# of 2-methylthionicotino-nitrile, Pyrazolopyridine and Pyridopyrazolotriazine Derivatives

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Síntesis, reacciones y caracterización de derivados de 2-metiltionicotinonitrilo, pirazolopiridina y piridopirazolotriazina

Síntesi, reaccions i caracterització de derivats de 2-metiltionicotinonitril, pirazolopiridina i piridopirazolotriazina

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RESUMEN

Se obtienen las 4,6-diaril-1H-pirazolo[3,4-b]piridin-3-aminas 4a-c en estado muy puro y se usan como buenos productos de partida para el presente estudio. El compuesto 4a se diazotiza para dar la correspondiente sal de diazonio 11 y, además, se hace reaccionar con 2-bromo-1-feniletanona para dar el correspondiente derivado de pirazolo[3,4-b]piridin-2-il)-1-feniletanona 7 que se usa para preparar los derivados de hidrazona 8 y de formamida 10 mediante reacción con hidrato de hidrazina y ácido fórmico, respectivamente. El compuesto 11 se utiliza para preparar derivados de piridopirazolotriazina vía acoplamiento con diversos compuestos que contienen –CH2- activos. Se determina la estructura química de los nuevos compuestos heterocíclicos sintetizados a partir de los datos de IR, 1H-RMN, espectros de masas y análisis elementales.

Palabras clave: **Cianoetantioamida. 2-metiltionicotinonitrilo. Pirazolopiridina. Hidrazona. Formamida. Pirazolopiridinilhidrazono. Piridopirazolotriazina.**

SUMMARY

4,6-Diaryl-1*H*-pyrazolo[3,4-*b*]pyridin-3-amines 4a-c were obtained in very pure state and used as the good starting materials for the present study. Compound 4a diazotized to give the corresponding diazonium salt 11 and also, reacted with 2-bromo-1-phenylethanone to give the corresponding pyrazolo[3,4-*b*]pyridin-2-yl)-1-phenylethanone derivative 7 which in turn, used for the preparation of the hydrazone and formamide derivatives 8 and 10 respectively through its reaction with hydrazine hydrate and formic acid respectively. Compound 11 was used for the preparation of pyridopyrazolotriazine derivatives via its coupling with several active –CH_2- containing compounds. Considering the data from IR, ^{1}H NMR, the mass spectra and elemental analyses the chemical structures of the newly synthesized heterocyclic compounds were elucidated.

Key words: **Cyanoethanethioamide. 2-methylthionicotinonitrile. Pyrazolopyridine. Hydrazone. Formamide. Pyrazolopyridinylhydrazono and Pyridopyrazolotriazine.**

RESUM

S'obtenen les 4,6-diaril-1H-pirazolo[3,4-b]piridin-3-amines 4a-c en estat molt pur i s'empren com a bons productes de partida per al present estudi. El compost 4a es diazotitza per donar la corresponent sal de diazoni 11 i a més, es fa reaccionar amb 2-bromo-1-feniletanona per donar el corresponent derivat de pirazolo[3,4-b]piridin-2-il)-1-feniletanona 7, que s'empra per preparar els derivats d'hidrazona 8 i de formamida 10 mitjançant reacció amb hidrat d'hidrazina i àcid fòrmic, respectivament. El compost 11 s'utilitza per preparar derivats de piridopirazolotriazina via acoblament amb diversos compostos que contenen –CH2- actius. Es determina l'estructura química dels nous compostos heterocíclics sintetitzats a partir de les dades de IR, 1H-RMN, espectres de masses i anàlisis elementals.

Mots clau: **Cianoetantioamida. 2-metiltionicotinonitrilo. Pirazolopiridina. Hidrazona. Formamida. Pirazolopiridinilhidrazono. Piridopirazolotriazina.**

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INTRODUCTION

In previous papers[1-22] the synthesis of pyrazolopyridine and pyridopyrazolotriazine derivatives were described. As a continuation of our research on the synthesis of these ring systems and owing to the reported biological activities of pyrazolopyridine[23-25] and as well as that of triazines,[26-30] we were interested to synthesize several derivatives of these ring systems that are required for several chemical transformation as well as for our medicinal chemistry program.

RESULTS AND DISCUSSION

The synthetic potentiality of **1a-c** was used to build up new ring containing active functional groups, this goal achieved through their reaction with hydrazine hydrate. Thus, it has been found that **1a** reacted with methyl iodide in methanolic sodium methoxide to afford the corresponding 4-(4-bromophenyl)-2-(methylthio)-6-phenylnicotinonitrile **2a** which in turn, reacted with hydrazine hydrate in ethanol to give the sulfur free product that formulated as 4-(4-bromophenyl)-6-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-amine **4a** through the non-isolable product **3a**. Chemical structure of **4a** was elucidated based on the spectroscopic and elemental analyses (cf. Exp. Part). A further elucidation of structure **4a** arose from its preparation authentically, thus **1a** reacted with hydrazine hydrate to afford directly **4a** through the hydrogen sulfide molecule removal. It is remarkable to report here that the products of the two pathways were identical in all physical and chemical properties (cf. Exp. Part). Similarly, 1*H*-pyrazolo[3,4-*b*]pyridin-3-amine derivatives **4b,c** were synthesized by the reaction of either **1b,c** or **2b,c** with hydrazine hydrate and their structures were elucidated by considering the data of elemental and spectroscopic analyses (cf. Exp. Part and Chart 1).

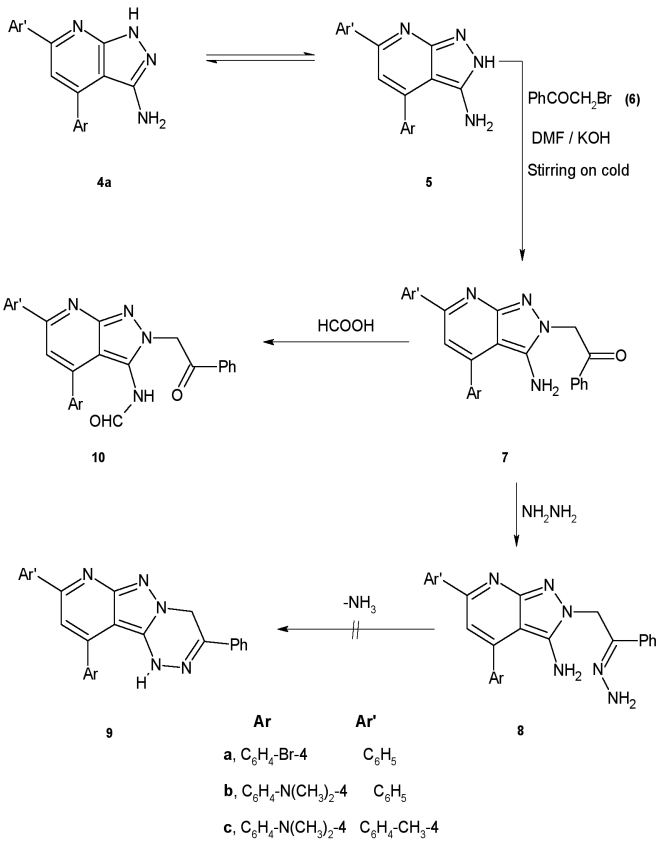


Chart 2

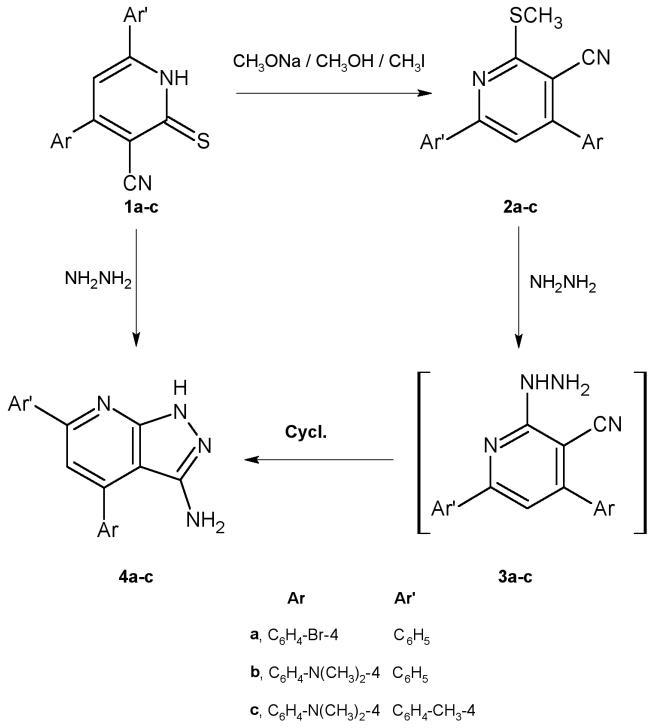


Chart 1

The chemical reactivity and synthetic potentiality of **4a** was investigated through its reaction with 2-bromo-1-phenylethanone **(6)** in stirred DMF/KOH on cold to give the corresponding 2-(3-amino-4-[4-bromophenyl]-6-phenyl-2*H*-pyrazolo[3,4-*b*]pyridin-2-yl)-1-phenylethan-one **(7)**. The reaction seemed to be proceeded through the dehydrobromination between the tautomer **5** and **6**.

The IR, ^{1}H NMR, and elemental analyses of this reaction product found to be in a good agreement with the assigned structure (cf. Exp. Part and Chart 2). Furthermore, the structure of compound **7** was confirmed chemically through its reaction with both hydrazine hydrate and formic acid. Thus, it has been found that compound **7** reacted with hydrazine hydrate under reflux 3-5 hours to afford the reaction product which assumed to be formed via the condensation of **7** with hydrazine hydrate to give the final isolable hydrazone derivative **8** which confirm the presence and chemical reactivity of CO group. The IR (cm^{-1}) of this reaction product showed no bands of C=O and instead the newly formed = N-NH_2 group was detected.

On the other hand, the ^{1}H NMR spectrum of this reaction product revealed the signals of NH_2 at pyrazole ring and =N-NH_2 protons. Moreover, its mass spectrum gave m/z = 497 (M+, 14.9%) which corresponding to the molecular weight of the molecular formula $C_{26}H_{21}BrN_6$ of the assigned structure. Several peaks such as 364 [M-CH_2-C(Ph) = N-NH_2, 100%], 335 (364-N_2, 20%) and 270 (335-$C_3H_5N_2$, 13.1%) were detected and their detec-

tion elucidates structure **8** (cf. Exp. Part). Considering the above-mentioned data in addition to that of elemental analyses it is concluded that this reaction product formulated as 2-(3-amino-4-(4-bromophenyl)-6-phenyl-2*H*-pyrazolo[3,4-*b*]pyridin-2-yl)-1-phenyl-ethanone hydrazone **8** not triazine derivative **9** (cf. Chart 2 and Exp. Part).

The position and chemical reactivity of NH_2 in **7** could be established through its reaction with formic acid. It has been found unexpectedly that the IR (cm^{-1}) of this reaction product showed the bands of C=O, NH function and the ^{1}H NMR (δppm) showed the signals of aldehydic, NH and -$\underline{CH_2}$COPh protons. Moreover, the mass spectrum of this reaction product gave m/z = 511 (M^+, 11.1%) which corresponding to the molecular weight of the molecular formula $C_{27}H_{19}BrN_4O_2$ of the assigned structure, in addition to the peak at m/z = 405 (M-COPh, H, 71.5%) and m/z = 77 (for the fragment Ph, 100%). Considering the above mentioned data we can conclude that *N*-[4-(4-bromophenyl)-2-(2-oxo-2-phenylethyl)-6-phenyl-2*H*-pyrazolo[3,4-*b*]pyridin-3-yl]formamide **10** represents the reaction product (cf. Chart 2 and Exp. Part).

The chemical reactivity of **4a** was further investigated via its reaction with nitrous acid to give the corresponding 4-(4-bromophenyl)-6-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-3-diazonium chloride **(11)**. Compound **11** used as a good synthon for the preparation of several pyrido[2',3':3,4]pyrazolo[5,1-*c*]triazine derivatives **15a-f**. Thus, it has been found that compound **11** coupled with each of malononitrile, ethyl cyanoacetate and 2-cyanoethanethioamide **(12a-c)** in stirred ethanol-sodium acetate on cold. The IR (cm^{-1}) of the reaction product in case of **12a** showed the bands of CN, NH_2 groups. The reaction product in case of **12b** showed the bands of NH_2, CO (ester) in its IR spectrum and its 1H NMR spectrum revealed the signals of $COOCH_2CH_3$ protons. On the other hand, the reaction product in case of **12c** showed the bands of NH_2, C=S in IR spectrum. Moreover, the mass spectra of these reaction products gave m/z = 442, 489 and 476 and these corresponding to the molecular weights of the molecular formulas $C_{21}H_{12}BrN_7$, $C_{23}H_{17}BrN_6O_2$ and $C_{21}H_{14}BrN_7S$ respectively in addition to several fragments confirm the structures **15a-c** (cf. Chart 3 and Exp. Part). Considering the above-mentioned data (cf. Exp. Part) we concluded that the reaction seemed to be proceeded via dehydrochlorination between each of **12a-c** and **11** to afford the corresponding non-isolable derivatives **13a-c**, **14a-c** respectively which spontaneously cyclized to afford the corresponding triazines **15a-c**.

Similarly, synthon **11** reacted with each of diethylmalonate, acetylacetone and ethyl acetoacetate **12d-f** under the same above-mentioned experimental conditions to afford the corresponding pyrido-[2',3':3,4]pyrazolo[5,1-*c*][1,2,4]triazines **15d-f** via the non-isolable intermediates **13d-f** respectively. By considering the data of IR, ^{1}H NMR and elemental analyses (cf. Exp. Part) the chemical structures of each of **15d-f** were elucidated. Moreover, the mass spectra of **15d-f** gave m/z = 490, 458 and 488 which corresponding to the molecular weights of the molecular formulas $C_{23}H_{16}BrN_5O_3$, $C_{23}H_{16}BrN_5O$ and $C_{24}H_{18}BrN_5O_2$ of the assigned structures. The presence of broad band in IR spectrum of **15d** confirm the presence of more stable enol-form and this confirmed further by the detection of peak at 489 (M^+–1) at mass spectrum (cf. Chart 4 and Fig. 1). The presence of a peak at m/z = 488 in mass spectrum for the reaction product of **11** with **12f** confirm the structure **15f** and reject that of **15g** and this also, further confirmed by the presence of signal at δ(ppm) 1.4 (t, 3H, $COOCH_2\underline{CH_3}$) and 4.5 (q, 2H, $COO\underline{CH_2}CH3$) and absence of m/z = 460 for the molecular formula $C_{22}H_{14}BrN_5O_2$ of the structure **15g** (cf. Charts 4, Fig. 2, and Exp. Part). An authentic samples of pyrido[2',3':3,4]pyrazolo[5,1-*c*]-[1,2,4]triazines **15a-f** obtained through another pathway via the reaction of each of **12a-f** with **11** in ethanol containing the catalytic amounts of triethylamine under reflux 3-5hrs. It is important to report here that compounds obtained through the two pathways are identical in all physical and chemical properties.

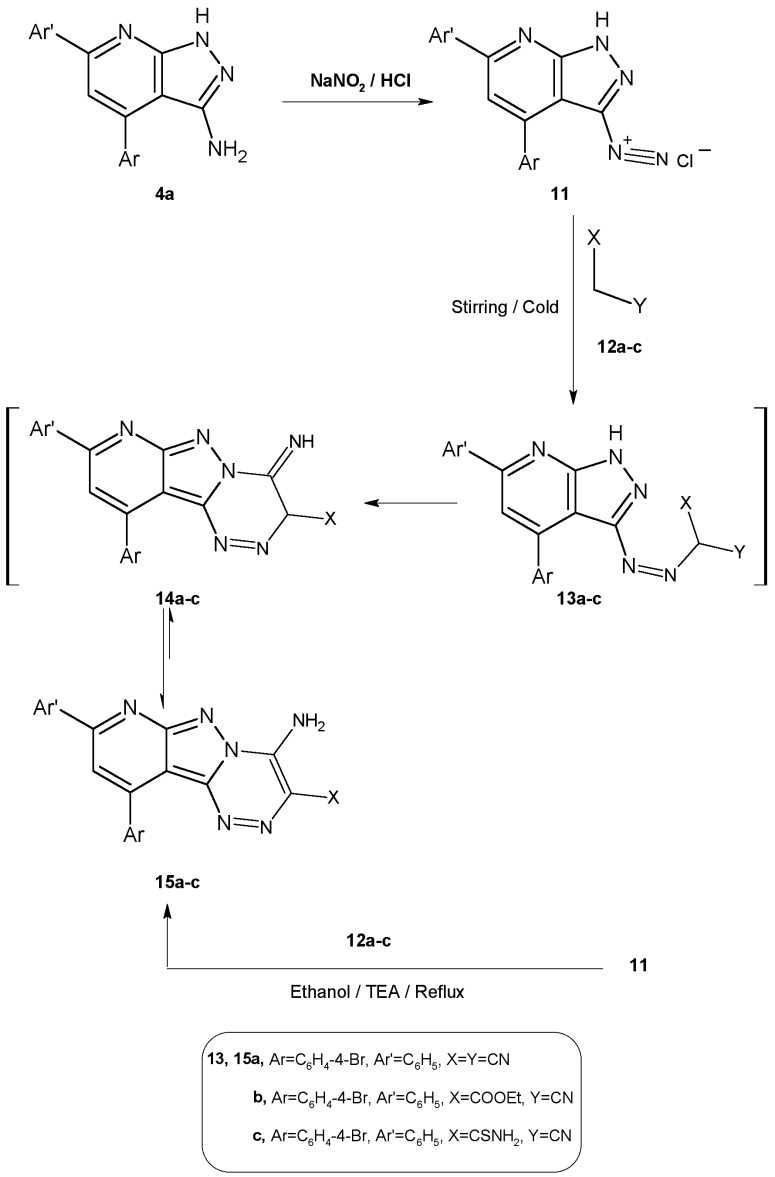
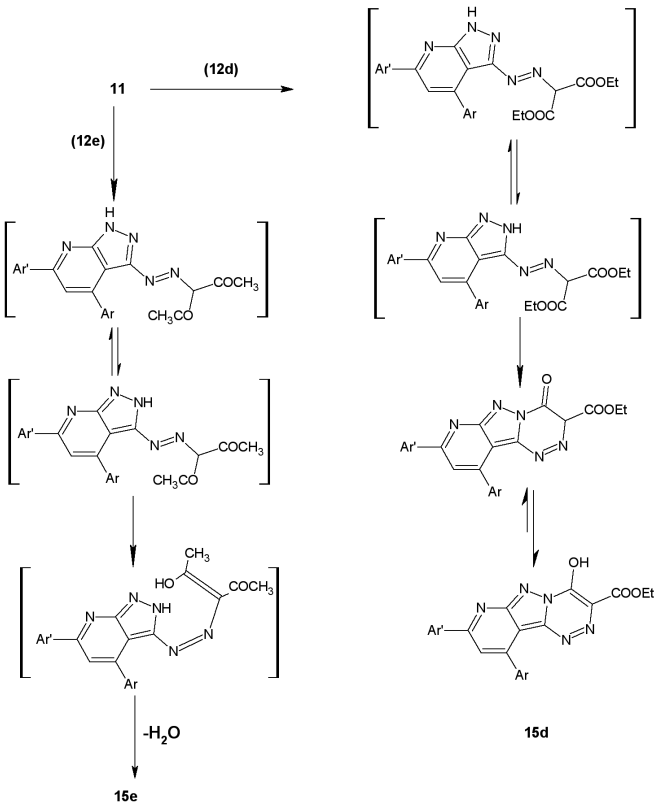
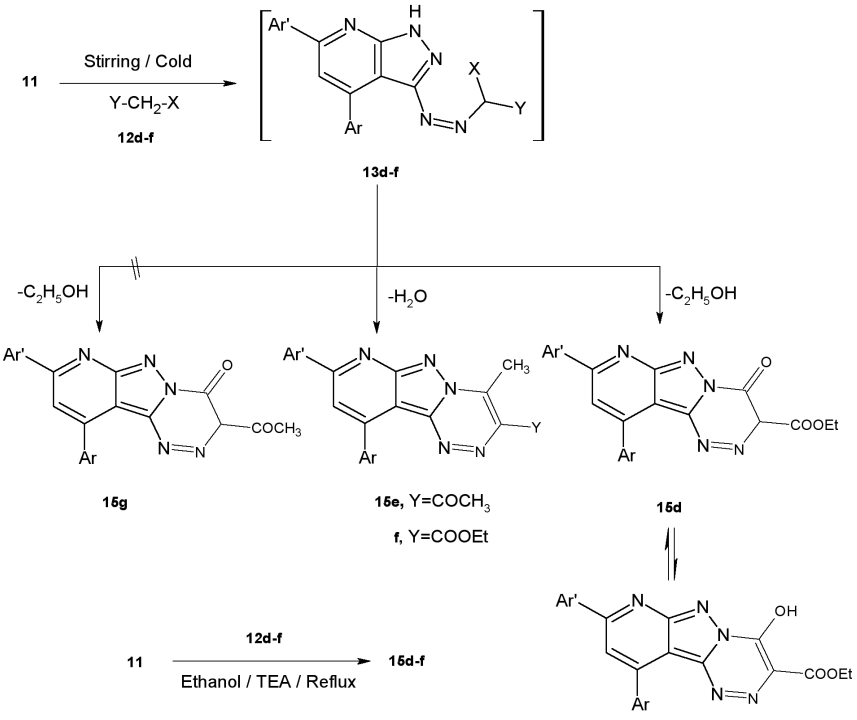


Chart 3

Figure 1





Ar=C_6H_4-4-Br, Ar'=C_6H_5

12d, X=Y=COOEt
e, X=Y=$COCH_3$
f, X=$COCH_3$, Y=COOEt

Chart 4

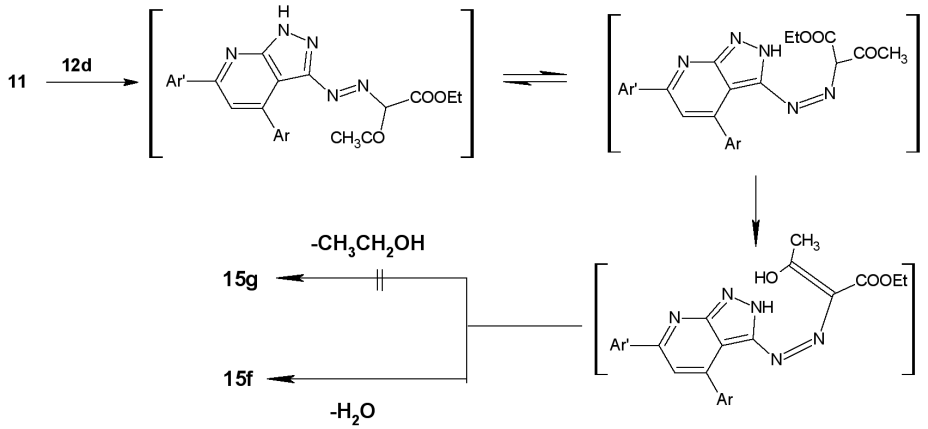


Figure 2

EXPERIMENTAL

All melting points were uncorrected. I.R. (KBr discs) spectra were recorded on a Shimadzu FTIR-8201PC Spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian Mercury 300 MHz., and a Varian Gemini 200 MHz. spectrometers using TMS as an internal standard and $CDCl_3$, DMSO-d_6, and $(CD_3)_2CO$ as solvents. Chemical shifts were expressed as δ (ppm) units. Mass spectra were recorded on Shimadzu GCMS-QP1000EX using an inlet type at 70 eV. The Microanalytical Center of Cairo University performed the microanalyses.

Synthesis of 2a-c: (General Procedure): Mix each of 2-thioxopyridine derivatives **1a-c** (0.1 mole) and iodomethane (0.15 mole) in methanolic sodium methoxide (0.23 g of sodium with about 30-50 mL methanol). Stir on cold for 1-1.5 hours then pour onto ice-cold water and acidified with concentrated HCl. Collect the formed solids by filtration and wash with water then crystallize from the proper solvent to afford **2a-c** respectively.

4-(4-bromophenyl)-2-(methylthio)-6-phenylnicotinonitrile 2a: crystallized from acetic acid as yellowish-white crystals (64%); m.p 260 ºC; **IR** (ν cm^{-1}): 2218 (CN) and 1605 (C=C); *Anal. for* $C_{19}H_{13}BrN_2S$ (381.28): Calcd./Found (%): C,59.85/60.10, H,3.44/3.50, Br,20.96/21.0, N,7.35/7.30, S,8.41/8.50.

4-[4-(dimethylamino)phenyl]-2-(methylthio)-6-phenylnicotinonitrile 2b: crystallized from ethanol as pale yellow crystals (64%); m.p 222 ºC; **IR** (ν cm^{-1}): 2218 (CN) and 1605 (C=C); *Anal. for* $C_{21}H_{19}N_3S$ (345.46): Calcd./Found (%): C,73.01/73.10, H,5.54/5.50, N,12.16/12.20, S,9.28/9.30.

4-[4-(dimethylamino)phenyl]-6-(4-methylphenyl)-2-(methylthio)-nicotinonitrile 2c: crystallized from ethanol as orange crystals (66%); m.p 220 ºC; **IR** (ν cm^{-1}): 2222 (CN) and 1602 (C=C); *Anal. for* $C_{22}H_{21}N_3S$ (359.48): Calcd./Found (%): C,73.50/73.50, H,5.89/5.90, N,11.69/11.50, S,8.92/9.0.

Synthesis of 4a-c: A mixture of **1a-c** or **2a-c** (0.01 mole of each) and hydrazine hydrate (20-25 mL) and pyridine (20 mL) was heated under reflux for 20 hours till the odour of H_2S or CH_3SH ceased. The products so formed after cooling were filtered off, washed with cold ethanol, and crystallized from the proper solvent to give **4a-c** respectively.

4-(4-Bromophenyl)-6-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-amine 4a: crystallized from ethanol as yellow crystals (58 %); mp.232-4 ºC; **IR** (cm^{-1}): 3466, 3302, 3194 (NH_2, NH), 2858 (sat. CH) and 1642 (C=N); *Anal. for* $C_{18}H_{13}BrN_4$ (365.22): Calcd./Found (%): C,59.19/59.30, H,3.59/3.60, Br,21.88/21.70, N,15.34/15.40.

4-[4-(Dimethylamino)phenyl]-6-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-amine 4b: crystallized from ethanol as yellow crystals (65 %); mp.256-8 ºC; **IR** (cm^{-1}): 3446, 3287, 3185 (NH_2, NH) and 1638 (C=N); *Anal. for* $C_{20}H_{19}N_5$ (329.39): Calcd./Found (%): C,72.93/73.0, H,5.81/5.9, N,21.26/21.30.

4-[4-(Dimethylamino)phenyl]-6-(4-methylphenyl)-1*H*-pyrazolo[3,4-*b*]-pyridin-3-amine 4c: crystallized from ethanol as yellow crystals (65%); mp.256-8 ºC; **IR** (cm^{-1}): 3462, 3309, 3194 (NH_2, NH) and 1641 (C=N); *Anal. for* $C_{21}H_{21}N_5$ (343.42): Calcd./Found (%): C,73.44/73.3, H,6.16/6.20, N,20.39/20.40.

Synthesis of 7: A solution of **4a** and potassium hydroxide (0.01 mole of each) in DMF (30 mL) stirred with 2-bromo-1-phenylethanone **(6)** (0.01 mole) for 30 minutes on cold. Pour onto ice-cold water, the solid so formed was filtered off, washed with water, and crystallized from ethanol to give 7.

2-(3-Amino-4-(4-bromophenyl)-6-phenyl-2*H*-pyrazolo[3,4-*b*]pyridin-2-yl)-1-phenylethanone 7: as yellow crystals (60 %); mp.194-6 ºC; **IR** (cm^{-1}): 3418, 3294, 3189 (NH_2), 3059 (CH-aromatic) and 1692 (C=O); ^{1}**H-NMR** (δ): 2.60 (s, 2H, -CH_2-), 5.67 (s, br., 2H, NH_2) and 7.08-7.89 (m, 15H, aromatic and pyridine-CH protons); MS: 483 (M^+, 11.1%) which corresponding to the molecular weight of the molecular formula $C_{26}H_{19}BrN_4O$ of the assigned structure, 484 (M+1, 10.6 %), 485 (M+2, 8.5 %), 482 (M^+–H, 9.8%), 380 (M^+–PhCN, 72.5%), 379 (482-PhCN, 96.6%), 377 (482-PhCO, 100%), 363 (M^+–$PhCOCH_2$, 1.6%), 105 (PhCO, 41.7%), 103 (PhCN, 1.5%) and 77 (Ph, 61.8%); *Anal. for* $C_{26}H_{19}BrN_4O$ (483.35): Calcd./Found (%): C,64.61/65.0, H,3.96/4.0, Br,16.53/16.40, N,11.59/11.60.

Synthesis of 8: A mixture of **7** (0.01 mole), hydrazine hydrate (20-25 mL) and ethanol (25 mL) was heated under reflux for 5-7 hours. The product so formed after cooling was filtered off, washed with cold ethanol, and crystallized from diluted ethanol to give **8**.

2-(3-amino-4-(4-bromophenyl)-6-phenyl-2*H*-pyrazolo[3,4-*b*]pyridin-2-yl)-1-phenylethanone hydrazone 8: as yellow crystals (57%); mp.114-6 ºC; **IR** (cm^{-1}), 3311 (NH_2), 3055 (CH-aromatic) 2966(aliphatic CH) and 1578 (C=N); ^{1}**H-NMR**

(δ): 1.55 (s, 2H, -CH_2-), 5.41 (s, br., 2H, NH_2 at pyrazole), 6.75 (s, br., 2H, NH_2, N=NH_2) and 7.13-8.02 (m, 15H, aromatic and pyridine-CH protons); **MS:** 497 (M^+, 14.9%) which corresponding to the molecular weight of the molecular formula $C_{26}H_{21}BrN_6$ of the assigned structure, 496 (M^+-H, 23.4%), 480 (M^+–NH_2, 46.9%), 377 (M^+–PhC = N–NH_2, 73.1%), 364 (M^+–133, –CH_2-C(Ph)-N = NH_2, 100%), 335 (364-N_2, H, 20%); *Anal. for* $C_{26}H_{21}BrN_6$ (497.38): Calcd./Found (%): C,62.78/62.80, H,4.26/4.30, Br,16.06/16.10, N,16.90/17.10.

Synthesis of 10: A mixture of **7** (0.01 mole) and formic acid (20-25 mL) was heated under reflux for 5-7 hours. The product so formed after cooling was filtered off, washed with cold ethanol, and crystallized from dioxane to give **10**.

***N*-[4-(4-bromophenyl)-2-(2-oxo-2-phenylethyl)-6-phenyl-2*H*-pyrazolo-[3,4-*b*]pyridin-3-yl]formamide 10:** as pale yellow crystals (67%); mp. 262-4 ºC; **IR** (cm^{-1}): 3178 (NH), 3058 (CH-aromatic), 2965 (aliphatic CH), 1699 (CO) and 1580 (C=N); **^{1}H-NMR** (δ): 2.11 (s, 2H, -$\underline{CH_2}$-COPh), 6.26 (s, br., 1H, NH), 7.51-8.23 (m, 15H, aromatic and pyridine-CH protons) and 10.26 (s, 1H, -CHO); **MS:** 511 (M^+, 11.1%) which corresponding to the molecular weight of the molecular formula $C_{27}H_{19}BrN_4O_2$ of the assigned structure, 512 (M+1, 15 %), 513 (M+2, 11.3 %), 510 (M^+–H, 13.7%), 405 (M+–COPh, 71.5%), 392 (M+-CH2-COPh, 1.4%), 377 (M^+–NCH_2COPh, 54.4 %), 363 (377–N, 3.5 %), 334 (363-CHO, 1.6%), 77 (Ph, 100%); *Anal. for* $C_{27}H_{19}BrN_4O_2$ (511.36): Calcd./Found (%): C,63.42/63.50, H,3.75/3.70, Br,15.63/15.70, N,10.96/11.10.

Synthesis of 11: Mix **4a** (0.01 mole), HCl (1.5 mL) and acetic acid (5 mL). Dissolve the formed salt in about 10 ml cold water. Add a mixture sodium nitrite (0.01 mole) and cold water drop wise. Stir for 30 min. then filter the formed solid, wash with water and crystallize the formed solid from ethanol to give **11**.

4-(4-bromophenyl)-6-phenyl-1*H*-pyrazolo[3,4-b]pyridine-3-diazonium chloride (11): as yellow crystals (62%); mp.180-2 ºC; **IR** (cm^{-1}): 3454 (NH), 3048 (CH-aromatic) and 2232 (N≡N); *Anal. for* $C_{18}H_{11}BrClN_5$ (412.67): Calcd./Found (%): C,52.39/52.40, H,2.69/2.70, Br,19.36/19.30, Cl,8.59/8.60, N,16.97/17.0.

Synthesis of 15a-f: ***(General Procedure):***
Method A: A solution of **12a-f** (0.01 mole) in ethanol (50 mL) containing fused sodium acetate (2g) was stirred for 30 min. in ice-cold mixture. Add a mixture of each of **11** in ethanol (50 mL) drop wise, stir for 1hr after complete addition. The solids so obtained were filtered off, washed with water and crystallized from the proper solvent to give **15a-f** respectively.

Method B: A solution of **11** (0.01 mole) in ethanol (50 mL) and each of **12a-f** (0.01 mole) in the presence of triethylamine (0.5 mL) was heated under reflux for 3 hrs. The solids so obtained were filtered off and crystallized from the proper solvent to give **15a-f** respectively.

4-Amino-10-(4-bromophenyl)-8-phenylpyrido[2',3':3,4]pyrazolo[5,1-*c*][1,2,4]triazine-3-carbonitrile 15a: crystallize from ethanol-DMF mixture as orange crystals (60%); mp. >320 ºC; **IR** (cm^{-1}): 3413, 3323, 3159 (NH_2) and 2227 (CN); **MS:** 442 (M^+, 56.7 %) which corresponding to the molecular weight of the molecular formula $C_{21}H_{12}BrN_7$ of the assigned structure, 443 (M+1, 100 %), 444 (M+2, 25.22 %), 441 (M^+–H, 100 %), 425 (M^+–NH_2, 32.38 %), 268 (M^+–$C_6H_2N_7$, 25.29 %); *Anal. for* $C_{21}H_{12}BrN_7$ (442.27): Calcd./Found (%): C,57.03/57.0, H,2.73/2.80, Br,18.07/18.10, N,22.17/22.20.

Ethyl 4-amino-10-(4-bromophenyl)-8-phenylpyrido [2',3':3,4] pyrazolo- [5,1-*c*][1,2,4]triazine-3-carboxylate 15b: crystallize from ethanol-DMF mixture as orange crystals (58%); mp. >300 ºC; **IR** (cm^{-1}), 3398, 3220, 3124 (NH_2), 2927 (CH-aliphatic) and 1693 (C=O); **^{1}H-NMR** (δ): 1.25 (t, 3H, $\underline{CH_3}CH_2COO$), 4.18 (q, 2H, $CH_3\underline{CH_2}COO$), 7.50-8.41 (m, 10H, aromatic and pyridine-CH protons) and 8.78 (s, br. 2H, NH_2); MS: 489 (M^+, 16.36%) which corresponding to the molecular weight of the molecular formula $C_{23}H_{17}BrN_6O_2$ of the assigned structure, 490 (M+1, 54.75%), 491 (M+2, 12.97%), 488 (M^+–H, 53.34%), 459 (488-C_2H_5, 14.86%), 416 (M^+–$COOC_2H_5$, 51.89%), 388 (416–N_2, 19.22%), 364 (M^+–$COOC_2H_5$-N_2-C_2, 100%), 334 (364-NNH_2, 8.88%), 103 (PhCN, 7.30%); *Anal. for* $C_{23}H_{17}BrN_6O_2$ (489.32): Calcd./ Found (%): C,56.45/56.50, H,3.50/3.60, Br,16.33/16.20, N,17.17/17.20.

3-[Aminosulfanylidyne)methyl]-10-(4-bromophenyl)-8-phenylpyrido-[2',3':3,4]pyrazolo[5,1-*c*][1,2,4]triazin-4-amine 15c: crystallize from ethanol-DMF mixture as yellow crystals (60 %); mp. >320 ºC; **IR** (cm^{-1}), 3457, 3318, 3162 (two NH_2) and 2925 (CH-aliphatic); **MS:** 477 (M+1, 16 %), 475 (M^+–H, 16.62%), 459 (475-NH_2, 37.08%), 443 (475-S, 100%), 416 (M^+–$CSNH_2$, 27.54%), 388 (416-N_2, 21.54%), 103 (PhCN, 21.69%); *Anal. for* $C_{21}H_{14}BrN_7S$ (476.35): Calcd./Found (%): C,52.95/53.0, H,2.96/3.10, Br,16.77/16.80, N,20.58/20.60, S,6.73/6.70.

Ethyl 10-(4-bromophenyl)-4-oxo-8-phenyl-3,4-dihydropyrido[2',3':3,4]–pyrazolo[5,1-*c*][1,2,4]triazine-3-carboxylate 15d: crystallize from ethanol-DMF mixture as orange crystals (56 %); mp. >300 ºC; **IR** (cm^{-1}): 3400, 3200 (H-bonded OH), 2981 (CH-aliphatic) and 1714 (CO ester); MS: 489 (M^+–H, 0.59 %), 460 (489-CH_3CH_2, 1.23 %), 458 (M^+-OH, CH_3, 1.58 %), 428 (458-OCH_2, 1.86 %), 400 (428-N_2, 1.62 %), 388 (400-C, 1.58 %), 285 (388-PhCN, 5.38%), 73 (COOEt, 81.16%), 68 (–N=N–C–CO–, 24.46%), 103 (PhCN, 5.46 %), 73 ($COOC_2H_5$, 81.16%); Anal. for Molecular Formula $C_{23}H_{16}BrN_5O_3$ (490.30): Calcd./Found (%): C,56.34/56.50, H,3.29/3.30, Br,16.30/16.40, N,14.28/14.30.

1-[10-(4-Bromophenyl)-4-methyl-8-phenylpyrido [2',3':3,4]pyrazolo-[5,1-*c*][1,2,4]triazin-3-yl]ethanone 15e: crystallize from ethanol-DMF mixture as orange crystals (52%); mp. 320 ºC; **IR** (cm^{-1}): 3073 (CH aromatic), 2923 (CH-aliphatic) and 1697 (CO acetyl); **^{1}H-NMR** (δ): 1.27 (s, 3H, CH_3), 2.11 (s, 3H, $CO\underline{CH_3}$), 7.63-8.48 (m, 10H, aromatic and pyridine-CH protons); **MS:** 458 (M^+, 30.56%) which corresponding to the molecular weight of the molecular formula $C_{23}H_{16}BrN_5O$ of the assigned structure, 459 (M+1, 100 %), 460 (M+2, 26.49 %), 415 (M^+–$COCH_3$, 8,71%), 416 (459-$COCH_3$, 29.76%), 387 (415–N_2, 8.21 %), 388 (416–N_2, 9.72 %); 103 (PhCN, 3.02%); Anal. for Molecular Formula $C_{23}H_{16}BrN_5O$ (458.31): Calcd./Found (%): C,60.27/60.30, H,3.52/3.60, Br,17.43/17.40, N,15.28/15.30.

Ethyl 10-(4-bromophenyl)-4-methyl-8-phenylpyrido[2',3':3,4] pyrazolo-[5,1-*c*][1,2,4]triazine-3-carboxylate 15f: crystallize from ethanol-DMF mixture as orange crystals (58 %); mp. 258-60 ºC; **IR** (cm^{-1}): 3049 (CH aromatic), 2923 (CH-aliphatic) and 1719 (CO ester); **^{1}H-NMR** (δ): 1.49 (s, 3H, CH_3), 1.57 (t, 3H, $\underline{CH_3}CH_2COO$), 4.63 (q, 2H, $COO\underline{CH_2}CH_3$) and 7.26-8.37 (m, 10H, aromatic and pyridine-CH protons); **MS:** 488 (M^+, 15.98%) which corresponding to the molecular weight of the molecular formula $C_{24}H_{18}BrN_5O_2$ of the assigned structure, 489 (M+1, 54.94%), 460 (M+1–C_2H_5, 12.79%), 459 (M^+–C_2H_5, 38.04%), 415 (M^+–$COOC_2H_5$, 98.03%), 416 (M+1-$COOC_2H_5$, 63.17%), 387 (415-N_2, 12.60%), 388 (416-N_2, 50.95%), 361 (388-CCH_3, 7.37%), 348 [M^+–$N_2C(COOC_2H_5)$ = $C(CH_3)$, 10.82%]; Anal. for Molecular Formula $C_{24}H_{18}BrN_5O_2$ (488.33): Calcd./Found (%): C,59.03/59.10, H,3.72/3.80, Br,16.36/16.40, N,14.34/14.20.

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