Asian Journal of Chemistry Vol. 9, No. 3 (1997), 379–387

Reactions of Phthalic Anhydride with Alcohols

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Phthalic anhydride has been converted to its monoesters by reaction with simple alcohols under a variety of conditions. The monoesters are each transformed into the corresponding diesters by reaction with alcohols under acid-catalysed dehydrating conditions. Phthalic anhydride on hydrolysis yields phthalic acid which with alcohols either directly or through the intermediacy of O-phthaloyl chloride has been transformed into the diesters.

INTRODUCTION

Phthalic anhydride is a valuable petrochemical yielding a variety of commercially important products/intermediates[1]. Its most important reaction is with nucleophiles. Phthalic anhydride reacts with a variety of nucleophiles, such as oxygen nucleophiles, nitrogen nucleophiles, carbon nucleophiles etc. The nature of the product obtained in these reactions depends on the nature of the nucleophile, reaction conditions etc.[2–4] Although the reactions of phthalic anhydride with alcohols have been widely studied, no simple study seems to have been done. We now wish to report the reactions of phthalic anhydride with simple alcohols under different conditions.

RESULTS AND DISCUSSION

(i) *Formation of monoesters*: Treatment of phthalic anhydride with n-butanol in refluxing benzene for 4 h followed by processing gave mono-n-butyl phthalate in 80% yield. The product thus obtained was found to be homogeneous in that it was free from traces of phthalic anhydride and di-n-butyl phthalate.

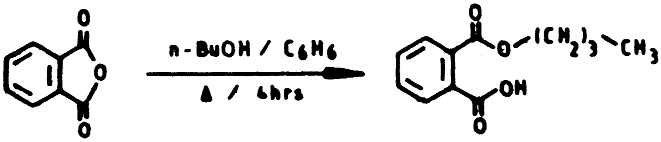

Fig. 1

The structure of the product is supported by its melting point, TLC, IR and ^{1}H NMR spectra. The IR spectrum recorded in KBr phase showed absorptions at 3500 cm^{-1} (weak, broad, free —OH), 3000 cm^{-1} (medium, very broad, bonded —OH), 1740 and 1720 cm^{-1} (unsplit doublet, very strong, 2 × —CO—) etc. The

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^1H NMR spectrum recorded in DMSO-d^6/TMS showed signals at δ 0.95 (t, 3H, —CH_3), 1.6 (m, 4H, —CH_2—CH_2—CH_3), 4.3 (t, 2H, —O—CH_2—), 7.9 (m, 4H, aryl protons).

The formation of monoester can be explained by the following two mechanisms—one, where a hemi-acetal-like intermediate is formed and two, where the reaction goes by addition-displacement pathway.

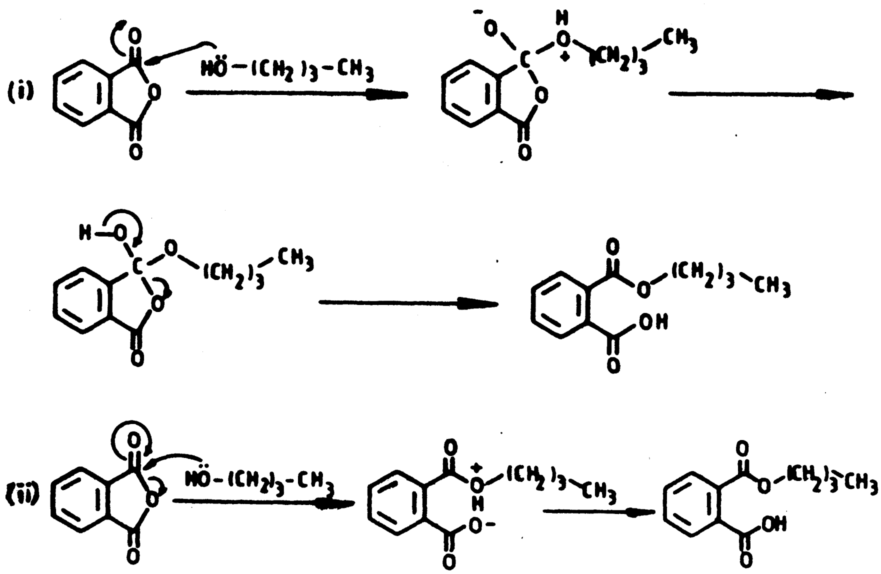


Fig. 2

However, in the present case, the second mechanism seems to be operating since the first one is known[5] to occur only in carbohydrate chemistry involving aldehyde/ketonic carbonyl and hydroxyl groups. Furthermore, acetalisation is an acid-catalysed reaction[5].

Similar treatment of phthalic anydride with n-butanol in refluxing toluene or xylene and subsequent processing, however, gave the monoester in 64 and 52% yields respectively. Direct condensation of phthalic anhydride with n-butanol at 100°C for 4 h yielded mono-n-butyl phthalate as a clean product although in lower yield (56%). Treatment of phthalic anhydride with n-butanol in pyridine as solvent at 100°C for 4 h resulted in the monoester in 59% yield. It is obvious from this reaction that pyridine is only acting as a solvent and not as a base catalyst. Attempts were made to condense phthalic anhydride with n-butanol in dimethyl sulphoxide and dimethyl formamide respectively as solvents at room temperature. However, these experiments were unsuccessful and gave phthalic acid as the only product. Results of this study are summarised in Table-1.

The reaction of phthalic anhydride with n-butanol in refluxing benzene has been extended to other alcohols like methanol, ethanol, i-propanol, n-octyl alcohol etc. and the results are shown in Table-2.

TABLE-1
CONDENSATION OF PHTHALIC ANHYDRIDE WITH n-BUTANOL IN DIFFERENT SOLVENTS YIELDING MONO-N-BUTYL PHTHALATE AS PRODUCT

S.No.	Solvent	Conditions	Yield of the monoester (%)
1.	Benzene	Reflux/4 h	80
2.	Toluene	Reflux/4 h	64
3.	Xylene	Reflux/4 h	52
4.	n-Butanol itself	100°C/4 h	56
5.	Pyridine	100°C/4 h	59
6.	DMSO	Room temp./4 h	Nil
7.	DMF	Room temp./4 h	Nil

TABLE-2
CONDENSATION OF PHTHALIC ANHYDRIDE WITH DIFFERENT ALCOHOLS IN REFLUXING BENZENE

S.No.	Alcohol used	Product obtained	Molar yield (%)	m.p. (°C)	m.p. (°C) (Lit.)
1.	Methanol	Monomethyl phthalate	42	82–85	82–84[6] 83–84[7, 8] 82.4–82.7[9]
2.	Ethanol	Monoethyl phthalate	66	68–70	47–48[10]*
3.	i-Propanol	Mono-i-propyl phthalate	59	79–81	78–80[11]
4.	n-Butanol	Mono-n-butyl phthalate	80	72–73	73.1–73.5[9]
5.	n-Octanol	Mono-n-octyl phthalate	76	—	21.6–22.5[9]
				(Liquid at room temperature)	

*Goggans and Capenhaver (Ref. 9) reported that this is the melting point (47–48°C) for product obtained by Amann (Ref. 10) which was *not* in a state of purity.

The reaction of phthalic anhydride with n-butanol has been studied under base-catalysed conditions also. Thus, treatment of phthalic anhydride with sodium n-butoxide in 1 : 1 molar ratio in n-butanol at room temperature for a few minutes and subsequent processing gave mono-n-butyl phthalate as a clean crystalline product (57 % yield). The sodium n-butoxide required for this purpose was prepared and used *in situ by* dissolving sodium metal in n-butanol at room temperature.

The reaction of phthalic anhydride with sodium n-butoxide/n-butanol at room temperature has been extended to other alkoxide/alcohol mixtures and the results are shown in Table-3. In all the cases, the alkoxides were generated *in situ* by reaction of sodium metal with the alcohol at room temperature and used as such.

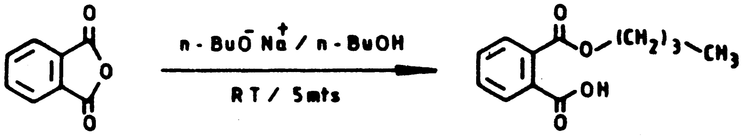


Fig. 3

TABLE-3
CONDENSATION OF PHTHALIC ANHYDRIDE WITH ALKOXIDE/ALCOHOLS AT ROOM TEMPERATURE FOR 5–10 MIN

S.No.	Alkoxide/Alcohol used	Product obtained	Molar yield (%)	m.p. (°C)
1.	Sod. methoxide/Methanol	Monomethyl phthalate	72	81–84
2.	Sod. ethoxide/Ethanol	Monoethyl phthalate	76	68–71
3.	Sod. i-propoxide/i-Propanol	Mono-i-propyl phthalate	68	78–80
4.	Sod. n-butoxide/n-Butanol	Mono-n-butyl phthalate	57	72–73
5.	Sod. n-octanolate/n-Octanol	Mono-n-octyl phthalate	66	(Liquid at room temp)

Similar condensation of phthalic anhydride with n-butanol containing KOH at room temperature for 5 min resulted in monoester as clean, crystalline product in 35% yield.

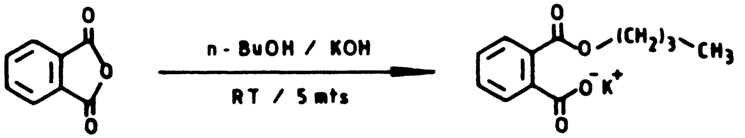


Fig. 4

The reaction probably goes by the following mechanism:

$$n\text{-}Bu\text{-}OH + KOH \rightleftharpoons n\text{-}BuO^-K^+ + HOH$$

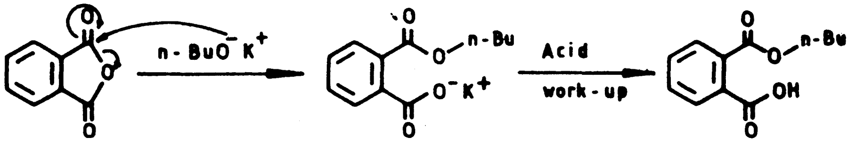


Fig. 5

(ii) *Formation of diesters*: Treatment of phthalic anhydride with n-butanol in refluxing benzene in the presence of a trace of *p*-toluene-sulphonic acid using a Dean-Stark apparatus for 6 h followed by processing gave di-n-butyl phthalate in 76% yield.

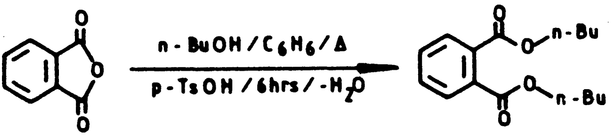


Fig. 6

The product obtained above was found to be homogeneous in that it was free from traces of the monoester, phthalic anhydride etc. The structure of the product is supported by its spectral data. Its IR spectrum recorded as a neat liquid showed absorptions at 2950 cm^{-1} (sharp, strong, —CH— stretching), 1735 cm^{-1} (very strong, unsplit doublet, 2 × —CO— stretching vibrations), 1600, 1580 cm^{-1} etc.

The ^1H NMR spectrum of di-n-butyl phthalate recorded in $CDCl_3/TMS$ showed signals at δ 0.9 (t, 6H, $2 \times CH_3$), 1.5 (m, 8H, $2 \times —CH_2—CH_2—$), 4.3 (t, 4H, $2 \times —O—CH_2—$) and 7.5 (AA′BB′, 4H, phenyl protons).

The above reaction of phthalic anhydride with n-butanol in refluxing benzene in the presence of *p*-toluenesulphonic acid using Dean-Stark apparatus to prepare diesters has been extended to methanol, ethanol, i-propanol and n-octanol. The results are shown in Table-4.

TABLE-4

FORMATION OF DIESTERS FROM PHTHALIC ANHYDRIDE AND ALCOHOLS IN BENZENE/*p*-TOLUENESULPHONIC ACID/Δ/DEAN-STARK ($—H_2O$)

S.No.	Alcohol used	Diester formed	Molar yield (%)	b.p. (760 mm) found (°C)	b.p. (760 mm) (°C) (Lit. value)	
1.	Methanol	Dimethyl phthalate	68	280–2	282	12 (a)
2.	Ethanol	Diethyl phthalate	90	296–8	298–9	12 (b)
3.	i-Propanol	Di-i-propyl phthalate	70	312–15	130 (12 mm)	12 (c)
4.	n-Butanol	Di-n-butyl phthalate	76	> 300	340	12 (d)
5.	n-Octanol	Di-n-octyl	59	> 300	384	12 (e)

The formation of diesters in the above reaction occurs by the following pathway

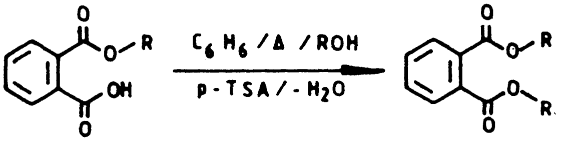


Fig. 7

That the monoesters are intermediates in the above reaction has been proved by taking the monoesters, prepared earlier by the alkoxide reactions and treating them with respective alcohols in refluxing benzene in the presence of *p*-toluenesulphonic acid with Dean-Stark removal of water.

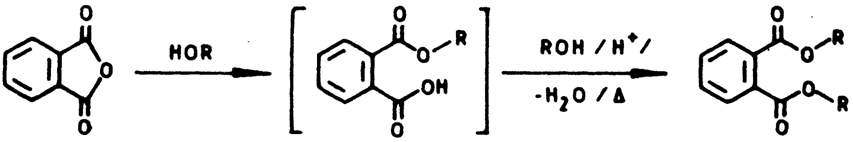


Fig. 8

Treatment of phthalic anhydride with aq. NaOH at room temperature for 15 min followed by processing led to phthalic acid which was characterised by its m.p., TLC and IR spectrum. Heating a mixture of phthalic acid and thionyl chloride on a steam-bath (100°C) under reflux for a few hours yielded phthaloyl chloride which after removal of thionyl chloride and without isolation, was treated *in situ* with a mixture of pyridine + n-butanol. The reaction mixture on processing gave di-n-butyl phthalate in 76% yield.

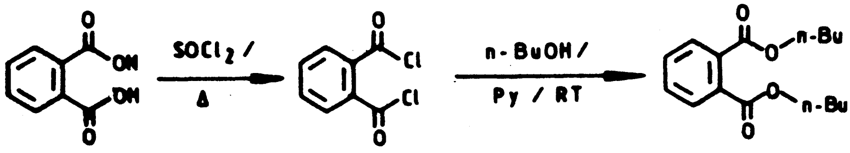


Fig. 9

The above reaction of phthalic acid with thionyl chloride and subsequent treatment with n-butanol in pyridine has been extended to other alcohols, such as methanol, ethanol, i-propanol, n-octanol etc. The results of this study are shown in Table-5.

TABLE-5
PREPARATION OF DIESTERS FROM PHTHALIC ACID AND ALCOHOLS THROUGH PHTHALOYL CHLORIDE

S.No.	Alcohol used	Product obtained	Molar yield (%)	b.p. (°C) (760 mm)
1.	Methanol	Dimethyl phthalate	68	280–2
2.	Ethanol	Diethyl phthalate	64	298–9
3.	i-Propanol	Di-i-propyl phthalate	79	312–15
4.	n-Butanol	Di-n-butyl phthalate	76	> 300
5.	n-Octanol	Di-n-octyl phthalate	86	> 300

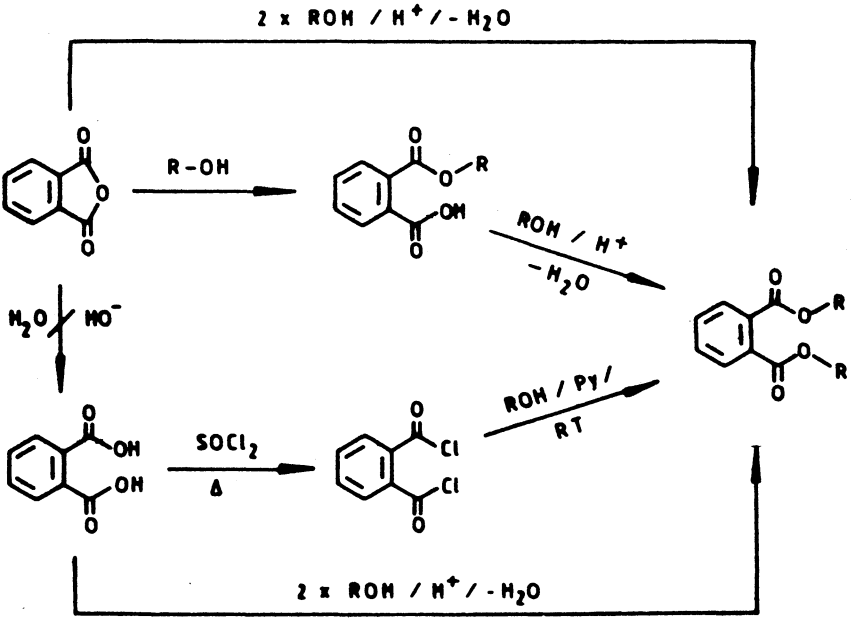
All the above reactions reported in this paper are summarised in Scheme-1 which is shown in Fig. 10

EXPERIMENTAL

The chemicals used in this work were mostly of LR/AR grade obtained from commercial suppliers. Solvents were purified by simple distillation before use. IR spectra were recorded on Perkin-Elmer 446 instrument using polystyrene as external reference standard. ^{1}H NMR spectra were recorded on a Varian Associates 100 MHz instrument with TMS as internal reference standard. TLC was done on small glass plates using silica-gel-G as adsorbent and iodine was used for spotting purposes. Melting points were recorded in open-capillary tubes in sulphuric acid baths and are uncorrected. Yields are reported to the extent products have been isolated from reaction mixtures.

(i) Preparation of monoesters

(a) *Reaction of phthalic anhydride with n-butanol in benzene under reflux for 4 h*: Phthalic anhydride (1.48 g, 10 mM) was taken in a round bottom flask, treated with benzene and warmed on a steam-bath for 5 min. On cooling to room temperature a clear solution was obtained. To this was added n-butanol (2 mL, 22 mM) and the mixture refluxed on a steam-bath for 4 h. At the end of this period, the reaction mixture was cooled to room temperature and extracted with aq. $NaHCO_3$ (5%, 2 × 15 mL) in a separatory funnel. The aq. $NaHCO_3$ layer was neutralised with conc. HCl (to pH 2.0) and extracted with benzene (2 × 20 mL). The benzene layer



SCHEME-1

Fig. 10

was separated and evaporated to dryness in a china dish giving mon-n-butyl phthalate as residue. Yield = 1.65 g (80% molar), m.p. 72–3°C (Table-1).

The above reaction of phthalic anhydride was carried out with methanol, ethanol, i-propanol and n-octyl alcohol in benzene under reflux for 4 h and processed similarly to obtain respective monoesters. (Table-2).

(b) *Reaction of phthalic anhydride with n-butanol in toluene/xylene under reflux for 4 h*: This reaction was carried out exactly as in the case of benzene except that toluene/xylene was used as solvent and processed similarly to obtain mono-n-butyl phthalate (Table-1).

(c) *Direct reaction of phthalic anhydride with n-butanol at 100°C for 4 h*: Phthalic anhydride (1.48 g, 10 mM) was dissolved in n-butanol (7 mL) in a round bottom flask by warming and then heated under reflux on a steam-bath at 100°C for 4 h. At the end of this period, the reaction mixture was evaporated to dryness on a steam-bath and the residue treated with benzene (25 mL). The benzene layer was extracted with aq. $NaHCO_3$ (5%, 2 × 15 mL). The aq. $NaHCO_3$ layer was neutralised with a dropwise addition of conc. HCl in the cold when a white crystalline solid separated out. This was filtered, washed with water and dried to obtain mono-n-butyl phthalate. Yield = 1.25 g (56% molar). m.p. 71–2°C (*cf.* Table-1).

(d) *Reaction of phthalic anhydride with n-butanol in the presence of pyridine at 100°C for 4 h*: A solution of phthalic anhydride (1.48 g, 10 mM), pyridine (7 mL) and n-butanol (3 mL, 32 mM) was heated on a steam-bath (100°C) for 4 h. At the end of this period, the raction mixture was evaporated to dryness on a steam-bath (100°C) yielding a residue. The latter on trituration with cold water (3 × 15 mL) gave mono-n-butyl phthalate as a clean, crystalline solid. Yield = 1.235 g (59% molar). m.p. 72–3°C (*cf.* Table-1).

(e) *Reaction of phthalic anhydride with n-butanol in DMSO-DMF at room temperature for 4 h*: A mixture of phthalic anhydride (1.48 g, 10 mM), n-butanol (3 mL, 32 mM) and DMSO or DMF (20 mL) was stirred at room temperature for 6 h. At the end of this period, the reaction mixture was poured onto crushed ice. The resulting mixture was extracted with ether (3 × 100 mL), the ether extract dried over anh. Na_2SO_4 and evaporated to yield a white crystalline solid (1.1 g) which was found to be phthalic acid by comparison with an authentic sample (mp, mmp, TLC etc.).

(f) *Reaction of phthalic anhydride with sodium n-butoxide at room temperature for 5 min*: Phthalic anhydride (1.48 g, 10 mM) was dissolved in n-butanol (3.5 mL, 38 mM) with warming at room temperature. To this was added a solution of sod. n-butoxide (0.2 g, of sodium metal in 5 mL of n-butanol) and the mixture stirred at room temperature for 5 min. It was then evaporated to dryness on a steam-bath yielding a thick white residue. The latter was treated with water (10 mL) and brought to acidic pH with a dropwise addition of conc. HCl. The separated product was filtered, washed with water and dried to obtain mono-n-butyl phthalate. Yield = 1.27 g (57% molar), m.p. 72–3°C.

The above reaction of phthalic anhydride was carried out with sodium methoxide, sodium ethoxide, sodium i-propoxide and sodium n-octanolate in the respective alcoholic media at room temperature for 5 min and processed similarly to obtain the respective monoesters. (Table-3).

(g) *Reaction of phthalic anhydride with n-butanol-KOH*: To a solution of phthalic anhydride (1.48 g, 10 mM) in n-butanol (5 mL) was added a solution of KOH (0.56 g) in n-butanol (3 mL) at room temperature. The resulting mixture, which showed exothermicity on mixing, was stirred for 5 min and evaporated to dryness on a steam-bath (100°C) yielding a residue. The latter was treated with cold water (10 mL) and brought to acidic pH with a dropwise addition of conc. HCl. The separated product was filtered, washed with water and dried to obtain mono-n-butyl phthalate. Yield = 1.23 g (55% molar), m.p. 70–71°C.

(ii) Preparation of diesters

(a) *Condensation of phthalic anhydride with n-butanol in benzene/p-toluenesulphonic acid using Dean-Stark apparatus*: A mixture of phthalic anhydride (1.48 g, 10 mM), n-butanol (3 mL, 32 mM), benzene (50 mL) and *p*-tolunesulphonic acid (50 mg) was heated under reflux with Dean-Stark removal of water for 6 h. At the end of this period, the reaction mixture was cooled to room temperature, diluted with fresh benzene (25 mL) and washed with water (2 × 25 mL) in a separatory funnel. The aqueous washings were discarded while the benzene layer was dried (anhydrous Na_2SO_4) and evaporated to obtain an oily residue which was di-n-butyl phthalate. Yield = 2.14 (76% molar), b.p. > 300°C.

The above reaction of phthalic anhydride was carried out with methanol, ethanol, i-propanol and n-octanol and processed exactly as above to obtain the respective diesters (Table-4).

(b) *Reaction of phthalic acid with thionyl chloride and subsequent butylation in the presence of pyridine*: A mixture of phthalic acid (1.66 g, 10 mM) and thionyl chloride (5 mL) was heated under reflux on a steam-bath for 1 h. The condenser was than removed and the unreacted thionyl chloride eliminated from the flask by heating it on a steam-bath in fume-hood for 1 h. To the residue in the flask were then added pyridine (5 mL) and n-butanol (5 mL). The reaction mixture was heated under reflux on a steam-bath for 3 h. At the end of this period, the reaction mixture was evaporated on a steam-bath to yield a residue which was taken up in benzene (50 mL). The benzene layer was washed with water (2 × 15 mL), dried and evaporated to obtain a residue which was di-n-butyl phthalate. Yield = 2.12 g (76% molar), b.p. > 300°C.

The above reaction of phthalic acid was carried out with methanol, ethanol, i-propanol and n-octanol and processed exactly as above to yield the respective diesters (Table-5).

ACKNOWLEDGEMENTS

The authors are thankful to Dr. K. Syam Sundar, Professor and Head, Department of Chemistry, J.N.T. Univ., College of Engineering, Hyderabad for providing laboratory facilities and for constant encouragement. They are very grateful to the U.G.C., New Delhi for financial support of the work done.

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(*Received*: 13 September 1996; *Accepted*: 21 January 1997) AJC-1215