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Note

The synthesis of some new (1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl) diarylmethanol

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The (1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)diarylmethanols were synthesized by ethyl 1-aryl-5-methyl-1*H*-1,2,3-triazole-4-carboxylate. The yielded products are investigated with NMR, MS, IR, elemental analyses and X-ray crystallographic techniques.

Keywords: 1,2,3-Triazole, methanol, synthesis, Grignard reaction

In recent years, the remarkable efficacy of compounds having a 1,2,3-triazole nucleus has been demonstrated with inducing antibacterial [1-3], antifungal[4], antiviral[5], antimicrobial[6], anti-inflammatory and analgesic[7] activities in various publication. Some 1,2,3-triazole derivatives have also been synthesized to inhibit tumour proliferation, invasion, metastasis[8], and anti-HIV activity[9-14]. 1,2,3-Triazole and related compounds have attracted much attention due to their indispensable roles in medicine, agriculture and industry. For the sake of the obtaining new biologically active agents, some new 1,2,3-triazole derivatives were synthesized by Grignard reaction.

In this paper, the synthesis of (1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)diarylmethanols **6a-i** is described. The route of synthesis is showed in **Scheme I**.

Results and Discussion

The crystal structure of **6e** is show in **Figure 1**. 1,2,3-Triazole derivatives were synthesized in laboratory in recent years[15]. In this paper, compounds **6a-i** were synthesized by Grignard reaction.

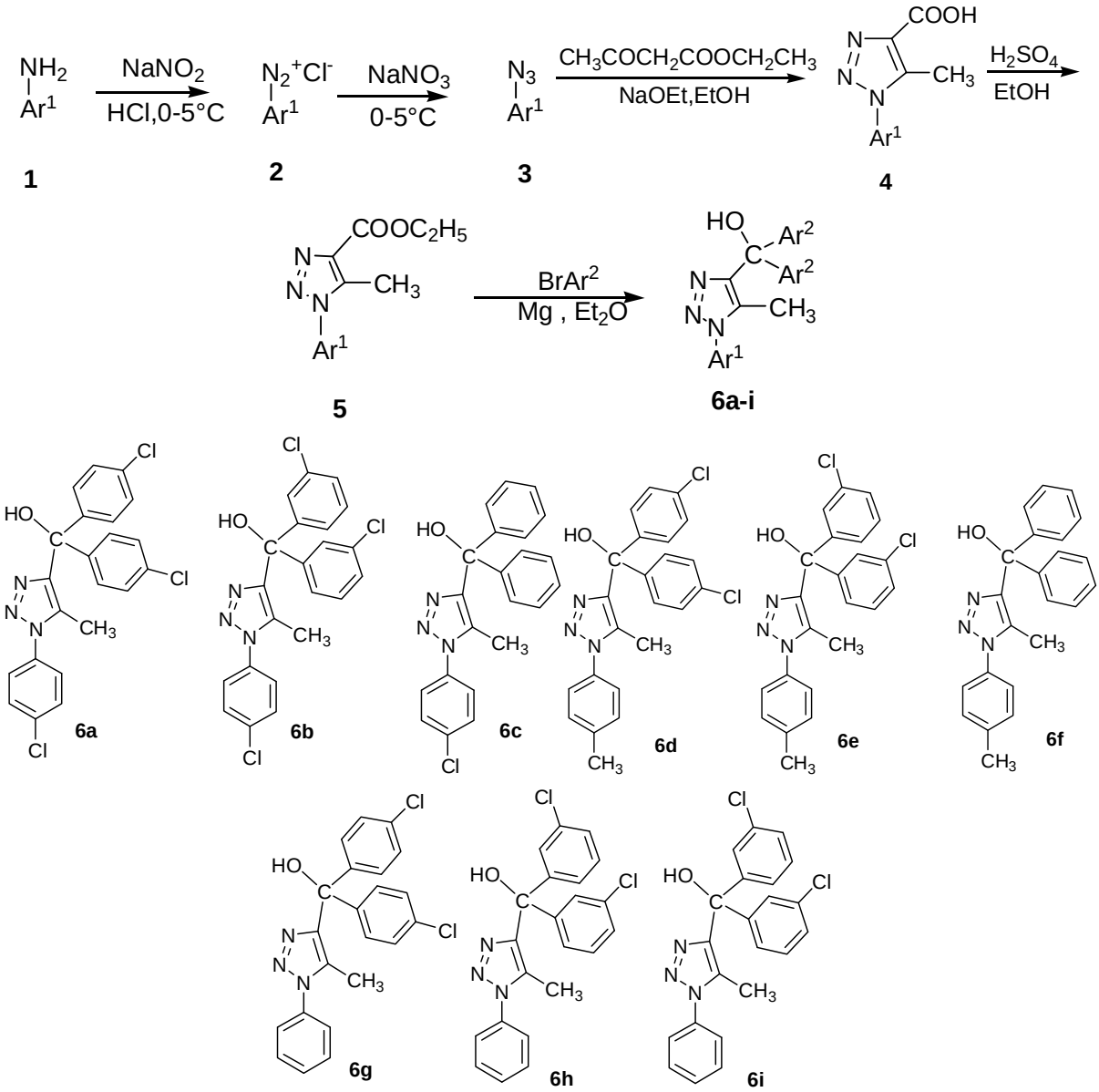
It is preferred to use ammonium chloride instead of dilute hydrochloric acid in the process of synthesis. When the concentration of hydrochloric acid is higher, some compounds of **6a-i** could be changed and the hydroxyl group is substituted by chlorine atom. When the product was crystallized in ethanol, the chlorine atom was substituted by ethoxy. For example, The compound 1-(4-chlorophenyl)-4-(ethoxydiphnylmethyl)-5-methyl-1*H*-1,2,3-triazole was obtained, yield 90%, m.p. 156-58°C. ^{1}H NMR: ($CDCl_3$-d_1), δ 1.201-1.256 (t, 3H, J = 7.2Hz, CH_3CH_2O-), 1.991 (s, 3H, TRZ-H), 2.204-2.274 (q, 2H, J = 7.2, CH_3CH_2O-), 7.188-7.616 (m, 14H, Ar^1, Ar^2-H). MS *m/z*: 403(M^+), 405(M+2), 374, 373, 354, 345, 330, 316, 287, 273, 254, 238, 212, 188, 156, 153(100), 147, 111, 78; IR: 3062, 3025, 2972, 2903, 2888, 1518, 1490, 1444, 1260, 1208, 1120, 1087, 1069, 940, 898, 819, 774, 756, 726, 700 cm^{-1}. There is no obvious broad peak observed near 3300 cm^{-1} in the IR spectrum. 4-(Ethoxy-diphenylmethyl)-5- methyl-1-*p*-tolyl-1*H*-1,2,3-triazole, yield 89%, m.p. 118-20°C. ^{1}H NMR ($CDCl_3$-d_1), δ 1.217-1.264 (t, 3H, J = 7.2Hz, CH_3CH_2O), 1.959 (s, 3H, TRZ-H), 2.430 (s, 3H, Ar^1-CH_3), 3.233-3.304 (q, 2H, J = 7.2, CH_3CH_2O-), 7.192-7.338 (m, 10H, Ar^1, Ar^2-H), 7.624-7.647 (d, 4H, Ar^2-H). MS *m/z*: 383 (M^+), 355, 354, 338, 326, 310, 296, 287, 254, 238, 212, 185, 133, 106(100), 91, 77, 65, 52; IR: 3062, 3025, 2976, 2917, 2864, 1494, 1462, 1444, 1257, 1213, 1119, 1089, 1069, 1006, 972, 895, 842, 816, 755, 726, 701 cm^{-1}. There is no obvious broad peak observed near 3300 cm^{-1} in the IR spectrum, too. Their IR spectra are different from **6c** and **6g**.

The crystal structure of **6e** by X-ray diffraction was obtained. In the ring system, in the group, it can be seen that four rings are not in plane with each other as shown in **Figure 1**.

In this reaction, Grignard reaction showed that when the 1,2,3-triazole derivatives reacted with bromobenzene in the ratio of 1:1(mole), the triazole always cannot react completely. But the product can be purified easily by stirring in the solution of sodium hydroxide after recrystallizing.

In Grignard reaction it was found that the ^{1}H NMR peak of TRZ-CH_3 is shown at δ 1.740-1.824. It is different from chemical shifts value (at about 2.600) of reported one[15,16]. This is probably due to the existence of Ar^2. The IR spectra of compounds **6a-i**

showed the characteristic bands at 3273-3499 (O-H),



Scheme I

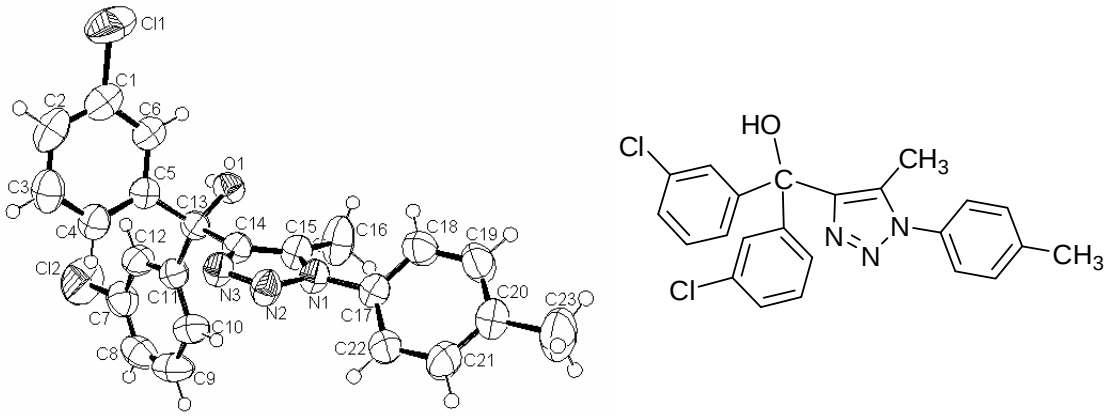


Figure 1 — ORTEP drawing of the title compound **6e** showing the atom numbering scheme.

Table I—Physical data and IR spectral date of compounds **6a-i**

Compd	m.p. (°C)	Yield (%)	Found/(Calcd)(%) C	H	N	IR (KBr, cm^{-1})
6a	182-83	81	59.50 (59.41	3.45 3.63	9.64 9.45)	3299 (b, -OH), 3065, 2921 (w, CH_3), 1495 (s, Ar), 1400, 1091, 1039, 1009, 916, 822, 527
6b	146-48	84	59.21 (59.41	3.65 3.63	9.55 9.45)	3273 (b, -OH), 3065, 2925 (w, CH_3), 1591, 1571, 1497, 1471 (s, Ar), 1420, 1090, 1039, 1008, 883, 834, 791, 711, 524
6c	161-62	89	70.11 (70.30	4.63 4.83	11.25 11.18)	3375 (b, -OH), 3068, 2939 (w, CH_3), 1495 (s, Ar), 1446, 1095, 1051, 1008, 901, 835, 757, 701, 527
6d	172-74	86	65.35 (65.10	4.42 4.51	9.77 9.90)	3265 (b, -OH), 3085, 2921 (w, CH_3), 1517, 1490 (s, Ar), 1400, 1344, 1264, 1093, 1013, 824, 811, 525
6e	146-48	83	65.01 (65.10	4.60 4.51	9.95 9.90)	3376 (b, -OH), 3072, 2922 (w, CH_3), 1590, 1570, 1516, 1470 (s, Ar), 1420, 1366, 1140, 1099, 1041, 877, 816, 790, 709, 538
6f	153-54	88	77.85 (77.72	5.84 5.96	11.67 11.82)	3341 (b, -OH), 3060, 2918 (w, CH_3), 1517, 1490 (s, Ar), 1447, 1204, 1139, 1055, 1009, 888, 828, 755, 696 (s, Ar)
6g	161-62	84	64.21 (64.40	4.33 4.18	9.94 10.24)	3225 (b, -OH), 2928 (w, CH_3), 1597, 1490 (s, Ar), 1422, 1397, 1260, 1092, 1051, 1014, 918, 812, 765, 688, 525
6h	166-68	86	64.33 (64.40	4.10 4.18	10.44 10.24)	3479 (b, -OH), 3065 (w, CH_3), 1593, 1571, 1500, 1472, 1422 (s, Ar), 1179, 1099, 1051, 885, 791, 769, 752, 694, 538
6i	144-46	85	77.56 (77.40	5.73 5.61	12.10 12.31)	3415 (b, -OH), 3061, 3023 (w, CH_3), 1592, 1494 (s, Ar), 1448, 1162, 1119, 1093, 894, 764, 699 (s, Ar)

Table II —^{1}H NMR and mass spectral date for compounds **6a-i**

Compd	^{1}H NMR ($CDCl_3$) δ,ppm	Mass *m/z*
6a	7.499-7.526 (d, 2H, *J* = 8.1Hz, Ar^1-3,5), 7.359-7.386 (d, 2H, *J* = 8.1Hz, Ar^1-2,6), 7.302-7.329 (d, 4H, *J* = 8.1Hz, Ar^2-3,5), 7.253-7.284 (d, 4H, *J* = 8.1Hz, Ar^2-2,6), 4.110 (s, 1H, -OH), 1.821 (s, 3H, TRZ-CH_3)	443, 447, 445, 415, 153, 151, 140, 137, 112, 111, 108, 93, 91, 78, 70, 65, 56, 52.
6b	7.504-7.528 (d, 2H, *J* = 7.2Hz, Ar^1-3,5), 7.377-7.401 (d, 2H, *J* = 7.2Hz, Ar^1-2,6), 7.383-7.393 (t, 2H, Ar^2-H), 7.250-7.319 (m, 4H, Ar^2-H), 7.180-7.215 (m, 2H, Ar^2-H), 4.113(s, 1H, -OH), 1.824(s, 3H, TRZ-CH_3)	443, 447, 445, 415, 413, 304, 251, 206, 153, 139, 136, 112, 111, 76, 72, 58, 56, 52.
6c	7.491-7.518 (q, 2H, *J* = 8.1Hz, Ar^1-3,5), 7.258-7.413 (m, 12H, Ar^1, Ar^2-H), 4.100 (s, 1H, -OH), 1.780 (s, 3H, TRZ-CH_3)	375, 377, 348, 346, 270, 184, 153, 136, 111, 106, 92, 77, 70, 56, 52.
6d	7.259-7.292 (m, 12H, Ar-H), 4.100 (s, 1H, -OH), 2.437 (s, 3H, Ar^1-CH_3), 1.776 (s, 3H, TRZ-CH_3)	423, 425, 394, 377, 284, 155, 137, 112, 111, 92, 91, 77, 65, 56, 52.
6e	7.401 (s, 2H, Ar^2-6), 7.186-7.299 (m, 10H, Ar^1, Ar^2-H), 4.413 (s, 1H, -OH), 2.551 (s, 3H, Ar^1-CH_3), 1.789 (s, 3H, TRZ-CH_3)	423, 425, 394, 378, 155, 140, 136, 137, 133, 111, 108, 91, 77, 65, 52.
6f	7.274-7.377 (m, 14H, Ar^1, Ar^2-H), 4.325 (s, 1H, -OH), 2.428 (s, 3H, Ar^1-CH_3), 1.740 (s, 3H, TRZ-CH_3)	355, 326, 250, 166, 134, 133, 106, 91, 77, 66, 52.
6g	7.518-7.540 (m, 3H, Ar^1-3,4,5), 7.405-7.458 (m, 2H, Ar^1-2,6), 7.254-7.354 (m, 8H, Ar^2-H), 4.110 (s, 1H, -OH), 1.807 (s, 3H, TRZ-CH_3)	409, 411, 379, 233, 156, 140, 119, 111, 83, 81, 78, 77, 70, 56, 52.
6h	7.532-7.567 (q, 3H, Ar^1-3,4,5), 7.454-7.473 (m, 2H, Ar^1-2,6), 7.405 (s, 2H, Ar^2-2), 7.196-7.307 (m, 6H, Ar^2-4,5,6), 3.920 (s, 1H, -OH), 1.813 (s, 3H, TRZ-CH_3)	409, 411, 380, 233, 156, 140, 119, 111, 78, 77, 56, 52.
6i	7.499-7.549 (m, 3H, Ar^1-3,4,5), 7.424-7.469(m, 2H, Ar^1-2,6), 7.256-7.360 (m, 10H, Ar^2-H), 4.169(s, 1H, -OH), 1.752(s, 3H, TRZ-CH_3)	341, 312, 296, 205, 156, 119, 106, 77, 56, 52.

1091-1099 (C-O) cm^{-1} (**Table I**). The ^{1}H NMR and mass spectral data for compound **6a-i** are given in **Table II**.

Experimental Section

All melting points were uncorrected and determined on an XT_4-100x microscopic melting point apparatus. IR spectra were obtained in KBr discs on a Nicolet AVATAR 360 FT-IR spectrometer and a Nicolet NEXUS 670 FT-IR. MS were performed on a ZAB-HS instrument. ^{1}H NMR spectroscopy ($CDCl_3$) was recorded on an Avance Mercury plus-300 instrument with TMS as an internal standard. 5-Methyl-1-subsituted-1,2,3-triazol-4-caroxylic acids and Ethyl 1-

aryl-5-methyl-1*H*-1,2,3-triazol-4-carboxylate **5** were prepared by literature[15] method**.**

(1-Aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)diarylmethanols 6a-i.

Three-necked round-bottomed flask (250 mL) was fitted with an efficient stirrer unit, a dropping funnel and an efficient reflux condenser; calcium chloride guard-tubes were placed on the top of the funnel and on the condenser. All parts of the apparatus must be thoroughly dry. The 0.96 (0.04 mole) of fresh magnesium turnings and a few crystals of iodine was placed in the flask. The bottom of the flask was heated with a bath of hot water until the iodine commences to vaporize and is then allowed to cool. While 5 mL of sodium-dried diethyl ether is added, 2 mL a mixture of 0.04 mole of the bromo-benzene and 30 mL of sodium-dried diethyl ether is added directly to the flask. After reaction has started for a few minutes, the remainder of the bromo-benzene and ether were dropped into the flask by the dropping funnel under stirring. Stirring and refluxing were continued for an hour after the drop-addition was completed.

A mixture of ethyl 1-aryl-5-methyl-1*H*-1,2,3-triazole-4- carboxylate (0.2 mole) in benzene was added in completely, stirring is continued for 2~3 hrs at room temperature. The mixture was decomposed by ice, water and ammonium chloride. The organic layer was separated and the solvent was distilled off. The crude product was recrystallized from benzene to give **6a-i**. The product was stirred in sodium hydroxide solution to remove unreacted ethyl 1-aryl-5-methyl-1*H*-l,2,3-triazol-4-carboxylate if it was necessary.

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