
CHAPTER - 3

PREPARATION AND APPLICATIONS OF
SPACER BOROHYDRIDE EXCHANGE RESIN

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EXCHANGE RESINABSTRACT

Spacer borohydride exchange resin (spacer BER) was prepared and used as reducing agent for the reduction of aldehydes and ketones. It has been observed that it is more effective reducing agent than corresponding borohydride exchange resin prepared from commercial anion exchange resin, Amberlyst A-26 and Amberlite IRA-400. The spacer BER reduces aldehydes and ketones in methanolic solutions with ease both by column as well as batchwise process.

The spacer BER was prepared starting from (2% crosslinked) chloromethylated polystyrene by amination reaction followed by quaternization with alkyl halide and then by treatment with aqueous sodium borohydride solution. The capacity of this spacer BER was determined. The stability and shelf life of spacer BER were also studied.

To study the effect of steric hinderence on the rate of reduction, the reaction was carried out by increasing steric bulk at nitrogen atom of spacer borohydride exchange resin.

INTRODUCTION

Majority of the polymeric reagents are based on polystyrene supports on account of their facile preparation, easy characterization, and comparatively good mechanical properties. Another type of support commonly used is based on poly (vinyl - pyridines)¹. The investigations of reagent functions based on polar polymeric supports have been very rare except for the acylating and oxidizing reactive functions based on polyamide (nylon) supports^{2,3}.

It is increasingly recognized that when polymers are used as supports for catalysts or organic reagents, the reactivity and selectivity of the supported catalysts or reagents may be seriously changed by so called polymer effects, the origins of which may be physical or chemical⁴⁻⁶.

The fact that majority of the organic reactions of synthetic importance occur in a polar environment suggest the importance of carrying out the polymer supported reactions in polar environments.

The synthetic reactions employed for polypeptides and other bio-polymers and a vast number of other preparative reactions require a polar environment for maximum

facilitation of the reaction. The reactivity of the non-polar polystyrene system in polar environments is limited and this has been a factor limiting the access to quantitative reactions⁷. In order to overcome this drawback of the polystyrene supports, polyacrylamide type supports were introduced by Sheppard and co-workers in the field of solid phase peptide synthesis^{8,9}. In many cases the yields of the peptide obtained were higher when compared to the synthesis using polystyrene resins^{10,11}.

The polymeric reagents have wide applications in various fields, particularly for solving problem in organic synthesis¹². The borohydride exchange resin (BER) reported by Gibson and Baily, prepared by using commercially available strongly anion exchange resin (Amberlyst A-26 or Amberlite IRA-400) has been used for various purposes like solvent purification, generation of volatile metal hydrides, reduction of metal ions and some aldehydes.

Similarly borohydride exchange resin has been used in the number of organic transformations including the reduction of benzyl and primary alkyl halide to the corresponding hydrocarbons¹³, the reduction of aliphatic acid chlorides to aldehydes¹⁴ and selective reduction of olefinic bonds in α, β - unsaturated cyanoacetates¹⁵. The BER also exhibited a high chemoselectivity not only between aldehydes and ketones but also between ketones¹⁶.

The BER exhibited chemoselectivity in the reduction of α, β - unsaturated carbonyl compounds to the corresponding alcohols¹⁷ as well.

The sequential use of two or more polymeric transfer agents on a single starting substrate offers a novel approach to organic synthesis. This is termed as "cascade reaction"¹⁸. The BER prepared from commercially available strongly basic anion exchange resin was found to be unsuitable for cascade reaction since the rate of reduction is very slow.

The present chapter deals with the preparation of spacer borohydride exchange resin (spacer BER) starting from crosslinked (2%) chloromethylated polystyrene, its capacity determination and effect of steric hinderence at the reactive site on the rate of reduction reaction of carbonyl compounds to corresponding alcohols.

The major thrust is on the incorporation of reducing agent on polystyrene which is readily available and cheap. The reagent was found to be suitable for the reduction of carbonyl compounds to corresponding alcohols in high yields. Similarly the rate of reduction reaction was found to be faster as compared to the BER prepared from commercial anion exchange resins (Amberlyst A-26 or Amberlite IRA-400)

PRESENT WORK

The BER prepared from strongly basic anion exchange resin (Amberlyst A-26, Amberlite IRA-400) has been widely used in various reduction reactions. It has been also used for the selective reductions of carbonyl compounds.

In order for a cascade to succeed, the substrate must be entirely converted to product prior to reaction product with the next polymeric reagent. BER prepared from commercially available strongly anion exchange resin Amberlite IRA-400 was found to be unsuitable for cascade reaction since the rate of reduction is very slow.

In order to overcome steric effect and to achieve reductions on a column for a cascade reaction a new BER has been prepared with a spacer (spacer BER). Spacer BER reduces aldehydes and ketones much faster than BER prepared from commercial anion exchange resin.

PREPARATION OF SPACER BER

The spacer BER was prepared by three step reactions, starting from crosslinked (2%) chloromethylated polystyrene beads. Commercially available chloromethylated polystyrene beads were refluxed with 3-Dimethylaminopropylamine in N, N-Dimethylformamide. The resulting polymer after washing with N, N-Dimethylformamide and methanol was

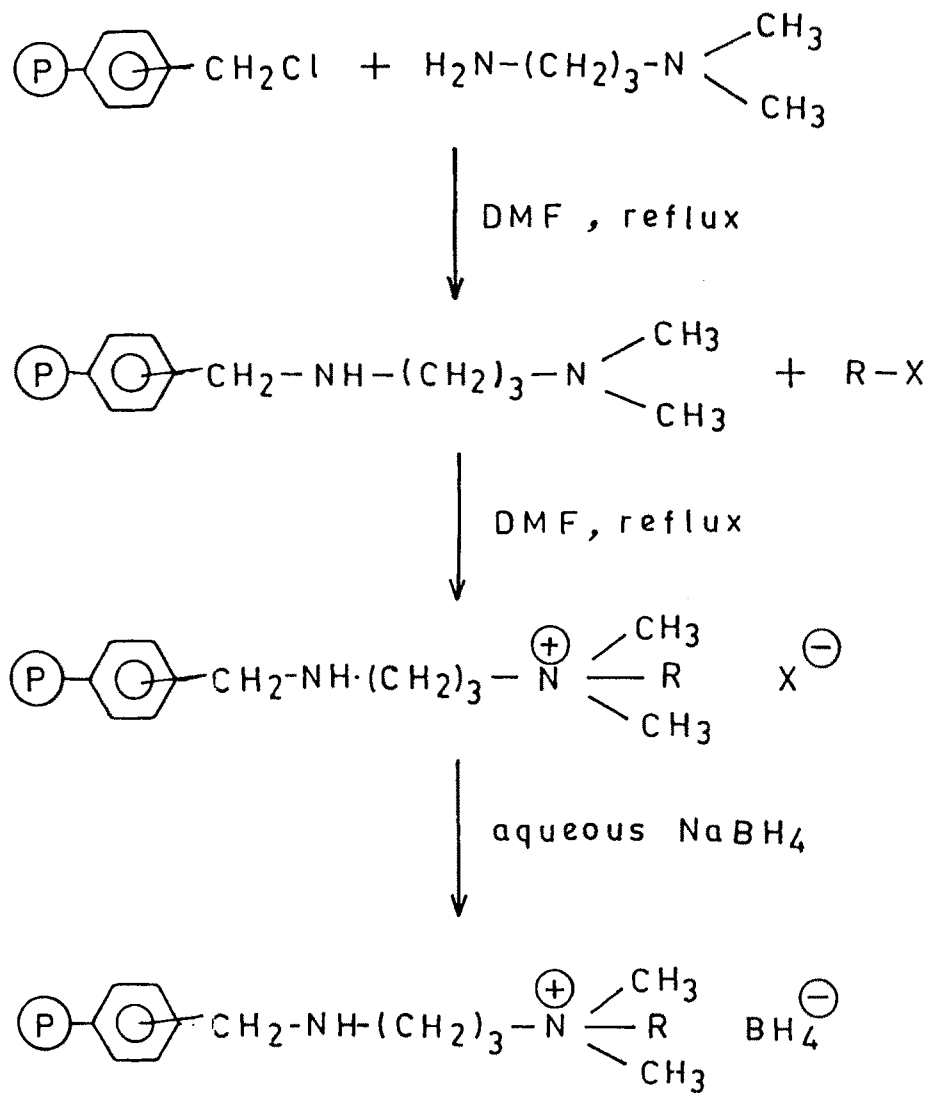
quaternized by refluxing with alkyl halide. The quaternized polymer was then washed with methanol and dried. Then aqueous sodium borohydride solution (0.5 M) was slowly passed through the quaternized polymer over a period of 60 minutes. The resulting polymer was washed with distilled water thoroughly until free from excess of sodium borohydride. The spacer BER was then dried by keeping it with calcium chloride in vacuo, at room temperature.

The dried resin was then analysed for its borohydride content by hydrogen evolution on acidification with 0.8 N hydrochloric acid.

The scheme-III.1 explains the procedure for the preparation of spacer BER.

The spacer BER-A was prepared by using methyl iodide where as spacer BER-B and spacer BER-C were prepared by using ethyl iodide and isobutyl bromide respectively. The structures of spacer BER prepared are shown in Chart-A.

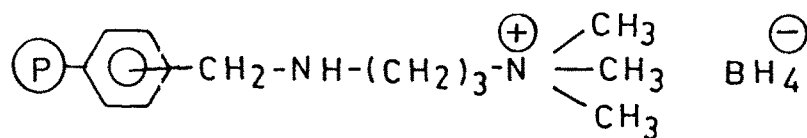
SCHEME III.1 - PROCEDURE FOR PREPARATION OF SPACE BER.



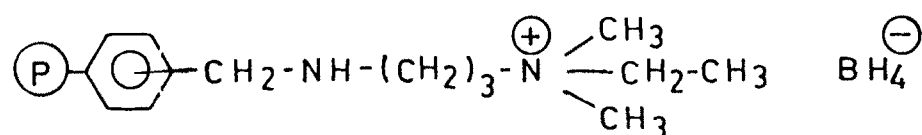
SPACER BER

R-X = alkyl halide

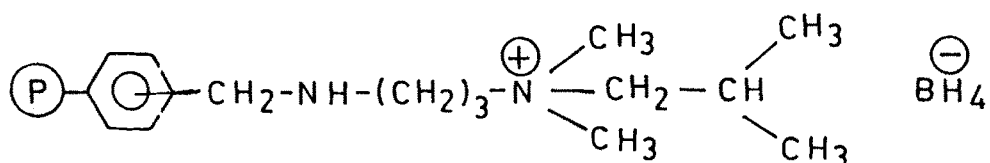
CHART A) STRUCTURES OF SPACER BER
PREPARED .



SPACER BER (A)



SPACER BER (B)



SPACER BER (C)



DETERMINATION OF CAPACITY OF SPACER BER

The capacity of spacer BER was determined by passing sodium nitrate solution through the column containing quaternized polymer and then titrating the effluent against silver nitrate solution using potassium chromate as an indicator.

The capacity of spacer BER was found to be 0.52 mili equivalents/gm. of the dry resin.

STABILITY AND SHELF LIFE OF SPACER BER

The spacer BER obtained in the form of fine beads were found to be stable under the ordinary laboratory conditions. The reagent can be stored indefinitely without appreciable loss in the capacity. In order to determine the stability of reagent, it was kept with calcium chloride in vacuo at room temperature for a period of three months and the capacities were determined by the same procedure.

Table - 1 : Stability of spacer BER

Polymeric reagent	Initial capacity (m.equi./gm.)	Capacity after weeks (m.eq./gm.)					
		2	4	6	8	10	12
Spacer BER(A)	0.52	0.52	0.52	0.52	0.52	0.51	0.51

REDUCTION REACTION WITH SPACER BER

The spacer BER was found to be useful for the reduction of carbonyl compounds to corresponding alcohols in high yields. The reduction reaction can be carried out by columnwise method as well as by batchwise method.

The rate of reduction reaction is faster with spacer BER than the BER prepared by using Amberlyst A-26 and Amberlite IRA-400.

The results are shown in table-2.

Table - 2 : Reduction of Benzaldehyde to Benzyl alcohol
at room temperature in methanol
(Batchwise method)

Sr. No.	Starting material	Exchange resin used	Time (hrs)	Isolated Yield (%)
1.	Benzaldehyde	BER ^a	2	95
2.	Benzaldehyde	spacer BER(A)	0.33	97
3.	Benzaldehyde	spacer BER(B)	0.50	97
4.	Benzaldehyde	spacer BER(C)	1.2	95

BER^a - BER prepared from Amberlite IRA-400

The observation of table - 2 reveals that the time required for the reduction of benzaldehyde with spacer

BER(C) is more than spacer BER(A). This particular observation prompted us to examine the spacer BER for the selective reduction of α, β - unsaturated carbonyl compounds. However it was observed that the selectivity is lost with spacer BER.

The results are shown in table-3

Table - 3 : Reduction of Cinnamaldehyde to 3-phenyl propanol with spacer BER.

Sr. No.	Starting material	Exchange resin used	Time (hrs)	Isolated Yield (%)
1.	Cinnamaldehyde	spacer BER(A)	0.75	95
2.	Cinnamaldehyde	spacer BER(C)	1.75	95

SOLVENT EFFECT

To investigate the effect of solvent on the reaction rate, we used protic as well as aprotic solvents for the reaction.

It was observed that the reaction goes satisfactorily in protic and aprotic solvent as well without much affecting the yields of reaction. The reaction is faster in protic solvent like methanol than in aprotic solvent.

The results are shown in table - 4.

Table - 4 : Reduction of Benzaldehyde to benzyl alcohol with spacer BER in different solvents.

Sr. No.	Solvent used	Reaction time (hrs)	Isolated Yield (%)
1.	Methanol	0.33	97
2.	Ethanol	1.2	95
3.	Benzene	16	89
4.	Ether	16	90

REGENERATION OF SPACER BER

The easy recovery of the polymer makes it possible to regenerate and reuse it. This is very important from an economic point of view because polymer supported reagents will generally be more expensive than the analogous non-supported reagents.

The spacer BER once used can be regenerated. For this purpose the used spacer BER was treated with dilute hydrochloric acid. After removing the excess of chloride ions, it was treated with aqueous sodium borohydride solution. The capacities were determined after each regeneration by the same procedure. The observations indicate that spacer BER can be regenerated and reused.

Table - 5 : Capacity of spacer BER after regeneration

Polymeric reagent	Initial capacity (m.equi./gm.)	Capacity after regeneration (m.equi./gm.)			
		1 st	2 nd	3 rd	4 th
spacer BER (A)	0.52	0.52	0.52	0.52	0.51

EXPERIMENTALGENERAL

The (2%) crosslinked chloromethylated polystyrene was supplied by Thermax Private Limited, Chemical Division, 97-E, Bhosari, Pune 411 026, India, as a gift sample.

3-Dimethylaminopropylamine (by Fluka chemicals).

N, N-Dimethylformamide (by E. Merck Pvt. Ltd.) and alkyl halides (by Sisco research laboratory Pvt. Ltd; Bombay) were used. The other chemicals like benzaldehyde and methanol were commercially available and distilled before use. (N, N-Dimethylformamide was distilled by using Dean-Stark apparatus and vacuum distillation technique).

PROCEDURE FOR THE PREPARATION OF SPACER BER

The amination of crosslinked (2%) chloromethylated polystyrene beads was done by refluxing the beads (5 gms) with 3-Dimethylaminopropylamine (10 ml) in N,N-Dimethylformamide (30 ml) for two hours. The beads were then filtered, washed first with DMF (120 ml) and then in methanol soxhlet for three hours. The beads were dried by keeping with calcium chloride in vacuo at room temperature for four hours.

The resulting polymer was quaternized by refluxing with alkyl halide (10 ml) in DMF (30 ml) for three hours.

The beads were filtered and washed in methanol soxhlet for three hours and dried. (The washing of polymer in methanol soxhlet is shown in diagram A). Then 50 ml of aqueous sodium borohydride solution (0.5 M) was slowly passed through quaternized polymer over a period of 60 minutes.

The resulting polymer (spacer BER) was washed with distilled water thoroughly until free from excess of sodium borohydride. The spacer BER was then dried by keeping it with calcium chloride in vacuo at room temperature for twelve hours.

The dried resin was then analysed for its borohydride content by hydrogen evolution on acidification with 0.8 N hydrochloric acid.

DETERMINATION OF CAPACITY OF SPACER BER

1 gm of quaternized polymer was taken in an ion exchange column. Then 200 ml of 1 N NaNO_3 was passed through the column at the rate of about $2 \text{ cm}^3/\text{min}$. The effluent was titrated against 0.05 N AgNO_3 solution using 5% potassium chromate as an indicator. From this value, the capacity of spacer BER was determined.

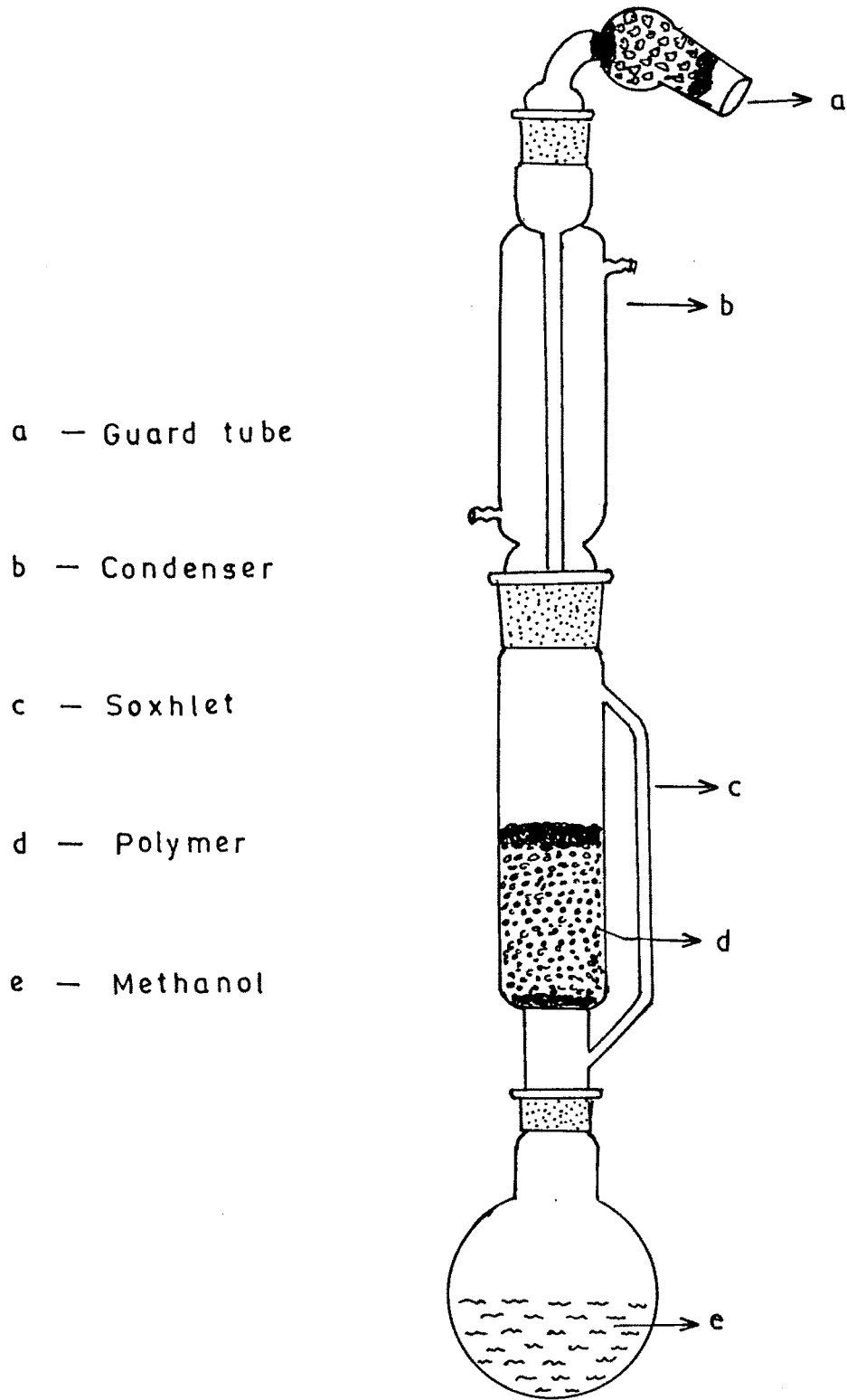


Diagram (A) - Washing of polymer in methanol soxhlet .

PROCEDURE FOR THE REDUCTION

A) BATCHWISE : Spacer BER (400 mg, 0.208 mmole) was added to a stirred solution of carbonyl compound (5 mg, 0.05 mmole) in methanol (5 ml) and the reaction mixture was stirred at room temperature. The progress of reaction was monitored by TLC. After the completion of reaction, the resin was filtered off, washed with the solvent (5 ml) and the product was isolated by the evaporation of filtrate under reduced pressure. The products obtained were essentially pure and were characterized by comparison with authentic sample and IR spectral analysis.

B) COLUMNWISE : A solution of carbonyl compound (5 mg, 0.05 mmole) in methanol was passed through a column (0.2 cm diameter) containing 2 gms of spacer BER(A) over a period of 1.75 hrs. Column was then washed with methanol. Removal of the solvent furnished corresponding alcohol.

REGENERATION OF SPACER BER

2 gms of spacer BER (after its use for reduction reaction) was activated by treating it with dilute hydrochloric acid (15 ml) for three hours. The resulting polymer was washed thoroughly with distilled water until free from excess of chloride ions. Then 20 ml of aqueous sodium borohydride solution (0.5 M) was slowly passed

through the polymer over a period of 60 minutes. The resulting polymer was washed thoroughly with distilled water until free from excess of sodium borohydride. The polymer was then dried and its capacity was determined by the same procedure. The regenerated polymer can be reused.

SPECTRAL DATA

Fig. 1 : IR spectrum of spacer BER (A)

Fig. 2 : IR spectrum of Benzyl alcohol.

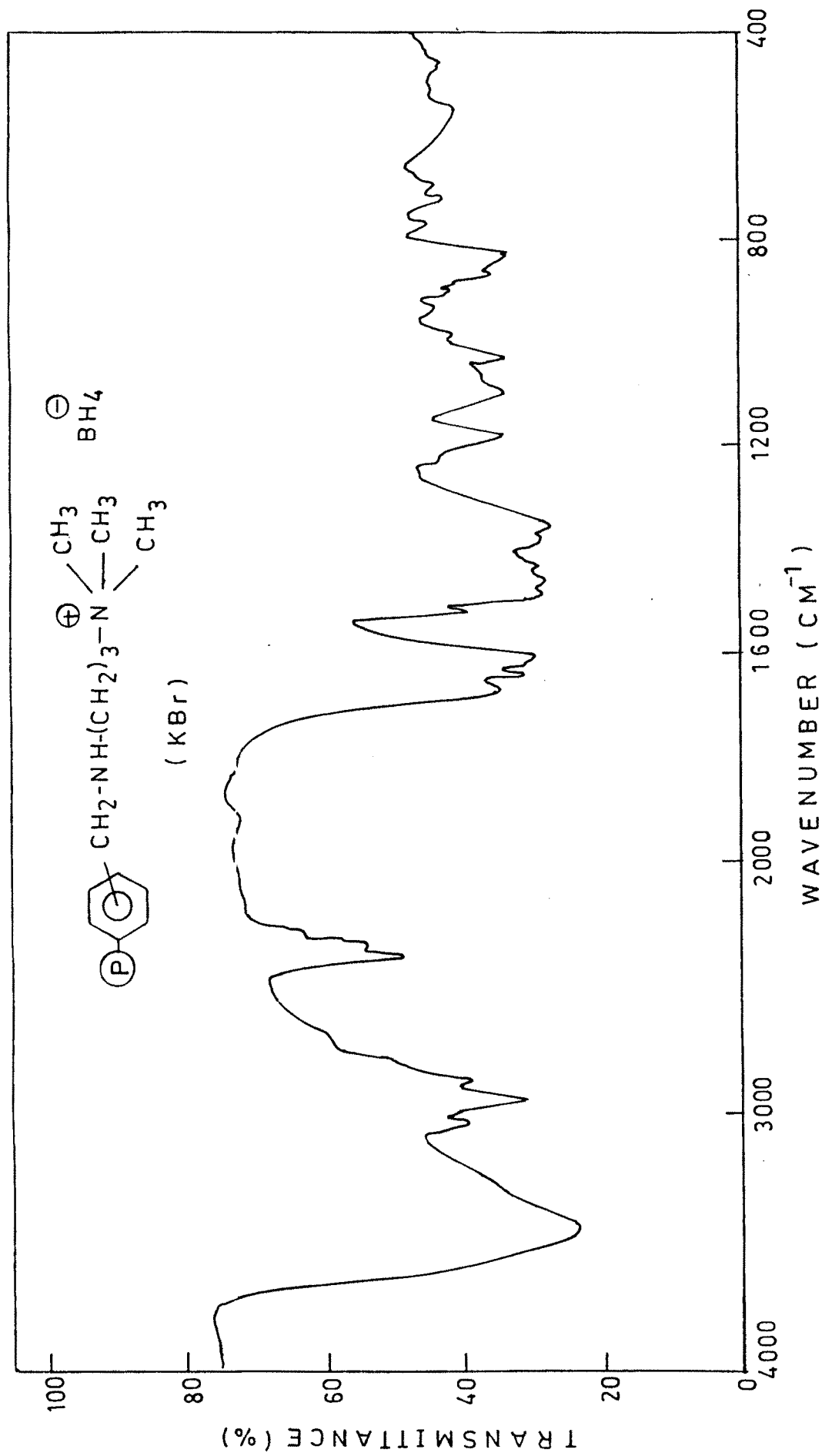


Fig. 1

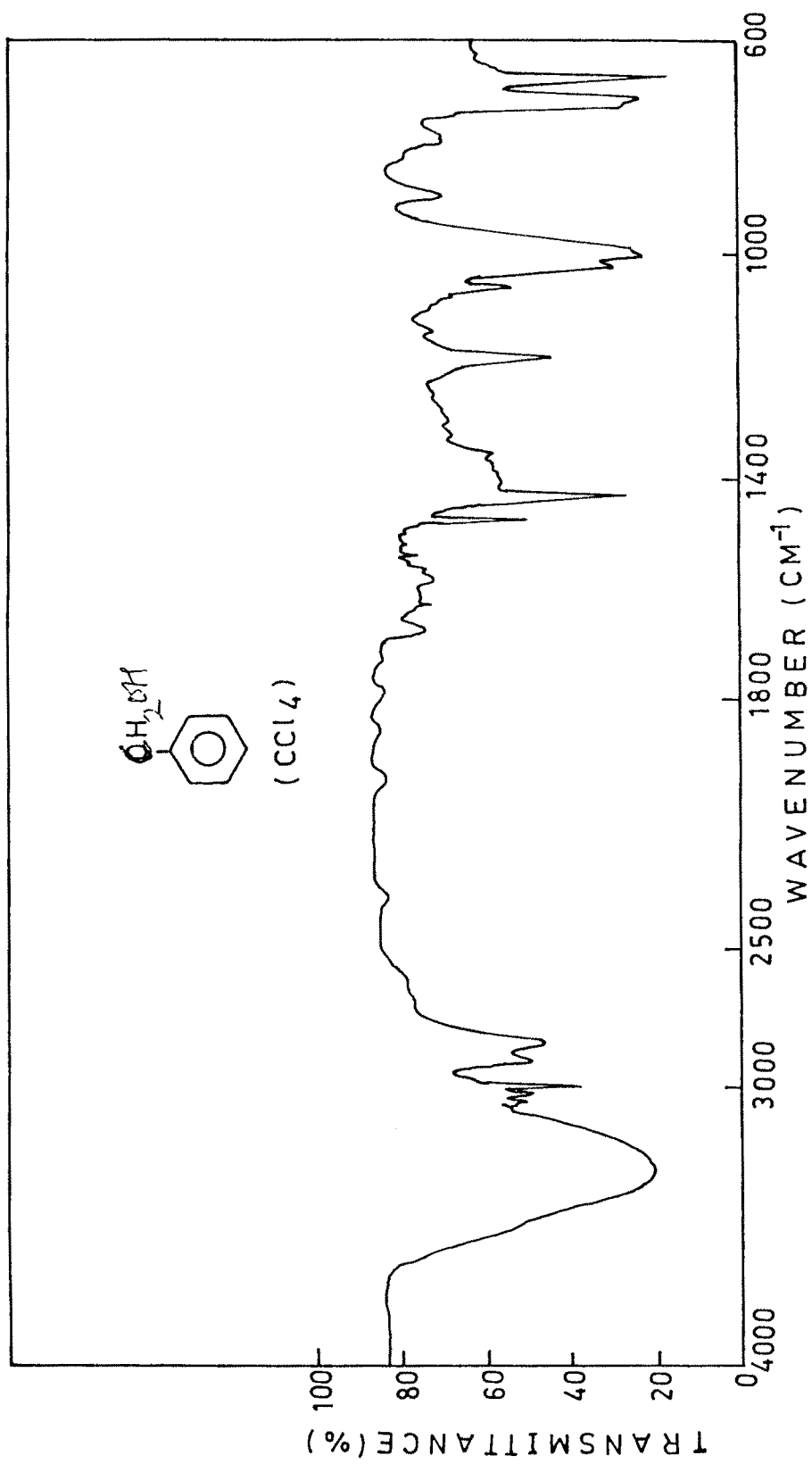


Fig. 2

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