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Synthesis and Biocidal Nature of Oxamic Acids

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Synthesis of seven oxamic acids, *viz.*, N-*p*-nitrophenyl oxamic acid, N-*p*-chlorophenyl oxamic acid, N,N-*o*-phenylene dioxamic acid,N,N′-*m*-phenylene diamine dioxamic acid, N-*o*-phenol oxamic acid, N-pyridino-*p*-carboxy oxamic acid and N-pyrazole oxamic acid was carried out by refluxing the pure aromatic amino compounds with anhydrous diethyloxalate and characterized by their physico-chemical studies. All compounds were biocidal in nature.

Key Words: Oxamic acids, Physico-chemical properties, Biocidal nature.

INTRODUCTION

Oxamic acids are the N-amino derivatives of aliphatic dibasic acids having the general formula R—NH—CO—COOH where R is variable. Aschon[1] synthesized *m*-toluidinyl oxamic acid by condensing freshly distilled *m*-toluidine with anhydrous oxalic acid. Oxamic acids are versatile reagents for spectrophotometric titration[2–5], organic and inorganic analysis[6], solvent extraction[7–9], paper[10] and ion exchange chromatography[11]. They are also used in the analysis of trace elements[12]. John *et al.*[13] and Sharma *et al.*[14, 15] have evaluated the biological activity of oxamic acids and their metal complexes. In the present paper, we are reporting our extended studies[16] on the synthesis and biocidal studies of seven more oxamic acids.

EXPERIMENTAL

General method of preparation of oxamic acids : 1 : 1 molar mixture of mono amino compound (0.025 M) (in the case of *p*-nitroaniline, *p*-chloroaniline, aminophenol, 2-amino-4-carboxypyridine and 2-aminopyrazole) and 1 : 2 molar mixture of diamino-compound (*o*-phenylene diamine or *m*-phenylene diamine) with freshly distilled diethyloxalate (0.025 M) were refluxed in a round-bottom flask, fitted with an air condenser for about 2–3 h. After cooling the contents of the flask, 25 mL absolute alcohol was added to dissolve the formed ester. The insoluble oxamide simultaneously formed was filtered out. The filtrate was treated with sodium carbonate solution (6.0 g in 50 mL water). The mixture was steam-distilled for 1 h. On cooling the solution at room temperature, the sodium

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salt of the oxamic acid was obtained. The desired free acid was obtained by adding an appropriate amount of conc. hydrochloric acid to the sodium salt. The impure product was dissolved in ammonium hydroxide and filtered to remove the solid impurity if any. The free acid from this filtrate was obtained by adding conc. hydrochloric acid again to get solid. This solid was again filtered, repeatedly washed with cold water, ethanol and dried in a vacuum desiccator over P_2O_5.

The physico-chemical properties of the compounds are given as under

(i) N-*p*-nitrophenyl oxamic acid (N-*p*-NPOXA): Light yellow, m.p. 110°C, m.f. $C_8H_6N_2O_5$, % Analysis, Found (Calcd.): C, 46.10 (45.70), H, 2.75 (2.80), N, 12.85 (13.3), .

(ii) N-*p*-Chlorophenyloxamic acid (N-*p*-CPOXA): Light pink, m.p. 110°C, m.f. $C_8H_6NO_3Cl$, % Analysis, Found (Calcd.): C, 47.40 (48.20), H, 2.90 (3.10), N, 11.07 (11.11).

(iii) N,N′-*o*-phenylene diamine dioxamic acid .(N-N′-*o*-PDDOXA): Brown, m.p. 140°C, m.f. $C_{10}H_8N_2O_6$; % Analysis, Found (Calcd.): C, 48.0 (47.6), H, 3.03 (3.17), H, 11.04 (11.14).

(iv) N,N′-*m*-phenylene diamine dioxamic acid,(N-N′-*m*-PDDOXA): Brown, m. p. 138°C, m.f. $C_{10}H_8N_2O_6$; % Analysis, Found (Calcd.): C, 48.10 (47.6), H, 3.03 (3.17), H, 11.04 (11.20).

(v) N-*o*-phenol oxamic acid (N-*o*-PLOXA) White, m.p. 130°C, m.f. $C_8H_7NO_4$; % Analysis, Found (Calcd.): C, 51.4 (53.0), H, 3.90 (3.86), N, 7.63 (7.73).

(vi) N-Pyridino-*p*-carboxy oxamic acid (N-Py-*o*-CAOXA): White, m.p. 145°C, m.f. $C_8H_6N_2O_5$; % Analysis, Found (Calcd.): C. 46.0 (45.71), H, 2.96 (2.85), N, 13.21 (13.33).

(vii) N-Pyrazole oxamic acid (N-PzOXA): Pinkish white, m.p. 125°C, m.f. $C_6H_6N_2O_3$, % Analysis, Found (Calcd.): C, 45.6 (46.75), H, 3.70 (3.89), N, 17.74 (18.8).

RESULTS AND DISCUSSION

All compounds are stable at room tempeature. They can be represented by the general formula R—N—C—C—OH, where R is an amino moiety. Physical

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properties and elemental analysis indicate that all the compounds are coloured and stable at room temperature. They are fairly soluble in common organic solvents and mineral acids. The calculated values of elemental analysis (C, H, N) considerably resemble their analyzed values which indicate their purity and correct molecular formula. IR spectral data (Table-1) indicate their skeleton structure obtained on the condensation of amino-compounds with anhydrous diethyl oxalate, which is well in agreement with their proposed structure. The obtained minimum inhibitory concentration values (Table-2) reveal that all the oxamic acids are biologically active and their biocidal behaviour is specific and discriminating depending on the nature of bacteria and fungi and also depends both on the type of substituants on the benzene ring and its position of substitution.

TABLE-1
IR SPECTRAL DATA (IN cm^{-1}) OF OXAMIC ACIDS

N-*p*-NPOXA	N-*p*-CPOXA	N,N′-*o*-PDDOXA	N,N′-*m*-PDDOXA	N-*o*-PLOXA	N-Py-*p*-CAOXA	N-Pz-OXA	Probable Assignments
3260 s	3240 m	3250 s	3230 s	33260 s	3210 s	3220 s	OH and NH-hydrogen bonding
1770 m	1765 m	1730 m	1730 m	1760 m	1750 m	1745 m	Carbonyl stretching
1580 m	1570 m	1560 w	1540 w	1570 w	1510 w	1550 w	Aromatic C=C stretching
1510 m	1505 m	1540 m	1510 m	1560	1520 m	1550 m	Mixing of CO and NH bond
1350 m	1380 m	1375 m	11310 m	1350 m	1370 m	1365 m	C—N stretching
1165 m	1170 m	1110 m	1140 m	1120 m	1180 m	1110 m	In-plane C—H deformation
830 s	720 m	720 m	720 m	950 s	930 s	945 s	Out-of- plane C—H deformation
740	720	720 s	720 s	750 s	930 s	720 s	

TABLE-2
MIC VALUE (MOLAR CONCENTRATION × 10^{-4}) OF OXAMIC ACIDS

Compound	Bacteria		Fungi	
	S. aureus	*E. coli*	*A. niger*	*C. Albicans*
N-*p*-NPOXA	2.15	2.15	1.05	1.05
N-*p*-CPOXA	2.51	2.51	1.26	1.26
N,N′-*o*-PDDOXA	1.25	1.25	1.05	1.05
N,N′-*m*-PDDOXA	1.25	1.25	1.05	1.05
N-*o*-PLOXA	2.51	2.51	1.26	1.26
N-Py-*p*-CAOXA	1.25	1.25	1.05	1.05
N-Pz-OXA	2.43	2.43	4.86	4.86

All the oxamic acids were tested for their antibacterial activity against *Staphylococcus* (gram + ve) and *Escherichia coli* (gram –ve) bacteria and for antifungal activity agaisnt two common fungi, *Aspergillus niger* (*AN*) and *Candida albicans* (*CA*) by serial dilution method[17, 18] using pencillin as a standard (Table-2). The culture media for growing the bacteria at the optimum temperature 37°C was prepared in double-distilled sterilized 250 mL water by dissolving agar 0.375 g, peptone 1.50 g and yeast extract 0.75 g. Similarly, 250 mL culture media for growing the fungi at 28°C was prepared by dissolving agar 6.25 g, dextrose 5.0 g and peptone 2.5 g. Both the culture media were sterilized in an autoclave at 121°C under 15 pounds pressure for about 1/2 h The inhibition of the bacteria was recorded after 24 h whereas the inhibition of fungi was recorded after 96 h.

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