Organic Reactions in the Aqueous Medium Part-VII: Effect of Sonication on the Reactions of Salicyladehyde with Ammonium Compounds

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Summary: The unstirred reactions of ammonium carbonate and phosphate with salicylaldehyde yielded varying amounts of hydrosalicylamide (III) depending upon molar ratio (1:1 to 1:4) and the reaction medium (water/methanol). Under similar conditions ammonium bicarbonate and acetate afforded a mixture of (III) and tricyclobenzoxine (IV) when the salts and aldehyde were treated in 1:3 and 1:4 molar ratio respectively. When these reactions were repeated in the ultrasonic bath, only (III) was obtained under these conditions. Sonication generally improved the yield of (III) and significantly reduced the duration of the reactions.

Introduction

Salicylaldehyde when reacted with excess ammonium carbonate has been reported to yield hydrosalicylamide in water [1]. However, attempts made to reproduce this work were not very fruitful. This necessitated the reinvestigation of the reaction of salicyladehyde with different ammonium compounds. Consequently, in an earlier work we reported that the reaction of this aldehyde with gaseous ammonia yields exclusively N-unsubstituted salicylaldehyde-imine (II) in non-polar solvents and hydrosalicylamide (III) generally in the polar solvents [2]. In the present work the reactions of salicylaldehyde have been carried out with various ammonium salts in different molar ratios in polar solvents (water and methanol) to investigate the effects of sonication on these reactions.

Results and Discussion

The reaction of salicylaldehyde with ammonia in non-polar solvents predominantly yields its N-unsubstituted-imine (II) [2]. On the other hand, it was observed that this aldehyde on reaction with ammonia in water and methanol affords hydrosalicylamide (III). Consequently, the reactions of this aldehyde with different ammonium salts have been reinvestigated in water and methanol which afford hydrosalicylamide (III) and tricyclobenzoxine (IX) under different conditions and the results are reported in Table-1.

It is obvious from Table-1 that under unstirred conditions, salicylaldehyde on reaction with ammonium carbonate and triammonium phosphate in different molar ratios yielded only hydrosalicyalamide (III) both in water and methanol. Moreover, this aldehyde on reaction with ammonium bicarbonate also yields only (III) in these solvents when the salt and aldehyde ratio is restricted to 1:1 and 1:2. However, with higher molar ratios of 1:3 and 1:4, the reaction with this salt yields a mixture of (III) and (IV). The pH values ranged from 7-8.5 in all these reactions. In the acidic salts like ammonium chloride and ammonium dihydrogen phosphate no such products could be obtained. This suggests that under the acidic conditions the nucleophilic attack by these ammoniating agents may not be possible.

Interestingly, the reaction mixtures of ammonium acetate and salicylaldehyde in different molar ratios did not afford any of these products in water, even if kept at room temperature (30 ± 2°) for over two weeks. However, when the molar ratio of the salt to the aldehyde was 1:1 and 1:2 (III) was obtained in good yield (81%) in methanol. Higher molar ratios (1:3 and 1:4) gave a mixture of (III) and (IV) in the same solvent but yield of (IV) was good (64%) in the latter case. Formation of (IV) through this procedure in achieved under very simple conditions as compared with a previously reported method [3], which demands quite vigorous conditions.

The reactions of this aldehyde with different ammonium compounds have also been carried out

Table-1: Effect of Sonication on the reaction of salicylaldehyde with ammonium salts

Molar ratio (Duration)→		1:1 (Hours)		1:2 (Hours)		1:3 (Hours)			1:4 (Hours)		
(Salt : aldehyde)		Room temp. (30 ± 2°) unstirred	Sonication	Room temp. (30 ± 2°) unstirred	Sonication	Room Temp. (30 ± 2°) unstirred		Sonication	Room temp. (30 ± 2°) unstirred		Sonication
Ammonium salt	Medium	III%	III%	III%	III%	III%	IV%	III%	III%	IV%	III%
Ammonium acetate	H_2O	-	-	-	-	-	-	-	-	-	-
	CH_3OH	57(24)	53(2) 64(4) 69(6)	81(24)	89(6)	56(24)	25(24)	85(4) 90(6)	3(24)	64(24)	71(4) 88(6)
Ammonium carbonate	H_2O	32(48)		59(48)		75(48)			80(40)	-	-
	CH_3OH	51(48)	63(6)	71(48)	82(6)	65(48)	-	75(6)	63(48)	-	69(6)
Ammonium bicarbonate	H_2O	40(48)		58(48)		57(48)			60(48)	-	
	CH_3OH	35(48)	42(6)	73(48)	78(6)	25(48)	11(48)	35(6)	7(48)	18(48)	25(6)
Ammonium phosphate	H_2O	15(48)		36(48)		38(48)	-		37(48)	-	
	CH_3OH	28(48)	32(6)	35(48)	40(6)	36(48)		42(6)	35(48)	-	41(6)

in methanol in the ultrasonic bath for different durations and the results also recorded in Table-1. It is clear from these results that sonication generally improves the yield of hydrosalicylamide (III) in all the experiments. Sonication also goes a long way in reducing the duration of the reaction from 24 hrs/48 (in different salts) to about 6 hrs. for comparatively better yield of (III). It did not yield (IV) in all the experiments carried in the ultrasonic bath.

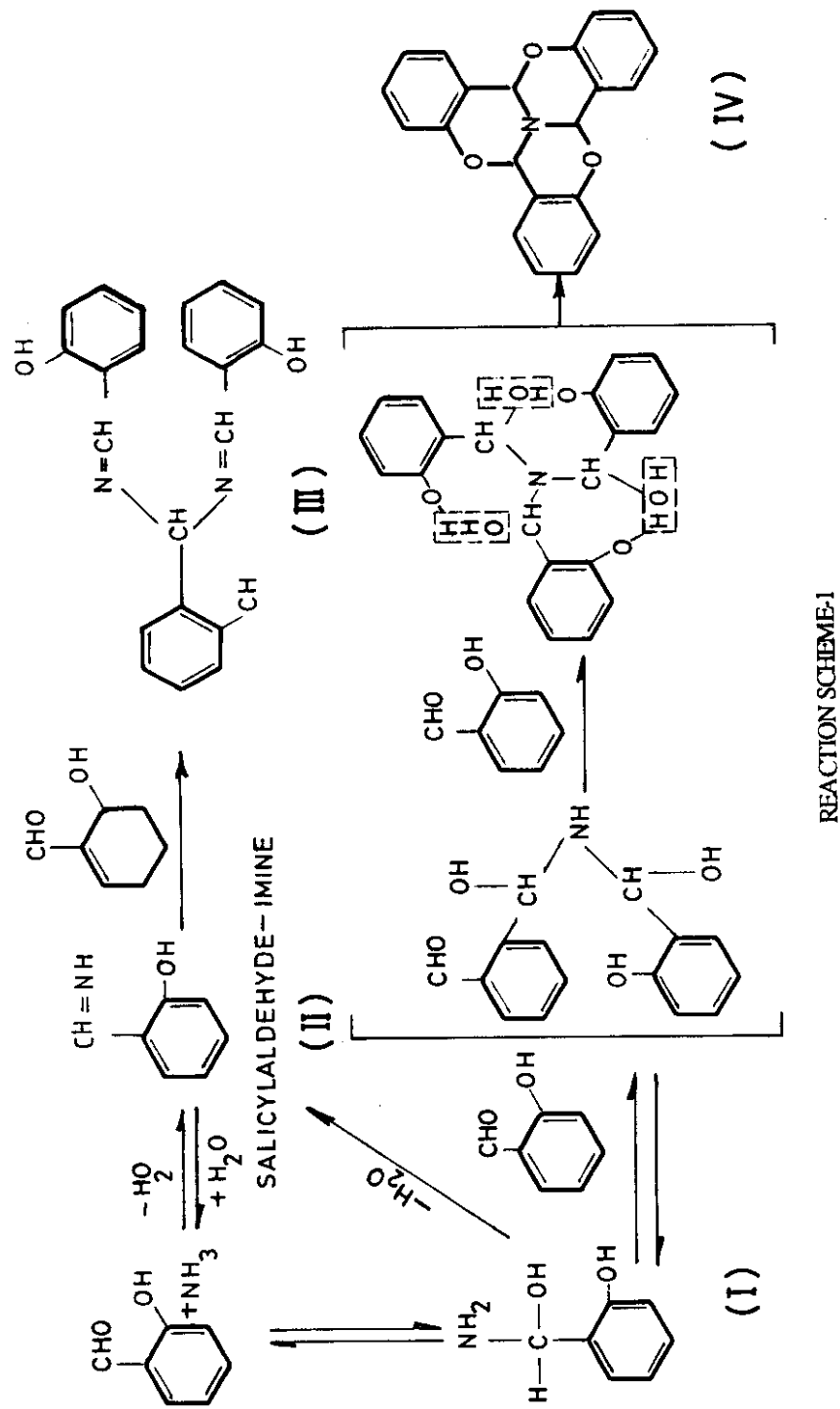
In order to explain the mode of different products. Reaction Scheme-1 has been shown, where nucleophilic addition of ammonia has been proposed to form hemiaminal (carbinol amine) (I) as the first step in conformity with earlier reports [4,5]. This undergoes dehydration yielding salicylaldehyde-imine (II). The latter on reaction with more of aldehyde was found to transform into hydrosalicylamide (III). It has also been reported [2] that (II) when left in open changes to salicylaldehyde (with liberation of ammonia) and eventually transforms to hydrosalicylamide (III) as shown in the Reaction Scheme-1. To explain the formation of (IV) as a major product in the unstirred reaction of ammonium acetate and the aldehyde, especially in 1:4 molar ratio, it is assumed that hemiaminal (1) may successively react with excess aldehyde to afford an intermediate, which on dehydration converts to tricyclobenzoxine (IV). However, we failed to obtain (IV) in all the experiments carried out with different molar ratios of the aldehyde and various ammonium salts under ultrasonic conditions. It may be inferred from these observations that formation of (IV) proceeds via slow molecular condensation and dehydration. On the other hand, under ultrasonic conditions kinetic energy is quite high which enhances the rate of molecular collision [6] and thus does not favour the formation of (IV). This was confirmed by repeating the unstirred reaction of the ammonium salt and the aldehyde (in 1:4 molar ratio) in a refrigerator (10 ± 1°) when the yield of (IV) increased from 64 to 69%, since rate of molecular collisions also decreases on cooling.

Experimental

All the chemicals used were of analytical grade. The solvents used were distilled before use. Doubly distilled water was used in all the desired experiments. The reaction mixtures consisting of appropriate amount of the ammonium salts, salicylaldehyde and water/methanol taken in conical flasks, plugged with loose cotton, were left at room temperature (30 ± 2°C) unstirred for 24/48 hrs. Thereafter, products were separated by filtration.

Identical experiments were also run in the ultrasonic bath (300 Ultra Sonic - Jencons Scientific Ltd.), when the temperature increased from 30 ± 2°C to 42 ± 3°C for different durations. In order to facilitate settling of the product the reaction mixtures were cooled in the ice-bath for about 2 hrs., before filtration.

Initial values of pH were recorded on a Henna H-8417 digital pH meter by mixing and shaking the reactants. The final pH of the mother liquors, after the products were isolated by filtration, were also noted. The products, dried at


SALICYLALDEHYDE-IMINE
(I)
(II)
(III)
(IV)
REACTION SCHEME-I

room temperature in a vacuum desiccator, were purified by crystallisation from the appropriate solvents. Since different molar ratios of the reactants were used in all the experiments, the reported % yields are based on that reactant which is either equal or lesser than the theoretically required amount in a particular reaction. Melting point were determined on a Kofler microscope hot state and are uncorrected. Infrared absorption spectra were recorded on a Beckman Acculab-10. Infrared spectrophotometer. Mass spectra were run at Chemistry Department, Monash University (Australia). The NMR spectra were recorded on Hitachi Perkin Elmer R-24, 60 MHz spectrophotometer using TMS as internal standard.

Reaction of salicylaldehyde with

Ammonia

Gaseous ammonia was passed to a reaction mixture consisting of salicylaldehyde (1.22 g; 0.01 mole) and water/methanol (20 mL) until the contents got saturated with it. Bright yellow product, hydrosalicylamide (III) (N, N'-bis(2-hydroxybenzylidene-2-hydroxy-α,α-tolyldiamine), filtered off and recrystallised from acetone had m.p. 163-164° (lit. 164°) [1] and the yields were (1.095 g, 95%) in water and (0.968 g, 84%) in methanol. Its mixture melting point with an authentic sample remained undepressed. Their I.R. and NMR spectra were also superimpossible.

Ammonium acetate

Ammonium acetate (0.77 g, 0.01 mole) was added to four different flasks containing methanol (20 mL) followed by addition of salicylaldehyde (1.22 g, 0.01 mol; 2.44 g, 0.02 mole; 3.66 g, 0.03 mole and 4.88 g, 0.04 mole) in each flask. The reaction mixture was left unstirred and work up after 24 hours yielded (III) (0.657 g, 57 % and 1.401 g, 81%) in the first two flasks respectively. The third flask gave (III) (0.968 g, 56%) and (IV) (0.823 g, 25%), while the fourth flask afforded (III) (0.052 g, 3%) and IV (2.106 g; 64%). Hydrosalicylamide (III) and (IV) (tricyclobenzoxine) were separated by dissolving (III) in acetone, while (IV), m.p. 244-245°, was practically insoluble in this solvent. The mass spectrum of (IV) indicated molecular ion at m/z 329 corresponding to its molecular formula, $C_{21}H_{15}O_3N$. It was further confirmed by combustion analysis.

Identical experiments were run in the ultrasonic bath for different durations. When the ratio of the reactants was 1:1, (III) formed in 53% (0.611 g), 64% (0.738 g) and 69% (0.796) when sonication was carried out for 2,4 and 6 hrs. respectively. Sonication for 6 hrs, afforded (III) (1.539 g, 89%) when salt and aldehyde ratio was 1:2. Higher reactant ratios (1:3 and 1:4) yielded (III) (1.470 g, 85%; 1.557 g, 90%) and (1.228 g, 71%; 1.522 g; 88%) for 4 and 6 hrs. sonication respectively.

The reaction of salicylaldehyde with this ammonium salt in water practically yielded no product even if the reaction was extended upto two weeks.

*Ammonium carbonate**

*(According to BDH Laboratory Supplies, England the product consists of approximately equimolar proportion of ammonium bicarbonate and ammonium carbonate).

Ammonium carbonate (0.96 g, 0.01 mole) was added to four flasks containing salicylaldehyde (1.22 g, 0.01 mole; 2.44 g, 0.02 mole; 3.66 g, 0.03 mole and 4.88 g, 0.04 mole) and water (20 mL). The reactants were kept unstirred for 48 hrs. and work up afforded (III) (0.369 g, 32%; 1.361 g, 59%; 2.595 g, 75% and 2.768 g, 80%) respectively. Similar experiments were carried out in methanol (20 mL), which afforded (III) (0.588 g, 51%; 1.638 g, 71 %; 2.249 g; 65% and 2.179 g, 63%) respectively.

Four identical experiments were also subjected to sonication for 6 hours using methanol (20 mL) as a medium. The work up gave only (III) (0.726 g, 63%; 1.891 g, 82%; 2.595 g, 75% and 2.387 g, 69%).

Ammonium bicarbonate

Ammonium bicarbonate (0.79 g, 0.01 mole) in water (20 mL) was mixed with salicylaldehyde (1.22 g, 0.01 mole; 2.44 g, 0.02 mole; 3.66 g, 0.03 mole and 4.88 g, 0.04 mole in four different flasks. The unstirred reactants yielded (III) (0.461 g; 40%; 1.003 g, 58%; 0.986 g, 57% and 1.038 g, 60%) respectively. When identical experiments were carried out in methanol (20 mL) % yield of (III) was 35(0.404 g) and 73 (1.262 g) for the salt and

aldehyde ratio of 1:1 and 1:2 respectively. When these reactants were in 1:3 and 1:4, a mixture of (III) (0.432 g, 25%) and (IV) (0.362 g, 11%) was obtained in the case of former experiment, while the latter experiment afforded (III) (0.121 g, 7%) and (IV) (0.592 g, 18%). When all these experiments in methanol (20 mL) were run for 6 hrs, in the ultrasound bath, only (III) (10.461 g, 42%; 1.349 g, 78%; 0.605 g, 35% and 0.432 g, 25% respectively) was obtained.

Ammonium phosphate

Equal amount of ammonium phosphate (1.49 g, 0.01 mole) was added to four flasks containing salicylaldehyde (1.22 g, 0.01 mole; 2.44 g, 0.02 mole; 3.66 g, 0.03 mole and 4.88 g, 0.04 mole) and water (20 mL). The work up after 48 hours, yielded (III) (0.173 g, 15%, 0.830 g, 36%; 1.315 g, 38% and 1.707 g, 37%) respectively. When these experiments were carried out in methanol (20 mL) corresponding % of (III) was 28, 35, 36 and 35, while sonication for 6 hrs, afforded (III) 36%, 40%, 42% and 41 respectively.

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