Synthesis and reactions of 2,6-bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethylamino)methylene]pyridine

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Abstract

The versatile multifunctional hitherto unreported 2,6-bis-[3-oxo-3-propanenitrile-2-(*N,N*-dimethylamino)methylene]pyridine **3** was prepared by the reaction of pyridine-2,6-bis-(3-oxo-3-propanenitrile) **2** with dimethylformamide-dimethylacetal (DMF-DMA). Several new pyrazole, isoxazole, pyrimidine, pyrazolopyrimidine, triazolopyrimidine and imidazopyrimidine derivatives have been synthesized by the reactions of 2,6-bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethylamino)methylene]pyridine **3** with several nitrogen binucleophiles.

Keywords: Enaminonitrile, 2,6-disubstituted pyridine, pyrazole, isoxazole, pyrimidine and pyrazolopyrimidine

Introduction

Multifunctional building blocks are of special interest for drug design and organic synthesis due to three reasons, at least. First, these compounds can be used to tether two molecular fragments responsible for binding to the biological target, thus they can act as linkers. Second, if one functional group is not engaged in connection between the core of building block and the rest of a molecule being constructed, then it can participate in important interactions with a biological target. Finally, many multifunctional building blocks can undergo cyclization reactions, allowing rapid advance toward prospective heterocyclic units.

Enaminonitriles are multifunctional highly reactive reagents extensively used for synthesis of otherwise not readily obtainable, heterocyclic compounds,¹⁻⁴ and can be used as starting material for the preparations of *N*-1 and/or *N*-2 substituted pyrazoles.⁵⁻⁹ On the other hand a great deal of interest has been focused on the synthesis of the functionalized pyridine derivatives due to their biological activities.¹⁰⁻¹³ In view of these observations and in continuation of our previous work on the synthesis of heterocyclic systems for biological evaluations,¹⁴⁻¹⁷ we report herein a facile route to various pyrazoles, isoxazoles, pyrimidines, pyrazolopyrimidine and

triazolopyrimidine, incorporating 2,6 pyridine moiety. In this manner, we have found that 2,6-bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethylamino)-methylene]pyridine **3** is an excellent building block for the synthesis of the target objectives.

Results and Discussion

Treatment of pyridine-2,6-bis(3-oxo-3-propanenitrile) **2** with dimethylformamide-dimethylacetal (DMF-DMA) in dry THF afforded a yellow crystalline product identified as 2,6-bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethylamino)methylene]pyridine **3** (Scheme 1). The structure of the isolated product was confirmed on the basis of its elemental analysis and spectral data. For example, its ^1H NMR spectrum displayed a singlet signals at δ 2.98, 3.11 and 6.75 characteristics for methyl groups and CH of enamine protons, respectively.

Scheme 1

The reactivity of the enaminonitrile **3** towards some nitrogen nucleophiles was investigated. Thus, treatment of compound **3** with hydrazine hydrate, in refluxing ethanol, afforded a product for which two possible structures **5a** and **6a** can be formulated (Scheme 2). The spectral data of the isolated product was incomplete agreement with structure **5a**. Similarly, compound **3** reacted with phenyl hydrazine in refluxing ethanol, in the presence of a catalytic amount of piperidine, and afforded a yellow crystalline product of **5b** (Scheme 2). The other possible structure **6b** was easily excluded on the basis of spectral data [see experimental part]. The formation of compounds **5a** and **5b** are assumed to take place *via* a Michael type addition of the amino group of hydrazines to the enamine double bond in **3** to form non-isolable intermediate **4** which readily undergoes intramolecular cyclization into the pyrazole derivatives **5a** and **5b** *via* the loss of dimethylamine and water molecules (type A, Scheme 2).

Scheme 2

The structures of the expected pyrazoles **6a,b** were excluded as a result of the lack of carbonyl group in IR and ^{13}C NMR spectra. Moreover, the absolute structure of **5b** was completely solved by X-ray diffraction analysis as shown in Figure 1.

Figure1. X-Ray crystal structure of compound **5b**.

Table 1. Selected bond angles and bond lengths of compound **5b**

Bond	Angle	Bond	Length (Å°)
N11—N12—C1	120.5	N12—N11	1.374
C7—N12—N11	112.6	N20—N21	1.368
N12—N11—C9	104.6	N12—C1	1.435
C7—C8—C9	106.0	C7—C8	1.387

In a similar manner, the enaminonitrile **3** reacted with hydroxylamine hydrochloride, in the presence of potassium carbonate, and afforded white solid of 2,6-bis[4-cyano-isoxazol-5-yl]pyridine (**8**) that not readily soluble in most of organic solvent. Compound **8** is assumed to be formed *via* the Michael type addition of the amino group of hydroxylamine to the enamine double bond in the enaminonitrile **3**¹⁸⁻²¹ to form non-isolable intermediate **7** which underwent intramolecular cyclization *via* the loss of dimethylamine and water molecules to afford the isoxazole derivative **8** (type A, Scheme 2). The IR spectrum of the later product revealed the lack of absorption band corresponding to carbonyl group and showed band at 2206 cm⁻¹ corresponding to nitrile function, its mass spectrum revealed molecular ion peak at *m/z* 263 (M⁺).

Enaminonitrile **3** reacts also with guanidine hydrochloride in refluxing ethanol, in the presence of anhydrous potassium carbonate to give a single product (as examined by TLC) that was identified as 2,6-bis[2-amino-5-cyanopyrimidin-4-yl]pyridine **10** according to its elemental analysis and spectral data. Thus, the IR spectrum of compound **10**, showed an amino and nitrile absorption bands at 3317, 3184 and 2219, respectively, which are compatible with the assigned structure which seemed to be formed *via* the cyclization mode of type A (Scheme 3).

The foregoing results and our synthetic strategy towards new class of 2,6-disubstituted pyridines prompted us to investigate the behavior of the enaminonitrile **3** towards urea derivatives.

Few examples of acid catalyzed dimethylamine substitution reactions of enaminones with amido-*N*-nucleophiles such as ureas have been described in the literature,^{22,23} probably due to the very low nucleophilic reactivity of amide nitrogen atoms. Thus, treatment of the enaminonitrile **3** and excess of urea (6 equiv) in DMF as polar solvent at 60 °C, in the presence of excess HCl, afforded the corresponding uriedopropenate and thiouriedopropenate derivatives **11a,b** which subsequently cyclized into pyridyl uraciles **12a,b** when treated with sodium ethoxide solution (Scheme 3). The structures of the synthesized products were established on the basis of their elemental analysis and spectral data [see the experimental part].

Scheme 3

The behaviors of the enaminonitrile **3** towards some heterocyclic amines as potential precursors for fused heterocyclic systems²⁴ were also investigated. Thus, treatment of compound **3** with 5-amino-3-phenyl-1*H*-pyrazole **13**, in refluxing ethanol in the presence of a catalytic amount of piperidine, furnished a single product identified as 2,6-bis[6-cyano-2-phenylpyrazolo[1,5-*a*]pyrimidin-7-yl]pyridine **14** (Scheme 3). Further evidence for the proposed structure **14** was obtained by an independent synthesis of compound **14** *via* treatment of 5-*N,N*-dimethylaminomethyleneimino-3-phenyl-1*H*-pyrazole **17** with the oxopropanenitrile **2**, in refluxing ethanol and in the presence of a catalytic amount of piperidine, to afford a product identical in all respects (mp, TLC and spectra) with that obtained from the reaction of the enaminonitrile **3** with 5-amino-3-phenyl-1*H*-pyrazole **13**. The formation of compound **14** can be explained on the basis of an initial Michael addition of exocyclic NH₂ in **13** to the enamine double bond in **3** to afford non-isolable intermediate undergo intramolecular cyclization to afford compound **14** (Scheme 4). However, structures **15** and **16** were easily excluded on the basis of elemental analysis and spectral data (see experimental part).

Scheme 4

Experimental Section

General. All melting points were measured on a Gallenkamp melting point apparatus. The infrared spectra were recorded in potassium bromide discs on a Pye Unicam SP 3-300 and Shimadzu FT IR 8101 PC infrared spectrophotometers. The NMR spectra were recorded on a Varian Mercury VXR-300 NMR spectrometer. ^1H NMR (300 MHz) and ^{13}C NMR (75.46 MHz) were run in deuterated chloroform (CDCl_3) or dimethylsulfoxide ($\text{DMSO}-d_6$). Chemical shifts were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP1000 EX mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical Centre of Cairo University, Giza, Egypt. All reactions were followed by TLC (Silica gel, Aluminum Sheets 60 F₂₅₄, Merck). Compounds **13**,²⁵⁻²⁷ **17**²⁸ and **2**²⁹ were prepared according to literature procedures.

Material and reagents

Sodium hydride, hydrazine hydrate, phenyl hydrazine, 2,6-pyridine dicarboxylic and guanidine hydrochloride were purchased from Aldrich Chemical CO. triethylamine and piperidine were purchased from British Drug Houses (BDH). Dimethylformamide-dimethylacetal (DMF-DMA) was obtained from Merck CO, Germany. Hydrochloric acid, sulfuric acid, potassium carbonate, urea and thiourea were purchased from El-Nasr Pharmaceutical and Chemical CO. (ADWIC).

Solvents

Acetonitrile, THF, diethyl ether, dimethylformamide, and pyridine purchased from Aldrich Chemical CO. Ethanol, methanol, petroleum ether; chloroform were BDH reagents. Acetic acid and acetic anhydride were purchased from EL-Nasr Pharmaceutical and Chemical Co. (ADWIC), Egypt.

Crystallographic analysis

The crystals were mounted on a glass fiber. All measurements were performed on an ENRAF NONIUS FR 590. The data were collected at a temperature of 25 °C using the ω scanning technique to a maximum of a 20 of 22.9860. The structure was solved by direct method using SIR 92 and refined by full-matrix least squares. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located geometrically and were refined isotropically.

Crystal data

For compound **5b**: $\text{C}_{25}\text{H}_{15}\text{N}_7$, $M = 413.43$, Triclinic, $a = 6.6268$ (5), $b = 13.6234$ (12), $c = 13.4353$ (13) Å, $v = 1133.4$ (2), $\alpha = 75.134$ (3), $\gamma = 89.996$ (5) °, $\beta = 75.705$ (4) °, space group: $P2_1/c$, $Z=2$, $D_x = 1.223$ Mg m⁻³, $\theta_{\text{max}} = 27.485$ °. Figure 1 illustrates the structure as determined. Full data can be obtained on request from the CCDC.³⁰

Pyridine-2,6-bis(3-oxo-3-propanenitrile) (2). To a mixture of diethyl-2,6-pyridinedicarboxylate **1** (4.46 g, 20 mmol) and acetonitrile (2.70 mL, 50 mmol), in dry THF (50 mL), was added sodium hydride (4 g, 50 %). The reaction mixture was refluxed for 2h, and then allowed to cool. The solid that precipitated was filtered off, washed with diethyl ether and dried. The crude product was dissolved in water (30 mL) and the resulting alkaline solution was treated with diluted hydrochloric acid until it becomes acidic (pH 5). The precipitated solid product was filtered off, washed with water, dried and finally recrystallized from ethanol/dioxan to afford brown crystals of pyridine-2,6-bis(3-oxo-3-propanenitrile)²⁵ **2**. Yield (1.70 g, 80 %, brown crystals); mp: 185-186 °C. IR (KBr): ν 2264 (CN), 1720 (C=O) cm^{-1} . ¹H NMR (DMSO-*d*₆): δ 3.74 (s, 4H, 2CH₂), 8.57-8.24 (m, 3H, pyridine). ¹³C NMR (DMSO-*d*₆): δ 29.6, 116.4, 123.7, 126.4, 165.7, 190.7. MS *m/z* (%): 213 [M^+] (75), 145 (100). Analysis for C₁₁H₇N₃O₂ (213.19) Calcd: C, 61.97; H, 3.31; N, 19.71. Found: C, 61.94 ; H, 3.34; N, 19.7

2,6-Bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethyl amino)methylene]pyridine (3). A mixture of oxopropanenitrile **2** (2.13g, 10 mmol) and dimethylformamide-dimethylacetal (DMF-DMA) (3.99 mL, 30 mmol) in dry THF (20 mL) was stirred for 4 h at room temperature. The solvent was removed by distillation under reduced pressure, and the solid product obtained was washed with diethyl ether, filtered off, dried and crystallized from ethanol to afford yellow crystal of 2,6-bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethyl amino)methylene]pyridine **3**. Yield (3.05g, 94 %, yellow crystal); mp: 206-208 °C. IR (KBr): ν 2194 (CN), 1655 (C=O) cm^{-1} . ¹H NMR (DMSO-*d*₆): δ 2.98, 3.11 (2s, 12H, 4CH₃), 6.75 (s, 2H, 2CH enamine), 7.95-8.03 (m, 3H, pyridine). ¹³C NMR (DMSO-*d*₆): δ 40.5, 48.3, 79.8, 119.3, 124.5, 139.3, 146.4, 154.6, 160.1, 187.2. MS *m/z* (%): 323 [M^+] (73), 280 (56), 199 (57), 123 (100), 80 (74). Analysis for C₁₇H₁₇N₅O₂ (323.35) Calcd: C, 63.15; H, 5.30; N, 21.66. Found: C, 63.12; H, 5.42; N, 21.59.

Pyridine-2,6-bis-(1*H*-pyrazol-5-yl-4-carbonitrile) (5a). A mixture of hydrazine hydrate (80 %, 1.30 mL) and enaminonitrile **3** (0.32 g, 1 mmol) in absolute ethanol (20 mL), was stirred at room temperature for 10 h. The solid that precipitate was collected by filtration, washed with ethanol and dried. Recrystallization from ethanol afforded pyridine-2,6-bis-(1*H*-pyrazol-5-yl-4-carbonitrile) **5a**. Yield (0.21 g, 80 %, white solid), mp: 225-227 °C. IR (KBr) cm^{-1} : ν 3297 (NH), 2231 (CN). ¹H NMR (DMSO-*d*₆): δ 6.08 (s, 2H, 2CH-pyrazole-H), 7.52-7.79 (m, 3H, pyridine-H's), 8.75 (s, 2H, 2NH D₂O-exchangeable). ¹³C NMR (DMSO-*d*₆): δ 89.9, 117.9, 123.1, 131.2, 138.39, 148.8, 155.4. MS *m/z* (%): 261 [M^+] (100), 235 (68), 142 (14), 64 (49). Analysis for C₁₃H₇N₇ (261.24) Calcd: C, 59.67; H, 2.70; N, 37.53. Found: C, 59.65; H, 2.75; N, 37.62.

Pyridine-2,6-bis-(1*H*-1-phenyl-pyrazol-5-yl-4-carbonitrile) (5b). To a solution of the enaminonitrile **3** (0.32 g, 1 mmol) in ethanol (10 mL), were added phenyl hydrazine (0.32 g, 3 mmol) and few drops of piperidine. The reaction mixture was refluxed for 5 h, then left to cool. The yellowish solid precipitate was collected by filtration, washed with ethanol and dried.

Recrystallization from ethanol/dioxan afforded pyridine-2,6-bis-(1*H*-1-phenyl-pyrazol-5-yl-4-carbonitrile) **5b**. Yield (0.39g, 94 %, yellow crystal), mp: 175-176 ° C. IR (KBr) cm^{-1} : ν 2232 (CN). ^1H NMR (DMSO- d_6): δ 7.05-7.34 (m, 10H, ArH's), 7.69-7.85 (m, 3H, pyridine-H's), 8.21 (s, 2H, 2CH-pyrazole H). ^{13}C NMR (DMSO- d_6): δ 94.3, 113.8, 125.9, 126.1, 129.6, 129.7, 138.8, 139.3, 143.6, 145.7, 146.7. MS m/z (%): 413 [M^+] (100), 242 (21), 216 (32), 114 (82). Analysis for $\text{C}_{25}\text{H}_{15}\text{N}_7$ (413.43), Calcd: C, 72.63; H, 3.66; N, 23.71. Found: C, 72.53; H, 3.70; N, 23.65.

Reaction of 2,6-bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethyl amino)methylene]pyridine (3) with hydroxylamine hydrochloride and guanidine. To a mixture of the enamionitrile **3** (0.32 g, 1 mmol) and hydroxylamine hydrochloride (0.14 g, 2 mmol) or guanidine hydrochloride (0.19 g, 2 mmol) in ethanol (10 mL), was added anhydrous potassium carbonate (0.28 g, 2 mmol). The resulting mixture was refluxed for 10 h, and allowed to cool to room temperature then diluted with water (30 mL). The solid products that formed were collected by filtration, washed with water and dried and recrystallized from the proper solvent to afford compounds **8** and **10** respectively.

2,6-Bis[4-cyanoisoxazol-5-yl]pyridine (8). Yield (0.19g, 72 %, white solid); mp: > 300 °C. (not readily soluble in most of organic solvent). IR (KBr) cm^{-1} : ν 2206 (CN). MS m/z (%): 263 [M^+] (23), 219 (17), 179 (25), 77 (35), 68 (100). Analysis for $\text{C}_{13}\text{H}_5\text{N}_5\text{O}_2$ (263.22), Calcd: C, 59.32; H, 1.91; N, 26.61. Found: C, 59.41; H, 1.95; N, 26.65.

2,6-Bis[2-amino-5-cyanopyrimidine-4-yl]pyridine (10). Yield (0.25 g, 79 %, white solid), mp: > 300 °C (Ethanol/ DMF). IR (KBr) cm^{-1} : ν 3317-3184 (NH_2), 2219 (CN). ^1H NMR (DMSO- d_6) δ : 6.70 (br.s, 4H, 2 NH_2 D_2O -exchangeable), 7.94-8.28 (m, 3H, pyridine-H's), 8.75 (s, 2H, pyrimidine.-H).). ^{13}C NMR (DMSO- d_6): δ 93.9, 117.7, 125.1, 139.6, 152.8, 163.7, 164.9, 165.2. MS m/z (%): 315 [M^+] (11), 289 (23), 247 (15), 223 (13), 144 (16), 92 (31). Analysis for $\text{C}_{15}\text{H}_9\text{N}_9$ (315.29), Calcd: C, 57.14; H, 2.88; N, 39.98. Found: C, 57.20; H, 2.91; N, 40.10.

Reaction of 2,6-Bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethylamino)methylene]pyridine (3) with urea derivatives

A mixture of 2,6-bis[3-oxo-3-propanenitrile-2-(*N,N*-dimethylamino)methylene]pyridine **3** (0.323 g, 1 mmol) and appropriate urea (12 mmol) was dissolved in DMF (20 mL) followed by the addition of hydrochloric acid(5 mL). The resulting mixture was stirred at 60 ° C for 7 h. the solvent was evaporated in *vacuo* and the residue was treated with ice-water. The solid precipitate was collected by filtration, washed with water, dried and crystallized from ethanol to give compounds **11a,b**.

2,6-Bis[5-cyano-3-oxo-3-(prop-1-enyl)urea]pyridine (11a). Yield (0.22 g, 62 %, pale yellow solid), mp: 200-202 °C. IR (KBr) cm^{-1} : ν 3338, 3237 (NH, NH_2), 2216 (CN). 1718, 1659 (2C=O). ^1H NMR (DMSO- d_6): δ 4.25 (br.s, 4H, 2 NH_2 D_2O -exchangeable), 6.11 (s, 2H, 2C=CH), 7.83-8.08 (m, 3H, pyridine-H's), 8.10 (s, 2H, 2NH D_2O -exchangeable). MS m/z (%):

353 [M⁺] (15), 83 (65), 66 (100). Analysis for C₁₅H₁₁N₇O₄ (353.29), Calcd: C, 50.99; H, 3.14; N, 27.75. Found: C, 50.85; H, 3.25; N, 27.83.

2,6-Bis[5-cyano-3-thio-3-(prop-1-enyl)urea] pyridine (11b). Yield (0.23 g, 65 %, pale yellow solid), mp: 210-212 °C. IR (KBr) cm⁻¹: ν 3341, 3198 (NH, NH₂), 2211 (CN), 1710, 1645 (2C=O). ¹H NMR (DMSO-*d*₆): δ 3.97 (br.s, 4H, 2NH₂ D₂O-exchangeable), 6.51 (s, 2H, 2C=CH), 7.81-8.13 (m, 3H, pyridine-H's), 8.70 (s, 2H, 2NH D₂O-exchangeable). MS *m/z* (%): 385 [M⁺] (62), 315 (17), 104 (13) 77 (100). Analysis for C₁₅H₁₁N₇O₂S₂ (385.42), Calcd: C, 46.74; H, 2.88; N, 25.44. Found: C, 46.82; H, 2.75; N, 25.47

Synthesis of oxypyrimidine and thiopyrimidine derivatives (12a,b)

Sodium ethoxide solution [prepared from sodium metal (0.11g) and absolute ethanol (20 mL)], was added to ethanolic solution of **11a,b**. The resulting mixture was refluxed with stirring for 10 h. the reaction mixture was neutralized with HCl and the obtained suspension was poured on ice water. The formed solid products were collected by filtration, washed with water, dried and finally recrystallized from the appropriate solvent, to afford the corresponding pyridy derivatives **12a,b**.

2,6-Bis[5-cyano-1,2-dihydro-2-oxopyrimidin-4-yl]pyridine (12a). Yield (0.21 g, 66%, yellow solid), mp: 225-227 °C. IR (KBr) cm⁻¹: ν 3338 (NH), 2216 (CN). ¹H NMR (DMSO-*d*₆) δ : 7.83-8.08 (m, 3H, pyridine-H's), 8.75 (s, 2H, pyrimidine.-H). 9.51 (s, 2H, 2NH D₂O-exchangeable). ¹³C NMR (DMSO-*d*₆): δ 85.2, 116.7, 121.3, 140.2, 148.2, 156.6, 167.5, 178.2. MS *m/z* (%): 317 [M⁺] (25), 246 (68), 76 (100). Analysis for C₁₅H₇N₇O₂ (317.26) Calcd: C, 56.79; H, 2.22; N, 30.90. Found: C, 56.85; H, 2.25; N, 30.85.

2,6-Bis[5-cyano-1,2-dihydro-2-thiopyrimidin-4-yl]pyridine (12b). Yield (0.23 g, 65 %, yellow solid), mp: 219-221 °C. IR (KBr) cm⁻¹: ν 3331 (NH), 2211 (CN). ¹H NMR (DMSO-*d*₆) δ : 7.71-8.12 (m, 3H, pyridine-H's),), 8.97 (s, 2H, pyrimidine.-H). 9.71 (s, 2H, 2NH D₂O-exchangeable). ¹³C NMR (DMSO-*d*₆): δ 90.9, 117.7, 125.1, 139.62, 152.8, 163.7, 164.9, 165.2. MS *m/z* (%): 349 [M⁺] (42), 104 (57), 76 (100). Analysis for C₁₅H₇N₇S₂ (349.39), Calcd: C, 51.56; H, 2.02; N, 28.06. Found: C, 51.59; H, 2.05; N, 28.15.

2,6-Bis[6-cyano-2-phenylpyrazolo[1,5-*a*]pyrimidin-7-yl]pyridine (14)

Method A. To a mixture of the enamionitrile **3** (0.32 g, 1 mmol) and 5-amino-3-phenyl-1H-pyrazole **13** (0.32 g, 2 mmol) in ethanol (20 mL), was added a few drops of piperidine. The resulting mixture was refluxed for 5 h, and allowed to cool to room temperature. The solid product that formed was collected by filtration, washed with ethanol, dried and finally recrystallized from ethanol to afford 2,6-bis[6-cyano-2-phenylpyrazolo[1,5-*a*]pyrimidin-7-yl]pyridine **14** [Yield (0.42 g, 82%]

Method B. To a mixture of compound **2** (0.21 g, 1 mmol) and (*E*)-*N,N*-dimethyl-*N'*-(3-phenyl-1H-pyrazol-5-yl)formamidine **17** (0.43 g, 2 mmol) in ethanol (10 mL) was added few drops of piperidine. The reaction mixture was heated under reflux for 9 h, and then left to cool. The precipitated solid product was collected by filtration, washed with ethanol, dried, and

recrystallized from ethanol to afford products identical in all respect (mp, TLC, IR, NMR) with that of method A Yield (0.45 g, 87%).

Yellow solid, mp: 280-282 °C. IR (KBr) cm^{-1} : ν 2215 (CN), ^1H NMR ($\text{DMSO}-d_6$): δ 6.95-7.43 (m, 10H, ArH's), 7.65 (s, 2H, 2CH-pyrazole), 7.85-8.01 (m, 3H, pyridine-H's), 8.87 (s, 2H, pyrimidin-H). ^{13}C NMR ($\text{DMSO}-d_6$): δ 91.1, 101.9, 115.3, 126.5, 127.2, 129.6, 130.6, 136.3, 137.6, 148.3, 156.2, 163.3, 164.3, 169.8 MS m/z (%): 515 [M^+] (10), 346 (21), 315 (17), 77 (100). Analysis for $\text{C}_{31}\text{H}_{17}\text{N}_9$ (515.54), Calcd: C, 72.22; H, 3.32; N, 24.45. Found: C, 72.25; H, 3.37; N, 24.40.

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30. Crystal data for compound **5b** (ref. CCDC 790224) can be obtained on request from the director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EW, UK