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N-Bromoisonicotinamide: New, mild, stable, effective and efficient oxidant for organic substrate

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ABSTRACT

N-Bromoisonicotinamide (NBIN) is prepared by standard procedure and characterized. The physical constant, the formal redox potential, elemental analysis and spectral characterization (IR and ^{1}H NMR) confirm the presence of nitrogen-halogen bond. It is found to be a stable and mild oxidant of low cost. It is prepared by a simple method, giving high yield in a short period of time. Its formal redox potential shows NBIN can be used as effective source of positive halogen. It will be a valuable addition to the existing oxidants. It is screened for antimicrobial activity against bacteria and fungi at various concentrations using disc diffusion method.

Key words: N-Bromoisonicotinamide, oxidant,N-halocompoumds.

INTRODUCTION

The role of N – halo compounds in the kinetic study of oxidation of organic compounds is very wide. A considerable attention has been focused on the chemistry of N- halogeno compounds[1-7]. The diverse nature of the compounds is due to their ability to act as sources of halogenonium cations, hypo halite species and nitrogen anions which act both as bases and nucleophiles. Among the N-halo compounds, N-bromonicotinamide (NBN) has been used as the oxidant for amino acids[8]. In the search of new halo compounds, the latest development involves the study of synthesis, characterization and antimicrobial activities of yet another oxidant, N-Bromoisonicotinamide (NBIN).

The present paper deals with the synthesis, characterization and usage of NBIN for the facile oxidation of organic substrates. This oxidant offers advantages like easy method of synthesis, low cost, low toxicity and mild nature with appreciable stability.

EXPERIMENTAL

N-Bromoisonicotinamide (m.p 211 ^{0}C) was prepared by the method described in literature. 12 g isonicotinamide was added to 100 ml of an ice-cold solution of sodium hypobromite, freshely prepared from 14.4 g (0.09 mol) of bromine and 9.0 g (0.23 mol) of sodium hydroxide. After shaking for ten minutes, the mixture was filtered rapidly with suction into a cold solution of 9ml of glacial acetic acid and 25 ml of ice-cold water. The bromamide precipitated was filtered off, washed and recrystallized from ethanol (yield 80%).

RESULTS AND DISCUSSION

The purity of NBIN (Fig.1.) was confirmed by elemental analysis (C 35.79 %, H 3.14 %, N 13.27 %, Br 39.48 % and O 8.40%). The IR spectra of NBIN showed the presence of secondary amide (1660 cm^{-1}), a carbonyl group (1500 cm^{-1}) and N-Br bond (1250 cm ^{1}).The ^{1}H NMR signals for the pyridine ring protons have the same chemical shifts in both INA and NBIN, while the peak corresponding

to NH_2 signal is slightly shifted to a larger value, the integration of the peak was half. This indicates that only one proton of the NH_2 group is substituted by the bromine atom. ^{1}H NMR δ: 9 (due to C_2-H and C_6-H), 8.2 (due to C_3-H and C_5-H), 4.4 (broad singlet due to CO-NH proton coupled with C_3-H and C_5-H).

NBIN was found be soluble in water, acetic acid, dimethyl sulphoxide, dimethyl formamide, sparingly soluble in ethanol, but insoluble in carbon tetrachloride, ethyl acetate,chlorobenzene and dioxane. Stock solution of NBIN was prepared in 70% acetic acid mixture and kept in the amber coloured bottle (to prevent interaction with light). It showed no appreciable change in concentration and appearance over a period of one month indicating a fair degree of stability.A digital potentiometer (Equiptronics dual channel potentiometer EQ-603) with a smooth platinum electrode and a saturated aqueous calomel electrode was used for the determination of formal redox potential of NBIN / INA couple.The formal redox potential of NBIN/INA couple was determined by measuring the potential in mixtures containing varying concentration ratios of NBIN and INA in 70% acetic acid and 0.1 M HCl. Since dilute solutions of both NBIN and INA (isonicotinamide) were used, the activities were replaced by concentration terms in the Nernst equation.

$$E_{obs} = E^{o}\frac{2.303RT}{F} + \log\frac{[NBIN]}{[INA]}$$

A plot of E_{obs} against log [NBIN] / [INA] from the above equation was made which yield a straight line with non-zero intercept (Fig.2.) and the potential from it was calculated to be 0.808 V at 25 ^{0}C. This value shows it is a fairly strong oxidizing agent.

The value of formal redox potential of the NBIN / INA couple viz. (0.808 V at 25 ^{0}C) is comparable to the value of 0.797 V for N-bromonicotinamide[8], +1.14 V for chloramine-T[9], +1.16 V for bromamine-T[10] and +1.02 V for N-chloronicotinamide[11]

NBIN is fairly stable. NBIN can serve as an efficient reagent for oxidation, halogenation, and polymer induced cyclisation, peroxidation, side chain substitution similar to other known N-bromo compounds. The active oxidizing species while using NBIN are Br_2, Br^+, Br_2^+, HOBr, H_2OBr, depending upon the p^H of the medium. NBIN can be used for a variety of synthetic reactions like ortho oxidation, peroxidation, effective oxidation,preferential halogenation, which shows its selectivity.

Table 1: Antimicrobial activity of N-Bromoisonicotinamide

S. No	Name of the microorganisms	Zone of the inhibition in mm Sample-NBIN				Standard
		50	100	200	250	
1	Staphylococcus aureus (NCM 2079)	10	15	15	16	32
2	Klebsiella aerogenes (NCM 2098)	8	10	10	12	30
3	Proteus vulgaris (NCM 2027)	—	10	10	10	32
4	Salmonella typhi (NCN 2023)	8	10	10	12	30
5	Candida alebicans (NCM 3102)	8	8	10	10	31
6	Aspergillus niger (NCM 105)	8	10	10	15	32

Antimicrobial activity

The antibacterial activity was carried out by disc diffusion technique[12]. The test microorganisms of Gram positive *Staphylococcus aureus* and Gram negative *Proteus vulgaris, Salmonella typhi, Klebsiella aerogenes* and *Fungus Candida alebicans, Aspergillus niger* were obtained from National Chemical Laboratory (NCL), Pune and maintained by periodical sub culturing on nutrient agar and sabouraud dextrose medium for

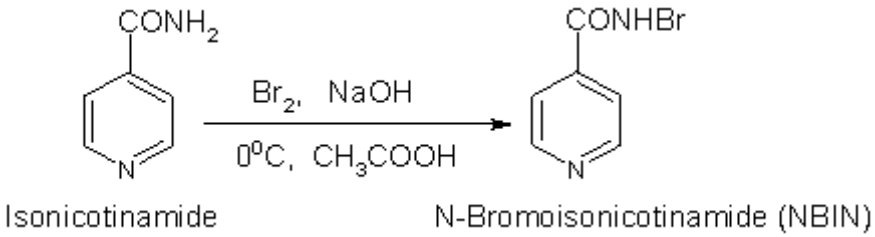

Fig. 1:

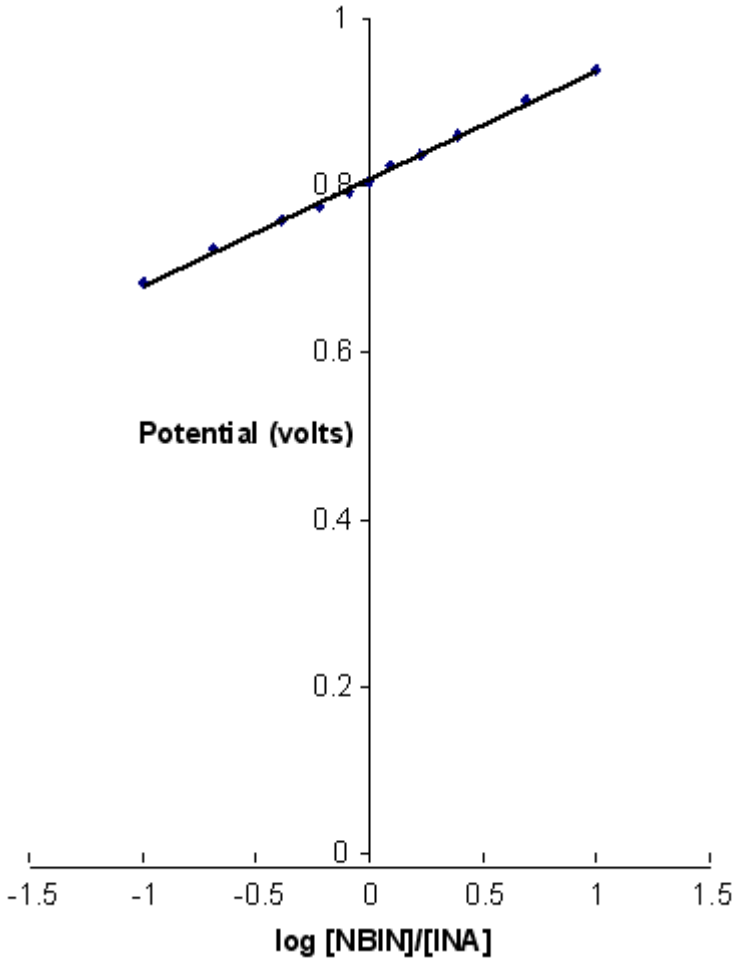

Fig. 2: Determination of E^0 [NBIN]/[INA] potentiometrically in a mixture of 0.1 mol dm^{-3} HCl and 70% acetic acid-30% water (v/v) at 25°C

bacteria and fungi respectively. The effect produced by the compound was compared with the effect produced by the positive control (Reference: Standard ciprofloxacin 5µg/disc for bacteria and standard fluconazole 100 units/disc for fungi). All the observations are given in Table-1.

Preparation of disc

A known quantity of the compound NBIN was dissolved in water. The required quantity of the compound is loaded on the sterile discs using micropipette. Discs impregnated with known concentration of the compound are placed on Muller Hinton agar plate that has been inoculated uniformly over the entire plate with a culture of the bacterium and fungi to be tested. Dried discs are stored in sterile containers till use.

Preparation of inoculum

The microbial strains are inoculated in peptone water and sabouraued dextrose broth and incubated at 37 ^{0}C and 25 ^{0}C for 6 to 18 hrs for bacteria and fungi respectively.

Disc diffusion method was performed to look for the antimicrobial activity of various extracts (Table-1). The zone of inhibition of growth was measured by making use of Tripartigan rule (Hoechst) (NCCLS, 1993)[13].

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