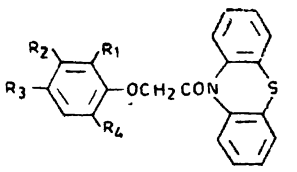
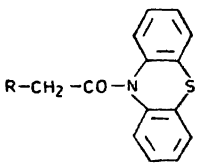


(1–10)



(11) R = α-Naphthoxy
(12) R = β-Naphthoxy

Synthesis and Biological Evaluation of some Novel *N*-2-(Phenoxy/bromo/nitro/methyl/ naphthoxy and substituted-phenoxy)-acetylphenothiazine

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PHENOXY- and naphthoxyacetic acids and their various derivatives have been reported to possess a wide spectrum of biological activities[1]. These results prompted us to undertake the synthesis of the title compounds and to screen their anthelmintic activity.

Experimental

Naphthoxy- and various phenoxyacetic acids and their bromo, nitro and methyl substituted derivatives were synthesised by condensing the sodium salt of the appropriate phenols with $Cl-CH_2CO_2Na$[2].

To a solution of aryloxy acid (0.05 mol in 50 ml C_6H_6/EtOAc/CH_3OH) was added thionyl chloride (0.05–0.06 mol) and the mixture was refluxed on a water-bath for 6–8 h. The acid chloride were then added dropwise to an ice-cold solution of phenothiazine (0.036–0.037 mol in 25 ml EtOAc/MeOH/$C_2H_5OC_2H_5$) and 4 *N* NaOH solution (5 ml) with constant stirring. The separated compounds were filtered, washed and purified over the column of silica gel.

Following this methods all the compounds were prepared (Table 1). The structures of the compounds were checked by elemental analyses and ir spectra; ν_{max} 620–880, 900–1 040, 1 240–1 260, 1 280–1 350 and 1 630 (phenothiazine and aromatic ring, amide and nitro groups), 1 110–1 180 (C–O–C) and 2 940 cm^{-1} (methyl group) respectively. Purity of the compounds was checked by tlc.

Biological activity : The anthelmintic activity of all the compounds was carried out by the reported method of Watkins[3]. The solution of the compounds (**1**–**12**) was made in ethylene glycol (0.1%, w/v). The piperazine citrate (standard drug) was made of the same concentration in ethylene glycol. Normal saline solution was prepared in distilled water.

Compounds **5** (MPT-5, MLT-10), **6** (MPT-12, MLT-17), **7** (MPT-6, MLT-9), **8** (MPT-14, MLT-22) and **9** (MPT-24, MLT-32) showed promising activity

TABLE 1—PHYSICAL DATA OF COMPOUNDS*

Compd. no.	R_1	R_2	R_3	R_4	Yield %	Mol. formula	M.p ** °C
1.	H	H	H	H	50	$C_{20}H_{15}O_2NS$	99–100[a]
2.	NO_2	H	H	H	80	$C_{20}H_{14}O_4N_2S$	260–62[b]
3.	H	NO_2	H	H	60	$C_{20}H_{14}O_4N_2S$	100–02[b]
4.	H	H	NO_2	H	80	$C_{20}H_{14}O_4N_2S$	70–72[b]
5.	NO_2	H	NO_2	NO_2	70	$C_{20}H_{12}O_8N_4S$	61–62[c]
6	Br	H	Br	H	70	$C_{20}H_{13}O_2NSBr_2$	260–62[a]
7.	Br	H	Br	Br	60	$C_{20}H_{12}O_2NSBr_3$	99–100[c]
8.	CH_3	H	H	H	60	$C_{21}H_{17}O_2NS$	111–12[c]
9	H	CH_3	H	H	70	$C_{21}H_{17}O_2NS$	82–84[d]
10	H	H	CH_3	H	65	$C_{20}H_{17}O_2NS$	75–76[d]
11	—	—	—	—	75	$C_{20}H_{17}O_2NS$	278–70[c]
12	—	—	—	—	60	$C_{20}H_{17}O_2NS$	219–20[c]

*All compounds gave satisfactory C, H, N and S analysis and for **6**, **7** in addition Br analysis. **Solvent for crystallisation : [a]$CHCl_3$, [b]C_6H_6, [c]EtOAc, [d]MeOH.

as compared with the standard drug (MPT-60, MLT-68), where MPT=mean paralysis time and MLT=mean lethal time.

The toxicity was determined by the reported method[4]. No toxic symptoms were found upto the doses of test compounds 1000 mg/kg body weight.

Acknowledgement

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References

1. M. L. KHUBCHANDANI and S K. SRIVASTAVA, *Curr. Sci* , 1987, **56**, 264 ; P. G, STECHER, M. WINDHOLZ, D S. LEAHY, D. M. BOLTON, L G. EATON, "The Merk Index' , Merk, Inc , Rahmay, 1968, p. 117 , P B PATEL and K J SHAH, *J Indian Chem Soc* , 1973, **60**, 337
2 P ROBERT, *J Am Chem Soc* , 1941, **63**, 1768
3 T. I WATKINS, *J Pharm Pharmacol* , 1958, **10**, 209
4. J E. N. SLOAN, P. A KINGSBURY and D W. JOLLY, *J Pharm Pharmacol* , 1954, **6**, 720