SYNTHESIS AND ANTIBACTERIALA CTIVITIES OF FUSED PYRANOQUINOLINE DERIVATIVES

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Abstract
Ethyl 2-amino-4-aryl-6-chloro-4-H-pyrano[3,2-h]quinoline-3-carboxylate **1a-e** was converted into ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate **2a-e**. Several derivatives of the latter compound have been synthesized. Also, the synthesis of 7-aryl-5-chloropyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano- [3,2-h]quinoline and other related heterocycles are described
Key words: pyrrolo-, pyrazino-, pyranoquinoline, antibacterial activities.

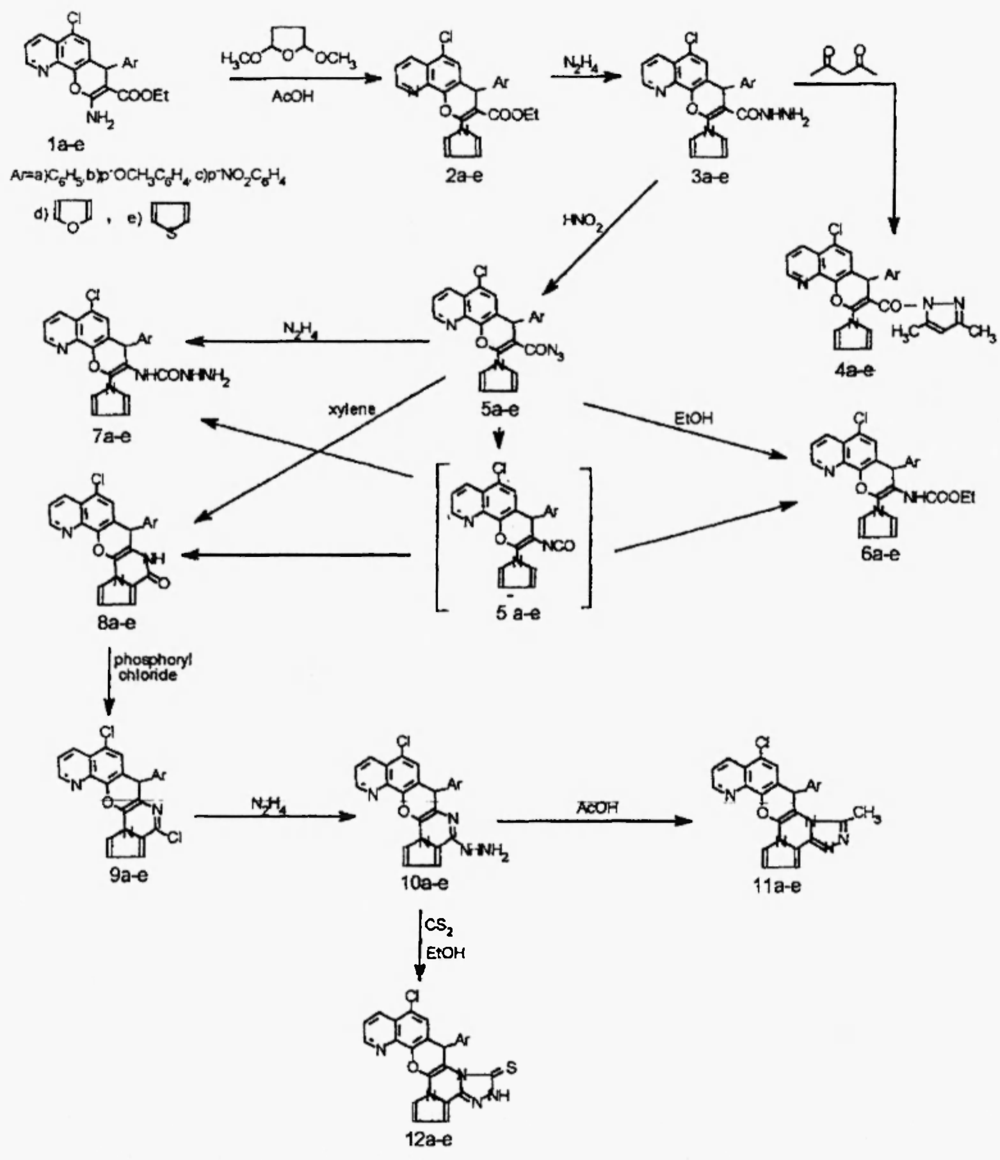
Introduction

Recent years have witnessed the synthesis and characterization a number of nitrogen-containing heteroaromatics. In fact, the biological activities of these compounds have drawn the attention of organic chemists for a long time. The synthesis of pyrano-quinoline derivatives has gaind very important goals to be used as antimicrobial activity (1-3). The pyrrolopyrazine derivatives were reported by Robba and his colleagues (4-8). We are presently involved in a program directed to the synthesis of pyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano[3,2-h]quinoline derivatives and related hexacyclic heterocycles (scheme-1).

Experimental

The time required for completion of each reaction was monitored by TLC. Melting points are uncorrected. NMR(δ, ppm) spectra were measured on an EM-360 90-MHZ spectrometer using TMS as internal standard. IR(γ, cm^{-1}) spectra were recorded on a Nicolet Jeol Technique in the rang of 4000-400 cm^{-1} 205 FTIR with KBr. Elemental analysis were determined on a perkin Elmer 240 C microanalyser. Mass spectra were recorded on Jeol JMS 600 instrement. Physical and spectral data are presented in table-1.

Ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate 1a-e:
A mixture of cinnamonnitrile derivatives (0.01 mol) and 5-chloro-8-quinolinol (0.01 mol) was heated under reflux in absolute ethanol (50 ml) using a catalytic amount of piperidine for 6h. The solvent was evaporated under reduced pressure, cooled and the precipitates were collected by filtration and recrystallized from methanol.


AcOH
N_2H_4
HNO_2
xylene
EtOH
phosphoryl chloride
CS_2
EtOH
1a-e
2a-e
3a-e
4a-e
5a-e
5 a-e
6a-e
7a-e
8a-e
9a-e
10a-e
11a-e
12a-e

Scheme 1

Table 1: Physical Data of Pyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano[3,2-h]quinoline derivatives and related heterocyclic heterocycles **1a-e-12a-e**.

Comp. No.	Yield %	Mp (°C)	Molecular Formula	IR (γ,cm^{-1}) (KBr)andMS	NMR (solvent) (δ,ppm)	Anal.Calcd/(Found)% C	H	N	S	Cl
1a	65	114-116	$C_{21}H_{17}N_2O_3Cl$	3273-3160(NH_2) 1735(CO),m/z 381,383	($CDCl_3$):5.10(1H,s), 3.70(3H,t),4.20(2H,q), 7.10-8.50(9H,m),8.90 (2H,s)	66.22 (66.34)	4.50 (4.46)	7.36 (7.43)		9.32 (9.26)
1b	79	101-103	$C_{22}H_{29}N_2O_4Cl$	3324-3180(NH_2), 1716(CO)	($CDCl_3$):2.20(3H,s), 3.80(3H,t),4.25(2H,q), 5.10(1H,s),7.00-8.45 (8H,m),8.90(2H,S)	64.30 (64.44)	4.66 (4.73)	6.82 (6 73)		8.64 (8.71)
1c	72	96-98	$C_{21}H_{30}N_3O_5Cl$	3390-3242(NH_2), 1700(CO)	(CF_3COOD):5.10(1H,s),3.70(3H,t),4.15(2H,q), 7.10-8.40(8H,m)	59.22 (59.34)	3.79 (3.73	9.87 (9.94)		8.34 (8.28)
1d	83	117-119	$C_{19}H_{15}N_2O_4Cl$	3360-3186(NH_2), 1711(CO)	(CF_3COOD):5.00(1H,s),3.50(3H,t),4.00(2H,q), 7.80-8.90(7H,m)	6154 (61.65)	4.08 (4.16)	7.56 (7.47)		9.57 (9.46)
1e	80	83-85	$C_{19}H_{15}N_2O_3ClS$	3324-3196(NH_2), 1716(CO)	(CF_3COOD):5.00(1H,s),3.50(3H,t),4.00(2H,q), 6.60-7.80(7H,m)	58.98 (58.85)	3.91 (3.83)	7.24 (7.33)	8.30 (8.22)	9.18 (9.30)
2a	62	126	$C_{25}H_{19}N_2O_3Cl$	1700(CO),m/z 419,421	($CDCl_3$):3.50(3H,t), 4.30(2H,q),5.10(1H,s) 6.40(2H,m),6.75(2H,m) 7.10-8.60(9H,m)	69.68 (69.82)	4.44 (4.48)	6.50 (6.41)		8.24 (8.16)
2b	71	89	$C_{26}H_{21}N_2O_4Cl$	1710(CO)	($CDCl_3$):3.50(3H,s), 4.30(2H,t),4.30(2H,q) 5.00(1H,s),6.50(2H,m) 6.80(2H,m),7.20-8.50 (8H,m)	67.74 (67,61)	4.59 (4.51)	6.08 (6.16)		7.70 (7.83)
2c	65	142	$C_{25}H_{18}N_3O_5Cl$	1700(CO)	($CDCl_3$):3.50(3H,t), 4.20(2H,q),5.10(2H,s) 6.50(2H,m),6.70(2H,m) 7.20-8.50(8H,m)	63.09 (63.20)	3.81 (3.76)	8.83 (8.78)		7.46 (7.35)
2d	74	176	$C_{23}H_{17}N_2O_4Cl$	1720(CO)	($CDCl_3$):3.50(3H,t), 4.30(2H,q),5.10(2H,s) 6.40(2H,m),6.60(2H,m) 6.80-8.20(7H,m)	65.63 (65.74)	4.07 (4.12)	6.66 (6.74)		8.44 (8.35)
2e	68	98	$C_{19}H_{15}N_2O_3ClS$	1720(CO)	($CDCl_3$):3.50(3H,t), 4.30(2H,q),5.10(2H,s) 6.40(2H,m),6.60(2H,m) 6.80-8.30(7H,m)	63.21 (63.33)	3.92 (3.84)	6.41 (6.31)	7.35 (7.42)	8.12 (8.21)
3a	65	134	$C_{23}H_{17}N_4O_2Cl$	1700(CO), 3324-3206(NH_2),3452(NH),m/z 417,419	(CF_3COOD):5.00(1H,s),6.40(2H,m),6.70(2H,m),7.10-8.60(9H,m)	66.26 (66.15)	4.11 (4.16)	13.44 (13.50)		8.52 (8.61)
3b	75	151	$C_{24}H_{19}N_4O_3Cl$	1716(CO), 3312-3202(NH_2), 3450(NH)	(CF_3COOD):2.40(3H,s),5.10(1H,t),6.40(2H,m), 6.70(2H,m),7.10-8.40 (8H,m)	64.49 (64.58)	4.29 (4.34)	12.54 (12.47)		7.94 (7.85)
3c	69	121	$C_{23}H_{10}N_5O_4Cl$	1710(CO), 3300-3200(NH_2), 3450(NH)	(CF_3COOD):5.00(1H,s),6.40(1H,m),6.70(2H,m), 7.20-8.20(8H,m)	59.80 (59.95)	3.49 (3.42)	15.17 (15.23)		7.69 (7.54)
3d	78	159	$C_{21}H_{15}N_4O_3Cl$	1700(CO), 3320-3215 (NH_2),3435 (NH)	(CF_3COOD):5.10(1H,s),6.20(2H,m),6.60(2H,m),6.80-8.50(7H,m)	61.99 (61.86)	3.72 (3.67)	13.77 (13.69)		8.37 (8.50)
3e	72	>340	$C_{21}H_{15}N_4O_2Cl$	1700(CO), 3310-3200 (NH_2),3420 (NH)	(CF_3COOD):5.10(1H,s),6.20(2H,m),6.60(2H,m),6.90-8.40(7H,m)	59.63 (59.79)	3.58 (3.62)	13.25 (13.19)	7.59 (7.68)	8.39 (8.24)
4a	61	231	$C_{28}H_{21}N_4O_2Cl$	1700(CO),m/z 481,483	($CDCl_3$):1.80(6H,s), 5.00(1H,s),6.30(2H,m),6.55(2H,m),7.10-8.50 (9H,m)	69.91 (69.79)	4.40 (4.37)	11.65 (11.72)		7.38 (7.46)
4b	70	173	$C_{29}H_{23}N_4O_2Cl$	1700(CO),	($CDCl_3$):2.30(3H,s), 5.10(1H,s),6.30(2H,m) 6.50(2H,m),7.20-8.40 (8H,m)	70.36 (70.47)	4.68 (4.74)	11.32 (11.41)		7.17 (7.28)
4c	65	133	$C_{28}H_{20}N_5O_4Cl$	1710(CO)	($CDCl_3$):5.10(3H,s), 6.40(2H,m),6.60(2H,m) ,7.30-8.40(8H,m)	63.93 (63,83)	3.83 (3.77)	13.32 (13.24)		6.75 (6.65)
4d	74	>340	$C_{26}H_{19}N_4O_3Cl$	1700(CO)	($CDCl_3$):5.0(1H,s), 6.300(2H,m),6.50 (2H,m),7.10-8.20 (7H,m)	66.30 (66.42)	7.07 (4.13)	11.90 (11.81)		7.54 (7.42)

Table-1 continued

4e	68	112	$C_{20}H_{19}N_4O_2ClS$	1722(CO)	($CDCl_3$):5.0(1H,s), 6.30(2H,m),6.50(2H,m),7.20-8.40(7H,m)	64.11 (64.22)	3.93 (3.87)	11.51 (11.43)	6.59 (6.66)	7.29 (7.18)
5a	62	185	$C_{23}H_{14}N_5O_2Cl$	2213(N_3), 1716(CO),m/z 428,430	($CDCl_3$):5.10(1H,s), 6.40(2H,m),6.60(2H,m) 7.30-8.60(9H,m)	64.56 (60.68)	3.30 (3.38)	16.37 (16.48)		8.30 (8.19)
5b	67	108	$C_{24}H_{10}N_5O_3Cl$	2218(N_3), 1710(CO)	($CDCl_3$):2.50(3H,s), 5.10(1H,s),6.40(2H,m) 6.60(2H,m), 7.30-8.50(8H,m)	62.95 (62.82)	3.52 (3.47)	15.30 (15.43)		7.75 (7.82)
5c	61	194	$C_{23}H_{13}N_5O_4Cl$	2210(N_3), 1700(CO)	($CDCl_3$):5.10(1H,s), 6.40(1H,m),6.60(2H,m), 7.30-8.60(8H,m)	60.20 (60.31)	2.86 (2.94)	15.27 (15.49)		7.74 (7.81)
5d	70	338	$C_{21}H_{12}N_5O_3Cl$	2214(N_3), 1680(CO)	($CDCl_3$):5. 0(1H,s), 6.30(2H,m),6.50(2H,m), 6.80-8.10(7H,m)	60.36 (60.48)	2.90 (2.84)	16.76 (16.88)		8.50 (8 43)
5e	74	257	$C_{25}H_{12}N_5O_2ClS$	2216(N_3), 1670(CO)	($CDCl_3$):5. 0(1H,s), 6.30(2H,m),6.50(2H,m), 6.80-8.10(7H,m	58.12 (58.22)	2.79 (2.87)	16.14 (16.25	7.40 (7.51)	8.18 (8.25)
6a	72	>340	$C_{25}H_{20}N_3O_3Cl$	3375(NH), 1700(CO), m/z 446,448	(CF_3COOD):2.10(3H,t), 4.20(2H,q),5.10(1H,s), 6.30(2H,m),6.60(2H,m), 7.30-8.50(9H,m)	67.33 (67.47)	4.52 (4.58)	9.43 (9.36)		7.96 (8.04)
6b	76	192	$C_{26}H_{22}N_3O_4Cl$	3457(NH), 1705(CO)	(CF_3COOD):2.10(3H,t), 2.90(3H,s),4.10(2H,q), 5.10(1H,s),6.30(2H,m), 6.60(2H,m),7.20-8.40 (8H,m)	65.61 (65.45)	4.66 (4.58)	8.83 (8.92)		7.46 (7.62)
6c	70	>340	$C_{25}H_{10}N_3O_5Cl$	3421(NH), 1700(CO)	(CF_3COOD):2.10(3H,t), 4.10(2H,q),5.10(1H,s), 6.30(2H,m), 7.20-8.50 (8H,m)	61.16 (61.30)	3.90 (3.78)	11.42 (11.28)		7.23 (7.34)
6d	79	>340	$C_{23}H_{18}N_3O_4ClS$	3405(NH), 1705(CO)	(CF_3COOD):2.20(3H,t), 4.10(2H,q),6.20(2H,m), 6.40(2H,m),7.00-8.30(7H,m)	63.37 (63.22)	4.16 (4.24)	9.64 (9.75)		8.14 (8.29)
6e	82	285	$C_{23}H_{18}N_3O_3Cl$	3415(NH), 1700(CO),	(CF_3COOD):2.20(1H,t), 420(2H,q),6.20(2H,m), 6.40(2H,m),7.00-8.30 (7H,m)	61.11 (61.24)	4.01 (4.11)	9.30 (9.21)	7.10 (7.21)	7.85 (7.93)
7a	70	325	$C_{25}H_{18}N_5O_2Cl$	3340-3160 (NH_2),3347 (NH), 1690 (CO),m/z 432,434	(CF_3COOD):5.10(1H,s), 6.20-8.30(13H,m)	63.95 (63.81)	4.20 (4 14)	16.22 (16.15)		8.22 (8.30)
7b	75	246	$C_{24}H_{20}N_5O_3Cl$	3340-3210(NH_2),3450(NH),1670 (CO	(Cf$_3$COOD):3.20(3H,s), 5.10(1H,s),6.25-8.30 (12H,m)	62.40 (62.55)	4.36 (4.42)	15.16 (15.29)		7.69 (7 78)
7c	69	261	$C_{23}H_{17}N_6O_4Cl$	3331-3230 (NH_2),3340 (NH),1665 (CO)	(CF_3COOD):5.10 (1H,s),6.20-8.40 (12H,m)	57.92 (57.97)	3.59 (3.64)	17.63 (17.74)		7.44 (7.51)
7d	78	>340	$C_{21}H_{16}N_5O_3Cl$	3300-3200 (NH_2),3435 (NH),1670 (CO)	(CF_3COOD):5.00(1H,s), 6.30-8.45(11H,m)	59.78 (59.64)	3.82 (3.76)	16.60 (16.47)		8.42 (8.51)
7e	82	>340	$C_{21}H_{10}N_3O_2ClS$	3315-3203 (NH_2),3427 (NH), 1685 (CO)	(CF_3COOD):5.00(1H,s), 6.30-8.40 (11H,m)	57.58 (57.46)	3.68 (3.73)	15.99 (15.82)	7.33 (7.44)	8.11 (8.20)
8a	62	>340	$C_{23}H_{14}N_3O_2Cl$	3385(NH_2), 1690 (CO), m/z 400,402	(CF_3COOD):5.10(1H,s), 6.45-8.25(12H,m)	69.08 (69.20)	3.53 (3 61)	10.51 (10.62)		8.77 (8.26)
8b	65	196	$C_{24}H_{14}N_3O_3Cl$	2416(NH), 1690(CO)	(CF_3COOD):2.30(1H,s), 5.10(1H,s), 6.40-8.30(11H,m)	67.05 (67.21)	3.75 (3.82)	9.78 (9.87)		8.26 (8.32)
8c	61	>340	$C_{23}H_{13}N_4O_4Cl$	3390(NH), 1650(CO)	(CF_3COOD):5.10(1H,s), 6.40-8.30(11H,m)	62.09 (62.23)	2.95 (3.02)	12.60 (12.74)		7.98 (8.06)
8d	66	>340	$C_{21}H_{12}N_3O_3Cl$	3380(NH), 1700(CO)	(CF_3COOD):5.00(1H,s), 6.25-8.30(10H,m)	64.70 (64.44)	3.10 (3.19)	10.78 (10.86)		9.11 (9.26)

Table-1 continued

8e	69	>340	$C_{21}H_{12}N_3O_2Cl$	3380(NH), 1664(CO)	(CF_3COOD):5.00(1H,s), 6.25-8.30(10H,m)	62.13 (62.26)	2.98 (2.87)	10.35 (10.44)	7.91 (7.83)	8.75 (8.82)
9a	70	254	$C_{23}H_{13}N_3OCl_2$		($CDCl_3$):5.10(1H,s), 6.35-8.40(12H,m)	66.03 (66.17)	3.13 (3.07)	10.05 (10.14)		16.97 (16.83)
9b	73	242	$C_{24}H_{15}N_3O_2Cl_2$		($CDCl_3$):2.30(3H,s), 5.10(1H,s), 6.30-8.40(11H,m)	64.28 (64.39)	3.37 (3.43)	9.37 (9.45)		15.83 (15.72)
9c	68	228	$C_{23}H_{12}N_4O_3Cl_2$		($CDCl_3$):5.10(1H,s), 6.30-8.40(11H,m)	59.61 (59.74)	2.61 (2.56)	12.09 (12.18)		15.32 (15.20)
9d	74	298	$C_{21}H_{11}N_3O_2Cl_2$		($CDCl_3$):5.00(1H,s), 6.25-8.30(10H,m)	61.77 (61.64)	2.72 (2.68)	10.29 (10.18)		17.39 (17.27)
9e	77	291	$C_{21}H_{11}N_3OCl_2S$		($CDCl_3$):5.00(1H,s), 6.25-8.30(10H,m)	59.42 (59.31)	2.61 (2.58)	9.90 (9.82)	7.56 (7.66)	16.73 (16.60)
10a	64	294	$C_{23}H_{10}N_5OCl$	3320-3206 (NH_2),3450 (NH),m/z 414,416	(CF_3COOD):5.10(1H,s), 6.30--8.20 (12H,m)	66.74 (66.62)	3.90 (3.20)	16.92 (16.99)		8.58 (8.66)
10b	66	282	$C_{24}H_{18}N_5O_2Cl$	3300-3195 (NH_2),3416 (NH)	(CF_3COOD):2.30(3H,s), 5.10(1H,s), 6.30-8.20 (11H,m)	64.93 (64.80)	4.09 (4.15)	15.78 (15.91)		8.00 (7.89)
10c	62	257	$C_{23}H_{15}N_6O_3Cl$	3315-3202 (NH_2),3430 (NH)	(CF_3COOD): 5.10(1H,s), 6.30-8.30 (11H,m)	60.19 (60.30)	3.30 (3.41)	18.32 (18.44)		7.74 (7.81)
10d	68	>340	$C_{21}H_{14}N_5O_2Cl$	3300-3180 (NH_2),3446 (NH)	(CF_3COOD):5.00(1H,s), 6.20-8.25(10H,m)	62.45 (62.57)	3.49 (3.57)	17.35 (17.47)		8.79 (8.87)
10e	71	95	$C_{21}H_{14}N_5OClS$	3310-3165 (NH_2),3450 (NH)	(CF_3COOD):5.00(1H,s), 6.20-8.25(10H,m)	60.05 (60.15)	3.36 (3.42)	16.68 (16.81)	7.64 (7.58)	8.45 (8.38)
11a	55	118	$C_{25}H_{16}N_5OCl$		($CDCl_3$):2.10(3H,s), 5.10(1H,s), 6.30-8.10(12H,m)	68.56 (68.45)	3.68 (3.73)	16.00 (16.06)		8.11 (8 19)
11b	58	234	$C_{26}H_{18}N_5O_2Cl$		($CDCl_3$):2.10(3H,s), 3.20(3H,s), 5.10(1H,s), 630-8.20(11H,m)	66.73 (66.60)	3.88 (3.93)	14.97 (14.86)		7.59 (7.48)
11c	54	257	$C_{25}H_{15}N_5O_3Cl$		($CDCl_3$): 2.10(3H,s), 5.10(1H,s), 6.30-8.20(11H,m)	64.03 (64.13)	3.22 (3.16)	14.94 (14.84)		7.57 (7.66)
11d	60	>340	$C_{23}H_{14}N_5O_2Cl$		($CDCl_3$): 2.10(3H,s), 5.00(1H,s), 6.20-8.35(10H,m)	64.56 (64.43)	3.30 (3.24)	16.37 (16.25)		8.30 (8.43)
11e	63	195	$C_{23}H_{14}N_5OClS$		($CDCl_3$): 2.10(3H,s), 5.00(1H,s), 6.20-8.35(10H,m)	62.22 (62.36)	3.18 (3.25)	15.78 (15.67)	7.23 (7.17)	8.00 (8.11)
12a	59	191	$C_{24}H_{14}N_5OClS$	3330(NH), 1190(CS),m/z 356,358	(CF_3COOD):5.10(1H,s), 6.30-8.25(12H,m)	63.21 (63.32)	3.10 (3 01)	15.36 (15.45)	7.04 (7.13)	7.79 (7.88)
12b	62	>340	$C_{25}H_{15}N_5O_2ClS$	3400(NH), 1190(CS)	(CF_3COOD):2.50(3H,s), 5.10(1H,s), 6.30-8.30(11H,m)	61.78 (61.89)	3.32 (3.38)	14.41 (14.32)	6.61 (6.62)	7.30 (7.41)
12c	58	263	$C_{24}H_{13}N_9O_3ClS$	3350(NH), 1190(CS)	(CF_3COOD):5.10(1H,s), 6.30-8.30(11H,m)	57.53 (57. 43)	2.62 (2.56)	16.78 (16. 86)	6.41 (6.50)	7 09 (7.19)
12d	65	127	$C_{22}H_{12}N_5O_2ClS$	3325(NH), 1195(CS)	(CF_3COOD):5.10(1H,s), 6.20-8.30(10H,m)	59.25 (59.37)	2.71 (2.65)	15.71 (15.62)	7.20 (7.12)	7.96 (7.84)
12e	67	>340	$C_{22}H_{12}N_5OClS_2$	3340(NH), 1180(CS)	(CF_3COOD):5.10(1H,s), 6.20-8.30(10H,m)	57.18 (57.29)	2.62 (2.56)	15.16 (15.24)	13.89 (13.78)	7.68 (7.57)

Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate 2a-e:

A mixture of **1a-e** (0.01 mol) an 2,5-dimethoxytetrahydrofuran (0.01 mol) in acetic acid (50 ml) was heated under reflux for two hours. After cooling, the precipitates formed was filtered off and recrystallized from ethanol.

2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carbohydrazide 3a-e:

To a solution of the ester **2a-e** (0.01 mol) in hot ethanol (60 ml) was added an excess of hydrazine hydrate (5 ml, 98%) and the reaction mixture was refluxed for 5h. The solid product obtained was filtered off and recrystallized from acetic acid.

2-(1-pyrrolyl)-3-[(3,5-dimethylpyrazol-1-yl)carbonyl]-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolines 4a-e:

A mixture of **3a-e** (0.01 mol) and excess of acetylacetone (10 ml) was refluxed for 5h. The excess acetylacetone was eliminated in vacuo and the solid product was collected and recrystallized from ethanol.

2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-oylazide 5a-e: General Procedure:

To a solution of **3a-e** (0.01 mol) in glacial acetic acid (40 ml) a solution of sodium nitrite (0.01 mol in 10 ml water) was added at room temperature with stirring. Stirring was continued for 30 minutes and the precipitates were filtered off, washed with water and recrystallized from benzene.

Ethyl 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-carboxylate 6a-e:

Each compound of **5a-e** (0.01 mol) was heated under reflux in excess absolute ethanol (50 ml) for 2h. The reaction mixture was concentrated and left to cool. The solid product was recrystallized from ethanol.

4-[2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinoline-3-yl]semicarbazide 7a-e:

A mixture of **5a-e** (0.01 mol) and hydrazine hydrate (10 ml) was refluxed for 1h. On cooling the solid product obtained was filtered off, washed with ethanol and recrystallized from ethanol.

7-Aryl-5-chloro-9-oxo-8,9-dihydropyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano-[3,2-h]quinoline 8a-e:
Asolution of **5a-e** (0.01 mol) in xylene (15 ml) was refluxed for one hour and then allowed to cool. The formed product was filtered off and recrystallized from ethanol.

7-Aryl-5,9-dichloropyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano[3,2-h]quinoline 9a-e:
A suspension of **8a-e** (0.01 mol) in phosphoryl chloride (25 ml) was heated under reflux for 4 hours. The cold reaction mixture was poured into ice-water mixture, the residual solid product was worked up in an ammonium hydroxide-ice mixture, filtered ,washed with water and recrystallized from benzene.

7-Aryl-5-chloro-9-hydrazinopyrrolo[1",2":1',2']pyrazino[5,6:5',6']pyrano[3,2-h] quinoline 10a-e:
A mixture of **9a-e** (0.01 mol) and hydrazine hydrate (5 ml, 98%) in ethanol (25 ml) was heated under reflux for 5h. The product formed after cooling was filtered, washed with ethanol and recrystallized from dioxane.

7-Aryl-5-chloro-9-methyl[1,2,4]triazolo[3",4":3',4']pyrrolo[1",2":1',2']pyrazino-[5,6:5',6']pyrano[3,2-h]quinoline 11a-e:
A solution of **10a-e** (0.01mol) in acetic acid (30 ml) was heated under reflux for 6h. The reaction mixture was concentrated in vacuo and the solid product was collected, washed with water and recrystallized from acetic acid.

7-Aryl-5-chloro-9-thioxo-9,10-dihydro[1,2,4]triazolo[3",4":3',4'] pyrrolo-[1",2":1',2'] pyrazino[5,6:5',6']pyrano[3,2-h]quinoline 12a-e:
A mixture of 10a-e (0.01 mol), in carbon disulfide (3 ml) in ethanol (30 ml) and two pellets of potassium hydroxide was heated under reflux on water bath for 6h. The solid product obtained was dissolved in water then acidified with acetic acid and recrystallized from dioxane.

Antimicrobial Activity

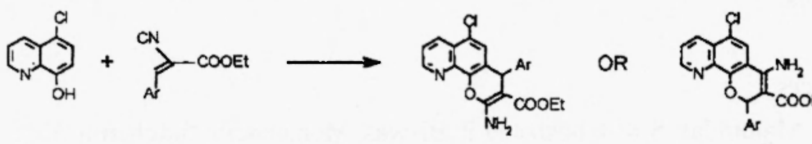
The antimicrobial activity of the synthesized compounds was tested against *Escherichia coli* and *staphylococcus aureus* using the agar cup diffusion technique(11) and results of the biological testing are given in Table 2. The data showed that most of the newly synthesized compounds exhibited remarkable effects.

Table 2: Antimicrobial Screening of compounds **1a-e-12a-e (inhibition zones mm)**

Compd.No.	Escherichia coli	Staphilococcus aureus	Compd.No.	Escherichia coli	Staphilococcus aureus
1a	18	25	**7a**	27	36
1b	29	33	**7b**	43	32
1c	-	17	**7c**	25	16
1d	26	39	**7d**	31	34
1e	45	62	**7e**	47	29
2a	20	29	**8a**	22	26
2b	33	35	**8b**	35	24
2c	19	-	**8c**	-	29
2d	17	21	**8d**	22	25
2e	36	50	**8e**	33	39
3a	22	31	**9a**	26	31
3b	37	27	**9b**	40	28
3c	26	19	**9c**	26	35
3d	23	28	**9d**	31	28
3e	42	57	**9e**	37	44
4a	18	21	**10a**	21	25
4b	23	19	**10b**	36	22
4c	18	24	**10c**	22	32
4d	-	16	**10d**	25	23
4e	22	-	**10e**	31	28
5a	24	33	**11a**	-	21
5b	40	29	**11b**	29	-
5c	14	22	**11c**	-	19
5d	27	31	**11d**	18	-
5e	44	61	**11e**	24	21
6a	19	21	**12a**	31	36
6b	25	19	**12b**	45	31
6c	23	-	**12c**	30	38
6d	26	23	**12d**	44	32
6e	24	31	**12e**	39	46
Tetracycline	12	15	**Tetracycline**	12	15

Results and discussions

It has been found that 5-chloro-8-quinolinol reacts with ylidennitriles in ethanol and in the presence of catalytic amount of piperidine for which two products **1a**-e and **1'a**-e seemed possible. Structures **1a**-e were establish for the reaction products based on ^{1}H-NMR spectra which revealed the presence of 4H-pyran proton at 5.00-5.10 ppm, thus the structure **1'a**-e were ruled out (9,10).



1a-e 1'a-e

The amino function of ethyl 2-amino-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolines **1a**-e were easily converted to the corresponding 1-pyrrolyl group (7) via the interaction with 2,5-dimethoxytetrahydrofuran in boiling acetic acid to give **2a**-e. The latter pyrrolyl ester was reacted with hydrazine hydrate to give the pyrrolyl hydrazide **3a**-e. The pyrazolyl derivatives **4a**-e were the product of the reaction between the hydrazides 3a-e and acetylacetone. The treatment of the hydrazides **3a**-e with nitrous acid gave the corresponding 2-(1-pyrrolyl)-4-aryl-6-chloro-4H-pyrano[3,2-h]quinolin-3-oylazides **5a**-e. This acid azide is versatile compound and could be transformed into a variety of derivatives. When **5a**-e were heated in boiling ethanol the ethyl carbamate **6a**-e were obtained. When they were reacted with hydrazine hydrate, the products were the semicarbazides 7a-e. Obviously these reactions went through the intermediate isocyanate **5a**-e formed via Curtius rearrangement of **5a**-e. Heating the acid azides **5a**-e in a high-boiling point inert solvent such as xylene led to Curtius rearrangement with concomitant ring closure of the isocyanate intermediate **5a**-e giving 7-aryl-5-chloro-9-oxo-8,9-dihydropyrrolo[1",2":1',2']pyrazino [5,6:5',6']-pyrano[3,2-h]quinolines **8a**-e. The formation of **8a**-e are due to the high reactivity of the isocyanate intermediate which could not be isolated under the reaction conditions used.

The latter oxo compounds **8a**-e could be transformed into the corresponding chloro derivatives 9a-e by heating with phosphoryl chloride under reflux. The reactivity of the chlorine atom of 9a-e was shown by its easy displacement using various nucleophilic reagents such as hydrazine hydrate to give **10a**-e. The hydrazine hydrate derivatives **10a**-e proved to be a useful compound for synthetics. The triazolo derivatives **11a-e** and **12a-e** were produced from the reaction of **10a-e** with acetic acid and carbon disulfide respectively Table 1. All the newly synthesized compounds were tested against *Escherichia coli* and *staphylococcus aureus* and the data are listed in Table 2.

Conclusions

This work reports a facile method for the synthesis of fused pyranoquinoline derivatives.

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Received on January 6, 2004.