SYNTHESIS OF SOME TRICYCLIC AND TETRACYCLIC RING SYSTEMS BUILT ON 4-HYDROXY-2-QUINOLONES

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ABSTRACT:

Few substituted 4-hydroxy-2-quinolones were reacted with cinnamonitrile to afford fused pyrano [3,2-c] quinolines. They were further subjected to ring formation by means of acetic anhydride with or without pyridine.

INTRODUCTION:

Ravenine[1,2] a alkaloid was isolated from "Ravenia Spectabilis" is a 4-hydroxy-2-quinolone derivative, while Flindersine isolated from "Flinderia australis " has been found to be a fused 4-hydroxy-2-quinolone skeleton. Many derivatives were obtained from this alkaloid[3,4]. 4-hydroxy-2-quinolones were much studied for its biological properties[5,6] and also as optical brightners and laser dyes[7]. Many efforts were carried out for preparation of fused system of 4-hydroxy-2-quinolones at 3,4-positions[8-12]. Earlier El-Nabi[13] has prepared few fused heterocyclic systems where the benzenoid part was unsubstituted.

In continuation of our earlier work on substituted 4-hydroxy-2-quinolones and their 3-substituted analogs[14,15], we report herein various ring formation reactions of 4-hydroxy-2-quinolones to study the effect of electron withdrawing or donating groups like OCH_3, Cl, NO_2, CH_3 on various biological activity.

In the present work, few substituted 4-hydroxy-2-quinolones 1a-e were treated with cinnamonitrile 2 in presence of triethyl amine as a catalyst which gave substituted pyrano [3,2 -c] quinolines. The 3a-e when treated with acetic anhydride, afforded to give tricyclic compounds 4a-e, while the same reagent in presence of pyridine gave a tetracyclic system substituted 10-methyl-7-phenyl-5, 9-dihydroquinolino [3', 4', 5,6] 4H-pyrano [2,3-d] pyrimidine-6, 8-dione. All fifteen compounds were characterized by spectral analysis.

EXPERIMENTAL:

All the melting points were determined in open glass capillaries in a liquid paraffin-bath and are uncorrected. Purity of compounds was checked by TLC system IR spectra were recorded in PERKIN ELMER SPECTRUM GX FT-IR Spectrophotometer and PMR spectra in DMSO-d_6 on a BRUKER AC (300MHz) FT NMR Spectrometer using TMS as internal standard (chemical shifts) in δ ppm.

7-methyl-4-hydroxy-2-quinolone 1d.

It was prepared according to reported method[14,16]. Other compounds were also prepared.

2-amino-8-methyl-5-oxo-4-phenyl-6-hydro-4H-pyrano[3,2-c]quinoline-3-carbo-nitriles 3d.

A mixture of 7-methyl-4-hydroxy-2-quinolone **1d**, (0.01mol.) and cinnamonitrile **2** (0.01mol.) absolute ethanol (30 ml) and catalytic amount of triethyl amine (0.1 ml) was taken in RBF, refluxed in water bath for 45 minute. The reaction mixture was cooled and the product was collected by filtration and recrystallized from N,N-dimethyl formamide(DMF). Yield, 68%, melting point, 260^{0}C, Molecular formula: $C_{20}H_{15}N_3O_2$ Calculated: C: 73.16%, H: 4.30%, N: 12.80%, O: 9.75%; Found: C: 73.10%, H: 4.22%, N: 12.77%, O: 9.79%. IR (KBr) cm^{-1}: 3474(N-H str.), 1672(C=O str.), 2203(C-N str.), 1645(C=C str.); 300 MHz ^{1}H NMR (DMSO-d_6) δ : 2.9 (3H, s, CH_3), 6.70-8.1(10H, m, 9H, aromatic, 2H, NH_2), 11.74(1H, s, NH).

N-(3-cyano-8-methyl-5-oxo-4-phenyl-6-hydro-4H-pyrano-[5,6-c]quinolin-2-yl) acetamide 4d.

A mixture of **3d** (0.01mol.) was refluxed in acetic anhydride (5ml) for 2 hours, then cooled and poured into crushed ice. The product thus formed was collected by filtration and washed with 100 ml. of water to get 75% yield, melting point, 115-18^{0}C, Molecular Formula: $C_{22}H_{18}N_3O_3$ Calculated: C: 70.96%, H: 4.87%, N: 11.31%, O: 12.89%; Found: C: 70.88%, H: 4.95%, N: 11.28%, O: 12.65%. IR (KBr) cm^{-1}: 3470(N-H str.), 1655(C=O str.), 1642(C=C str.), 1239(C-O-C asym. str.), 1032(C-O-C sym. str.);

300 MHz ^{1}H NMR (DMSO-d_6) δ : 2.25(3H, s, -NHCOCH_3), 2.94(3H, s, CH_3), 7.22-7.91(8H, m, aromatic), 9.20(1H, s, NH), 11.80(1H, s, NH)

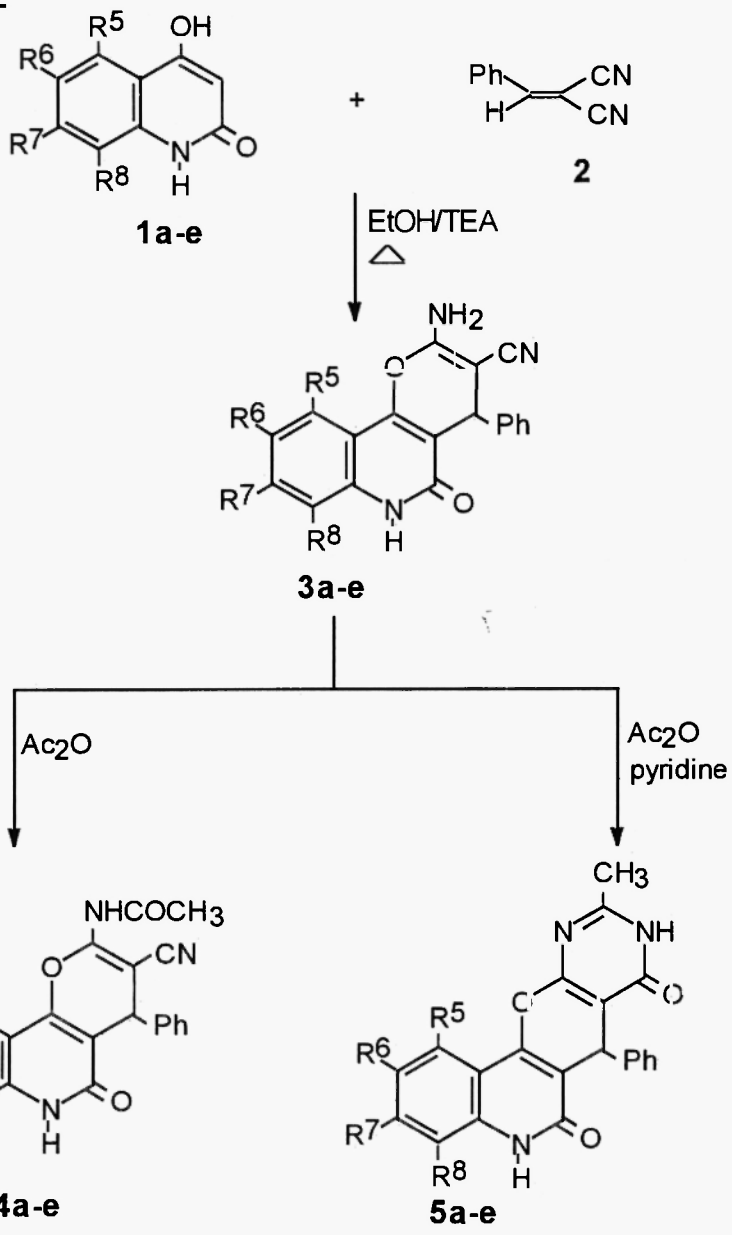
3,10-dimethyl-6-phenyl-5,9-dihydroquinolino[3',4',-5,6]4H-pyrano[2,3-d]pyrimidine -6,8-dione 5d.

A solution of **3d** (0.01mol.) in an acetic anhydride /pyridine mixture (2:1v/v) was heated at 80^{0}C for 10 hours, then cooled and poured into ice water. The product was collected by filtration, washed with chilled water, and recrystallized from absolute alcohol. Yield, 68% melting point, 128^{0}C, Molecular Formula: $C_{22}H_{17}N_3O_3$ Calculated: C: 71.15%, H: 4.61%, N: 11.31%, O: 12.92%; Found: C: 71.10%, H: 11.25%, N: 11.80%, O: 12.79%. IR (KBr) cm^{-1}: 3478(N-H str.), 1668(C=O str.), 2209 (C-N str.) 1647(C=C str.), 1232(C-O-C asym. str.), 1075(C-O-C sym. str.); 300MHz ^{1}H NMR (DMSO-d_6) δ : 2.72(6H, d, 2x CH_3), 6.77-8.11(8H, m, aromatic), 11.85(1H, s, NH).

Similarly, other compounds of 3a-e, 4a-e and 5a-e were also synthesized. The physical data are recorded in Table -1.

Antibacterial, Antitubercular and Anti-viral activities of these compounds are under progress.

REACTION SCHEME



Where;
R^5 or R^7 = Cl, CH_3; R^6 = OCH_3; R^8 = NO_2

Table-I : Physical constants of the compounds 3a-e, 4a-e and 5a-e

Compd.	R_5	R_6	R_7	R_8	Molecular Formuia	M. P. (^{0}C) (Reported)	Yield (%)	% of Nitrogen Found	% of Nitrogen Calcd.
3a	H	H	H	H	$C_{19}H_{13}N_3$	305(307)[15]	60	13.33	13.30
3b	NO_2	H	H	H	$C_{19}H_{12}N_4O_4$	95	67	15.55	15.45
3c	H	Cl	H	H	$C_{19}H_{12}N_3O_2Cl$	85	70	12.01	12.10
3d	H	CH_3	H	H	$C_{20}H_{15}N_3O_2$	260	68	12.80	12.77
3e	H	H	OCH_3	H	$C_{20}H_{15}N_3O_3$	48-50	86	12.17	12.10
4a	H	H	H	H	$C_{21}H_{15}N_3O_3$	261(260)[15]	60	11.68	11.76
4b	NO_2	H	H	H	$C_{21}H_{14}N_4O_5$	139	67	13.92	13.95
4c	H	Cl	H	H	$C_{21}H_{14}N_3O_3Cl$	>300	75	10.70	10.72
4d	H	CH_3	H	H	$C_{22}H_{17}N_3O_3$	115-118	53	11.28	11.31
4e	H	H	OCH_3	H	$C_{22}H_{17}N_3O_4$	124	55	10.88	10.85
5a	H	H	H	H	$C_{21}H_{15}N_3O_3$	337(337)[15]	58	11.70	11.76
5b	NO_2	H	H	H	$C_{21}H_{14}N_4O_5$	40	75	13.85	13.92
5c	H	Cl	H	H	$C_{21}H_{14}N_3O_3Cl$	145	72	10.77	10.79
5d	H	CH_3	H	H	$C_{22}H_{17}N_3O_3$	128	68	11.80	11.31
5e	H	H	OCH_3	H	$C_{22}H_{17}N_3O_4$	182	59	10.80	10.85

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