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Facile Syntheses of Bi-1,2,4-triazoles via Hydrazonyl Halides

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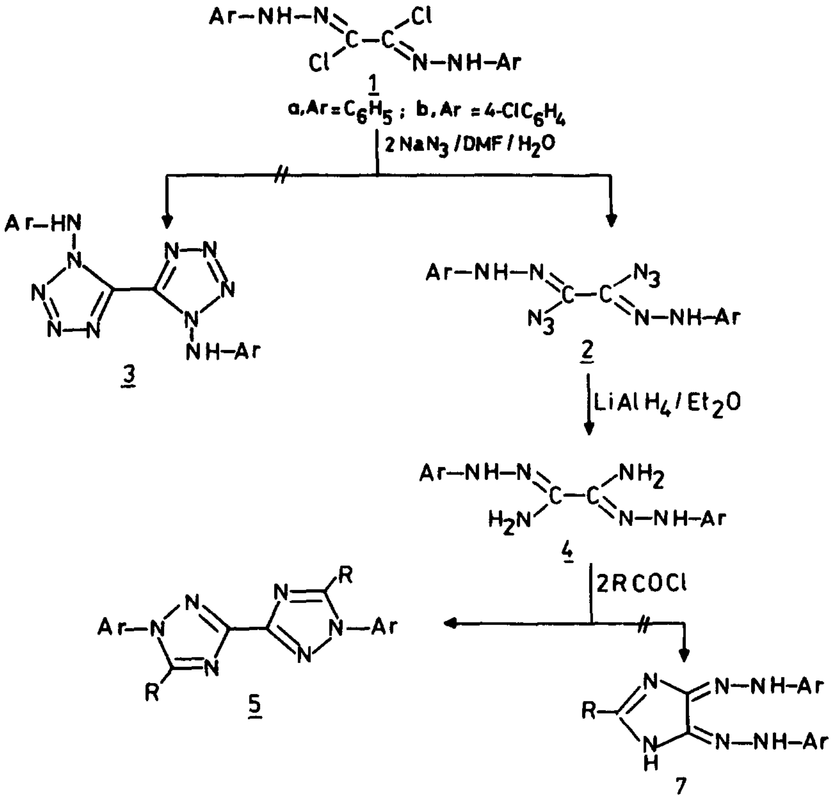
Abstract : *Reaction of oxalodihydrazonyl dihalides **1** with sodium azide afforded the corresponding di-azides **2**. Reduction of the latter with $LiAlH_4$ yielded the diamidrazones **4** which react with acyl halides to give the bi-1,2,4-triazoles **5**. The latter products were alternatively prepared by reaction of **2** with triphenylphosphine to give the phosphinimines **6** followed by treatment of the latter with acyl halides*

In continuation of our recent work on the use of hydrazonyl halides for synthesis of 3,5-bipyrazoline derivatives[1] , we report herein two facile routes for some bi-1,2,4-triazoles starting from oxalodihydrazonyl dihalides **1** . The chemistry of the latter has been rarely studied[2,3] although they have been known more than sixty years ago[4] .

Treatment of **1a,b** with sodium azide in aqueous dimethylformamide at room temperature afforded the corresponding N,N'-diaryloxalodihydrazonyl di-azides **2a,b** respectively in 80-85% yield (Scheme 1). The infrared spectra of the latter di-azides were characterized, in each case, by a strong azide absorption band at 2136 cm^{-1}. This finding excludes the isomeric bitetrazole structure **3** for the products isolated[5,6] . The structure of **2** was further evidenced by its chemical reduction to **4** (Scheme 1) .

Thus, when **2a,b** were treated with lithium aluminum hydride in ether, they yielded the di-amidrazones **4a,b** respectively in almost quantitative yield. The infrared spectra of **4** exhibited characteristic NH_2 bands in the region 3100 - 3480 cm^{-1}. Their ^{1}H-NMR spectra showed in each case, two broad signals in the regions δ 5.4 - 5.7 (s, 4H, 2 NH_2) and δ 8.2 - 8.35 (s, 2H, 2 NH Ar) ppm.



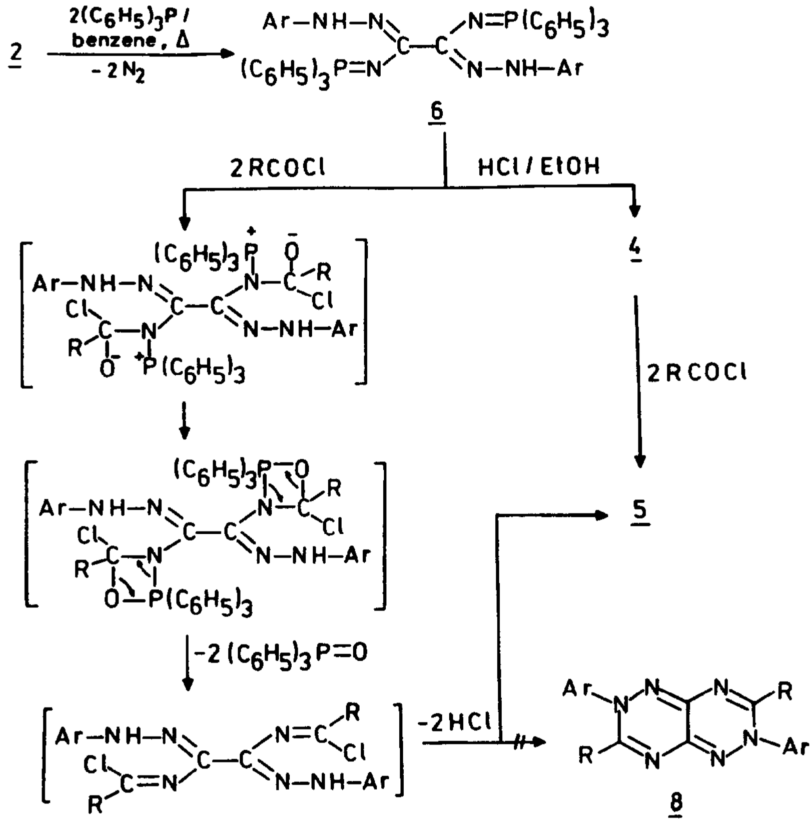
5	R / Ar
a	C_6H_5 / C_6H_5
b	4-$CH_3C_6H_4$ / C_6H_5
c	4-ClC_6H_4 / C_6H_5
d	3-$NO_2C_6H_4$ / C_6H_5
e	CH_2Cl / C_6H_5

	R / Ar
f	C_6H_5 / 4-ClC_6H_4
g	4-$CH_3C_6H_4$ / 4-ClC_6H_4
h	4-Cl C_6H_4 / 4-ClC_6H_4
i	3-$NO_2C_6H_4$ / 4-ClC_6H_4
j	CH_2Cl / 4-ClC_6H_4

Scheme 1

Reactions of 4 with acyl chlorides, in refluxing benzene gave products which were assigned the bi- 1,2,4-triazole structure 5. The other two possible isomeric structures 7 (Scheme 1) and 8 (Scheme 2) were discarded on the basis of the following findings. Unlike the related bis-1,2-diarylhydrazones[3], the isolated products were not susceptible to oxidation. The mass spectrum of 5a taken as a typical example of the series prepared, showed in addition to the molecular ion peak (m/e = 440), a peak at m/e = 220 corresponding to 1,5 - diphenyl - 1,2,4 - triazolyl radical cation fragment. The structural assignment of the isolated products 5 was further substantiated by their alternative synthesis outlined below(Scheme 2).

The diazides **2** reacted with triphenylophosphine in refluxing benzene to give the bis-phosphinimines **6** in fairly good yield (Scheme 2). The structures of the latter were consistent with their spectral data. For example, their IR spectra revealed the absence of the azide absorption band and the appearance of P = N band [7,8] in the region 1200 - 1300 cm^{-1}, and their ^{1}H- NMR spectra showed a singlet signal at δ 8.32 ppm due to NH proton resonance.



2,4,6	a	b
Ar	C_6H_5	4-ClC_6H_4

Scheme 2

The structure of **6** for the isolated products was further evidenced by their chemical transformations. Thus, hydrolysis of **6** in aqueous hydrochloric acid in ethanol gave the di-amidrazone **4** identical with that obtained above from reduction of **2** with lithium aluminum hydride. Futhermore, treatment of **6** with an excess of acyl chloride in refluxing benzene afforded products whose chemical analyses are compatible with either **5** or **8** . Structure **8** was discarded on the basis that the isolated products were found to be identical in all respects with the products **5** obtained above from acyl chlorides and the corresponding di-amidrazone **4** in refluxing benzene (Scheme 1) .

EXPERIMENTAL

Melting points were measured on Gallenkamp melting point apparatus and are uncorrected. The infrared spectra were recorded on Perkin-Elmer 1430 spectrometer. The ^{1}H-NMR spectra were recorded in deuterated chloroform on Varian T-60 NMR spectrometer using tetramethyl silane as an internal reference. Mass spectra were recorded on GCMS-QP 1000 Ex spectrometer. Elemental analyses were carried out at microanalytical laboratory, University of Cairo, Giza, Egypt.

N,N` -Diaryloxalodihydrazonyl diazides 2 .

To a stirred suspension of the appropriate dihydrazonyl dihalide **1** [2,10] (5 mmol) in dimethylformamide (30 ml), a solution of sodium azide (1.3g, 20 mmol) in water (20 ml) was added. The mixture was stirred at room temperature for 10h. The reddish-brown solid that precipitated was filtered, washed with water, dried and finally crystallized from benzene or dioxane/water. The azido products **2a,b** were obtained in 80-85% yield and their physical constants are given below :

2a : Yield (80%) ; mp. 121°C (decomp.) (benzene), IR (KBr) υ 3342 (NH), 2136 (N_3), 1593 (C=N) cm^{-1}. (Calcd. for $C_{14}H_{12}N_{10}$: C, 52.48; H, 3.15 ; N, 43.72. Found : C, 52.2; H, 3.1; N, 43.3).

2b : Yiels (85%) ; mp. 124°C (decomp.) (dioxane/water) ; IR (KBr) υ 3341 (NH), 2133 (N_3), 1601 (C=N) cm^{-1} ; (Calcd. for $C_{14}H_{10}Cl_2N_{10}$: C, 43.19; H, 2.59 ; N, 35.98 ; Cl, 18.22 . Found : C, 43.2 ; H, 2.8 ; N, 35.6; Cl, 18.0).

1,2-Bis(triphenylphosphinimino) glyoxal bis(arylhydrazones) 6 .

A mixture of diazido derivatives **2a,b** (2 mmol) and triphenylphosphine (1.2g, 4.5 mmol) in dry benzene (20 ml) was refluxed for 2-3h where a yellow precipitate was formed. The reaction mixture was cooled and the yellow product was collected, washed with ethanol, dried and finally crystallized from dioxane or chloroform. The bis-phosphinimine products **6a,b** were obtained in 70-75% yield and their physical constants are given below :

6a : Yield (75%) ; mp. 249-50°C (dioxane/water) ; IR (KBr) υ 3306 (NH), 1601 (C=N), 1320 (P=N) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 8.32 (s,2H, 2NH), 7.35-7.72 (m, 40 H, Ar-H)ppm. (Calcd. for $C_{50}H_{42}N_6P_2$: C,76.12; H, 5.37 ; N, 10.65. Found : C, 76.3; H, 5.5 ; N, 10.4).

6b: Yield (70%) ; mp. 223-25°C (chloroform) ; IR (KBr) υ 3308 (NH), 1599 (C=N) , 1312 (P=N) cm^{-1} ; (Calcd. for $C_{50}H_{40}Cl_2N_6P_2$: C, 70.0; H, 4.70 ; N, 9.79 ; Cl, 8.26. Found : C, 70.2 ; H, 4.8 ; N, 9.5 ; Cl,8.1) .

N^1, $N^{1`}$-Diaryloxaldiamidrazones 4.

Method A :

To a stirred suspension of the appropriate bis-azidohydrazone **2a,b** (5 mmol) in dry ether (50 ml), lithium aluminum hydride (0.6g, 15 mmol) in dry ether (20 ml) was added portionwise with constant stirring. After the addition was completed, the mixture was refluxed for 4h on a water bath. The reaction mixture was then cooled in ice-bath and then water (100 ml) was added with shaking. The precipitated inorganic solid was filtered off, and the ethereal layer was separated and dried over anhydrous sodium sulphate. Ether was then evaporated and the residue was triturated with ethanol where it solidified. The crude solid product was collected, dried and crystallized from ethanol to afford compounds **4** a,b in 65-72% yield.

4a : Yield (72%) ; mp. 223-24°C (ethanol) (lit.[9]: 225°C) ; IR (KBr) υ 3395, 3307 (NH_2) 3233 (NH), 1602 (C=N) cm^{-1}; ^1H-NMR ($CDCl_3$) δ 5.69 (s. 4H, $2NH_2$) , 8.38 (s,2H, 2NH), 7.07-7.23 (m, 10H, ArH). (Calcd. for $C_{14}H_{16}N_6$: C, 62.66 ; H, 6.01; N, 31.32 . Found : C, 62.9 ; H, 5.9 ; N, 31.0) .

4b : Yield (65%) ; mp.225-26°C (ethanol); IR (KBr) υ 3403, 3319 (NH_2) 3236 (NH), 1599 (C=N) cm^{-1}; (Calcd. for $C_{14}H_{14}Cl_2N_6$: C, 49.86 ; H, 4.18 ; N, 24.92 ; Cl, 20.03 . Found : C, 49.8 ; H,4.0 ; N,24.6 Cl, 19.8) .

Method B :

A suspension of the appropriate bis-phosphinimine derivatives **6a,b** (2 mmol) in a mixture of ethanol (20 ml) and hydrochloric acid (5 N, 10 ml) was refluxed for 10h. The reaction mixture was cooled and the precipitate was collected, washed with dilute sodium hydroxide solution followed by ethanol, dried and crystallized from ethanol to afford **4a,b** in 50-55% yield. Compounds **4a.b** are identical in all respects with those prepared by method A.

3,3'-Bi(1,5-disubstituted-1,2,4-triazoles) 5 .

Route A :

To a suspended solution of bis-phosphinimine **6a,b** (1 mmol) in dry benzene (20 ml) , was added the appropriate acyl chloride (3 mmol). The mixture was refluxed for 24h, then cooled. The solid that precipitated was collected, washed with ethanol, dried and finally crystallized from dioxane to afford white crystals of bitriazole derivatives **5** in 43-95% yield.

5a : Yield (45%) ; m.p. 259-60°C; IR (KBr) υ 1599 (C=N) cm^{-1} ; ^1H-NMR ($CDCl_3$) δ 7.15 - 7.6 (m, 20H, Ar-H); MS, m/e (%) 440 (M^+, 44.9) 337 (34.2) , 220 (6.3), 105 (6.8) , 91 (100), 77 (14.7), 64 (24.2) ; (Calcd. for $C_{28}H_{20}N_6$: C, 76.34 ; H, 4.57 ; N, 19.08 . Found : C, 76.4 ; H, 4.9 ; N, 18.9) .

5b : Yield (50%) ; m.p. 262°C ; IR (KBr) υ 1597 (C=N) cm^{-1} ; ^1H-NMR ($CDCl_3$) δ 2.35 (s. 6H, 2 CH_3Ar), 7.1-7.6 (m, 18H, ArH) ; (Calcd for $C_{30}H_{24}N_6$:C, 76.89 ; H, 6.16 ; N, 17.97 . Found : C, 77.1 ; H, C, 5.1 ; N, 17.8) .

5c : Yield (47%) ; m.p. 279°C; IR (KBr) υ 1600 (C=N) cm^{-1}; (Calcd. for $C_{28}H_{18}Cl_2N_6$: C, 66.02 ; H, 3.56 ; N, 16.5 ; Cl, 13.92. Found : C, 65.8 ; H, 3.6 ; N, 16.7 ; Cl, 13.8) .

5d : Yield (60%) ; m.p. 298-9°C ; IR (KBr) υ 1595 (C=N) cm^{-1}; (Calcd . for $C_{28}H_{18}N_8O_4$: C, 63.39 ; H, 3.42 ; N, 21.12. Found : C, 63.6 ; H, 3.4 ; N, 20.9) .

5e : Yield (43%) ; m.p 228-30°C ; IR (KBr) υ 1599 (C=N) cm^{-1} ; ^1H-NMR ($CDCl_3$) δ 4.7 (s,4 H; $2CH_2Cl$), 7.38-7.68 (m, 10 H, Ar-H) ; (Calcd. for $C_{18}H_{14}Cl_2N_6$: C, 56.11 ; H, 3.66 ; N, 21.82 . Found : C, 56.4 ; H, 3.8 ; N, 21.6) .

5f : Yield (93%) ; m.p. 264-5°C ; IR (KBr) ν 1600 (C=N) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.26-7.54 (m, 18H, ArH) ; (Calcd. for $C_{28}H_{18}Cl_2N_6$: C, 66.02 ; H, 3.56 ; N, 16.5 ; Cl, 13.92 . Found : C, 65.9 ; H, 3.4 ; N, 16.6 ; Cl, 14.1) .

5g : Yield (84%) ; m.p. 310-12°C ; IR (KBr) ν 1597 (C=N) cm^{-1} ; ^{1}H-NMR ($CDCl_3$) δ 2.4 (s, 6H, 2 CH_3-Ar) , 7.21-7.53 (m, 16H, Ar H) ; (Calcd . for $C_{30}H_{22}Cl_2N_6$: C, 67.04 ; H, 4.12 ; N, 15.64 ; Cl, 13.19 . Found : C, 67.3 ; H, 4.2 ; N, 15.4 ; Cl, 13.0) .

5h : Yield (95%) ; m.p. 288-90°C ; IR (KBr) ν1605 (C=N) cm^{-1}; (Calcd. for $C_{28}H_{16}Cl_4N_6$: C, 58.15 ; H, 2.79 ; N, 14.53 ; Cl, 24.52 . Found : C, 57.8 ; H, 3.0 ; N, 14.2 ; Cl, 24.3) .

5i : Yield (95%) ; m.p.329-31°C ; IR (KBr) ν 1595 (C=N) cm^{-1} ; (Calcd. for $C_{28}H_{16}Cl_2N_8O_4$: C, 56.10; H, 2.69 ; N, 18.69 ; Cl, 11.83. Found : C, 56.3 ; H, 2.7 ; N, 18.9 ; Cl, 11.6) .

5j : Yield (70%) ; m.p. 217-19°C ;IR (KBr) ν 1595(C=N) cm^{-1} ; ^{1}H-NMR ($CDCl_3$) δ 4.7 (s,4H, 2 CH_2Cl), 7.45 - 7.71 (m, 8 H , Ar H) ; (Calcd. for $C_{18}H_{12}Cl_4N_6$: C, 47.59 ; H, 2.66 ; N, 18.50 ; Cl, 31.23 . Found : C, 47.4 ; H, 2.7 ; N, 18.2 ; Cl, 31.1) .

Route B :

To a suspension of di-amidrazones **4** (1 mmol) in dry benzene (20 ml), was added the appropriate acyl chloride (3 mmol). The mixture was refluxed for 6h then cooled. The solid that precipitated was collected, dried and finally crystallized from dioxane to afford the bitriazole derivatives **5**. The compounds isolated were identical in all respects with those obtained above from **6** and acyl chlorides .

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