-4,5), 6.937~6.962(d, 1H, J=7.5Hz, Ar-6), 5.391(s, 2H -CH_2S-), 4.430~4.500(q, 2H, J=6.9Hz, -CO_2CH_2), 2.351 (s, 3H, -SCH_3-), 1.425~1.471(t, 3H, J=6.9Hz, -$CO_2CH_2CH_3$); IR(cm^{-1})(KBr disc), 3368, 3084, 3004,

2987, 2917, 1691, 1600, 1562, 1529, 1465, 1427, 1372, 1352, 1277, 1256, 1142, 1075, 1024, 992, 922, 899, 859, 806, 772, 744, 716, 697, 676, 649, 627, 562, 535, 438; MS M/Z(%), 326(M^+, 56), 297(2), 279(43), 251(16), 237(8), 223(3), 205(35), 191(4), 177(22), 166(9), 152(46), 138(17), 125(6), 111(40), 99(7), 90(7), 75(16), 61(100), 50(5), 43(16); HRMS (ESI) m/z calcd for $C_{13}H_{15}ClN_4O_2S$ $(M+H)^+$: 327.0677, found: 327.0679.

Ethyl 2-[(methylthio)methyl]-5-(phenylamino)-2*H*-1,2,3-triazole-4-carboxylate 6j: The white granular crystals, yield 51%, mp 62-63°C. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 7.984(s, 1H, -NH-), 7.498~7.548 (m, 2H, Ar-3,5), 7.310~7.334(d, 2H, J=7.2Hz, Ar-2,6), 6.957~7.007(m, 1H, Ar-4), 5.378 (s, 2H, -CH_2S-), 4.341~4.494(q, 2H, J=6.9Hz, -CO_2CH_2-), 2.337 (s, 3H, -SCH_3), 1.425~1.471 (t, 3H, J=6.9Hz, -$CO_2CH_2CH_3$); IR(cm^{-1})(KBr disc), 3356, 3207, 3067, 3008, 2985, 2954, 2918, 2510, 1922, 1841, 1778, 1691, 1600, 1571, 1525, 1479, 1442, 1389, 1359, 1308, 1254, 1140, 1080, 1025, 996, 906, 883, 844, 783, 749, 689, 652, 630, 565, 538, 500; MS M/Z(%), 292(M^+, 45), 260(100), 245(23), 217(6), 211(98), 196(18), 181(12), 171(24), 158(6), 149(9), 143(11), 130(33), 118(27), 110(5), 103(30), 91(13), 77(89), 69(6), 61(52), 51(19), 45(13); HRMS (ESI) m/z calcd for $C_{13}H_{16}N_4O_2S$ $(M+H)^+$: 293.1067, found: 293.1070.

2-((Methylthio)methyl)-2*H*-benzo[*d*][1,2,3] triazole (304658-78-4) 8a: The white granular crystals, yield 70%, mp 34-35°C. ^{1}H NMR (300 MHz,$CDCl_3$), δ = 7.861-7.891(d, 2H, *J* = 6.6 Hz, Ar-4,7), 7.386-7.418 (d, 2H, *J* = 6.6 Hz, Ar-5,6), 5.694 (s, 2H, N-CH_2-S-), 2.302 (s, 3H, -S-CH_3); IR(cm^{-1})(KBr disc), 3444, 3126, 3061, 3009, 2979, 2953, 2914, 2829, 1690, 1561, 1496, 1451, 1428, 1403, 1361, 1324, 1290, 1265, 1153, 997, 943, 845, 739, 702, 621, 512, 440; MS M/Z(%), 179(M^+, 17), 151(1), 133(67), 109(4), 104(21), 90(3), 77(100), 61(56), 51(27), 45(24), 39(12), 35(10).

1-((Methylthio)methyl)-1*H*-benzo[*d*][1,2,3]triazole (183164-38-7) 8b:The white lamellar crystals, yield 24%, mp 57-58°C (mp 60°C, Lit.16). ^{1}HNMR (300 MHz,$CDCl_3$), δ = 8.074-8.100(d, 1H, *J* = 8.1 Hz, Ar-4), 7.664-7.690 (d, 1H, *J* = 8.1 Hz, Ar-7), 7.506-7.537(ddd, 1H, *J* = 8.1, *J* = 6.9, *J* = 1.0 Hz, Ar-5), 7.388-7.439 (ddd, 1H, *J* = 8.1, *J* = 6.9, *J* = 1.0 Hz, Ar-6), 5.657-5.671 (d, 2H, *J* = 4.2 Hz, N-CH_2-S-), 2.085-2.099 (d, 3H, *J* = 4.2 Hz, -S-CH_3); IR(cm^{-1})(KBr disc), 3444, 3070, 3030, 2990, 2918, 1612, 1591, 1493, 1433, 1390, 1306, 1286, 1264, 1226, 1164, 1130, 1084, 985, 923, 862, 774, 746, 689, 662, 597, 570, 528, 429; MS M/Z(%), 179 (M^+, 8), 149(1), 132(59), 109(9), 104(24), 91(2), 77(100), 61(28), 51(39), 45(18), 39(9), 35(5).

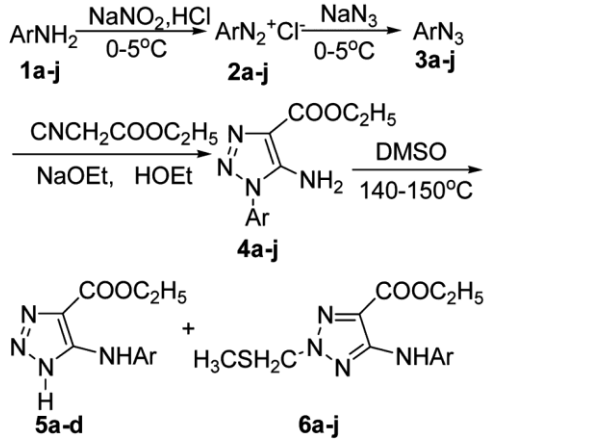
3,5-dimethyl-1-((methylthio)methyl)-1*H*-pyrazole 9: The pale yellow oily liquid; ^{1}HNMR (300 MHz,$CDCl_3$), δ = 5.829(s, 1H, Pyrazole ring-H), 5.000(s, 2H, -CH_2-S-), 2.276(s, 3H, -CH_3), 2.267 (s, 3H, -CH_3), 2.185(s, 3H, -S-CH_3); IR(cm^{-1}) (KBr disc), 3426, 2924, 2856, 2221, 1712, 1558, 1460, 1422, 1380, 1298, 1276, 1214, 1146, 1029, 979, 909, 792, 734, 649, 467; MS M/Z(%), 156(M^+, 19), 119(1), 109(100), 97(3), 82(11), 68(28), 61(18), 57(3), 53(11), 47(11), 42(37); HRMS (ESI) m/z calcd for $C_7H_{12}N_2S$ $(M+H)^+$: 157.0794, found: 157.0792.

Results and Discussion

Synthesis of the title compound

The structure of the title compound is shown in Scheme 3. In recent years, the synthesis and characteristics of s-triazolo[3,4-b]-1,3,4-thiadiazoles have been investigated[9]. These heterocyclic compounds contain 1,2,3-triazole, 1,2,4-triazole and 1,3,4-thiadiazole rings condensed through a C–N bond. In a continuation of our earlier studies[10], we now report some new compounds ethyl 5-(arylamino)-2-[(methylthio)methyl]-2*H*-1,2,3-triazole-4-carboxylate **6a-j**.

Compounds **5a-d** was obtained by Dimroth rearrangements by ethyl 5-amino-1-aryl-1*H*-1,2,3-

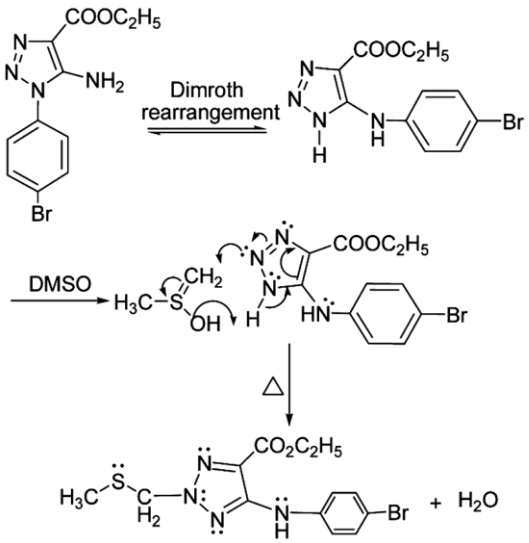


Scheme 3 — Synthesis of the title compound

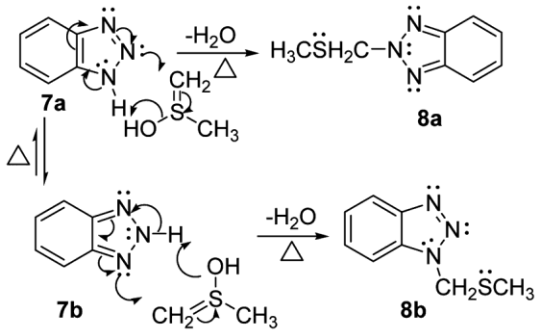
triazol-4-carboxyate **4a-j** when heated in DMSO. Then title compounds **6a-j** were synthesized by heating the mixture of compound **5a-j** with DMSO. The intriguing reaction is found on 1*H*-1,2,3-triazole derivatives with DMSO, the route of syntheses and reaction is shown in the following. The structures of these compounds were characterized with ^{1}H NMR, IR, MS and HRMS spectroscopy. The yields, melting points and reaction time are given in Table 1.

The structure of ethyl 2-methylthiamethyl-5-(4-bromoanilino)-*2H*-1,2,3-triazol-4-carbonate (**6d**) was confirmed by both spectroscopic means and X-ray crystallographic analysis (Fig. 1)[18-19].

The reactions of DMSO and (1*H*/2*H*)1,2,3-triazole derivatives are reported rarely[18-20] and The free-mediated reactions of DMSO and 1,2,3-triazole derivatives are not reported in literature. These compounds have potential applied valuable, so the study on this reaction is important. It was anticipated that the reaction mechanism is in following.



In order to study the reaction deeply and demonstrate the reaction mechanism, some characteristic compounds were selected. The products of these reactions are in keeping with anticipation. The reaction mechanism of benzotriazole and DMSO is in following:



The reaction of benzotriazole and DMSO gives two products due to the rearrangement of its H-shift.

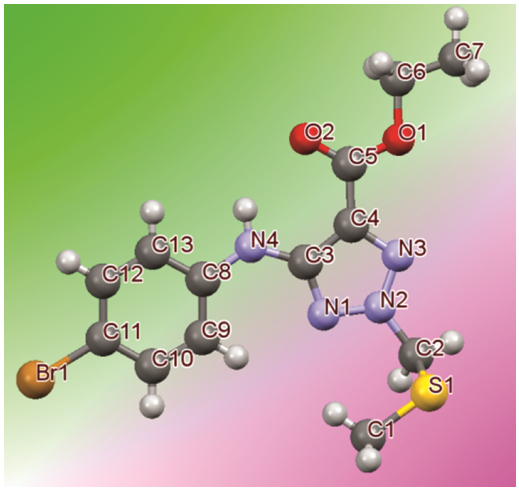
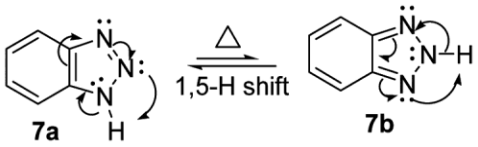


Fig. 1 — X-ray crystallographic structure of compound 6d (CCDC 286960)

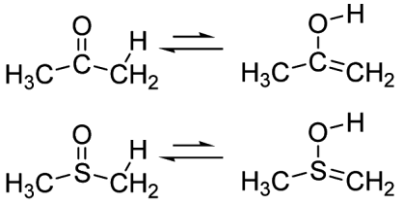
Table 1 — Yields, melting points (M.P.) and reaction time (T) of compounds 4a-j, 5a-d and 6a-j

Compd.	Yield (%)	M.P. (°C)	Compd.	Yield (%)	M.P. (°C)	T (h)
4a	86.0	150-151	5a	28.5	114-115	6
			6a	62.0	80-81	
4b	53.0	148-149	5b	32.2	91-92	6
			6b	60.5	76-77	
4c	84.5	169-170	5c	46.5	115-116	5
			6c	48.0	65-66	
4d	80.5	168-169	5d	30.5	164-165	8
			6d	62.5	102-103	
4e	78.0	159-160	6e	60.8	100-101	6
4f	66.5	129-130	6f	76.5	105-106	6
4g	80.5	159-160	6g	50.2	111-112	6
4h	84.2	148-149	6h	62.2	81-82	5
4i	80.2	157-158	6i	68.5	70-71	8
4j	76.6	136-137	6j	50.5	62-63	8

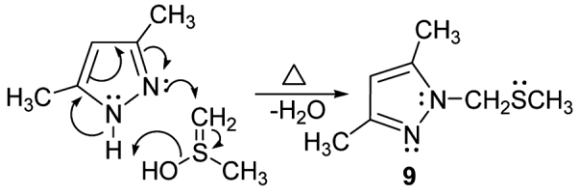
The rearrangement of benzotriazole could give 1*H*-benzotriazole and 2*H*-benzotriazole when it was heated.



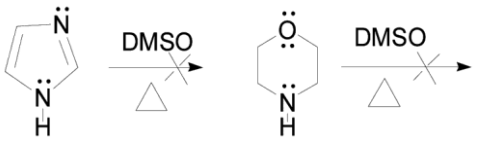
The 2-methylthiamethyl-benzotriazole is the product by reaction of 1*H*-benzotriazole with DMSO and 1-methylthiamethyl-benzotriazole is the product by reaction of 2*H*-benzotriazole with DMSO. The free-mediated reaction mechanism of benzotriazole and DMSO does not agree with Pummerer rearrangement reaction. The free-mediated reaction mechanism is a six ring transition state by enol of sulfur ketones and not acylsulfonium ylide(sulfur-substituted carbocation) of sulfoxide by activating agent to product α-Substituted sulfide for Pummerer rearrangement reaction[20-23].



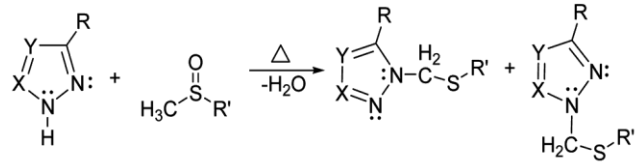
Acetone and dimethyl sulfide ketone all can form the tautomer. However, the carbonyl carbon of acetone can't keep lone pair electrons. In the same way, we use acetone cover for DMSO, but we can't get similar product of –NH-N= azole and sulfur ketones reaction.



3,5-Dimethyl-1-methylthiamethyl-pyrazole is only one reaction product of 3,5-dimethyl-pyrazole and DMSO.



The heating reaction mixture of imidazole or morpholine with DMSO has not produce similar products. This conclusion is comported with the result of the anticipation. The novel reaction is a powerful and practical method for the synthesis of azole compounds containing thio-function. The target compounds have potential applied prospect, so that the study is very important. The reaction mechanism is also suitable for the following types of reactions.



X, Y = N, R"-CH=, etc.; R, R', R" = Hydrocarbon group, Aryl, etc.

Conclusions

The reaction mechanism of –NH-N= azole derivatives and sulfur ketones derivatives is reported. The reaction mechanism is suitable for the synthesis of azole compounds containing thio-function. The free-mediated reaction mechanism of –NH-N= azole and DMSO does not agree with Pummerer rearrangement reaction mechanism. Some new (methylthio)methyl-triazole were synthesized by the azole compounds and DMSO. The new compounds were characterized by ^{1}H NMR, MS, IR, HRMS and single-crystal X-ray diffraction.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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References

1 Rani A, Singh G, Singh A, Maqbool U, Kaur G & Singh J, *RSC Adv*, 10 (2020) 5610.
2 Xu Z, *Eur J Med Chem*, 206 (2020) 112686.
3 Dong H R & Wu J G, *Heterocycl Commun*, 24 (2018) 109.
4 Dong H R, Wu J G & Gao Z L, *Synth Commun*, 47 (2017) 1783.
5 Bozorov K, Zhao J Y & Aisa H A, *Bioorg Med Chem*, 27 (2019) 3511.
6 Xu Z, Zhao S J & Liu Y, *Eur J Med Chem*, 183 (2019) 111700.
7 Gonzaga D T G, Rocha D R D, Silva F D C D & Ferreira V F, *Curr Top Med Chem*, 13 (2013) 2850.
8 Dong H R, Wu J G & Huo G Y, *J Mol Struct*, 1256 (2022) 132516.

9 Dong H R, Jin C Q & Chen Z B, *Indian J Chem*, 60B (2021) 1629.
10 Zheng Y C, Duan Y C & Ma J L, *J Med Chem*, 53 (2013) 8543.
11 Silva T B, Ji Kathya N K, Pauli F P, Galvao R M S, Faria A F M, Bello M L, Resende J A L C, Campos V R, Forezi L D S M, Silva F D C D, Faria R X & Ferreira V F, *Bioorg Chem*, 116 (2021) 105250.
12 Chen W B & Jin G Y, *Chem J Chin Univ*, 22 (2001) 1147.
13 Denisko Olga V, *Encyclopedia of Reagents for Org. Synth*. 2003, (https://doi.org/10.1002/047084289X.rn00362).
14 Wang H, He M, Li Y, Zhang H, Yang D, Nagasaka M, Lv Z, Guan Z, Cao Y, Gong F, Zhou Z, Zhu J, Samanta S, Chowdhury A D & Lei A, *J Am Chem Soc*, 143 (2021) 3628.
15 Katritzky A R, Bobrov S Y, Khashab N & Kirichenko K, *J Org Chem*, 69 (2004) 4269.
16 Katritzky A R, Bobrov S, Kirichenko K & Ji Y, *J Org Chem*, 69 (2004) 303.
17 Degl'Innocenti A, Capperucci A, Oniciu D C & Katritzky A R, *J Org Chem*, 65 (2006) 9206.
18 Katritzky A R, Oniciu D C, Ghiviriga I & Soti F, *J Org Chem*, 63 (1998) 2110.
19 Katritzky A R, Xie L & Serdyuk L, *J Org Chem*, 61(1996) 7564.
20 Wang B & Dong H S, *J Chem Crystallography*, 39 (2009) 95**.**
21 Tokatli A, Oezen E, Ucun F & Bahceli S, *Spectrochim Acta, Part A*, 78A (2011) 1201.
22 Zhang C X, Zheng L, Yan Q, Hu Q Q, Jia F C & Chen Y F, *ChemistrySelect*, 3 (2018) 10277.
23 Oae S & Numata T, *Isotopes in Organic Chemistry*, 5 (1980) 45.
24 KitaY & Shibata N, *Synlett*, (1996) 289. (doi.org/10.1055/s-1996-5400)
25 Murray A W, *Organic Reaction Mechanisms*, (2001) 473. (https://doi.org/10.1002/0470845805.ch15**).**