STUDY OF KRÖHNKE'S METHOD OF SYNTHESIS OF ALDEHYDES: CINNAMALDEHYDE FROM CINNAMYL BROMIDE

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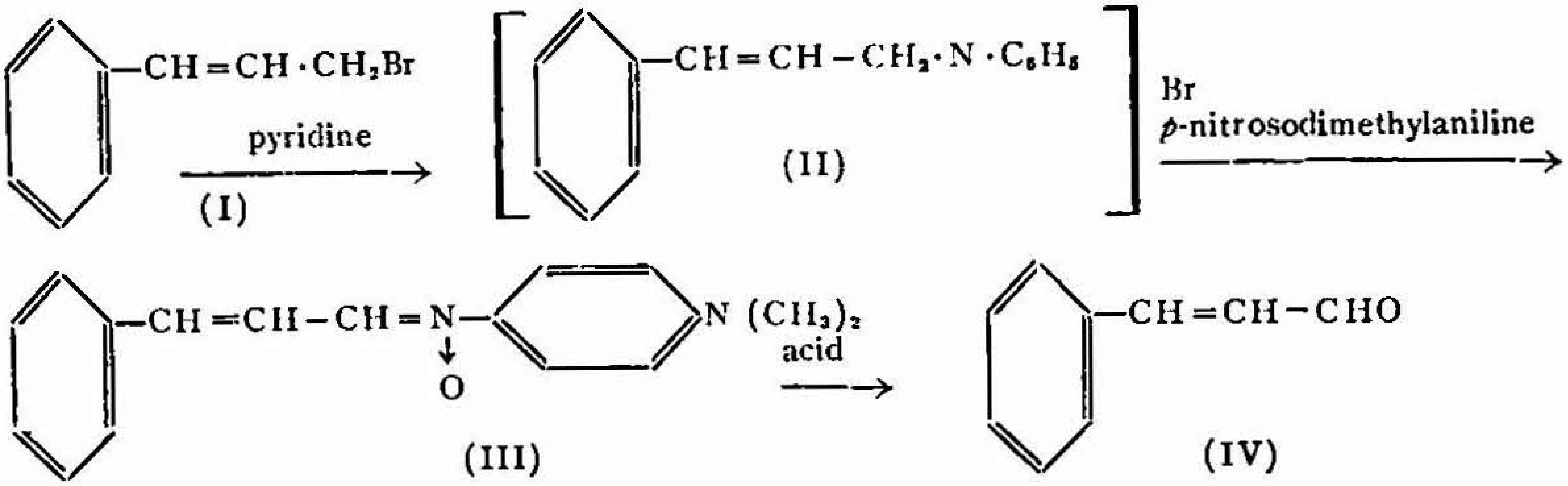
Conditions for the conversion of cinnamyl bromide (I) into cinnamaldehyde (IV) through cinnamyl pyridinium bromide (II) and styryl-N-(*p*-dimethylaminophenyl)-nitrone (III) have been studied. The intermediate pyridinium salt has been obtained in pure form for the first time. The pyridinium salt could be converted into the corresponding nitrone in 95% yield. It has been shown that the nitrone (III) can directly be converted into the semicarbazone of the corresponding aldehyde (IV).

Kröhnke[1] converted halogen compounds of the formulæ $\phi.CH_2X$, $RCOCH_2X$ and $RCH=CH\text{-}CH_2X$ into the corresponding aldehydes, $\phi.CHO$, $RCOCHO$, $RCH=CH\text{-}CHO$, by the hydrolysis of the nitrone obtained from the pyridinium salt and also put forward a mechanism for the reaction.[2] Karrer and Epprecht[3] utilised this method for the preparation of a few aliphatic α, β-unsaturated aldehydes and Reich[4] for the preparation of 3-acetoxypregnadien-(5, 17)-al-(21) and pregnadien-(4, 17)-one-(3)-al-(21) from the respective unsaturated bromides; the yields, however, were generally poor.

An attempt to extend the application of this method to β-cyclohexylidene ethyl bromide also resulted in a poor yield of cyclohexylideneacetaldehyde.[5] Possibly, the experimental conditions so far employed are not quite satisfactory. Therefore a systematic study of the reaction has been undertaken choosing cinnamyl bromide as starting material. The intermediate nitrone from it is a stable solid compound. Kröhnke (*loc. cit.*) himself has conducted the reaction with cinnamyl pyridinium perchlorate (prepared from cinnamyl pyridinium bromide) and obtained the intermediate styryl-N (*p*-dimethyl-aminophenyl)-nitrone in 70% yield (calculated from the perchlorate). In the present studies cinnamyl pyridinium bromide has been used in the place of cinnamyl pyridinium perchlorate and the reactions succeeded without special difficulty. Cinnamyl pyridinium bromide II was prepared in almost quantitative yield from cinnamyl bromide I and excess of absolute pyridine. The pyridinium salt could be isolated in crystalline form which was hitherto not reported. This pyridinium salt with *p*-nitrosodimethyl aniline and alkali gave styryl-N-(*p*-dimethyl-amino-phenyl) nitrone (III) which was hydrolysed to cinnamaldehyde (IV) by acid.



Of the three steps involved in this reaction the first and the third easily afforded almost quantitative yield and therefore the second, *viz.*, conversion of the pyridinium salt (II) to the nitrone (III), alone required special study. A number of reactions were studied under varying conditions and as a result the yield could be improved upto 95%. A summary of the more important experiments is given below, indicating the different conditions employed: *viz.*, change of solvents, volume of solvents, proportion of reagent, time and temperature. The melting point of the product isolated in each case is also given along with the yield.

From the table it is seen that the yield is increased and the time shortened as the concentration and proportion of the reactants are increased. An yield upto 79% was obtained during a period of only 5 minutes when the volume of the solvent (methyl alcohol) was reduced to the minimum (Expt. 13). Methyl alcohol is found to be slightly better than ethyl alcohol (Expts. 15, 16). The reaction takes place at 0° C. as smoothly as at room temperature (20–25°).

Cinnamyl pyridinium perchlorate also was prepared and converted into the nitrone by repeating Kröhnke's (*loc. cit.*) procedure and the nitrones obtained in both cases were found to be identical.

An attempt was made to prepare the nitrone using cinnamyl bromide-hexamethylenetetramine addition product in the place of cinnamyl pyridinium bromide but was unsuccessful.

Styryl-N-(*p*-dimethylaminophenyl)-nitrone reacted with semicarbazide hydrochloride to yield cinnamaldehyde semicarbazone just as benzaldoxime derivatives yielded benzaldehyde semicarbazone, described by Brady and

Peakin.[6] This method of preparing semicarbazones may be of use in those cases where the free aldehydes are unstable.

EXPERIMENTAL

Cinnamyl bromide (I)

Cinnamyl bromide was prepared by a slight modification of the method described by Rupe and Burgin.[7] Freshly distilled cinnamyl alcohol (30 g.) and absolute pyridine (3 g.) taken in 30 c.c. of anhydrous benzene was mixed little by little with phosphorus tribromide (26 g.) in 30 c.c. of anhydrous petrol ether under cooling. After keeping for 2 hours at room temperature and then half an hour at 50–55°, the reaction mixture was decomposed by water. The aqueous layer was extracted with benzene, the combined extract was washed with water, sodium bicarbonate solution and water, dried over sodium sulphate and distilled through a column. Cinnamyl bromide distilled at 102–03°/2·5 mm., yield 32·9 g.

Cinnamyl pyridinium bromide (II)

Cinnamyl bromide (5 g.) taken in a 100 c.c. round-bottomed flask was mixed with absolute pyridine (50 c.c.) and kept well stoppered. Shortly after mixing heat was evolved spontaneously. After 24 hours the excess of pyridine was distilled off under reduced pressure and the pasty residue was washed with sodium dried benzene by thorough shaking and decantation. When a few of such flasks containing the pasty pyridinium bromide was kept for 4 days more over dry benzene, the bromide in two of the flasks was found to have crystallized. The contents of the rest were crystallized by seeding them with traces of the crystalline salt. The crystallized compound was again washed with anhydrous benzene and dried under vacuum. The yields were generally quantitative. The crystals were extremely deliquescent, easily soluble in alcohol, chloroform and insoluble in benzene. and petrol ether. It melted at 95–98° (in sealed tube). For analysis a sample was repeatedly washed with absolute benzene and dried under high vacuum at 80–85°. Found: Br, 28·55; $C_{14}H_{14}NBr$ requires Br, 28·95 per cent.

Styryl-N-(p-*dimethylaminophenyl*)*-nitrone (III)*

Cinnamyl pyridinium bromide was dissolved in pure or dilute solvent and mixed with the required amounts of *p*-nitrosodimethyl aniline, dissolved in pure solvent, if necessary by warming. In all cases I N sodium hydroxide solution, equivalent to the bromide taken was added. They were then kept for different periods of time, diluted with water till the precipitation was complete, filtered, washed with distilled water and dried to constant weight. In some cases more precipitate appeared in the filtrate on keeping. The results of the experiments are summarized below, *Table showing the results of experiments for the conversion of cinnamyl pyridinium bromide to styryl-N-(*p*-dimethylaminophenyl)-nitrone*

Expt.	Cinnamyl pyridinium bromide	*p*-Nitroso dimethyl aniline	Solvent	Time	Temperature	Melting point	Yield	
							g.	%
	g.	g.			°C.	°C.		
1	6·9	3·9	170 c.c. 88% ethanol	10 hrs.	20–25	177–178	2·65	40
2	6·9	3·9	do.	16 ,,	,,	166–170	3·8	57·5
3	6·9	3·9	110 c.c. ethanol	10 ,,	,,	176–178	2·8	42
4	6·9	3·9	75 c.c. methanol	10 ,,	,,	170–174	5·55	83
5	6·9	3·9	95 c.c. 30% dioxan	10 ,,	,,	169–171	3·9	58·8
6	6·9	3·9	50 c.c. 50% acetone	10 ,,	,,	170–173	5·65	84·8
7	5·4	3·0	85 c.c. methanol	10 ,,	,,	168–170	3·45	66·4
8	5·4	3·75	do.	10 ,,	,,	170–172	3·9	75
9	5·4	4·5	do.	10 ,,	,,	170–172	4·4	85·5
10	5·4	5·25	do.	10 ,,	,,	169–171	4·7	90·4
11	5·4	6	do.	10 ,,	,,	170–172	4·65	89·5
12	5·4	3	20 c.c. methanol	10 mts.	,,	162–165	4·3	83·6
13	5·4	3	do.	5 ,,	,,	161–164	4·1	78·9
14	5·4	3	do.	16 hrs.	,,	167–169	4·85	93·3
15	5·4	3	40 c.c. methanol	8 ,,	0	171–173	4·9	95
16	5·4	3	40 c.c. ethanol	8 ,,	0	170–172	4·55	87·6

For analysis a sample of the nitrone was repeatedly crystallized from ethyl alcohol and ethyl acetate; m.p., 180–82° (Kröhnke found the m.p. 180°). Found: N, 10·37; $C_{17}H_{18}ON_2$ requires N, 10·53 per cent.

Hydrolysis of styryl-N-(p-*dimethylaminophenyl*)*-nitrone* (*III*): *Formation of cinnamaldehyde* (*IV*)

5 g. of styryl-N-(*p*-dimethylaminophenyl)-nitrone was suspended in 100 c.c. of ether and decomposed by vigorous shaking with several lots of cold 2 N sulphuric acid till the aqueous layer was almost colourless. The combined aqueous layer was then extracted with a fresh amount of ether and the combined ether solution was washed with sodium bicarbonate solution, water and dried over anhydrous sodium sulphate. On distillation through a column, 2·25 g. of cinnamaldehyde was obtained, b.p. 96–97°/3 mm. (Semicarbazone m.p. 217°. No depression in m.p. when mixed with authentic cinnamaldehyde semicarbazone). A reddish brown residue was left behind in the flask after distillation.

semicarbazone of cinnamaldehyde from styryl-N-(p-*dimethylaminophenyl*)*-nitrone*

The nitrone (1 g.) dissolved in 170 c.c. of alcohol was mixed with semicarbazide hydrochloride (·83 g.). After keeping for 1 day at room temperature, the volume of alcohol was reduced to a few c.c. under suction and diluted with much water, stirred and filtered. The residue was then stirred thoroughly with dilute hydrochloric acid and filtered. The semicarbazone thus obtained weighed ·7 g. (m.p. 205–07°). Recrystallized from dioxan and alcohol, m.p. 217°, undepressed on admixture with an authentic specimen.

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