ISSN: 0974 - 7516 Volume 10 Issue 3

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 10(3), 2014 [83-89]

Pyridazine derivatives and related compounds, Part 15: Photochemical study of 3-azido-4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazine

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ABSTRACT

As an extension of our work in the photochemical study of nitrogen heterocyclic compounds such as 3-diazopyrazolopyridazine derivatives and [2+2] photocycloaddtion, in this paper we will studying the photolysis of 3-azidopyrazolopyridazine derivative in different solvents such as Methanol, Ethanol, Toluene, Benzene,…..etc. and reagent as diethyl malonate. The photochemistry of 3-azidopyrazolopyridazine has been investigated. The irradiation of 3-azido-4,5-diphenyl-1H-pyrazolo[3,4-c]pyridazine I in various solvents brings to a photolytic nitrene intermediate, which involve into a ring- opening to give 3-substituted pyridazine derivatives. While the photolysis in toluene and/or anisole the photo attacks reaction of nitrene is faster than the ring opining to give the corresponding 3-anilinopyrazolopyridazine derivatives. The photolysis in the presence of diethyl malonate led to a mixture of three pyridazine derivatives.

KEYWORDS

Azides;
Pyridazines;
Pyrazoles;
Pyrazolopyridazines;
3-Azidopyrazolopyridazine;
Photolysis of azidopyrazoles.

INTRODUCTION

Recently, it has been reported that some pyridazine derivatives display antihypertensive, anticancer, and anti-HIV activities[3-6]. In addition, it is well documented that substituted pyridazines possess antimicrobial, antifungal, and antiviral activities[7-9]. From this view of high biological activity of pyridazine the photochemistry studying of it will be interest. Photolysis of aryl and heteroaryl azides is well documented[10] to give rise to varied group of products, whose identity is influenced by many factors such as reaction medium, substituents, etc. The formation of aryl nitrenes from aryl azides has been studied extensively for the last several decades. Since aryl nitrenes undergo bimolecular reactions they have been used for photo affinity labeling bio-organic molecules and in several industrial processes such as microlithography[11]. Photolysis of azides in methanol, which have a built-in intramolecular triplet sensitizer, yields mainly carbamates Laser flash-photolysis of azide derivatives shows formation of their triplet-excited ketone, which decays by intramolecular energy transfer to form triplet nitrenes[12]. In contrast, Lwowski and coworkers demonstrated that photolysis of carbonazidic acid methyl ester in matrices yields methoxy isocyanate, which reacts further to produce isocyanic acid[13]. It was concluded that the excited state of carbonazidic acid methyl ester, rather than the singlet carbomethoxy nitrene, undergoes a Curtius rearrangement to form the methoxy isocyanate. Similarly, Teles and Maier have

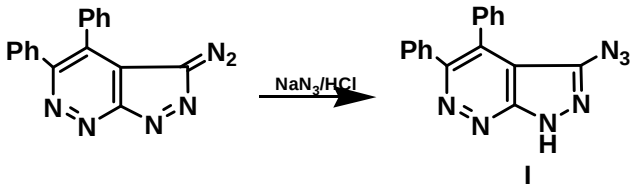
also shown that photolyzing carbonazidic acid methyl ester in matrices yields mainly methoxy isocyanate and a small amount of diazenedicarboxylic acid dimethyl ester, formaldehyde and isocyanic acid[14].

Rodney and coworkers were the first observation the intermolecular triplet sensitization of alkyl azides leads to bimolecular reactivity, by forming triplet alkyl nitrenes. The intermolecular triplet-sensitized photolysis of 1-azidoadamantane with acetone, acetophenone and benzophenone leads to the formation of di-(adamantan-1-yl)-1,2-diazene as the major product via dimerization of triplet adamantan-1-yl nitrene. The triplet alkyl nitrene also abstracts an H-atom from the solvent to form adamantan-1-yl amine, adamantan-1-yl-benzyl amine and adamantan-1-yl benzylidene amine[15]. Generally, accepted pathway includes primary formation of an open-shell singlet nitrene[16] by lose of N_2 followed by intersystem crossing (ISC) to the ground state triplet nitrene and/or cycloaddition to a neighboring C=C double bond in arene system. On the other hand, pyridazine derivatives and heterocyclic annelated pyridazines continue to attract considerable attention for their application in agriculture and in practical for their biological activity for use as potential drugs[17,18]. Only a few reports can be found about the photolysis of aryl azides or alkyl azides and alkoxycarbonyl azides. There are no reports in the photolysis of heterocyclic azides derivatives. So, in this paper we will study the photochemical reaction of 3-azidopyrazolopyridazine derivatives toward different solvents and reagent.

RESULTS AND DISCUSSION

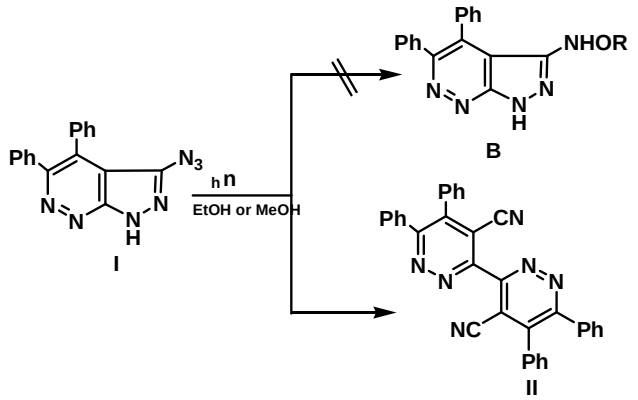
In a previous paper directed towards the synthesis of new pyridazine derivatives[1,2], we presented the photolysis of 3-diazo-4,5-diphenylpyrazolo[3,4-*c*]pyridazine in different reagents[1]. As an extension of our work we present in this paper reports of the photolysis of azido derivative in different reagents. Photolysis at room temperature were carried out with a high-pressure mercury lamp (300 w, λ 320 nm) through Pyrex filter under argon gas.

3-Azido-4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazine I was prepared in 85% yield as a yellow crystals (mp 167 °C) by addition of sodium azide in portion-wise to 3-diazo-4,5-diphenylpyrazolo[3,4-*c*]pyridazine[19] in conc. HCl at room temperature. The processes are quick and are readily carried out in a beaker or open flask. The reaction progress was completed until no diazo compound could be detected by TLC as well as no coupling color with β-naphthol. (Equation 1)



Equation 1

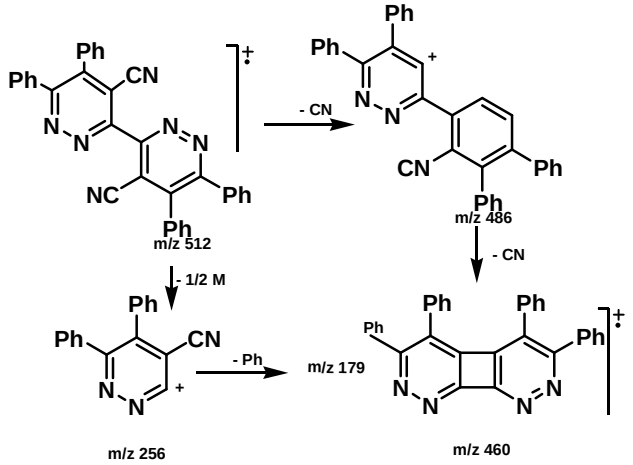
We starting our study by Irradiation of the azido derivative I in methanol and/or ethanol resulted in the formation of 3,3'-bis(4-cyano-5,6-diphenylpyridazine) II in moderate yield not compound B, which confirmed with IR give new strong beak at 2239 cm^{-1} for the new two CN groups and the disappearance for the N_3 group which appear at 2150 cm^{-1}; the ^{1}H-NMR appear new beaks for two new phenyl groups at δ 7.60-7.90 ppm. (cf. exp. section). (Scheme 1)



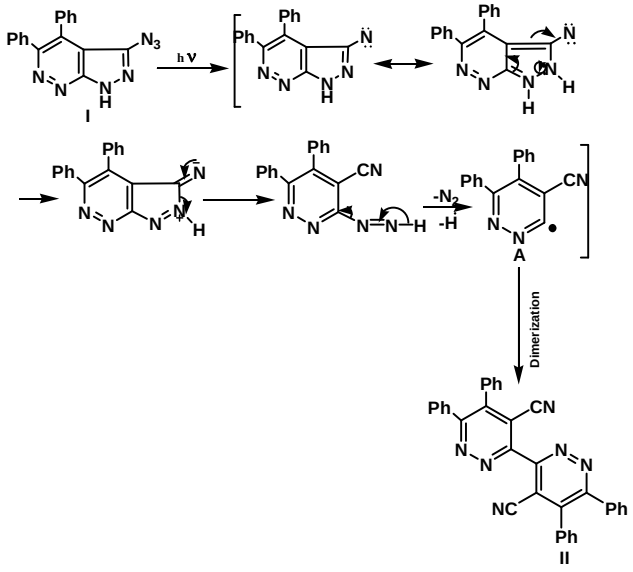
Scheme 1

The mass spectrum exhibited a characteristic 100% molecular ion peak at *m/z* 512 and the fragmentations are outlined as follows:

Mechanism for the transformation of I into II could involve the formation of a singlet nitrene followed by ring opening concerted with nitrogen molecule and hydrogen radical elimination producing the radical species which dimerized to form II (Scheme 3). This means that methanol or ethanol work only as a solvent not reacted with the nitrene and it is a good solvent to make the dimer II.



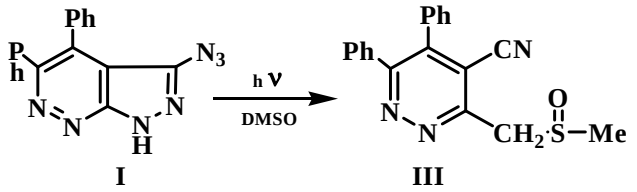
Scheme 2



Scheme 3

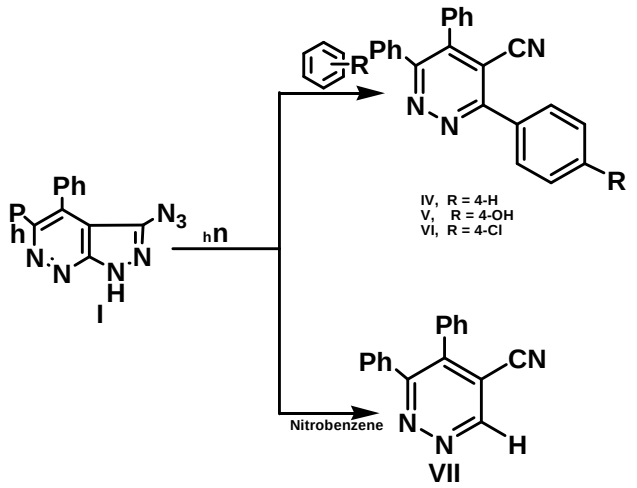
When the irradiation was occurred in dimethyl sulfoxide (DMSO) the reaction take the same mechanism but dimethylsulphoxide is more reactive than Methanol or ethanol and reacted with the radical A to give 3-methanesulfonylmethyl-5,6-diphenylpyridazine-3-carbonitrile III as the major product we can isolated from the reaction mixture which confirmed with IR, new beak at 2218 and 1065 cm^{-1} for the new CN and S=O groups and the ^{1}H-NMR with two new bands at 2.56 and 3.38 ppm for the new CH_3 and CH_2 of the sulfoxid group (cf. exp. section). (Equation 2)

On the other hand, when the irradiation occurred in electron deficient solvents such as benzene, Phenol, chlorobenzene and nitrobenzene we found the reaction also take the same mechanism that in benzene, phenol and chlorobenzene the pyrazole ring is opened in first and



Equation 2

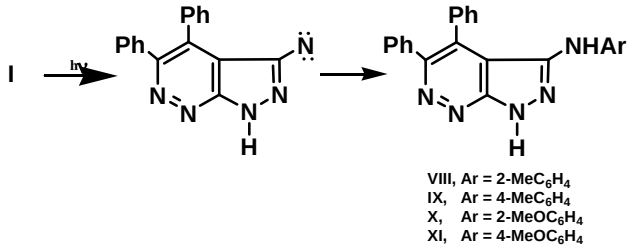
they reacted with the reactive intermediate A to have 4-cyano-3,5,6-triphenylpyridazine IV in 50% yield, 4-cyano-3(*p*-hydroxyphenyl),5,6-triphenylpyridazine V in 89.6% yield, and 4-cyano-3(*p*-chlorophenyl),5,6-triphenylpyridazine VI in 51.2% yield, respectively All this compounds were confirmed by different spectroscopic data such as IR for compound V shows 3454, 3360 cm^{-1} for new OH group and 2234 cm^{-1} for the new CN group and ^{1}H-NMR shows the characteristic beaks 6.80 and 7.5 (d. of d.) with J = 7.0 for the 4H of new phenol ring and 12.99 for the new OH (D_2O exchangeable) of phenol ring (cf. exp. section).. But in nitrobenzene we have 3,4-diphenylpyridazine-5-carbonitrile VII in 68.6% yield, hydrogen in position 6 this is means that the nitrobenzene is a very boor solvent and it is a very unreactive compound it is inhabited also to form the dimer II, ^{1}H-NMR Shows δ 9.7 ppm for the characteristic pyridazine hydrogen-6. (Scheme 4)



Scheme 4

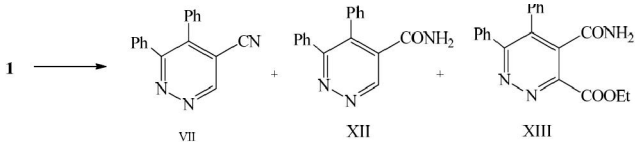
Moreover, the irradiation of 3-azido derivative I in electron reach solvents such as toluene and anisole, we found that the reactivity of these solvents are more and they attached with the nitrine faster than the ring opening give the corresponding nitrile instead gave a mixture of *ortho* and *para* substituted anilino derivatives VIII,

IX, X, and XI, respectively. We separated these compounds by the main chromatographic procedures and crystallized from the proper solvents. Anilino compounds could be explained assuming that the photo attack reaction of the nitrene compound with toluene and anisole is faster than the ring opening to give the corresponding anilino derivatives. These compounds were confirmed with different elemental analysis and spectroscopic data IR for compound VIII shows 3420 cm^{-1} for the new two NH groups, ^{1}H-NMR also shows singlet beak at δ 1.24 ppm for new $-CH_3$, 6.88-7.23 ppm multiple for the new 4H of the toluene ring and two singlet beaks at 9.8 and 12.01 for the two NH groups (D_2O exchangeable), and the Mass spectra shows the ion peak at 377, for the *para* substituted the ^{1}H-NMR shows the characteristic doublet of doublet beak of the toluene or anisole at δ 6.07, 7.05 with J = 9.3 and 6.35, 7.15 with J = 7.5 respectively. (cf. exp. section).



Scheme 5

Lastly, after all the previous study of the photochemical reaction of 3-azidopyrazolopyridazine with different solvents we found that there are two ways depending on the reactivity of the solvents. So, we will test the photolysis of compound I with some reagent such as diethyl malonate we used it as solvent and reactant. The TLC analysis of the crude product shows the presence of three products. These compounds were separated by column chromatography on silica gel (60-120 mesh) by proper solvent led to the isolation of 3,4-diphenylpyridazine-5-carbonitrile VII in 10.8% yield. The carboxamides XII, XIII were also obtained in 34.3% and 37.8% yields, respectively. This means that the ring opening is faster than the reaction of diethyl malonate with the nitrine. The structures were confirmed with different spectroscopic data and elemental analysis IR for compound XIII shows 3313 cm^{-1} for NH_2 group, two beaks at 1739, and 1660 cm^{-1} for the two carboxylic groups, and ^{1}H-NMR shows quartet and triplet beaks at δ 4.05, and 1.2 ppm for $-CH_2-CH_3$ of ester group and 6.51 ppm for the NH_2 group, D_2O exchangeable (cf. exp. section).



Scheme 6

The photoreaction of 3-azido derivative I with a variety of reagents proceeds smoothly to yield substituted 4-cyanopyridazine, substituted aminopyrazolopyridazine and/or pyridazine-carboxamide derivatives, depending on the nature of the reagent, the photoreaction described here would be an efficient and novel method for their synthesis.

EXPERIMENTAL

Melting points were determined on a Büchi 510 apparatus and are reported uncorrected. IR spectra were recorded as potassium bromide disks on a Perkin-Elmer 383 spectrophotometer. ^{1}H-NMR spectra were obtained on a Bruker Ac 200 F instrument. Mass spectra were obtained at 70 eV by using a AEI MS 30 mass spectrometer. Elemental analysis (C, H, N) were carried out using a Perkin-Elmer 240C Microanalyzer the Microanalytical Laboratory-Cairo University. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using U.V. light (254 and 366 nm). The photoreactions were carried out in a Pyrex immersion apparatus equipped with 300 w high-pressure mercury lamps at room temperature. Commercially available reagents and solvents were usually reagent grade and distilled or recrystallized prior to use.

3-Azido-4,5-diphenyl-1*H*-pyrazolo[3,4-c]pyridazine (I)

To a solution of 3-diazo derivative (0.6 g, 2 mmol) in conc. hydrochloric acid (5 mL), sodium azide (0.4 g, 6 mmol) was added in portion-wise at room temperature with stirring. A yellow deposit product was separated, filtered and recrystallized from benzene (0.54 g, 85%), m.p. 167 °C. IR: (KBr), ν cm^{-1}; 3150 (NH), 2150 (N_3), 1650 (C=N) and 1520 (C=C); ^{1}H-NMR

(DMSO-d_6, TMS): □ ppm 7.10-7.60 (m, 10H, 2Ph); 14.5 (s, 1H, NH) and. Anal. Calcd for $C_{17}H_{11}N_7$: C, 65.16%; H, 3.54%; N, 31.29%. Found: C, 65.00%; H, 3.40%; N, 31.20%.

General procedure for photochemical reactions

A sample of compound I in the appropriate anhydrous solvent was irradiated in a Pyrex immersion apparatus equipped with (300 w, □ 320 nm) high-pressure mercury lamps at room temperature and under argon gas until disappearance of the starting material. After removing the solvent under reduced pressure, the residue was recrystallized.

3,3'-Bis(4-cyano-5,6-diphenylpyridazine) (II)

Irradiation of compound I (0.5 g, 1.6 mmol) in methanol (250 mL) for 40 h the solvent was evaporated to half under reduced pressure to have, Pale yellow crystals (0.2 g, 24.4%), m.p. 298-299 °C (crystalized from methanol). IR: (KBr), ν cm^{-1}; 3085 (C-H, aromatic), 2239 (C≡N), 1630 (C=N), and 1442, 1338, 1258, 1120; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 6.91 – 7.46 (m, 10H, 2Ph), 7.60-7.90 (m, 10H, 2Ph); MS *m/z*: 512 (M^+, 100%), 435 (M^+ - Ph, 9.5% ion A), 409 (ion A – CN, 10.1%), 256 (½ M^+, 10.1%), and 178 (½ M^+-Ph, 97.6%). Anal. Calcd for $C_{34}H_{20}N_6$: C, 79.67%; H, 3.93%; N, 16.39%. Found: C, 79.50%; H, 3.80%; N, 16.20%.

3,3'-Bis(4-cyano-5,6-diphenylpyridazine) (II)

Using the same procedure, irradiation of compound I (0.5 g, 1.6 mmol) in absolute ethanol (250 mL) for 3 h gave the bicyclic product *II* (0.24 g, 30.5%), identical m.p., mixed m.p. and IR spectrum with the aforementioned sample.

3-Methanesulfonylmethyl-5,6-diphenylpyridazine-3-carbonitrile (III)

Irradiation of compound I (0.5 g, 1.6 mmol) in dimethylsulfoxide (250 mL) for 14 h. The reaction mixture was poured into ice water (100 mL), the solid filtered off and recrystallized from ethanol to give (0.3 g, 56.3%), m.p. > 300 °C. IR: (KBr), ν cm^{-1}; 3090 (CH, aromatic), 2920, 2850 (CH, aliphatic), 2218 (C≡N), 1633 (C=N), 1445, 1338 and 1065 (S=O); ^{1}H-NMR (DMSO-d_6, TMS): ? ppm 2.56 (s, 3H, CH_3), 3.38 (s, 2H, CH_2), 7.36 – 7.56 (m, 10H, 2Ph); MS *m/z*: 332 (M^+-1, 6.2%), 331 (M^+-2, 9.9%, ion A), 313 (ion A – H_2O, 6.7%, ion B), 285 (ion B - N_2, 38.0% ion C), 271 (ion C – CH_3, 77.1%), 256 (M^+ - $CH_2S(=O)Me$, 100%). Anal. Calcd for $C_{19}H_{15}N_3OS$: C, 68.44%, 4.54%; N, 12.60%. Found: C, 68.31%; H, 4.40%; N, 12.40%.

4-Cyano-3,5,6-triphenylpyridazine (IV)

Irradiation of compound I (0.5 g, 1.6 mmol) in benzene (250 mL) for 2 h, the solvent was reduced to the hafe under reduced pressure and filter the solid (0.3 g, 51.7%), m.p. 157-158 °C (crystalized from benzene). IR: (KBr), ν cm^{-1}; 3057 (CH, aromatic), 2128 (CN), 1607 (C=N), and 1445, 1358, 1225, 1129; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 6.58 – 7.54 (m, 15H, 3Ph); MS *m/z*: 333 (M^+, 34.3%), 256 (M^+ - Ph, 100%), 179 (M^+ - 2Ph, 70.9%). Anal. Calcd for $C_{23}H_{15}N_3$: C, 82.86%; H, 4.54%; N, 12.60%. Found: C, 82.70%, H, 4.40%; N, 12.50%.

4-Cyano-3-(p-hydroxyphenyl)-5,6-diphenylpyridazine (V)

Irradiation of compound I (0.5 g, 1.6 mmol) in phenol (50 mL) for 60 h. The reaction mixture was evaporated on a steam-bath and the residue was washed with diethyl ether, the solid product was filtered off and recrystallized from benzene to give (0.5 g, 89.6%) of, m.p. 165-166 °C. IR: (KBr), ν cm^{-1}; 3454, 3360 (OH), 3146, 3054 (CH, aromatic), 2229 (CN), 1624 (C=N), 1444, 1382, 1231 cm^{-1}; ^{1}H-NMR (DMSO-d_6, TMS): ? ppm 6.80 (d, J = 7.0, 2H, aromatic), 7.50 (d, J = 7.0, 2H, aromatic), 7.66 – 7.90 (m, 10H, 2Ph), 12.99 (s, 1H, OH, D_2O exchangeable); MS *m/z*: 349 (M^+, 6.2%), 256 (M^+ - C_6H_4OH, 75%). Anal. Calcd for $C_{23}H_{15}N_3O$: C, 79.06%; H, 4.33%; N, 12.04%. Found: C, 78.90%; H, 4.20%; N, 11.90%.

3-(*p*-Chlorophenyl)-4-cyano-5,6-diphenylpyridazine (VI)

Irradiation of compound I (0.5 g,1.6 mmol) in chlorobenzene (150 mL) for 16 h. The reaction mixture was evaporated and the residue was washed with diethyl ether, the solid product was filtered off and recrystallized from benzene to give (0.3 g, 51.2%) of m.p. 191-192 °C. IR: (KBr), ν cm^{-1}; 3010 (CH, aromatic), 2134 (C≡N), 1639 (C=N), 1453, 1206, 1160 and 696 (C-Cl); ^{1}H-NMR (DMSO-d_6, TMS): ? ppm 7.70

(d, J = 6.5, 2H, aromatic), 7.50 (d, J = 6.5, 2H, aromatic), 7.20 – 7.42 (m, 10H, 2Ph); MS *m/z*: 370 (M^{+2},6.1%), 368 (M^+, 11.4%), 256 (M^+-C_6H_4Cl, 13.9%). Anal. Calcd for $C_{23}H_{14}ClN_3$: C, 74.89%; H, 3.83%; N, 11.39%. Found: C, 74. 71%, H, 3.69%; N, 11.20%.

3,4-Diphenylpyridazine-5-carbonitrile (VII)

Irradiation of compound I (0.5 g, 1.6 mmol) in nitrobenzene (150 mL) for 6 h, gave (0.3 g, 68.6%), m.p. 143-144 °C. IR: (KBr), ν cm^{-1}; 3021 (CH, aromatic), 2129 (C≡N), 1605 (C=N), 1443, 1380, 1177; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 7.40 – 7.56 (m, 10H, 2Ph), 9.7 (s, 1H, C-H, pyridazine ring); MS *m/z*: 257 (M^+, 58%), 256 (M^+-H, 100%, ion A), 230 (ion A – CN, 25%). Anal. Calcd for $C_{17}H_{11}N_3$: C, 79.36%; H, 4.31%; N, 16.33%. Found: C, 79.25%; H, 4.20%; N, 16.19%.

3-(*o*-Toluidino)-4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazine (VIII)

Irradiation of compound I (0.5 g,1.6 mmol) in toluene (250 mL) for 3 h. The resulting reaction mixture was concentrated to its third volume, the solid obtained was collected by filtration to give (0.3 g, 49.9%) of, m.p. 141 – 142 °C (toluene). IR: (KBr), ν cm^{-1}; 3420 (NH), 3040 (CH, aromatic) 2922, 2855 (CH, aliphatic), 1609 (C=N), 1580, 1428, 1382 and 753, 701 attributed to the ortho substituted; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 1.24 (s, 3H, CH_3), 6.88 – 7.23 (m, 4H, toluene aromatic protons), 7.39 – 7.64 (m, 10H, 2Ph), 9.8 (s, 1H, NH, D_2O exchangeable), 12.01 (s, 1H, pyrazole NH, D_2O exchangeable), MS *m/z* : 377 (M^+, 43.1%), Anal. Calcd for $C_{24}H_{19}N_5$: C, 76.36%; H, 5.08%; N, 18.56%. Found: C, 76.20%; H, 4.90%; N, 18.40%.

3-(*p*-Toluidino)-4,5-diphenyl-1H-pyrazolo[3,4-c]pyridazine (IX)

The filtrate was evaporated under reduced pressure and the residue was triturated with diethyl ether and methylene chloride (8:2) column chromatography to give (0.15 g, 25%) of, m.p. 228 – 229 °C (from ethanol). IR: (KBr), ν cm^{-1}; 3150 (NH), 3090 (CH, aromatic), 2927 (CH, aliphatic, 1633 (C=N) and 870, 836 for the *para* substituted; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 1.23 (s, 3H, CH_3), 6.07 (d, *J* = 9.2, 2H, toluene protons), 7.05 (d, *J* = 9.3, 2H, toluene protons), 7.55 – 7.95 (m, 10H, 2Ph), 9.76 (s, 1H, NH, D_2O exchangeable), 12.55 (s, 1H, pyrazole NH, D_2O exchangeable); MS *m/z* : 377 (M^+, 9.5%), 376 (M^+ - 1, 10.5%), 286 (M^+ - $C_6H_4CH_3$, 10.1%, ion A), 271 (ion A - NH, 77%, ion B), 256 (ion B - NH, 100%). Anal. Calcd for $C_{24}H_{19}N_5$: C, 76.36%; H, 5.08%; N, 18.56%. Found: C, 76.22%; H, 4.90%; N, 18.41%.

3-(*o*-Anisidino)-4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazine (X)

Irradiation of compound *I* (0.5 g, 1.6 mmol) in anisole (150 mL) for 14 h. The resulting reaction mixture was concentrated to its third volume, the solid obtained was filtered off to give (0.2 g, 30.3%) of, m.p. 134-135 °C (anisole). IR: (KBr), ν cm^{-1}; 3421 (NH), 3059 (CH, aromatic), 2924, 2854 (CH, aliphatic), 1601 (C=N), 1490, 444, 1381 for aromatic system, and 763, 698 attributed to the *ortho* substituted; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 3.32 (s, 3H, -OMe), 6.90-7.29 (m, 4H, anisole protons), 7.33- 7.59 (m, 10H, 2Ph), 9.68 (s, 1H, NH, D_2O exchangeable), 12.01 (s, 1H, pyrazole NH, D_2O exchangeable), MS *m/z*: 393 (M^+, 50.2%), Anal. Calcd for $C_{24}H_{19}N_5O$: C, 73.26%; H, 4.86%; N, 17.81%. Found: C, 73.10%; H, 4.70%; N, 18.70%.

3-(*p*-Anisidino)-4,5-diphenyl-1H-pyrazolo[3,4-c]pyridazine (XI)

The filtrate was evaporated under reduced pressure and the residue was triturated with diethyl ether to give (0.25 g, 38.01%) of, m.p. 271-272 °C (benzene). IR: (KBr), ν cm^{-1}; 3320 (NH), 3054 (CH, aromatic), 2932, 2850 (CH, aliphatic), 1620 (C=N), 1516, 1150 for aromatic system and 890, 870 for the *para* substituted; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 3.75 (s, 3H, OCH_3), 6.35 (d, *J* = 7.6, 2H, anisole protons), 7.15 (d, *J* = 7.5, 2H, anisole protons), 7.25 – 7.40 (m, 10H, 2Ph), 9.37 (s, 1H, NH, D_2O exchangeable), 12.22 (s, 1H, pyrazole NH, D_2O exchangeable); MS *m/z*: 393 (M^+, 30.1%), 362 (M^+ - OMe, 4.0%, ion A), 271 (ion A – NHC_6H_4, 3.0%, ion B), 256 (ion B – NH, 100%). Anal. Calcd for $C_{24}H_{19}N_5O$: C, 73.29%; H, 4.83%; N, 17.81%. Found: C, 73.10%; H, 4.90%; N, 17.70%.

3,4-Diphenylpyridazine-5-carboxamide (XII)

Irradiation of compound I (1.0 g,3.2 mmol) in di-

ethyl malonate (150 mL). After 5 h the reaction mixture was evaporated under reduced pressure. TLC analysis of the crude product showed the presence of three compounds, which was separated through column chromatography (2.0 × 60 cm) on silica gel (60-120 mish) and was eluted with pet-ether 40/60 °C. The material was collected and recrystallized from chloroform to give (0.15 g, 34.3%) of, m.p. 267 – 268 °C. IR: (KBr), ν cm^{-1}; 3310 (NH), 3125, 3061 (CH, aromatic), 1663 (C=O amide), 1567 (C=N), and 1443, 1380, 1200 for the aromatic system; ^{1}H-NMR (DMSO-d_6, TMS): ? ppm *6.92* (s, 2H, NH_2, D_2O exchangeable), 7.35 – 7.55 (m, 10H, 2Ph), 9.74 (s, 1H, H-6 pyridazin ring); MS m/z: 274 (M^+, 26.4%), 273 (M^+-1, 100%), 258 (M^+ - NH_2, 10.1%, ion A), 230 (ion A - C=O, 18.5%). Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.16%; H, 4.76%; N, 15.27%. Found: C, 74.00%; H, 4.60%; N, 15.10%.

3,4-Diphenylpyridazine-5-nitrile (VII)

The second fraction was collected when eluted with pet. Ether 40/60 °C - methylene chloride (8:2) gave (0.09 g, 10.85%) of m.p. 143-144 °C.

Ethyl 4-carboxamido-5,6-diphenylpyridazine-3-carboxylate (XIII)

The third fraction was collected when eluted with methylene chloride-methanol (8:2) gave (0.21 g, 37.1%) of, m.p. 259 – 260 °C. IR: (KBr), ν cm^{-1}; 3427 (NH_2), 3062, 3006 (CH, aromatic), 2931, 2885 (CH, aliphatic), 1739 (C=O ester), 1660 (C=O amide), 1600 (C=N), and 1444, 1269, 1076 for the aromatic system; ^{1}H-NMR (DMSO-d_6, TMS): □ ppm 1.2 (t, J = 8.3, 3H, CH_3), 4.05 (q, J = 8.1, 2H, CH_2), 6.51 (s, 2H, NH_2, D_2O exchangeable,), 7.28 – 7.54 (m, 10H, 2Ph), ^{13}C-NMR (DMSO-d_6, TMS): δ ppm 16.3 (-$\underline{C}H_3$), 68.5 (-$\underline{C}H_2$), 129.5. 130.2, 131.6, 135.2, 139.6, 140.5 (aromatic carbons), 143.2 (C4, pyridazine ring), 147.2 (C5, pyridazine ring), 155.9 (C6-pyridazine ring), 166.2 (C3, pyridazine ring), 175.6 ($\underline{C}$=O, ester), 185.9 ($\underline{C}$=O, amide), MS *m/z*: 347 (M^+, 1.6%), 274 (M^+ - COOEt, 22.6%, ion A), 273 (ion A – 1, 100%, ion B), 257 (ion B –NH_2, 29.5%, ion C), 229 (ion C – C=O, 11.2%). Anal. Calcd for $C_{20}H_{17}N_3O_3$: C, 69.15%; H, 4.93%; N, 12.10%. Found: C, 69.00%; H, 4.80%; N, 12.00%.

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