Synthesis of New 2,2'-Disubstituted 5,5'-Dimethyl-4,4'-bitriazoles and 2-(4-Triazolyl)quinoxalines

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Thermal rearrangement of 3-acylisoxazole arylhydrazones allowed facile preparation of 2*H*-1,2,3-triazoles which were firstly reacted with isoamyl nitrite and then with an opportune arylhydrazine to produce the corresponding α-hydroxyiminohydrazones **8a-h**. The reaction of compounds **8a-h** with phosphorus pentachloride afforded the desired 4,4'-bitriazoles **1a-h**. The α-hydroxyiminoketone derivative **7** or the α-diketone **14** reacted easily with 1,2-phenylenediamine to afford 1,2,3-triazoles **2a-c** bearing the quinoxaline moiety at position 4. Improved yields of the quinoxalines **2a-c** were obtained when 1,2-phenylenediamine was reacted with the dioxime **15**.

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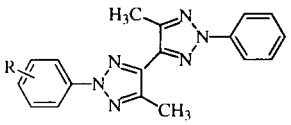
Introduction.

1,2,3-Triazoles and their benzo derivatives constitute a class of compounds which have attracted considerable attention in industry and agriculture primarily due to their significant biological activities. Thus, owing their importance, an impressive number of 1,2,3-triazole derivatives have been described in the literature [1]. Many 1,2,3-triazole derivatives possess bacteriostatic activity; in particular, some 4-alkyl-1,2,3-triazoles as well as 2-phenyl-1,2,3-triazole-4-carboxylic acid derivatives have been reported to inhibit the growth of different microorganisms [2-4]. Furthermore, virostatic, cytostatic, antimicrobial and antimycotic activities of 1,2,3-triazolecarboxamide derivatives have been reported [5].

From a synthetic point of view, alkyl- and aryl-substituted derivatives of 1,2,3-triazole ring system were firstly obtained from oxidative ring closure of dihydrazones and substituted dihydrazones of α-diketones and by ring closure of α-diazoimines, α-diazoamides and triazenes [6]. One of the most versatile route to 1*H*-1,2,3-triazoles consists of the thermal 1,3-dipolar cycloaddition of azides to alkynes; a wide range of substituents can be incorporated into the alkyne and azide component thus allowing the preparation of a variety of substituted 1,2,3-triazole derivatives [7,8]. In particular, the 4,4'-ditriazole system (structure **3** as an example) has been obtained by the cycloaddition of phenyl azides to alkadiynes; the system has been also obtained by cyclocondensation of a suitable 1,2,3-triazole-ketohydrazone derivative in the presence of ammonium acetate [9-11].



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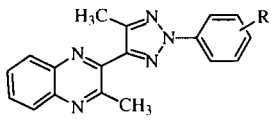

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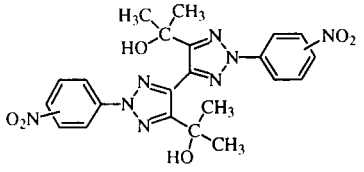

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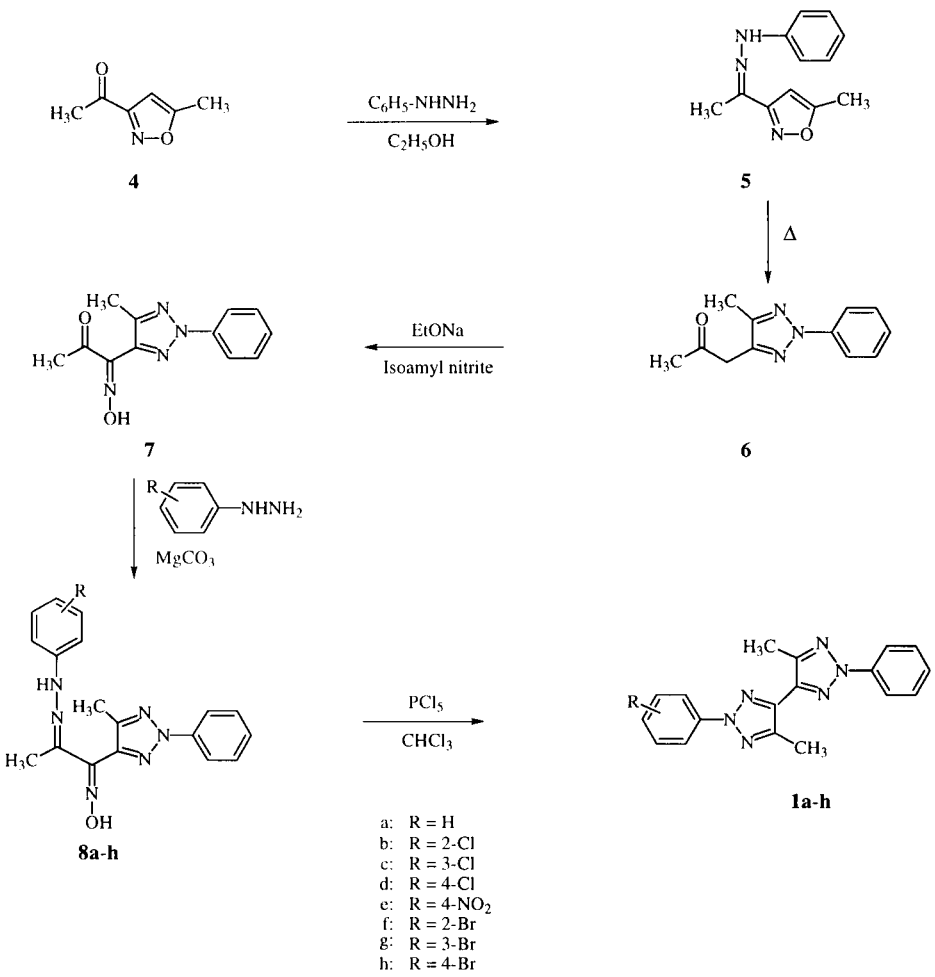
Our interest toward the triazole heterocycle commenced some years ago when some of us described the synthesis of new 1,2,4-triazoles and their thiadiazole condensed derivatives [12,13]. In an ongoing project aimed to explore the potential biological properties of the triazole heterocycle and in particular due to our interest for the 4,4'-ditriazole system, we undertook the preparation of some new 4,4'-ditriazole derivatives **1** as well as 1,2,3-triazoles **2** bearing a quinoxaline heterocycle at position 4. Considering that only few references have been reported hitherto in the literature for the preparation of the 4,4'-ditriazole system, we had an interest to reinvestigate and to improve the preparation of the title compounds using chemistry previously described [14].

In Scheme 1, we detail the synthesis of our desired 4,4'-ditriazoles starting from 3-acylisoxazoles which is amenable for scale preparation of a large number of derivatives. Additionally, using simple variations of this synthetic scheme we gained facile access to the 1,2,3-triazoles **2** bearing the desired quinoxaline portion.

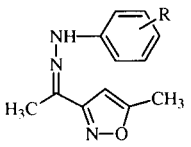
The hydrazone derivative **5** was simply prepared in 80% yield starting from the reaction of acetylisoxazole **4** with phenylhydrazine in ethanol at room temperature. Isomerization of 3-acylisoxazole arylhydrazones has

Scheme 1

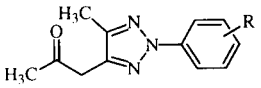


proved to be an excellent method for the synthesis of a variety of heterocyclic systems [15,16]. In particular, isomerization of 3-acylisoxazole arylhydrazones has widely been known to afford 1,2,3-triazoles; this well known rearrangement occurs readily in alcoholic potassium hydroxide or by melting with or without copper powder. Accordingly, the hydrazone derivative **5** was readily transformed into the 1,2,3-triazole **6** by warming at the melting temperature in a similar fashion to the work previously described [17].

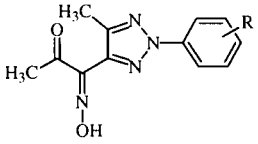
Starting from the easily prepared **6**, the 4,4'-ditriazoles **1a-h** were simply obtained as described in Scheme 1. The hydroxyimino derivative **7** was accessible by the reaction of the enolate of the ketone **6** with isoamyl nitrite at 0° C for 6 hours. The moderately strong band observed at 1600 cm^{-1} is characteristic of the new formed C=N-OH moiety while the N-OH was identified in the nmr spectra at δ 10.5 ppm. The hydroxyimino derivative **7** was reacted with the appropriate arylhydrazines in ethanol to afford in good yields the hydrazones **8a-h**. Compounds **8a-h** were simply cyclized to the 4,4'-ditriazole derivatives **1a-h** with phosphorus pentachloride in chloroform. The structures of new prepared 4,4'-ditriazoles were proved by an alternate synthesis of **1c,e**. Thus, starting from the hydrazones **9a,b**, we prepared easily new derivatives **10a,b**, **11a,b** and **12a,b**. The evidence for the structure of new triazoles **10a,b** was obtained from the nmr spectral data. Along with the expected signals, the CO-CH_2 protons appeared as a singlet at δ 3.89 ppm. The moderately strong band observed at 1720 cm^{-1} is characteristic of C=O group. By cyclization of **12a,b** compounds **1c,e** were obtained in good yields. The characterization data of **8b-h** and **1b-h** are given in Table 1, 2 and 3.



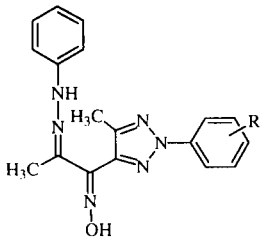
9a,b



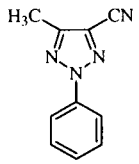
10a,b



11a,b



12a,b



13

a = 3-Cl
b = 4-NO_2

Table 1

Yields and Physical Data of Compounds **1b-h**

Compound	mp °C	Yield %	Formula (Mole Weight)	Analyses Calcd./Found C%	H%	N%
1b	125-126	65	$C_{18}H_{15}ClN_6$	61.63	4.31	23.96
			(350.8)	61.80	4.29	23.91
1c	170-172	55	$C_{18}H_{15}ClN_6$	61.63	4.31	23.96
			(350.8)	61.54	4.33	23.88
1d	204-207	68	$C_{18}H_{15}ClN_6$	61.63	4.31	23.96
			(350.8)	61.61	4.32	29.90
1e	273-274	60	$C_{18}H_{15}N_7O_2$	59.83	4.18	27.13
			(361.4)	59.72	4.20	27.08
1f	150-152	60	$C_{18}H_{15}BrN_6$	54.70	3.83	21.26
			(395.3)	54.76	3.85	21.19
1g	180-181	62	$C_{18}H_{15}BrN_6$	54.70	3.83	21.26
			(395.3)	54.54	3.83	21.28
1h	196-198	58	$C_{18}H_{15}BrN_6$	54.70	3.83	21.26
			(395.3)	54.60	3.84	21.18

The triazole derivative **7** has been proven to be a good precursor for either the preparation of the 4,4'-ditriazole derivatives **1a-h** or the quinoxaline derivatives **2a-c**. Initial attempts toward the cyclization of **7** and **11a,b** to **2a-c** by refluxing a mixture of the keto-oximes and the opportune amine in acetic acid were unsuccesseful (Scheme 2): the only product isolated was the nitrile **13**. Similar results were obtained when the cyclization was attempted in a sealed tube at 100 °C: also in this case the nitrile **13** was recovered as the principal compound together with traces of **2a-c**. After several attempts aimed to improve the yield of the desired derivatives **2a-c**, we found that these compounds can be synthesized (50-60% yield) by refluxing a mixture of **7**, **11a,b** and 1,2-phenylenediamine in methanol containing concentrated hydrochloric acid. Routinely, a stoichiometric ratio of 1:1.5 of the oxime to the diamine was employed to ensure complete conversion of the oxime into the cyclized product. In this case the nitrile **13** was obtained in low yield (5-10%).

The structures of novel compounds **2a,c** were also proved by an alternative synthesis as shown in Scheme 2. The oxime derivative **7** was hydrolyzed with hydrochloric acid to the diketone **14** which was in turn reacted with 1,2-phenylenediamine to give the desired **2a**. However, the yield is lower than the above described cyclization.

Interestingly, an alternative approach to the quinoxaline derivatives was devised employing the dioxime **15** that is easily prepared from the α-hydroxyiminoketone **7**. When **15** was reacted with 1,2-phenylenediamine in the presence of concentrated hydrochloric acid, product **2a** was obtained in good yield.

In summary, 3-acylisoxazole arylhydrazones are versatile intermediates giving various 4-acetonyl-1,2,3-triazoles, which are easily transformed into a large number of 4,4'-ditriazoles. The overall synthetic scheme allows the introduction of a wide range of substituents at the 2,2' positions. Moreover, simple modifications of the synthetic scheme make our approach applicable to the preparation of 1,2,3-triazoles bearing the quinoxaline moiety at position 4.

Table 2

Yields and Physical Data of Compounds **8b-h** and **12a,b**

Compound	mp °C	Yield %	Formula (Mole Weight)	Analyses Calcd./Found C%	H%	N%
8b	174-175	65	$C_{18}H_{17}ClN_6O$ (368.8)	58.62 58.55	4.65 4.66	22.79 22.75
8c	183-185	60	$C_{18}H_{17}ClN_6O$ (368.8)	58.62 58.68	4.65 4.63	22.79 22.85
8d	219-221	65	$C_{18}H_{17}ClN_6O$ (368.8)	58.62 58.47	4.65 4.66	22.79 22.71
8e	263-264	65	$C_{18}H_{17}N_7O_3$ (379.4)	56.99 57.12	4.52 4.50	25.84 25.79
8f	146-148	70	$C_{18}H_{17}BrN_6O$ (413.3)	52.31 52.17	4.15 4.17	20.33 20.28
8g	188-189	72	$C_{18}H_{17}BrN_6O$ (413.3)	52.31 52.40	4.15 4.16	20.33 20.25
8h	215-217	70	$C_{18}H_{17}BrN_6O$ (413.3)	52.31 52.22	4.15 4.17	20.33 20.30
12a	184-186	55	$C_{18}H_{17}ClN_6O$ (368.8)	58.62 58.77	4.65 4.63	22.79 22.72
12b	221-222	57	$C_{18}H_{17}N_7O_3$ (379.4)	56.99 56.84	4.52 4.54	25.84 25.76

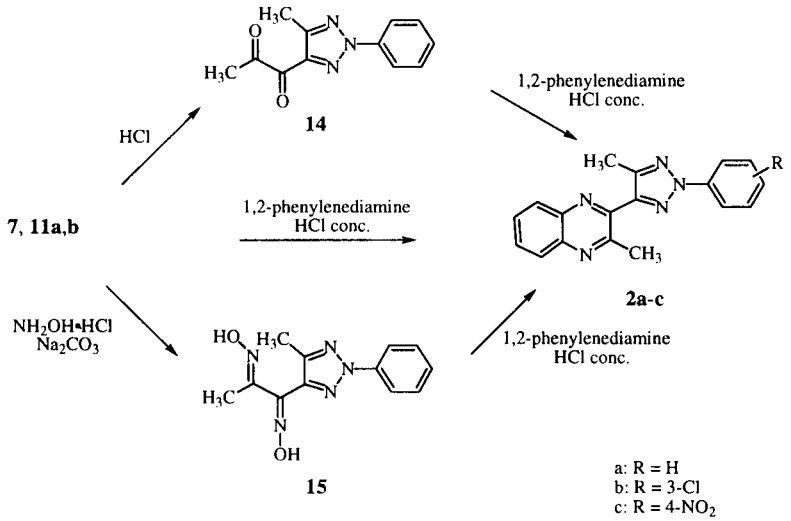
Table 3

^1H nmr and ^{13}C nmr Data of Compounds **1b-h**, **8b-h** and **12a,b**

Compound	^1H nmr, δ (ppm) (Deuteriodimethyl Sulfoxide)	^{13}H nmr, δ (ppm) (Deuteriodimethyl Sulfoxide)
1b [a]	2.69 (s, 3H); 2.76 (s, 3H); 7.25-7.71 (m, 7H); 8.06-8.13 (m, 2H)	11.7, 118.3, 127.1, 127.2, 127.4, 129.2, 129.7, 131.1, 144.8
1c [a]	2.73 (s, 6H); 7.26-7.53 (m, 5H); 7.96-8.10 (m, 4H)	11.9, 116.3, 118.3, 118.5, 127.0, 127.1, 129.3, 130.3, 135.1, 138.6, 139.6, 140.4, 144.8, 145.2
1d [a]	2.73 (s, 6H); 7.26-7.53 (m, 5H); 8.01-8.11 (m, 4H)	11.8, 118.4, 119.5, 127.1, 129.2, 129.3, 132.6, 138.2, 138.7, 139.3, 139.6, 144.7, 145.0
1e [a]	2.75 (s, 3H); 2.78 (s, 3H); 7.26-7.55 (m, 3H); 8.08-8.41 (m, 6H)	11.9, 12.0, 118.4, 121.3, 123.6, 127.3, 129.3, 130.3, 138.3, 139.5, 140.2, 144.9, 148.0
1f [a]	2.70 (s, 3H); 2.76 (s, 3H); 7.26-7.79 (m, 7H); 8.08-8.12 (m, 2H)	11.8, 118.2, 118.4, 127.1, 127.7, 128.1, 129.3, 130.1, 134.3, 139.7
1g [a]	2.73 (s, 6H); 7.26-7.52 (m, 5H); 8.00-8.10 (m, 3H); 8.25 (t, J = 2 Hz, 1H)	11.9, 116.8, 118.3, 121.3, 122.9, 127.1, 129.2, 129.9, 130.6, 138.6, 139.5, 139.8, 140.5, 144.8, 145.2
1h	2.22 (s, 3H); 2.25 (s, 3H); 7.21-7.61 (m, 7H); 7.94-8.01 (m, 2H)	10.1, 10.9, 114.0, 117.3, 126.7, 129.2, 131.0, 138.6, 139.6, 139.9, 144.0, 145.1, 147.8, 148.4
8b [a]	2.26 (s, 3H); 2.34 (s, 3H); 6.70-6.78 (m, 1H); 6.98-7.08 (m, 2H); 7.21-7.50 (m, 4H); 8.06-8.10 (m, 2H)	10.0, 11.1, 114.3, 117.8, 118.6, 118.8, 120.9, 127.2, 128.0, 129.2, 129.3, 138.4, 139.7, 140.8, 145.6, 150.6
8c	2.28 (s, 3H); 2.31 (s, 3H); 6.71-7.16 (m, 4H); 7.37-7.62 (m, 3H); 8.02-8.06 (m, 2H); 9.78 (s, 1H); 9.87 (s, 1H)	10.7, 11.4, 111.4, 112.3, 118.0, 119.0, 127.3, 129.7, 130.5, 133.7, 139.3, 140.2, 140.8, 145.0, 146.8, 149.0
8d	2.26 (s, 3H); 2.30 (s, 3H); 6.92 (d, J = 8.8, 2H); 7.14 (d, J = 8.8 Hz, 2H); 7.40 (m, 1H); 7.57 (d, J = 7.8 Hz, 2H); 8.03 (d, J = 7.8 Hz, 2H); 9.78 (s, 2H)	10.6, 11.4, 114.1, 117.9, 122.9, 127.2, 128.7, 129.7, 139.2, 140.2, 140.3, 144.2, 144.9, 149.0
8e	2.28 (s, 3H); 2.38 (s, 3H); 7.04 (m, 2H); 7.39-7.46 (m, 1H); 7.59 (m, 2H); 8.03 (d, J = 9.8 Hz, 4H); 9.51 (s, 1H); 10.48, (s, 1H)	10.7, 11.8, 112.0, 117.9, 125.8, 127.3, 129.8, 134.7, 139.1, 139.8, 144.6, 145.0, 148.7, 150.7
8f	2.26 (s, 3H); 2.35 (s, 3H); 6.70-7.13 (m, 3H); 7.36-7.61 (m, 4H); 8.03 (m, 2H); 8.35 (s, 1H); 9.55 (s, 1H)	10.7, 10.8, 107.8, 114.4, 117.9, 121.6, 127.3, 128.6, 129.7, 132.5, 139.1, 139.8, 141.5, 143.7, 145.0, 148.6
8g	2.26 (s, 3H); 2.30 (s, 3H); 6.83-7.10 (m, 4H); 7.37-7.61 (m, 3H); 8.03 (m, 2H); 9.72 (s, 1H); 9.89 (s, 1H)	10.8, 11.4, 111.8, 115.3, 118.0, 121.8, 122.2, 127.3, 129.8, 130.8, 135.1, 139.2, 140.2, 145.0, 146.9, 148.9
8h	2.22 (s, 3H); 2.26 (s, 3H); 6.83 (d, J = 8.8 Hz, 2H); 7.22 (d, J = 8.8 Hz, 2H); 7.37 (m, 1H); 7.54 (m, 2H); 7.99 (d, J = 8.8 Hz, 2H); 9.73 (s, 1H); 9.75 (s, 1H)	10.7, 11.5, 114.6, 117.9, 127.2, 129.7, 131.6, 134.6, 139.2, 140.2, 140.4, 144.5, 144.7, 148.9
12a	2.22 (s, 3H), 2.27 (s, 3H); 6.92-7.12 (m, 2H); 7.41-7.79 (m, 5H); 8.02-8.15 (m, 2H); 9.75 (s, 1H)	10.4, 10.9, 111.4, 112.6, 118.6, 118.9, 123.0, 125.2, 128.8, 130.9, 134.6, 138.9, 143.0, 146.5, 148.9, 155.1
12b	2.24 (s, 3H), 2.30 (s, 3H); 6.94-7.22 (m, 3H); 7.44-7.73 (m, 4H); 8.11 (m, 2H); 9.75 (s, 1H)	11.0, 11.9, 113.1, 118.6, 118.9, 123.0, 125.2, 128.8, 130.9, 138.9, 143.0, 146.5, 148.0, 155.1

[a] Spectra in deuteriochloroform.

Scheme 2



EXPERIMENTAL

Melting points were taken on a Buchi-Tottoli capillary apparatus and are uncorrected. Reaction courses and product mixtures were routinely monitored by thin-layer chromatography (tlc) on silica gel precoated F254 Merck plates. Infrared spectra (ir) were performed in potassium bromide and measured on a Perkin Elmer 1720 instrument. ^1H and ^{13}C nmr spectra were determined for solution in deuteriochloroform, unless otherwise specified, with a Bruker AC-200 spectrometer (tetramethylsilane as internal standard). All drying operations were performed over anhydrous magnesium sulfate.

1-[2-(3-Chlorophenyl)-5-methyl-2*H*-1,2,3-triazol-4-yl]-2-propanone (**10a**).

The hydrazone **9a** (1g, 4 mmoles) was introduced on the bottom of a test tube plunged in a sylicon oil bath, warmed to fusion and, cautiously, the temperature left to rise at about 240° C. As soon as generation of gas was evident, the test tube was taken away from the oil bath; the reaction went to completion in a few moments. The solid formed after cooling was taken up with boiling ethanol, refluxed with charcoal and then filtered. From the ethanolic solution a solid crystallized, 750 mg, yield 75%; mp 75°-76° C; ^1H nmr: δ 2.26 (s, 3H); 2.30 (s, 3H); 3.82 (s, 2H); 7.23-7.39 (m, 2H); 7.85-7.90 (m, 1H); 8.01 (m, 1H); ^{13}C nmr: δ 10.0, 29.4, 40.2, 116.2, 118.5, 126.8, 130.2, 135.0, 140.4, 141.6, 145.1, 203.6; ir: 1715, 1594, 1514.

Anal. Calcd. for $C_{12}H_{12}ClN_3O$: C, 57.72; H, 4.84; N, 16.83. Found: C, 57.67; H, 4.80; N, 16.79.

1-[2-(4-Nitrophenyl)-5-methyl-2*H*-1,2,3-triazol-4-yl]-2-propanone (**10b**).

Prepared as described for **10a**. Yield 78%; mp 153°-154° C; ^1H nmr: δ 2.31 (s, 3H); 2.33 (s, 3H); 3.89 (s, 2H); 8.08-8.11 (d, J = 8 Hz, 2H); 8.26-8.30 (d, J = 8 Hz, 2H); ^{13}C nmr: δ 10.0, 29.6, 39.9, 118.0, 125.0, 143.2, 143.4, 145.6, 146.7, 203.8; ir: 1720, 1590.

Anal. Calcd. for $C_{12}H_{12}N_4O_3$: C, 55.38; H, 4.65; N, 21.53. Found: C, 55.42; H, 4.66; N, 21.46.

1-Hydroxyimino-1-(2-phenyl-5-methyl-2*H*-1,2,3-triazol-4-yl)-2-propanone (**7**).

A solution of **6** (4 g, 18.6 mmoles) in 20 ml of absolute ethanol was added to a solution of sodium (0.5 g, 21.7 mmoles) in 20 ml of absolute ethanol. After cooling, isoamyl nitrite (3.7 ml, 27.8 mmoles) was added, and the mixture was stirred under cooling for 6 hours. The mixture was diluted with water (about 80 ml) and washed with diethyl ether; the water phase was acidified with diluted hydrochloric acid and extracted with diethyl ether. The organic layers were washed with a small amount of water, dried and evaporated. The residue was recrystallized from benzene: yield 3.0 g, (65%); mp 119°-120° C; ^1H nmr: δ 2.27 (s, 3H); 2.51 (s, 3H); 7.25-7.46 (m, 3H); 7.95-7.99 (m, 2H); 10.47 (s, 1H); ^{13}C (deuteriodimethyl sulfoxide) nmr: δ 10.6, 25.8, 118.1, 127.6, 129.7, 137.2, 138.9, 145.6, 149.3, 195.2; ir: 3283, 1677, 1600, 1507, 1462.

Anal. Calcd. for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94. Found: C, 58.91; H, 4.97; N, 22.88.

1-[2-(3-Chlorophenyl)-5-methyl-2*H*-1,2,3-triazol-4-yl]-1-hydroxyimino-2-propanone (**11a**).

Prepared as described for **7**. Yield 50%; mp 136°-137° C; ^1H nmr: δ 2.25 (s, 3H); 2.56 (s, 3H); 7.37-7.68 (m, 2H); 7.86-8.06 (m, 2H); 13.33 (s, 1H); ^{13}C nmr: δ 10.1, 25.3, 116.1, 117.2, 126.8, 130.9, 133.6, 137.4, 139.3, 145.7, 147.6, 195.8; ir: 3270, 1680, 1600, 1500.

Anal. Calcd. for $C_{12}H_{11}ClN_4O_2$: C, 51.72; H, 3.98; N, 20.1. Found: C, 51.66; H, 4.01; N, 20.03.

1-Hydroxyimino-1-[2-(4-nitrophenyl)-5-methyl-2*H*-1,2,3-triazol-4-yl]-2-propanone (**11b**).

Prepared as described for **7**. Yield 50%; mp 181°-182° C; ^1H nmr: δ 2.27 (s, 3H); 2.57 (s, 3H); 8.15 (d, J = 8.5, 2H); 8.38 (d, J = 8.5, 2H); 13.44 (s, 1H); ^{13}C nmr: δ 10.1, 25.2, 118.0, 125.0, 138.6, 142.2, 145.3, 146.9, 147.3, 196.8; ir: 3283, 1675, 1605, 1500.

Anal. Calcd. for $C_{12}H_{11}N_5O_4$: C, 49.83; H, 3.83; N, 24.21. Found: C, 49.72; H, 3.85; N, 24.19.

Genaral Procedure for the Preparation 1-Hydroxyimino-1-(5-methyl-2-phenyl-1,2,3-triazol-4-yl)-2-propanone Arylhydrazones (**8a-h**) and 1-(2-Aryl-5-methyl-1,2,3-triazol-4-yl)-1-hydroxyimino-2-propanone Phenylhydrazones (**12a,b**).

To a solution of **7** or **11a,b** was added (2.5 mmoles) in ethanol (10 ml) of the appropriate arylhydrazine (2.5 mmoles) together with magnesium carbonate (0.5 g) and the reaction mixture was refluxed for 1 hour, then filtered, and allowed to crystallize. The pure compounds were obtained after recrystallization from ethanol.

General Procedure for the Preparation of 2-Aryl-5,5'-dimethyl-2'-phenyl-4,4'-bi-1,2,3-triazoles (**1a-h**).

The appropriate arylhydrazones **8a-h** (18 mmoles) were suspended in 60 ml of dry chloroform and phosphorus pentachloride (4.5 g, 22 mmoles) was added to the mixture portionwise and with stirring at room temperature for 1 hour. The solution was cautiously diluted with water (30 ml). The organic layer was separated and diluted with 40 ml of ethanol. The solution was then evaporated, and desired compounds **1a-h** were crystallized from ethanol.

1-(2-Phenyl-5-methyl-2*H*-1,2,3-triazol-4-yl)-1,2-propanedione (**14**).

To a solution of **7** (730 mg, 3 mmoles) in ethanol (10 ml), 4 ml of concentrated hydrochloric acid and 3 ml of water were added. The solution was refluxed for 2 hours, then diluted with water and extracted with diethyl ether. Compound **14** was obtained after evaporation of the organic layer and chromatographic purification of the residue. Yield 380 mg (55%); mp 167°-168° C; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 2.54 (s, 3H); 3.36 (s, 3H); 7.42-7.62 (m, 3H); 7.92-8.02 (m, 2H); ^{13}C nmr: δ 9.7, 12.2, 120.0, 128.5, 129.2, 139.3, 142.7, 150.2, 156.2, 183.3; ir: 1650, 1510.

Anal. Calcd. for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33. Found: C, 62.99; H, 4.83; N, 18.28.

1-(2-Phenyl-5-methyl-2*H*-1,2,3-triazol-4-yl)-1,2-dihydroxyiminopropane (**15**).

To a solution of **7** (975 mg, 4 mmoles) in ethanol (20 ml), hydroxylamine hydrochloride (2 g, 2.8 mmoles) and a solution of sodium carbonate (1.5 g) in 5 ml of water were added. The mixture was warmed at 100° C for a few minutes and then allowed to cool. The dioxime crystallized as white needles which were recrystallized from ethanol to give 890 mg (yield 86 %) of the desired **15**; mp 232°-234° C; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 2.15 (s, 3H); 2.22 (s, 3H); 7.33-7.56 (m, 3H); 7.39-7.98 (m, 2H); 11.68 (s, 1H); 12.14 (s, 1H); ^{13}C nmr: δ 10.0, 10.4, 117.9, 127.4, 129.7, 139.1, 139.9, 144.8, 147.4, 153.2; ir: 3172, 1594, 1510.

Anal. Calcd. for $C_{12}H_{13}N_5O_2$: C, 55.59; H, 5.05; N, 27.01. Found: C, 55.48; H, 5.06; N, 26.97.

General Procedure for the Preparation of the Quinoxaline Derivatives **2a-c**.

To a solution of compound **7**, **11a**, **11b**, **14** or **15** (6 mmoles) in 50 ml of methanol containing 2 ml of concentrated hydrochloric acid, 1,2-phenylenediamine (650 mg, 6 mmoles) was added and the reaction mixture was refluxed for 60 hours, then evaporated, and purified by chromatography.

Synthesis from **7** afforded a side-product (about 10% yield) that was identified as 5-methyl-2-phenyl-1,2,3-triazole-4-carbonitrile **13**: mp 113°-114° C; ^{1}H nmr: δ 2.54 (s, 3H); 7.42-7.55 (m, 3H); 8.02-8.07 (m, 2H); ^{13}C nmr: δ 10.4, 111.6, 119.2, 121.9, 128.9, 129.5, 138.9, 150.4; ir: 2245, 1595, 1508.

Anal. Calcd. for $C_{10}H_8N_4$: C, 65.21; H, 4.38; N, 30.42. Found: C, 65.14; H, 4.38; N, 30.34.

2-(2-Phenyl-5-methyl-2*H*-1,2,3-triazol-4-yl)-3-methylquinoxaline (**2a**).

Yield (from **7**) 62%; mp 184°-186° C; ^{1}H nmr: δ 2.75 (s, 3H); 3.08 (s, 3H); 7.26-7.37 (m, 1H); 7.44-7.52 (m, 2H); 7.64-7.76 (m, 2H); 8.00-8.13 (m, 4H); ^{13}C nmr: δ 12.4, 25.2, 118.5, 127.3, 128.3, 129.0, 129.1, 129.3, 139.6, 140.4, 140.7, 144.2, 145.7, 147.3, 153.4, 178.1; ir: 1590, 1420, 1290, 975, 750, 715.

Anal. Calcd. for $C_{18}H_{15}N_5$: C, 71.74; H, 5.02; N, 23.24. Found: C, 71.59; H, 5.04; N, 23.28.

Yield of **2a** from **14** was about 15% less than the one obtained from **7**; yield from **15** was higher (70%).

3-Methyl 2-[2-(3-Chlorophenyl)-5-methyl-2*H*-1,2,3-triazol-4-yl]quinoxaline (**2b**).

Yield 48%; mp 194°-195° C; ^{1}H nmr: δ 2.75 (s, 3H); 3.09 (s, 3H); 7.26-7.47 (m, 2H); 7.68-7.81 (m, 2H); 7.99-8.10 (m, 4H); ^{13}C nmr: δ 12.4, 25.2, 116.6, 118.8, 127.3, 128.4, 129.0, 129.3, 130.2, 130.4, 135.2, 140.4, 140.8, 144.7, 145.4, 147.8, 153.3, 177.8; ir: 1594, 1460, 1375, 978, 905, 750, 722.

Anal. Calcd. for $C_{18}H_{14}ClN_5$: C, 64.38; H, 4.20; N, 20.86. Found: C, 64.55; H, 4.19; N, 20.80.

2-[2-(4-Nitrophenyl)-5-methyl-2*H*-1,2,3-triazol-4-yl]-3-methylquinoxaline (**2c**).

Yield 48%; mp 265°-267° C; ^{1}H nmr: δ 2.72 (s, 3H); 3.12 (s, 3H); 7.19-7.42 (m, 2H); 7.75-7.90 (m, 2H); 8.05-8.24 (m, 4H); ^{13}C nmr: δ 11.6, 24.7, 41.6, 116.8, 119.2, 127.5, 128.6, 129.8, 130.1, 130.2, 130.8, 136.1, 140.4, 140.9, 145.0, 145.4, 147.2, 155.5, 178.3; ir: 1605, 1450, 1370, 984, 745.

Anal. Calcd. for $C_{18}H_{14}N_6O_2$: C, 62.42; H, 4.07; N, 24.26. Found: C, 62.29; H, 4.09; N, 24.21.

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