SYNTHESIS OF SOME HETEROCYCLIC SULFONES RELATED TO QUINOLINOL

Ali A. ABDEL HAFEZ

Chemistry Department,
Faculty of Science, Assiut University, Assiut 71516, Egypt

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It is well known that pyrazolone derivatives possess antifugal and antibacterial activities[1]. Pyrazole and isoxazole derivatives are widely used in medicinal chemistry[2]. In continuation of our work on the synthesis of heterocycles containing the quinoline moiety[3 - 8] we synthesized different heterocyclic sulfones related to quinolinol.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded in KBr pellets on a Pye–Unicam Sp 200-G spectrophotometer. ^{1}H NMR spectra were measured in $(CD_3)_2SO$ on EM-360-90 MHz spectrometer. Elemental analyses were determined on a Perkin–Elmer microanalyzer. Physico-chemical and spectral data are given in Tables I and II.

Preparation of Quinolinoles *IIa – IIc*; General Procedure

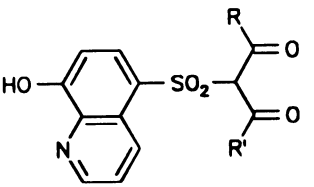
Respective active methylene compound (0.03 mol) was added to an alcoholic sodium ethoxid solution (1.4 g sodium in 100 ml ethanol) and stirred for 2 h. 8-Hydroxyquinoline-5-sulfonyl chloride (0.03 mol) was added and the reaction mixture was heated under reflux on a water bath for 7 h. The precipitated product was filtered off, washed with water and recrystallized from ethanol.

Preparation of Quinolinoles *IIIa*, *IIIb*, *VIa*, *VIb*, *IXa*, *IXb*; General Procedure

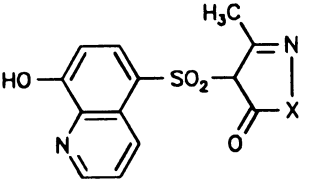
A mixture of *IIa*, *IIb* or *IIc*, respectively (0.001 mol) and hydrazine hydrate (99%, 0.001 mol) or phenylhydrazine in alcoholic sodium ethoxide solution (0.04 g sodium in 10 ml ethanol) was heated under reflux on a water bath for 10 h. The reaction mixture was filtered off and the filtrate was cooled, neutralized with acetic acid. Products were recrystallized from diluted acetic acid.

Preparation of Quinolinoles *IV*, *VII*, *X*; General Procedure

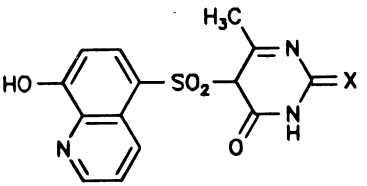
A mixture of the respective compound *II*, (0.001 mol), hydroxylamine hydrochloride (0.002 mol) and pyridine (10 ml) was heated under reflux for 6 h. The reaction mixture was cooled, poured into diluted HCl and recrystallized from ethanol.



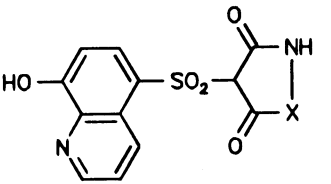
IIa, R = CH_3, R' = OC_2H_5
IIb, R = R' = OC_2H_5
IIc, R = R' = CH_3



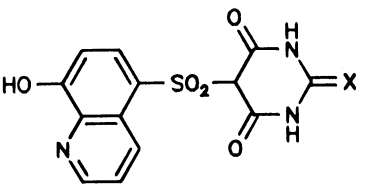
IIIa, X = NH
IIIb, X = NC_6H_5
IV, X = O



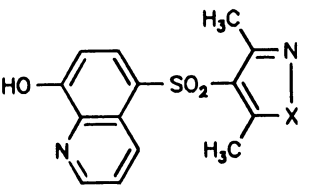
Va, X = O
Vb, X = S



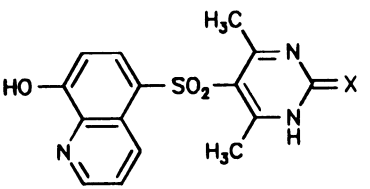
VIa, X = NH
VIb, X = NC_6H_5
VII, X = O



VIIIa, X = O
VIIIb, X = S



IXa, X = NH
IXb, X = NC_6H_5
X, X = O



XIa, X = O
XIb, X = S

TABLE I
Physico-chemical data of compounds *II* – *XI*

Compound	M. p., °C Yield, %	Formula	Calculated/Found			
			% C	% H	% N	% S
IIa	304 – 306 80	$C_{15}H_{15}NO_6S$	53.41 53.68	4.48 4.76	4.15 4.21	9.51 10.06
IIb	>340 75	$C_{16}H_{17}NO_7S$	52.31 52.52	4.66 5.00	3.81 4.01	8.73 8.69
IIc	>340 75	$C_{14}H_{13}NO_5S$	54.72 54.91	4.26 4.44	4.56 4.71	10.43 10.51
IIIa	278 – 280 52	$C_{13}H_{11}N_3O_4S$	51.15 51.00	3.63 3.53	13.77 13.89	10.50 10.56
IIIb	316 – 318 55	$C_{19}H_{15}N_3O_4S$	59.84 59.75	3.96 3.76	11.02 11.21	8.41 8.61
IV	288 – 290 63	$C_{13}H_{10}N_2O_5S$	50.98 50.89	3.29 3.39	9.15 9.36	10.47 10.54
Va	318 – 320 65	$C_{14}H_{11}N_3O_5S$	50.45 50.61	3.33 3.26	12.61 12.82	9.62 9.82
Vb	>340 60	$C_{14}H_{11}N_3O_4S_2$	48.13 48.01	3.17 3.26	12.03 12.19	18.35 18.61
VIa	143 – 145 43	$C_{12}H_9N_3O_5S$	47.06 47.00	2.61 2.92	13.73 13.61	10.46 10.59
VIb	248 – 250 54	$C_{18}H_{13}N_3O_5S$	56.55 56.85	3.16 3.00	11.00 10.81	8.38 8.12
VII	308 – 310 65	$C_{12}H_8N_2O_6S$	46.75 46.46	2.62 2.80	9.10 9.36	10.40 10.52
VIIIa	313 – 315 65	$C_{13}H_9N_3O_6S$	46.57 46.41	2.71 2.80	12.53 12.19	9.56 9.76
VIIIb	320 – 322 60	$C_{13}H_9N_3O_5S_2$	44.44 44.59	2.58 2.72	11.96 12.10	18.25 18.41
IXa	198 – 200 52	$C_{14}H_{13}N_3O_3S$	55.44 55.66	4.32 4.25	13.86 13.77	10.57 10.63
IXb	310 – 312 60	$C_{20}H_{17}N_3O_3S$	63.33 63.48	4.51 4.56	11.08 11.00	8.45 8.34
X	323 – 325 75	$C_{14}H_{12}N_2O_4S$	55.26 55.47	3.97 4.02	9.21 9.33	10.53 10.42
XIa	316 – 318 45	$C_{15}H_{13}N_3O_4S$	54.38 54.22	3.96 3.72	12.68 12.90	9.68 9.79
XIb	325 – 327 56	$C_{15}H_{13}N_3O_3S_2$	51.87 51.71	3.77 3.86	12.10 12.22	18.46 18.56

TABLE II
Spectral data of some synthesized compounds

Compound	IR ν, cm^{-1}	^1H NMR δ, ppm
IIa	1 360 (SO_2 asym.), 1 160 (SO_2 sym.), 1 750 (CO)	4.23 m, 2 H (CH_2); 1.17 t, 3 H (CH_3); 1.90 s, 3 H (CH_3CO); 7.60 m, 6 H (aromatic); 4.30 s, 1 H (CH)
IIb	1 350 (SO_2 asym.), 1 155 (SO_2 sym.), 1 720 (CO)	4.30 m, 4 H (2 CH_2); 1.20 t, 6 H (2 CH_3); 7.60 m, 6 H (aromatic), 4.40 s, 1 H (CH)
IIIa	1 600 (NC), 1 730 (CO), 3 150 (NH), 1 360 (SO_2 asym.), 1 160 (SO_2 sym.)	7.50 s, 1 H (4-pyrazolyl); 2.35 s, 3 H (CH_3 pyrazolyl); 7.65 m, 6 H (aromatic)
Va	1 600 (NC), 1 740 (CO), 3 100 (NH), 1 355 (SO_2 asym.), 1 155 (SO_2 sym.)	2.22 s, 3 H (CH_3 pyrimidine); 3.71 s, 1 H (pyrimidine); 3.90 s, 1 H (NH pyrimidine); 7.65 m, 6 H (aromatic)
Vb	1 600 (NC), 1 500 (NCS), 1 710 (CO)	
VIb	1 600 (NC), 1 730 (CO), 1 360 (SO_2 asym.), 1 160 (SO_2 sym.)	3.50 s, 1 H (NHCO); 7.45 s, 1 H (4-pyrazol); 6.20 m, 5 H (aromatic); 7.70 m, 6 H (quinolinol)
VII	1 355 (SO_2 asym.), 1 160 (SO_2 sym.), 1 740 (CO), 3 150 (NH)	
VIIIa	1 750 (CO), 3 120 (NH), 1 350 (SO_2 asym.), 1 150 (SO_2 sym.)	3.77 s, 2 H (2 NH pyrimidine); 7.66 m, 6 H (aromatic)
IXa	1 360 (SO_2 asym.), 1 160 (SO_2 sym.), 3 200 (NH), 1 600 (NC)	1.92 s, 6 H (2 CH_3); 7.78 s, 1 H (4-pyrazolyl); 7.65 m, 6 H (aromatic)
X	1 355 (SO_2 asym.), 1 160 (SO_2 sym.), 3 160 (NH), 1 580 (NC)	1.92 s, 6 H (2 CH_3, isoxazol); 3.78 s, 1 H (4-isoxazolyl); 7.65 m, 6 H (aromatic)
XIa	3 100 (NH), 1 600 (NC), 1 360 (SO_2 asym.), 1 160 (SO_2 sym.)	1.90 s, 6 H (2 CH_3 of pyrimidine ring); 3.85 s, 1 H (NH of pyrimidine)

Preparation of Quinolinoles *Va*, *Vb*, *VIIIa*, *VIIIb*, *XIa*, *XIb*; General Procedure

A mixture of the respective compound *II* (0.001 mol) and urea or thiourea in an alcoholic sodium ethoxide (0.02 g sodium in 10 ml ethanol) was heated under reflux on water bath for 8 h, cooled, neutralized with cold diluted HCl and the precipitate was washed with water and recrystallized from ethanol.

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