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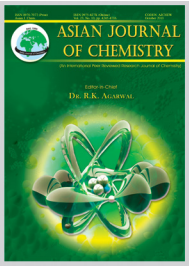

NOTE

Synthesis of Some Quinolone Derivatives with Possible Local Anaesthetics Activities

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Various new 7-[*N*-substituted acetyl amino]-2-methyl-4-quinolone were systheized by condensing 2-methyl-7-amino-4-quinolone with chloroacetyl chloride to get 2-methyl-7-chloroacetyl amino-4-quinolone, which on further reaction with various secondary amines to afford the required derivatives. The compounds were tested for their local anesthetic activity.

Key Words: Synthesis, Quinolone, Local anesthetic activity.

Quinolones and their derivative exhibit marked pharmacological properties[1-10]. In view of the therapeutic importance of quinolone, various new derivatives of quinolone consisting of a lypolytic end containing an aromatic nucleus, a hydrophyllic and consisting of a tertiary amino group and an intermediate alkyl chain is essential condition for local anesthetic activity[11-14], were synthesized by reported method[15], which involves condensation of 2-methyl-7-amino-4-quinolone with chloro acetyl chloride to get 2-methyl-7-chloro acetyl-4-quinolone. On further reaction with secondary amine to afford the required product which might confer better local anaesthetic activity and less toxicity.

Preparation of 2-methyl-7-nitro-4-quinolone (1): Place 0.25 mol of 3-nitroaniline in absolute alcohol and add 0.25 mol of acetoacetic ester (enol) in round bottom flask equipped with a reflux condenser. The contents were refluxed for 1 h and allowed product to stand overnight. The crude product was filter off and washed with ether and recrystallized from ethanol.

Preparation of 2-methyl-7-amino quinolone (2): 0.025 mol of 2-methyl-7-nitro quinolone (**1**) dissolved in 25 mL conc. HCl and 7.5 g granulated tin in a 100 mL round bottom flask fitted with reflux condenser and contents shaked to ensure through mixing of acid and were refluxed 100 ºC with vigorous shaking until the compound dissolve and its odour no longer persist cool the mixture and wash with 25 % NaOH to isolate the 2-methyl-7-amino quinolone which extracted with ether.

Preparation of 2-methyl-7-(chloroacetyl amine)-4-quinolone (3): 0.01 mol of chloroacetyl chloride was added drop wise with vigorous shaking to 0.01 mol of 2-methyl-7-amino-4-quinolone (**2**) dissolved in 25 mL ethanol and reaction mixture was stirred for 1 h, cool and pour the contents on crushed ice to separate solid which is filtered, dried and recrystallized by ethanol.

Preparation of 2-methyl-7-[*N*-Mophilinoacetyl amino]-4-quinolone: 0.01 mol of morpholine (2.4 mL) gradually added to 0.01 mol 2-methyl-7-(chloroacetyl amine)-4-quinolone dissolved in dry benzene containing K_2CO_3 (0.5 g). The reaction mixture was refluxed on water bath for *ca.* 8 h. Excess of solvent was distilled off and solid mass was extracted with water and recrystallized from ethanol (**Scheme-I**).

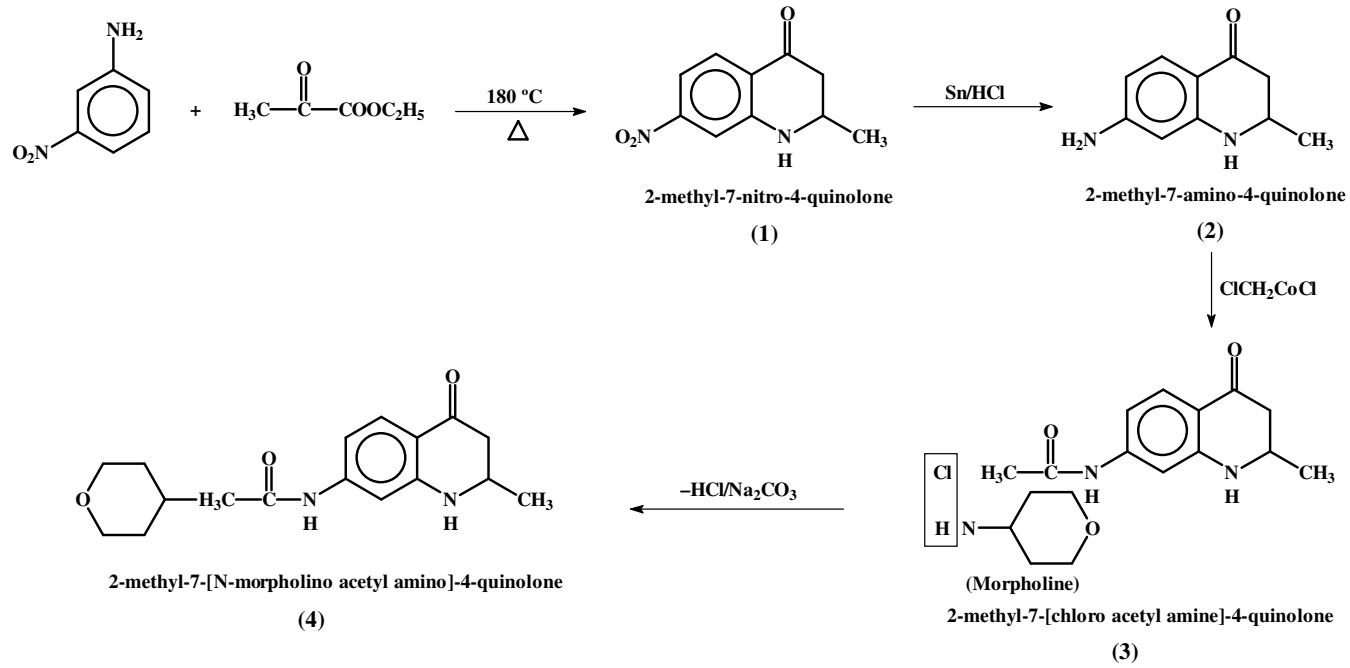
IR (KBr, ν_{max}, cm^{-1}) 3250 (NH) 1690 (N-C); 1340 (C-N); 1670 (C=O) pmr; -δ 2.9-3.2 (s-quinolone-CH_3); δ 6.4-9.6 (due to Ar-H); δ 8.9-9.8 (due to 1H; S-NH); δ 2.5-2.7 [(4H, t, $N(CH_2)_2$]; δ 3.6-3.9 [4H,t,O(CH2)2].

Similarly various 2-methyl-7-[*N*-substituted acetyl amino]-4-quinolone were synthesized accordingly and their analytical data are incorporated in Table-1. The synthesized compounds have been characterized by IR, PMR, spectral studies and elemental analysis. The purity of the compounds have been checked by TLC. The mps were determined in open capillaries and are uncorrected.

Biological activity: The preliminary investigation on local anesthetic activity of hydrochlorides of 2-methyl-7-[morpholino acetyl amino]-4-quinolone, 2-methyl-7-[diethyl acetyl amino]-4-quinolone, 2-methyl-7-[diisopropyl-acetyl-amino]-4-quinolone and 2-methyl-7-[dipiperidine acetyl amino]-4-quinolone in 2 % solution show surface anesthesia for 30, 34, 32 and 36 min respectively in frog's sciatic plexus by employing the method of Bulbring and Wajda[16].

TABLE-1

Comp. no.	Nature of (R) (m.w.)	m.f.	Yield (%)	m.p. (ºC)	Elemental analysis % of N	
					Calculated	Found
1	Morpholine (301)	$C_{16}H_{19}N_3O_3$	74	212	13.95	13.65
2	Dimethyl amine (259)	$C_{14}H_{17}N_3O_2$	71	203	16.22	16.04
3	Diethyl amine (287)	$C_{16}H_{21}N_3O_2$	67	209	14.63	14.41
4	Ethyl methyl amine 273)	$C_{15}H_{19}N_3O_2$	62	207	15.38	15.09
5	Dipropyl amine (315)	$C_{18}H_{25}N_3O_2$	70	216	13.33	13.13
6	Diisopropyl amine (315)	$C_{18}H_{25}N_3O_2$	66	213	13.33	13.02
7	Piperidine (299)	$C_{17}H_{21}N_3O_2$	63	210	14.04	13.68
8	Pyrrolidine (285)	$C_{16}H_{19}N_3O_2$	69	207	14.74	14.09
9	Diphenyl amine (383)	$C_{24}H_{21}N_3O_2$	61	221	10.97	10.26
10	*N*-Methyl aniline (321)	$C_{19}H_{19}N_3O_2$	64	217	13.08	12.71



Scheme-I

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