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Synthesis and antimicrobial activity of some new cyanopyridine and cyanopyrans towards *Mycobacterium tuberculosis* and other microorganisms

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2-Amino-3-cyano-6-(3,5-dibromo-4-methoxyphenyl)-4-aryl-pyridines **2a-i** are synthesized by the reaction of compounds (*2E*)-3-(3,5-dibromo-4-methoxyphenyl)-1-arylprop-2-en-1-one **1a-i** with malononitrile in the presence of ammonium acetate. Condensation of compounds **1a-i** with malononitrile in pyridine has yielded 2-amino-3-cyano-6-(3,5-dibromo-4-methoxyphenyl)-4-arylpyrans **3a-i.** The constitution of all the synthesized compounds have been established by elemental analyses, IR, ^{1}H NMR, and mass spectral data. All the compounds are screened for their antitubercular and antimicrobial activities.

Keywords: Cyanopyridine, cyanopyran, chalcone, antitubercular activity, antimicrobial activity

Many naturally occurring and synthetic compounds containing the cyanopyridine and cyanopyran scaffold possess interesting pharmacological properties. Among them, 2-amino-3-cyanopyridines have been identified as IKK – α inhibitors[1]. Cyanopyridine and cyanopyran derivatives are well-known for their versatile biological activities like antimicrobial[2], antitubercular[3], antiinflammatory[4], antitumor[5], antiviral[6], antifungal[7] etc. Looking to these multifold properties exhibited by them, we are reporting here the synthesis, antimicrobial and antitubercular activity towards *mycobacterium tuberculosis* of some cyanopyridines **2a-i** and cyanopyrans **3a-i** derivatives. In the present study, this strategy is used for the synthesis of these compounds in the hope that they may possess potent biological activities.

Chemistry

The synthesis of cyanopyridine and cyanopyran from chalcone was performed as shown in **Scheme I**. In the initial step, chalcones **1a-i** were synthesized by condensing 3,5-dibromo-4-methoxyacetophenone with aromatic aldehydes in the presence of catalytic amount of alcoholic KOH solution at RT[8-15]. The compounds **2a-i** were synthesized by reacting chalcone with malononitrile in presence of ammonium acetate in ethanol[16] while **3a-i** were synthesized by reacting chalcone with malononitrile in pyridine[17].

The purity of the synthesized compounds was controlled by TLC. Spectral data like IR, ^{1}H NMR, mass and elemental analysis of all the newly synthesized compounds were in full agreement with the proposed structures (**Table I**).

Biology

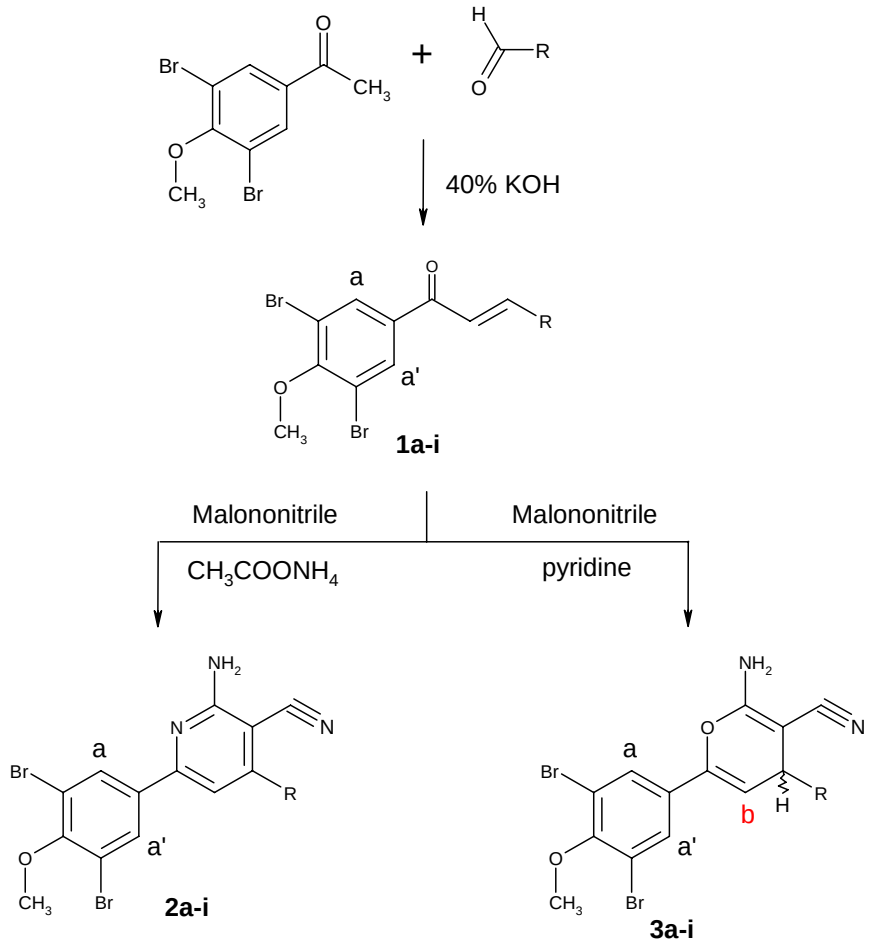
Antitubercular activity

The antitubercular evaluation of the compounds was carried out at Tuberculosis Antimicrobial Acquisition Coordinating Facility (TAACF) U.S.A[18]. Primary screening of the compounds for antitubercular activity has been conducted at 6.25 μg/mL against *Mycobacterium tuberculosis* H_{37}Rv ATCC 27294, in BACTEC 12B medium using the ALAMAR radiometric system.

The antitubercular activity data were compared with standard drug rifampin at 0.25 μg/mL concentrations, which showed 98% inhibition **Table II**.

Antimicrobial activity

The antimicrobial activity was assayed by using the cup-plate agar diffusion method[19] by measuring the zone of inhibition in mm. All the compounds were screened *in vitro* for their antimicrobial activity against varieties of bacterial strains such *Bacillus megaterium* ATCC 14518, *Bacillus substilis* ATCC 23857, *Escherichia coli* ATCC 25922, *Proteus*



R = Aryl

Scheme I

vulgaris ATCC 29213, and fungi *Aspergillus niger* ATCC 9029 at 40 µg/mL concentration. Standard drugs like ampicillin, amoxicillin, norfloxacin, benzyl penicillin and greseofulvin were used for the comparison purpose. The results are given in **Table II**.

Results and Discussion

From the evaluation of the antimicrobial data of the synthesized compounds it can be seen that the compounds **1c, 1i, 2f, 2i** and **3g** show moderate activity against *Mycobacterium tuberculosis*. The compounds **1c**, **1d, 2a, 2b**, **2c**, **2g**, **2h, 3a, 3b, 3d, 3f** and **3i** were active while **1a, 1h, 2e** and **2f** were moderately active against *B. megaterium*. The compound **2e** was active as well **2i**, **3b**, **3c**, **3h**, and **3i** were moderately active against *B. substilis*. The same way compounds **2a** and **2e** were active while **1e**, **1f**, **2b**, **2f** and **3b** were moderately active against *E. coli*. Similarly compounds **1d** were active while **1c**, **1e**, **1h**, **2e**, **3a**, **3b**, and **3i** show moderate activity against *P. vulgaris*. The compounds **1f**, **1i**, **2h**, **3e**, **3g**, and **3h** display moderate activity against *A. niger*.

Experimental Section

Melting points were determined in open capillary tubes with an electrothermal-9200 melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FTIR-8400 spectrophotometer in KBr. ^{1}H NMR spectra were recorded on a Bruker Avance II spectrometer (300 MHz) using TMS as an internal standard, chemical shift are given in δ, ppm. Mass spectra were determined using direct inlet probe on a GCMS-QP2010 mass spectrometer, Elemental analysis was performed on a Carlo Erba EA 1108 elemental analyzer. The results of elemental

Table I — Characterization data of compounds **1a-i**, **2a-i** and **3a-i**

Compd.	R	m.p. (^{o}C) (crystallization solvent)	Colour (yield%)	Mol. Formula (Mol. Wt.)	Calcd. (Found) (%)		
					C	H	N
1a	C_6H_5-	120-22 (methanol)	yellow (68)	$C_{16}H_{12}Br_2O_2$ (396.07	48.52 48.45	3.05 2.96	- -)
1b	3-Br-C_6H_4-	148-50 (methanol)	yellow (72)	$C_{16}H_{11}Br_3O_2$ (474.96	40.46 40.40	2.33 2.39	-)
1c	2-Cl-C_6H_4-	118-20 (methanol)	cream (66)	$C_{16}H_{11}Br_2ClO_2$ (430.52	44.64 44.52	2.58 2.61	-)
1d	4-Cl-C_6H_4-	125-26 (methanol)	cream (70)	$C_{16}H_{11}Br_2ClO_2$ (430.52	44.64 44.48	2.58 2.60	- -)
1e	4-N(CH_3)-C_6H_4-	145-47 (methanol)	pale yellow (65)	$C_{18}H_{17}Br_2NO_2$ (439.14	49.23 49.18	3.90 3.86	3.19 3.14)
1f	4-OCH_3-C_6H_4-	198-200 (ethanol)	cream (60)	$C_{17}H_{14}Br_2O_3$ (426.1	47.92 47.85	3.31 3.38	- -)
1g	3,4-$(OCH_3)_2$-C_6H_3-	234-36 (ethanol)	cream (65)	$C_{18}H_{16}Br_2O_4$ (456.13	47.40 47.31	3.54 3.59	- -)
1h	2-NO_2-C_6H_4-	110-12 (dioxane)	yellow (55)	$C_{16}H_{11}Br_2NO_4$ (441.07	43.57 43.55	2.51 2.59	3.18 3.14)
1i	3-NO_2-C_6H_4-	98-100 (dioxane)	yellow (63)	$C_{16}H_{11}Br_2NO_4$ (441.07	43.57 43.53	2.51 2.58	3.18 3.11)
2a	C_6H_5-	172-74 (dioxane)	white (65)	$C_{19}H_{13}Br_2N_3O$ (459.13	49.70 49.63	2.85 2.92	9.15 9.09)
2b	3-Br-C_6H_4-	126-8 (dioxane)	cream (60)	$C_{19}H_{12}Br_3N_3O$ (538.03	42.41 42.36	2.25 2.33	7.81 7.75)
2c	2-Cl-C_6H_4-	132-34 (dioxane)	cream (58)	$C_{19}H_{12}Br_2ClN_3O$ (493.58	46.23 46.19	2.45 2.49	7.18 7.10)
2d	4-Cl-C_6H_4-	170-71 (dioxane)	cream (70)	$C_{19}H_{12}Br_2ClN_3O$ (493.58	46.23 46.17	2.45 2.52	7.18 7.14)
2e	4-N(CH_3)-C_6H_4-	212-4 (dioxane)	yellow (72)	$C_{21}H_{18}Br_2N_4O$ (502.20	50.22 50.16	3.61 3.62	11.16 11.10)
2f	4-OCH_3-C_6H_4-	148-50 (dioxane)	cream (65)	$C_{20}H_{15}Br_2N_3O_2$ (489.16	49.11 49.06	3.09 3.16	8.56 8.51)
2g	3,4-$(OCH_3)_2$-C_6H_3-	268-70 (dioxane)	cream (68)	$C_{21}H_{17}Br_2N_3O_3$ (519.19	48.58 48.61	3.30 3.19	8.09 8.16)
2h	2-NO_2-C_6H_4-	134-36 (DMF)	yellow (58)	$C_{19}H_{12}Br_2N_4O_3$ (504.13	45.27 45.22	2.40 2.44	11.11 11.15)
2i	3-NO_2-C_6H_4-	168-70 (DMF)	yellow (55)	$C_{19}H_{12}Br_2N_4O_3$ (504.13	45.27 45.23	2.40 2.46	11.11 11.01)
3a	C_6H_5-	254-56 (ethyl acetate)	cream (62)	$C_{19}H_{14}Br_2N_2O_2$ (462.13	49.38 49.29	3.05 3.09	6.06 6.00)
3b	3-Br-C_6H_4-	210-12 (ethyl acetate)	white (65)	$C_{19}H_{13}Br_3N_2O_2$ (541.03	42.18 42.13	2.42 2.51	5.18 5.09)
3c	2-Cl-C_6H_4-	152-53 (ethyl acetate)	white (68)	$C_{19}H_{13}Br_2ClN_2O_2$ (496.58	45.96 45.89	2.64 2.67	5.64 5.69)
3d	4-Cl-C_6H_4-	130 132 (ethyl acetate)	white (70)	$C_{19}H_{13}Br_2ClN_2O_2$ (496.58	45.96 45.91	2.64 2.69	5.64 5.55)
3e	4-N(CH_3)-C_6H_4-	102-04 (dioxane)	yellow (64)	$C_{21}H_{19}Br_2N_3O_2$ (505.20	49.93 49.86	3.79 3.87	8.32 8.25)
3f	4-OCH_3-C_6H_4-	144-46 (ethyl acetate)	cream (65)	$C_{20}H_{16}Br_2N_2O_3$ (492.16	48.81 48.74	3.28 3.35	5.69 5.62)
3g	3,4-$(OCH_3)_2$-C_6H_3-	230-31 (dioxane)	cream (70)	$C_{21}H_{18}Br_2N_2O_4$ (522.19	48.30 48.24	3.47 3.38	5.32 5.40)
3h	2-NO_2-C_6H_4-	182-84 (DMF)	yellow (55)	$C_{19}H_{13}Br_2N_3O_4$ (507.13	45.00 44.93	2.58 2.67	8.29 8.22)
3i	3-NO_2-C_6H_4-	198-00 (DMF)	yellow (62)	$C_{19}H_{13}Br_2N_3O_4$ (507.13	45.00 44.96	2.58 2.64	6.06 6.00)

Table II — Antitubercular and antimicrobial screening of **1a-i, 2a-i** and **3a-i**

Compd	% Inhibition Antitubercular activity	Antibacterial activity				Antifungal activity
		B. megaterium	*B. substilis*	*E. coli*	*P. vulgaris*	*A. niger*
1a	25	18	12	10	10	10
1b	24	10	10	11	12	10
1c	65	32	16	12	14	12
1d	10	25	16	10	18	08
1e	00	12	11	18	16	10
1f	25	13	15	20	11	20
1g	45	14	11	11	10	11
1h	36	16	14	12	14	12
1i	71	11	12	13	11	18
2a	43	23	16	22	10	14
2b	25	26	14	18	11	12
2c	10	28	12	13	10	11
2d	03	10	10	16	12	10
2e	25	18	27	24	14	14
2f	55	17	11	17	12	15
2g	56	28	12	12	10	08
2h	25	24	15	15	08	20
2i	68	15	20	13	10	12
3a	36	22	12	14	14	10
3b	21	28	18	20	16	12
3c	65	14	20	12	12	12
3d	14	22	09	16	10	08
3e	10	08	16	11	12	20
3f	19	26	10	12	11	15
3g	53	13	11	14	10	18
3h	42	11	20	10	10	18
3i	10	27	21	08	14	16
Ampicillin	-	20	24	22	12	00
Amoxicillin	-	21	24	25	18	00
Norfloxacin	-	18	17	18	18	00
Benzyl penicillin	-	10	18	15	15	00
Greseofulvin	-	00	00	00	00	24
Rifampin	98	-	-	-	-	-

analyses (C, H, N) were within ± 0.4% of the theoretical values.

General procedure for the preparation of (2*E*)-1-(3,5-dibromo-4-methoxyphenyl)-3-aryl-prop-2-en-1-ones, 1a-i

A mixture of 3,5-dibromo-4-methoxyacetophenone (3.08 g, 0.01 mole) and different substituted arylaldehyde (0.01 mole) in methanol (25 mL) was stirred at RT for 24 hr. in the presence of catalytic amount of 40% KOH (0.5 mL). The resulting solution was poured onto crushed ice, thus the separated solid was filtered through Buchner funnel, dried and crystallized from suitable solvent.

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-phenyl-2-propen-1-one, 1a: IR (KBr, cm^{-1}): 3048 (Ar-C-H str.), 2958 (C-H str.), 1665 (C=O str.), 1051 (C-O str.), 1548 (C=C str.), 590 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.94 (s, 3H, -OCH_3), 7.15 (d, 1H, J = 12.2 Hz, -Hx), 7.24 (d, 1H, J = 12.3 Hz,

-Hy), 7.42-7.72 (m, 5H, Ar-H), 8.19 (s, 2H, Ar- Ha-a'); EI^+ *m/z*: 398 *(*M+2*)*, 396 *(*M^+*)*.

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(3-bromophenyl)-2-propen-1-one, 1b: IR (KBr, cm^{-1}): 3016 (Ar-C-H str.), 2945 (C-H str.), 1658 (C=O str.), 1086 (C-O str.), 1526 (C=C str.), 548 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.92 (s, 3H, -OCH_3), 7.21 (d, 1H, *J* = 13.0 Hz, -Hx), 7.48-7.53 (m, 2H, Ar-H), 7.63 (d, 1H, *J* = 13.0 Hz, -Hy), 7.69-7.89 (m, 2H, Ar-H), 8.12 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 475 (M^+).

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(2-chlorophenyl)-2-propen-1-one, 1c: IR (KBr, cm^{-1}): 3024 (Ar-C-H str.), 2937 (C-H str.), 1660 (C=O str.), 1068 (C-O str.), 1538 (C=C str.), 570 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.96 (s, 3H, -OCH_3), 7.18 (m, 1H, Ar-H), 7.26 (d, 1H, *J* = 14.2 Hz, -Hx), 7.52 (d, 1H, *J* = 14.1 Hz, -Hy), 7.68-7.92 (m, 3H, Ar-H), 8.16 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 432 (M+1), 431 (M^+).

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(4-chlorophenyl)-2-propen-1-one, 1d: IR (KBr, cm^{-1}): 3031 (Ar-C-H str.), 2930 (C-H str.), 1657 (C=O str.), 1052 (C-O str.), 1515 (C=C str.), 609 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.95 (s, 3H, -OCH_3), 7.16 (d, 1H, *J* = 14.6 Hz, -Hx), 7.25 (m, 2H, Ar-H), 7.51 (m, 2H, Ar-H), 7.59 (d, 1H, *J* = 14.6 Hz, -Hy), 8.19 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 431 (M^+).

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(4-*N*, *N*-dimethylphenyl)-2-propen-1-one, 1e: IR (KBr, cm^{-1}): 3028 (Ar-C-H str.), 2962 (C-H str.), 1651 (C=O str.), 1032 (C-O str.), 1548 (C=C str.), 586 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 2.92 (s, 6H, -$N(CH_3)_2$), 3.94 (s, 3H, -OCH_3), 6.82 (m, 2H, Ar-H), 7.09 (d, 1H, *J* = 13.8 Hz, -Hx), 7.16 (m, 2H, Ar-H), 7.32 (d, 1H, *J* = 13.6 Hz, -Hy), 7.58 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 440 (M^+).

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(4-methoxyphenyl)-2-propen-1-one, 1f: IR (KBr, cm^{-1}): 3059 (Ar-C-H str.), 2941 (C-H str.), 1666 (C=O str.), 1046 (C-O str.), 1534 (C=C str.), 549 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.90 (s, 3H, -OCH_3), 3.93 (s, 3H, -OCH_3), 6.75 (m, 2H, Ar-H), 7.15 (d, 1H, *J* = 15.1 Hz, -Hx), 7.28 (m, 2H, Ar-H), 7.46 (d, 1H, *J* = 15.2 Hz, -Hy), 7.88 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 426 (M^+).

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(3,4-dimethoxyphenyl)-2-propen-1-one, 1g: IR (KBr, cm-^{1}): 3038 (Ar-C-H str.), 2941 (C-H str.), 1670 (C=O str.), 1031 (C-O str.), 1526 (C=C str.), 564 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.82 (s, 6H, -OCH_3), 3.92 (s, 3H, -OCH_3), 6.81 (d, 1H, *J* = 7.5, Ar-H), 7.08 (m, 2H, Ar-H), 7.23 (d, 1H, *J* = 12.8 Hz, -Hx), 7.31 (d, 1H, J = 12.7 Hz, -Hy), 8.02 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 457 (M+1), 456 (M^+).

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(2-nitrophenyl)-2-propen-1-one, 1h: IR (KBr, cm^{-1}): 3063 (Ar-C-H str.), 2972 (C-H str.), 1666 (C=O str.), 1046 (C-O str.), 1534 (C=C str.), 549 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.95 (s, 3H, -OCH_3), 6.92 (d, 1H, *J* = 15.5 Hz, -Hx), 7.17 (m, 4H, Ar-H), 7.76 (s, 2H, Ar-Ha-a'), 7.89 (d, 1H, *J* = 15.5 Hz, -Hy); EI^+ *m/z*: 441 (M^+).

(2*E*)-1-(3,5-Dibromo-4-methoxyphenyl)-3-(3-nitrophenyl)-2-propen-1-one, 1i: IR (KBr, cm^{-1}): 3049 (Ar-C-H str.), 2956 (C-H str.), 1658 (C=O str.), 1034 (C-O str.), 1552 (C=C str.), 578 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.91 (s, 3H, -OCH_3), 6.88 (d, 1H, *J* = 14.3 Hz, -Hx), 7.20 (m, 4H, Ar-H), 8.03 (s, 2H, Ar-Ha-a'), 8.20 (d, 1H, *J* = 14.3 Hz, -Hy); EI^+ *m/z*: 538 (M^+).

General procedure for the preparation of 2-Amino-3-cyano-4-aryl-6-(3,5-dibromo-4-methoxyphenyl)pyridines, 2a-i: To a solution of (2*E*)-1-(3,5-dibromo-4-methoxyphenyl)-3-aryl-prop-2-en-1-ones **1a-i** (0.01 mole), in ethanol (20 mL) malononitrile (0.66 g, 0.01 mole) and ammonium acetate (6.2 g, 0.08 mole) were added. The content was heated under reflux for 12 hr. The resulting content was poured onto crushed ice, thus the solid separated was filtered through Buchner funnel and crystallized from suitable solvent which gives crystalline powder.

2-Amino-3-cyano-4-phenyl-6-(3,5-dibromo-4-methoxyphenyl)pyridine, 2a: IR (KBr, cm^{-1}) : 3378 (N-H str.), 3051 (Ar-C-H str.), 2940 (C-H str.), 2235 (C≡N str.), 1136 (C-O-C str.), 1528 (C=C str.), 541 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.95 (s, 3H, -OCH_3), 5.83 (s(b), 2H, -NH_2), 6.91 (m, 5H, Ar-H), 7.62 (s, 2H, Ar-Ha-a'), 7.85 (s, 1H, pyridine -C-H); EI^+ *m/z*: 459 (M^+).

2-Amino-3-cyano-4-(3-bromophenyl)-6-(3,5-dibromo-4-methoxyphenyl)pyridine, 2b: IR (KBr, cm^{-1}): 3357 (N-H str.), 3036 (Ar-C-H str.), 2925 (C-H str.), 2225 (C≡N str.), 1179 (C-O-C str.), 1512 (C=C str.), 563 (C-Br str.); ^1H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.91 (s, 3H, -OCH_3), 5.76 (s(b), 2H, -NH_2), 7.08 (m, 4H, Ar-H), 7.51 (s, 2H, Ar-Ha-a'), 7.98 (s, 1H, pyridine -C-H); EI^+ *m/z*: 460 (M+1), 459 (M^+).

2-Amino-3-cyano-4-(2-chlorophenyl)-6-(3,5-dibromo-4-methoxyphenyl)pyridine, 2c: IR (KBr, cm^{-1}): 3365 (N-H str.), 3042 (Ar-C-H str.), 2959 (C-H str.),

2228 (C≡N str.), 1163 (C-O-C str.), 1546 (C=C str.), 543 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.93 (s, 3H, -OCH_3), 5.82 (s(b), 2H, -NH_2), 7.12 (m, 4H, Ar-H), 7.63 (s, 2H, Ar-Ha-a'), 7.89 (s, 1H, pyridine -C-H); EI$^+$ *m/z*: 496 (M+2), 494 (M^+).

2-Amino-3-cyano-4-(4-chlorophenyl)-6-(3,5-dibromo-4-methoxyphenyl)pyridine, 2d: IR (KBr, cm^{-1}): 3361 (N-H str.), 3031 (Ar-C-H str.), 2937 (C-H str.), 2212 (C≡N str.), 1156 (C-O-C str.), 1561 (C=C str.), 603 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.97 (s, 3H, -OCH_3), 6.02 (s(b), 2H, -NH_2), 7.16 (m, 4H, Ar-H), 7.51 (s, 2H, Ar-Ha-a'), 7.85 (s, 1H, pyridine -C-H); EI$^+$ *m/z*: 495 (M+1), 494 (M^+).

2-Amino-3-cyano-4-(4-*N*,*N*-dimethylphenyl)-6-(3,5-dibromo-4-methoxyphenyl)-pyridine, 2e: IR (KBr, cm^{-1}): 3355 (N-H str.), 3046 (Ar-C-H str.), 2954 (C-H str.), 2224 (C≡N str.), 1149 (C-O-C str.), 1536 (C=C str.), 574 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.08 (s, 6H, -$N(CH_3)_2$), 3.92 (s, 3H, -OCH_3), 5.89 (s(b), 2H, -NH_2), 7.10 (m, 4H, Ar-H), 7.68 (s, 2H, Ar-Ha-a'), 7.92 (s, 1H, pyridine -C-H); EI$^+$ *m/z*: 502 (M^+).

2-Amino-3-cyano-4-(4-methoxyphenyl)-6-(3,5-dibromo-4-methoxyphenyl)-pyridine, 2f: IR (KBr, cm^{-1}): 3359 (N-H str.), 3062 (Ar-C-H str.), 2938 (C-H str.), 2236 (C≡N str.), 1161 (C-O-C str.), 1495 (C=C str.), 592 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.96 (s, 3H, -OCH_3), 3.98 (s, 3H, -OCH_3), 5.45 (s(b), 2H, -NH_2), 6.97 (s, 1H, pyridine -C-H), 7.50 (m, 4H, Ar-H), 7.70 (s, 2H, Ar-Ha-a'); EI$^+$ *m/z*: 491 (M+2), 489 (M^+).

2-Amino-3-cyano-4-(3,4-dimethoxyphenyl)-6-(3,5-dibromo-4-methoxyphenyl)-pyridine, 2g: IR (KBr, cm^{-1}): 3372 (N-H str.), 3053 (Ar-C-H str.), 2946 (C-H str.), 2240 (C≡N str.), 1141 (C-O-C str.), 1515 (C=C str.), 563 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.95 (s, 6H, -OCH_3), 3.98 (s, 3H, -OCH_3), 5.63 (s(b), 2H, -NH_2), 6.91 (m, 3H, Ar-H), 7.49 (s, 2H, Ar-Ha-a'), 7.73 (s, 1H, pyridine-C-H); EI$^+$ *m/z*: 520 (M^+).

2-Amino-3-cyano-4-(2-nitrophenyl)-6-(3,5-dibromo-4-methoxyphenyl)pyridine, 2h: IR (KBr, cm^{-1}): 3364 (N-H str.), 3047 (Ar-C-H str.), 2961 (C-H str.), 2234 (C≡N str.), 1168 (C-O-C str.), 1534 (C=C str.), 578 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.92 (s, 3H, -OCH_3), 5.79 (s(b), 2H, -NH_2), 7.09 (m, 4H, Ar-H), 7.59 (s, 2H, Ar-Ha-a'), 7.87 (s, 1H, pyridine -C-H); EI$^+$ *m/z*: 504 (M^+).

2-Amino-3-cyano-4-(3-nitrophenyl)-6-(3,5-dibromo-4-methoxyphenyl)pyridine, 2i: IR (KBr, cm^{-1}): 3370 (N-H str.), 3059 (Ar-C-H str.), 2972 (C-H str.), 2230 (C≡N str.), 1153 (C-O-C str.), 1561 (C=C str.), 586 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.94 (s, 3H, -OCH_3), 6.03 (s(b), 2H, -NH_2), 7.11 (m, 4H, Ar-H), 7.70 (s, 2H, Ar-Ha-a'), 7.84 (s, 1H, pyridine -C-H); EI$^+$ *m/z*: 504 (M^+).

General procedure for the preparation of 2-Amino-3-cyano-4-aryl-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3a-i: (2*E*)-1-(3,5-dibromo-4-methoxyphenyl)-3-aryl-prop-2-en-1-ones **1a-i** (0.01 mole), and malononitrile (0.66 g, 0.01 mole) in pyridine (20 mL) was heated under reflux for 10 hr. on oil-bath. The reaction-mixture was cooled and poured onto crushed ice. The residue was neutralized with 20% HCl, where upon a solid separated out, which was filtered through Buchner funnel and crystallized from suitable solvent to give crystalline powder.

2-Amino-3-cyano-4-phenyl-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3a: IR (KBr, cm^{-1}): 3370 (N-H str.), 3029 (Ar-C-H str.), 2876 (C-H str.), 2238 (C≡N str.), 1135 (C-O-C str.), 1471 (C=C str.), 550 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.93 (s, 3H, -OCH_3), 5.86 (s(b), 2H, -NH_2), 6.42 (d, 1H, J = 3.8 Hz, chiral-H), 6.83 (d, 1H, J = 3.7 Hz, pyran-Hb), 7.15 (m, 5H, Ar-H), 7.98 (s, 2H, Ar-Ha-a'). EI$^+$ *m/z*: 462 (M^+).

2-Amino-3-cyano-4-(3-bromophenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3b: IR (KBr, cm^{-1}): 3360 (N-H str.), 3046 (Ar-C-H str.), 2926 (C-H str.), 2229 (C≡N str.), 1162 (C-O-C str.), 1508 (C=C str.), 578 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.97 (s, 3H, -OCH_3), 5.72 (s(b), 2H, -NH_2), 5.98 (d, 1H, J = 3.5 Hz, chiral-H), 6.10 (d, 1H, J = 3.5 Hz, pyran-Hb), 6.92 (m, 4H, Ar-H), 8.02 (s, 2H, Ar-Ha-a'); EI$^+$ *m/z*: 542 (M+1), 541 (M^+).

2-Amino-3-cyano-4-(2-chlorophenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3c: IR (KBr, cm^{-1}): 3368 (N-H str.), 3068 (Ar-C-H str.), 2962 (C-H str.), 2235 (C≡N str.), 1147 (C-O-C str.), 1545 (C=C str.), 581 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.91 (s, 3H, -OCH_3), 5.62 (s(b), 2H, -NH_2), 5.82 (d, 1H, J = 3.6 Hz, chiral-H), 6.25 (d, 1H, J = 3.7 Hz, pyran-Hb), 6.91 (m, 4H, Ar-H), 8.08 (s, 2H, Ar-Ha-a'); EI$^+$ *m/z*: 497 (M^+).

2-Amino-3-cyano-4-(4-chlorophenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3d: IR (KBr, cm^{-1}): 3382 (N-H str.), 3056 (Ar-C-H str.), 2947 (C-H str.), 2214 (C≡N str.), 1103 (C-O-C str.), 1511 (C=C str.), 603 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ +

DMSO-d_6): 3.95 (s, 3H, -OCH_3), 5.56 (s(b), 2H, -NH_2), 6.75 (d, 1H, *J* = 3.2 Hz, chiral-H), 7.25 (d, 1H, *J* = 3.2 Hz, pyran-Hb), 6.81 (m, 4H, Ar-H), 7.70 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 497 (M^+).

2-Amino-3-cyano-4-(4-*N*,*N*-dimethylphenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3e: IR (KBr, cm^{-1}): 3364 (N-H str.), 3027 (Ar-C-H str.), 2892 (C-H str.), 2238 (C≡N str.), 1082 (C-O-C str.), 1563 (C=C str.), 523 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.08 (s, 6H, -$N(CH_3)_2$), 3.93 (s, 3H, -OCH_3), 5.64 (d, 1H, *J* = 3.9 Hz, chiral-H), 6.11 (s(b), 2H, -NH_2), 6.89 (d, 1H, *J* = 3.9 Hz, pyran-Hb), 7.15 (m, 4H, Ar-H), 7.86 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 507 (M+2), 505 (M^+).

2-Amino-3-cyano-4-(4-methoxyphenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3f: IR (KBr, cm^{-1}): 3376 (N-H str.), 3069 (Ar-C-H str.), 2938 (C-H str.), 2225 (C≡N str.), 1132 (C-O-C str.), 1523 (C=C str.), 561 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.96 (s, 3H, -OCH_3), 3.99 (s, 3H, -OCH_3), 5.89 (d, 1H, *J* = 4.1 Hz, chiral-H), 6.23 (s(b), 2H, -NH_2), 6.77 (d, 1H, *J* = 4.1 Hz, pyran-Hb), 7.32 (m, 4H, Ar-H), 7.79 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 493 (M^+).

2-Amino-3-cyano-4-(3,4-dimethoxyphenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3g: IR (KBr, cm^{-1}): 3378 (N-H str.), 3024 (Ar-C-H str.), 2962 (C-H str.), 2228 (C≡N str.), 1158 (C-O-C str.), 1541 (C=C str.), 579 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.94 (s, 6H, -OCH_3), 3.99 (s, 3H, -OCH_3), 5.65 (d, 1H, *J* = 3.7 Hz, chiral-H), 6.40 (s(b), 2H, -NH_2), 6.73 (d, 1H, *J* = 3.5 Hz, pyran-Hb), 7.41 (m, 3H, Ar-H), 7.96 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 524 (M+1), 523 (M^+).

2-Amino-3-cyano-4-(2-nitrophenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3h: IR (KBr, cm^{-1}): 3369 (N-H str.), 3051 (Ar-C-H str.), 2908 (C-H str.), 2238 (C≡N str.), 1143 (C-O-C str.), 1552 (C=C str.), 529 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.93 (s, 3H, -OCH_3), 5.42 (d, 1H, *J* = 3.3 Hz, chiral-H), 6.12 (s(b), 2H, -NH_2), 6.79 (d, 1H, *J* = 3.1 Hz, pyran-Hb), 7.32 (m, 4H, Ar-H), 7.94 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 507 (M^+).

2-Amino-3-cyano-4-(3-nitrophenyl)-6-(3,5-dibromo-4-methoxyphenyl)-*4H*-pyrans, 3i: IR (KBr, cm^{-1}): 3365 (N-H str.), 3043 (Ar-C-H str.), 2931 (C-H str.), 2235 (C≡N str.), 1108 (C-O-C str.), 1553 (C=C str.), 546 (C-Br str.); ^{1}H NMR 300 MHz ($CDCl_3$ + DMSO-d_6): 3.91 (s, 3H, -OCH_3), 5.58 (d, 1H, *J* = 3.6 Hz, chiral-H), 6.61 (s(b), 2H, -NH_2), 6.69 (d, 1H, *J* = 3.5 Hz, pyran-Hb), 7.63 (m, 4H, Ar-H), 7.88 (s, 2H, Ar-Ha-a'); EI^+ *m/z*: 507 (M^+).

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