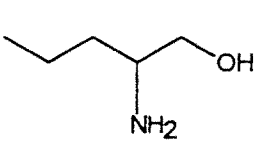
CHAPTER - 1

INTRODUCTION

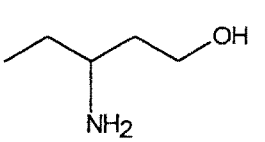
INTRODUCTION

Amino alcohols are versatile molecules, due to the presence of functionalities such as amino and hydroxyl in a single molecule. This combination makes them useful for countless industrial applications such as textiles, household products and pharmaceutical industries[1].

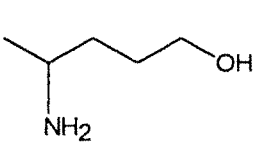
Depending upon the position of the hydroxyl and amino group, the amino alcohols may be classified accordingly as 1,2, 1,3 or 1,4 amino alcohols.



1,2 - amino alcohol



1,3 - amino alcohol

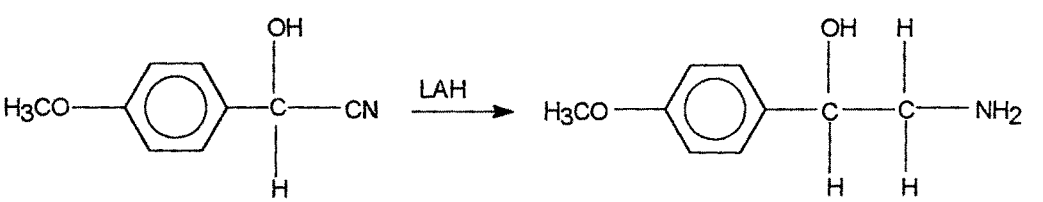


1,4 - amino alcohol

1.1 METHODS OF PREPARATION OF AMINO ALCOHOLS

Various methods are available for the synthesis of amino alcohols. Some of the important methods cited in the literature are discussed below :

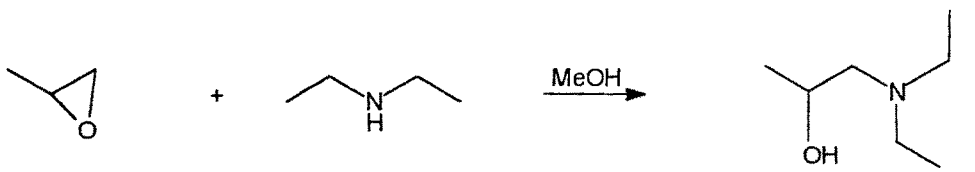
2-amino-1-alcohols are generally synthesised from cyanohydrin on reduction with lithiumaluminiumhydride. For example, it has been reported that β-p-methoxyphenyl-β-hydroxyethylamine **(2)** was obtained from p-methoxybenzaldehyde cyanohydrin **(1)** when it was reduced with lithiumaluminiumhydride[2] **(Scheme I.1)**.



1 **2**

Scheme I.1

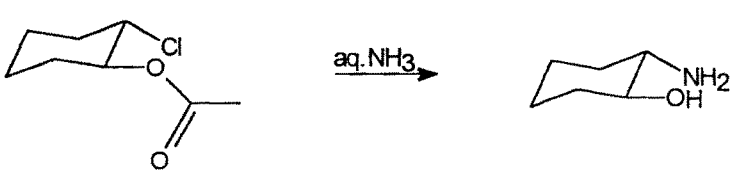
Propylene oxide **(3)** on heating with diethyl amine **(4)** in the presence of a catalytic amount of methanol resulted in the formation of 1,1-diethylamine-2-propanol[3] **(5) (Scheme I.2)**.



3 **4** **5**

Scheme I.2

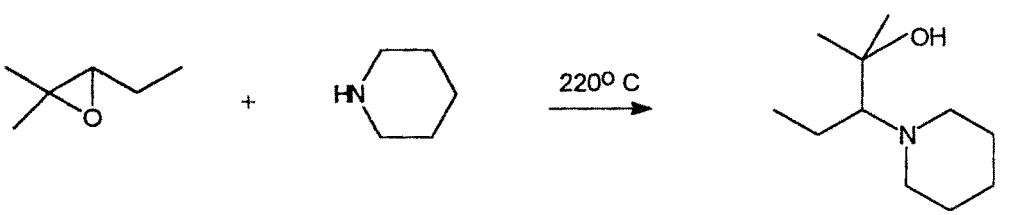
trans 2-Acetoxycyclohexylchloride **(6)** on treatment with aqueous concentrated ammonia has been reported to give *trans* 2-amino cyclohexanol[4] **(7) (Scheme I.3)**.



6 **7**

Scheme I.3

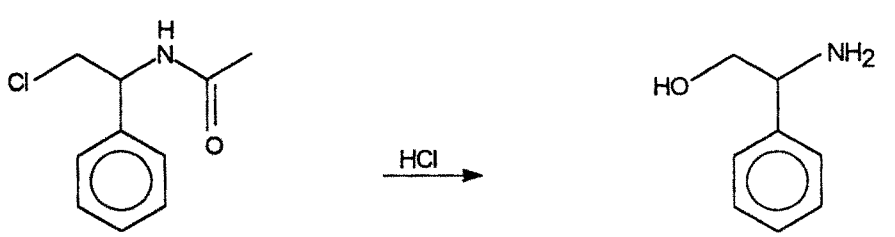
Colclough *etal*[5] in 1961 reported the formation of 2-methyl-3-piperidino-pentan-2-ol hydrochloride **(10)** by heating 2-methyl-2,3-epoxypentane **(8)** with piperidine **(9)** **(Scheme I.4)**.



8 **9** **10**

Scheme I.4

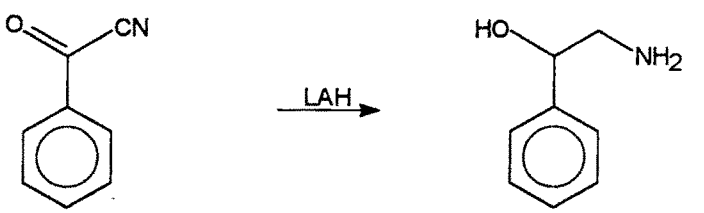
N-(2-Chloro-1-phenylethyl)acetamide **(11)** on heating with concentrated hydrochloric acid furnished β-hydroxy-α-phenylethylaminehydrochloride[6] **(12)** **(Scheme I.5)**.



11 **12**

Scheme I.5

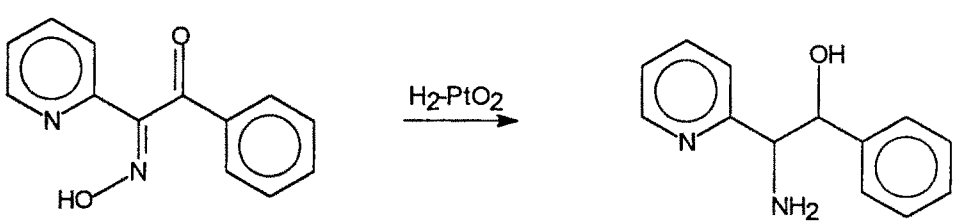
Benzoyl cyanide **(13)** on reduction with lithiumaluminiumhydride in ether resulted in the formation of ethanol amine[7] **(14) (Scheme I.6)**.



13 **14**

Scheme I.6

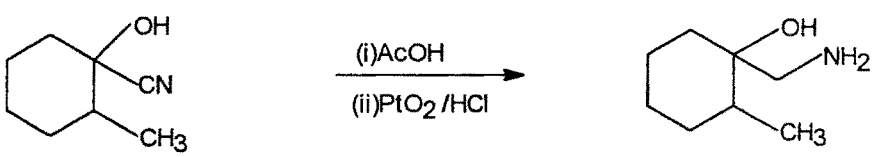
Isonitroso-α-phenacyl pyridine **(15)** in alcohol on reduction over platinum oxide at room temperature and atmospheric pressure produced 2-amino-1-phenyl-2-(α-pyridyl)ethanol[8] **(16) (Scheme I.7)**.



15 **16**

Scheme I.7

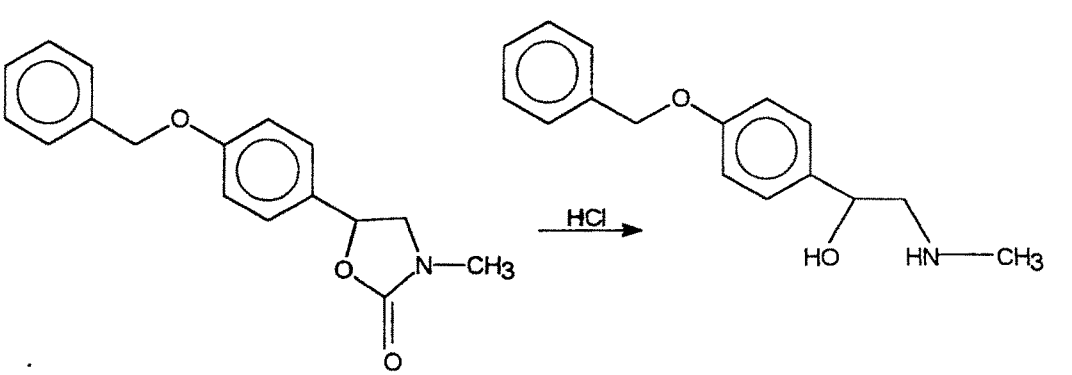
1-aminomethyl-2-methyl-1-cyclohexanol **(18)** was prepared by the hydrogenation of 1-cyano-2-methyl-1-cyclohexanol **(17)** with acetic acid in the presence of platinum oxide and hydrochloric acid[9] **(Scheme I.8)**.



17 **18**

Scheme I.8

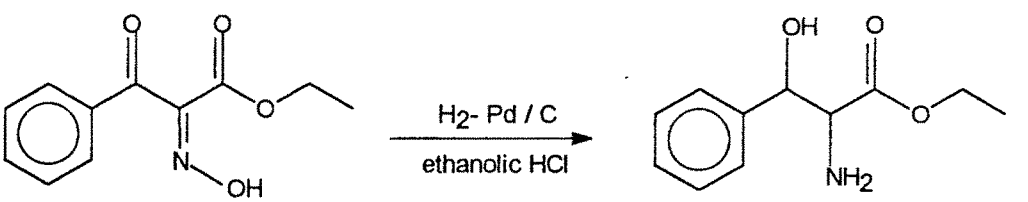
The hydrolysis of 5-(4'-Benzyloxyphenyl)-3-methyl 2-oxazolidinone **(19)** with hydrochloric acid has been reported[10] to yield the corresponding amino alcohol **(20) (Scheme I.9)**.



19 **20**

Scheme I.9

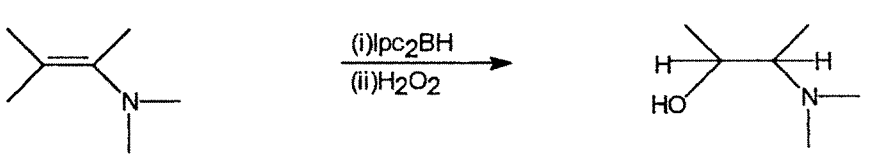
The hydrogenation of ethylbenzoyl oximino acetate **(21)** in ethanolic hydrochloric acid over palladium on charcoal resulted in the formation of β-phenyl serine ethyl ester[11] **(22) (Scheme I.10)**.



21 **22**

Scheme I.10

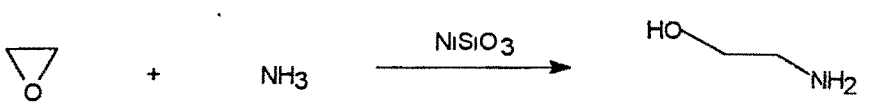
Chiral β-amino alcohols were prepared by the hydroboration of chiral or achiral enamines, with chiral organic borohydrides[12]. For example N,N-dimethyl-3-methyl-but-2-ene **(23)** on hydroboration with diisopinocamphenyl borane and further treatment with hydrogenperoxide resulted in the formation of N,N-dimethyl-3-methyl-3-hydroxy butane **(24) (Scheme I.11)**.



23 **24**

Scheme I.11

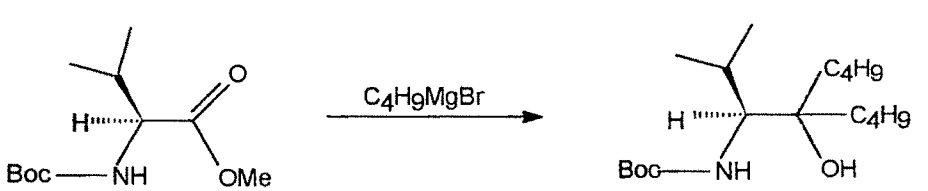
Satoyuki *etal* [13] reported the amination of alkylene oxides in presence of nickelsilicate resulting in the formation of 1,2-aminoalcohols. Ethanolamine **(27)** was thus prepared by the reaction of ethyleneoxide **(25)** with ammonia **(26) (Schemel.12)**.



25 **26** **27**

Scheme I.12

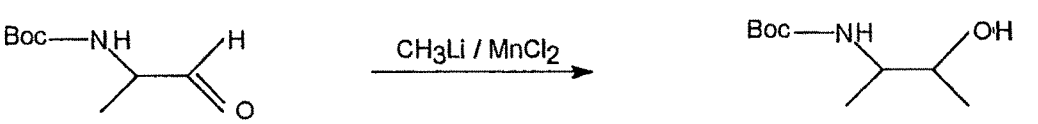
The methyl ester of t-butoxycarbonyl-L-Valine **(28)** on treatment with butyl magnesium bromide, led to the formation of corresponding valinol derivative[14] **(29) (Scheme I.13)**.



28 **29**

Scheme I.13

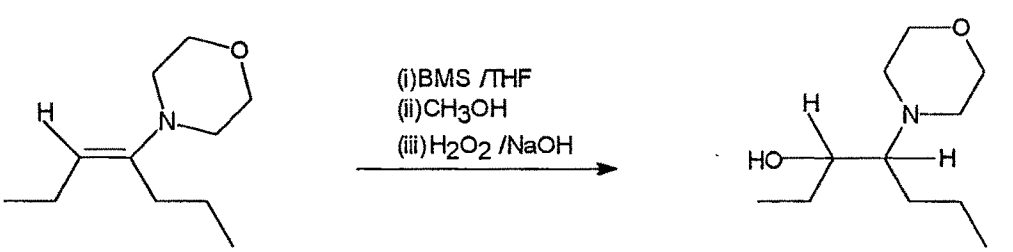
It was reported that N-protected-α-aminoaldehydes undergoes stereoselective addition with alkyl cuprates and the manganese reagents resulting in the formation of corresponding N-protected amino alcohols[15]. For example, N-(*t*-butoxycarbonyl)-3-amino-butan-2-ol **(31)** was obtained from N-(*t*-butoxycarbonyl)-2-aminopropionaldehyde **(30)** **(Scheme I.14)**.



30 **31**

Scheme I.14

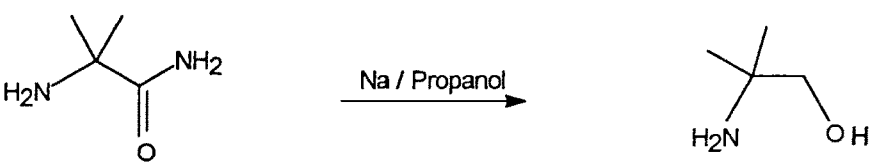
The hydroboration of the 4-morpholinohept-3-ene **(32)** with dimethyl sulfide-Borane (BMS), followed by methanolysis and oxidation with basic hydrogen-peroxide furnished 4-morpholino-3-hydroxyheptane[16] **(33)** **(Scheme I.15)**.



32 **33**

Scheme I.15

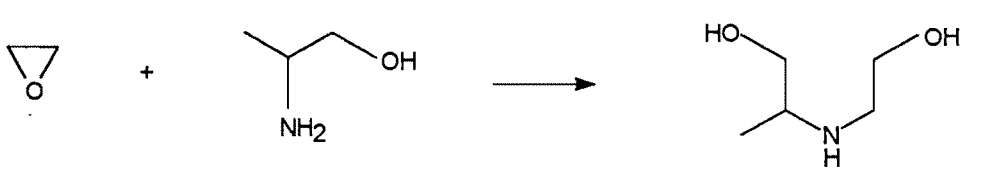
Enantiomerically pure 2,2-disubstituted 2-aminoethanols were synthesised by the reduction of α,α-disubstituted amides of amino acids using sodium metal in propanol[17], 2,2-dimethyl ethanolamine **(34)** was thus obtained on reduction of the amide of 2,2-dimethyl glycine **(35) (Scheme I.16)**.



34 **35**

Scheme I.16

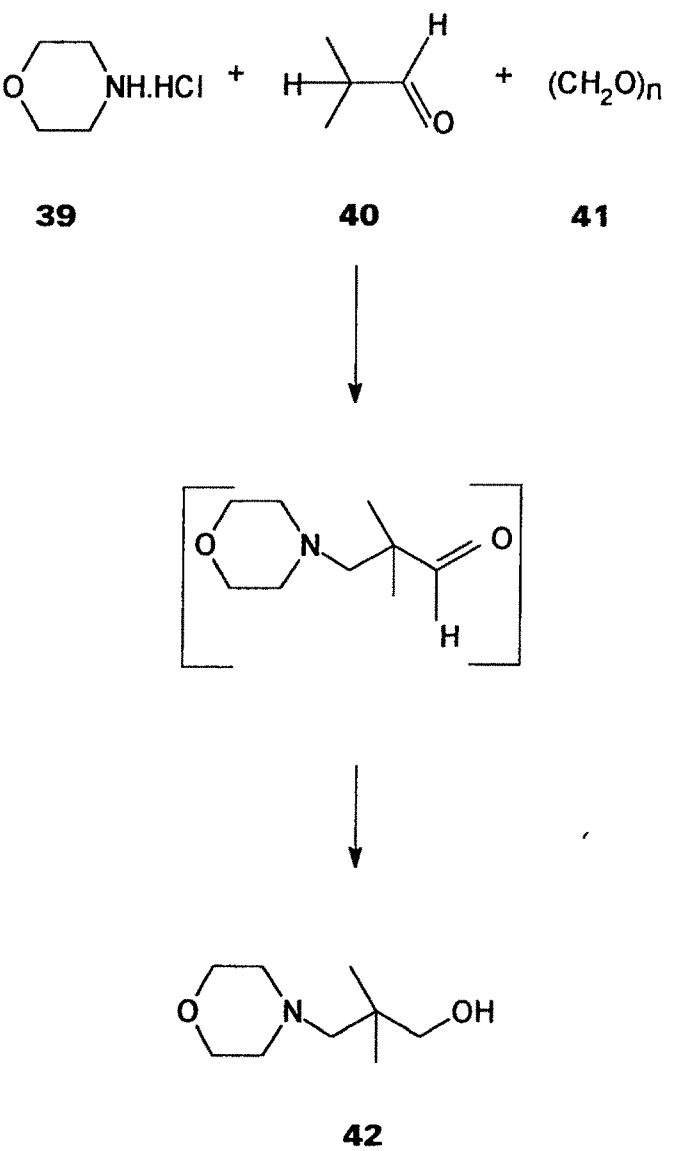
The reaction of ethylene oxide **(36)** and β-hydroxy isopropylamine **(37)** in alcohol results in the formation of α-methyl-β,β'-dihydroxy diethylamine[18] **(38) (Scheme I.17)**.



36 **37** **38**

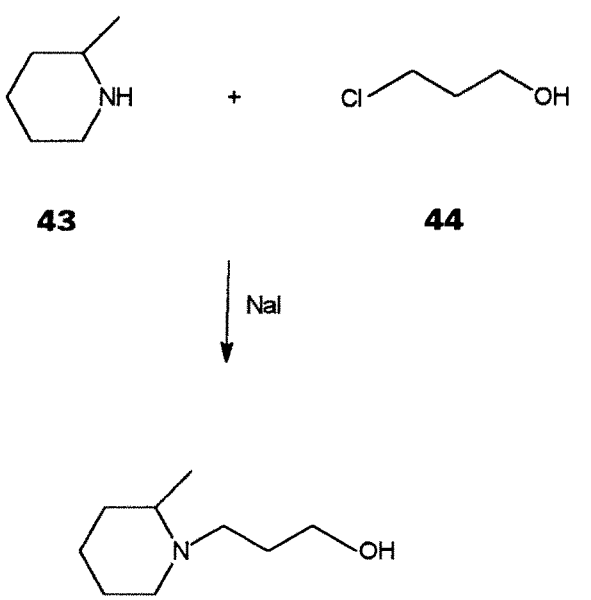
Scheme I.17

The reaction of morpholine hydrochloride **(39)**, isobutyraldehyde **(40)** and paraformaldehyde **(41)** in absolute ethanol produced 2,2-dimethyl-3(4-morpholinyl)-1-propanol[19] **(42) (Scheme I.18)**.



Scheme I.18

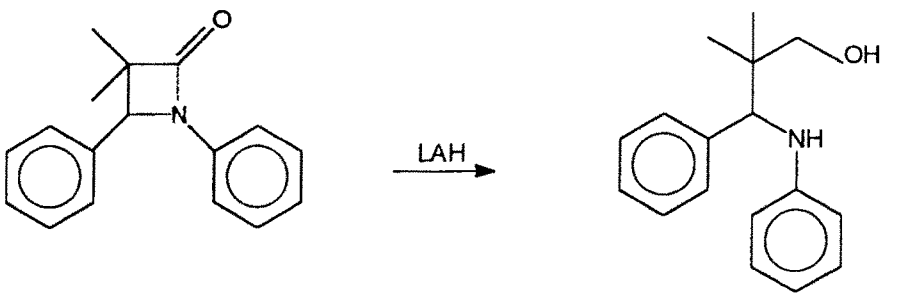
The reaction of 2-methyl piperidine **(43)** and trimethylene chlorohydrin **(44)** in absolute alcohol and sodium iodide resulted in the formation of 3-(2-methyl piperidyl)propanol[20] **(45) (Scheme I.19)**.



43 **44** **45**

Scheme I.19

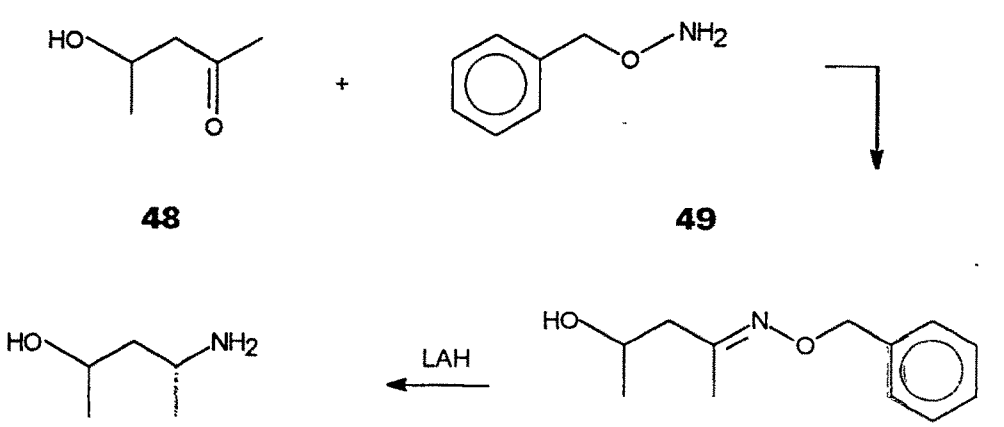
Vaughan *etal*[21] have reported the formation of 3-aminoalcohols. 3-Anilino-2,2-dimethyl-3-phenyl propanol **(47)** was produced by the reduction of 3,3-dimethyl-1,4-diphenyl-2-azetidinones **(46)** with lithiumaluminiumhydride **(Scheme I.20)**.



46 **47**

Scheme I.20

Acyclic 1,3-aminoalcohols were prepared from β-hydroxy ketones[22]. Pent-2-on-4-ol **(48)** on reaction with benzyloxyamine **(49)** resulted in the formation of **50** which on further reduction with lithiumaluminiumhydride furnished 2-amino-4-pentanol **(51) (Scheme I.21)**.

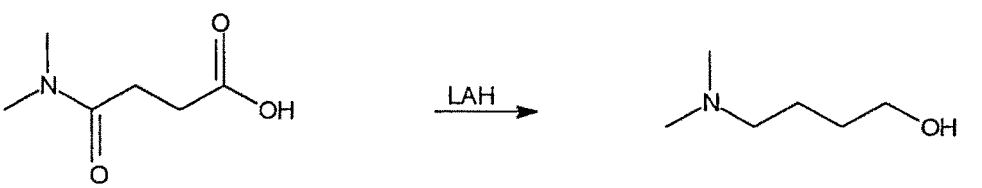


48 **49**

51 **50**

Scheme I.21

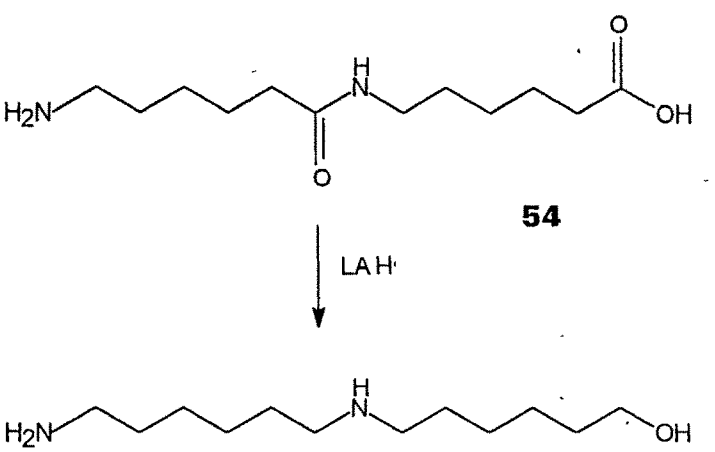
Avison *etal* [23] reported the reduction of N,N-dimethyl succinamic acid **(52)** with lithiumaluminiumhydride in dry ether to yield 4-N,N-dimethyl amino-1-butanol **(53) (Scheme I.22)**.



52 **53**

Scheme I.22

The reduction of ω (ω-aminocaproyl)aminocaproic acid **(54)** with lithiumaluminiumhydride has been reported to give ω (ω-aminohexyl)amino hexanol[24] **(55) (Scheme I.23)**.



54

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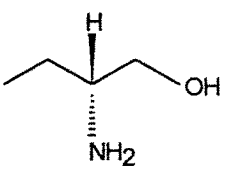
Scheme I.23

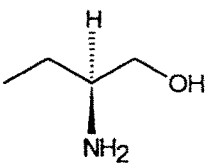
1.2 2-AMINO-1-BUTANOL

2-amino-1-butanol is well known in the pharmaceutical industry.



56

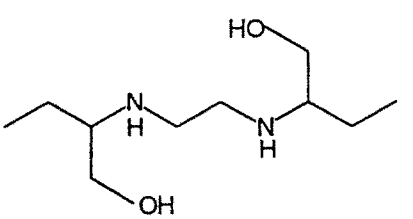
***(R)*-(-)-2-amino-1-butanol**



57

***(S)*-(+)-2-amino-1-butanol**

'**Ethambutol**' is an important antitubercular drug with an annual production in India alone exceeding 400 tonnes[25]. ***(S)*-(+)-2-amino-1-butanol (57)** is used as a synthetic precursor for ethambutol **(58)**.



58

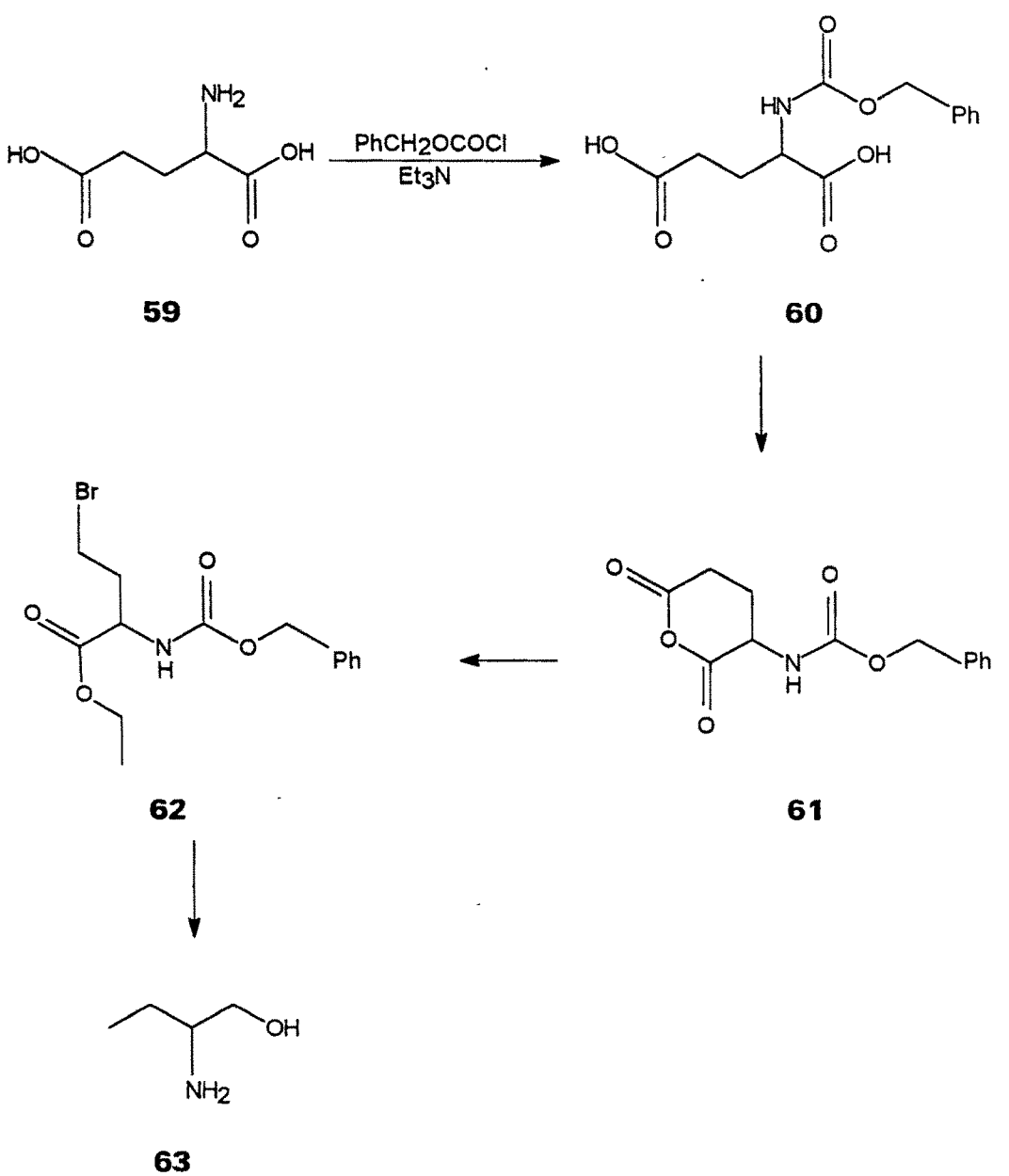
Ethambutol

Wilkinson *etal* [26] first reported the synthesis and chemotherapeutic evaluation of **'Ethambutol'**, the dextrorotatory form of 2,2'-(ethylene diimino)-di-1-butanol, which is four times as active as streptomycin against an established infection with the human strain of *mycobacterium tuberculosis*, in mice. It is also fully active against isoniazid and streptomycin resistant infection in mice. The sharp stereospecificity of the activity of this synthetic chemotherapeutic agent is in the following order :

dextro = 12 x meso => 200 x leavo

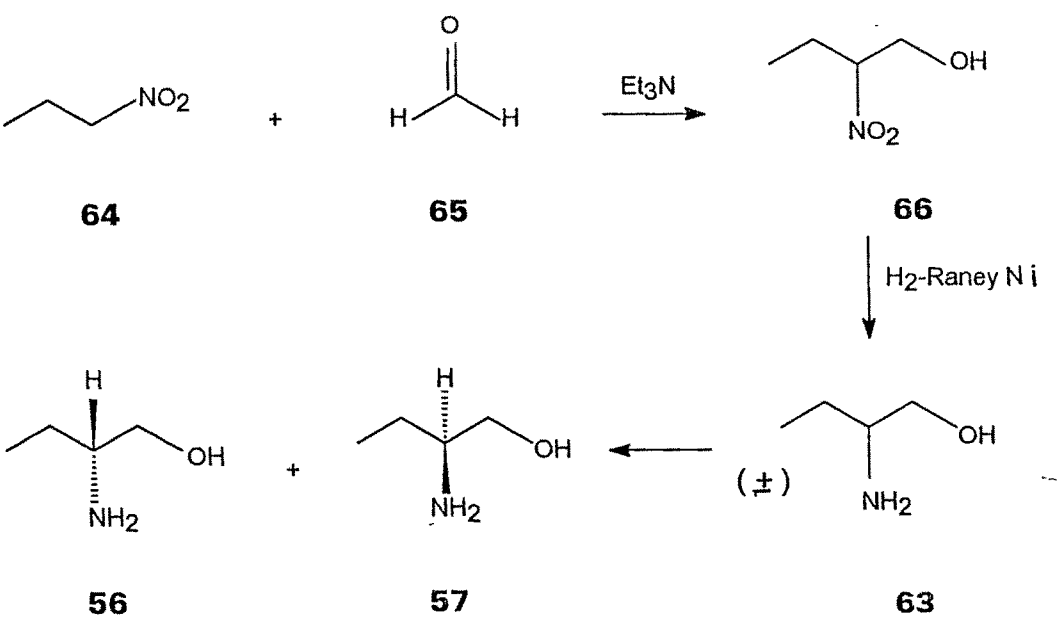
1.2.1 SYNTHESIS OF 2-AMINO-1-BUTANOL

Cook *etal* [27] have reported the preparation of ***(S)***-(+)-2-amino-1-butanol **(63)** from ***(S)***-(+)-glutamic acid **(59)** **(Scheme I.24)**.



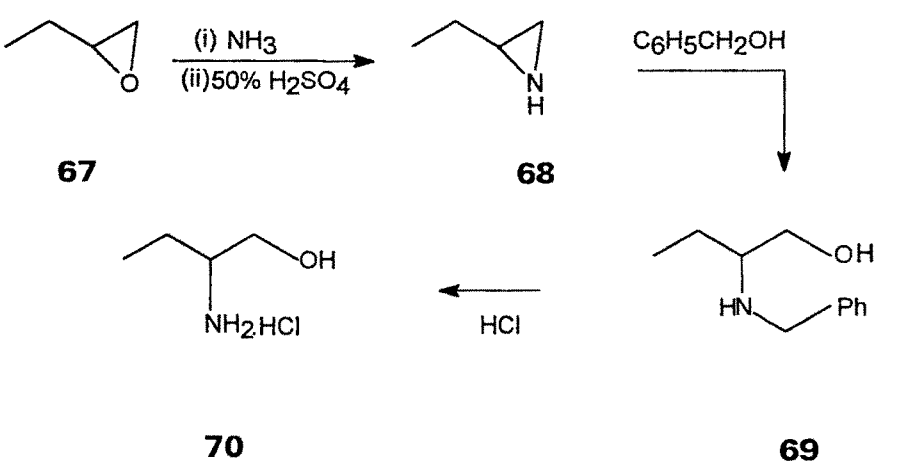
Scheme I.24

(S)-(+)-2-amino-1-butanol **(57)** was prepared in 31% overall yield by the reaction of 1-nitropropane **(64)** with formaldehyde **(65)** in presence of triethyl amine gave 2-nitro-1-propanol **(66)** which on reduction with Raney nickel and hydrogen resulted in the formation (±)-2-amino-1-butanol **(63)**. Resolution of (±)-2-amino-1-butanol with tartaric acid in anhydrous methanol furnished the desired isomer[28] **(Scheme I.25)**.



Scheme I.25

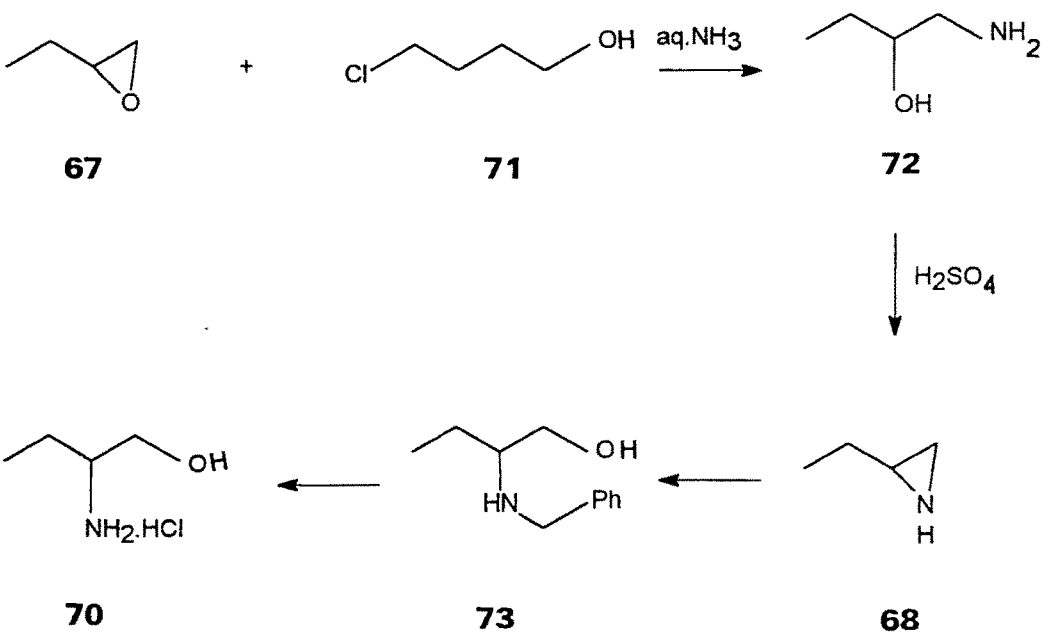
1,2-epoxybutane **(67)** is converted into 2-amino-1-butanol **(63)** by various methods. 1,2- epoxybutane **(67)** was reacted with ammonia and cyclized with 50% sulfuric acid to give 2-ethyl aziridine **(68)**. Treatment of 2-ethyl aziridine with benzylalcohol gave (±) N- benzyl 2-amino-1-butanol **(69)**, which on hydrolysis resulted in the formation of (±) 2-amino-1-butanol hydrochloride[29] **(70) (Scheme I.26)**.



67 **68** **70** **69**

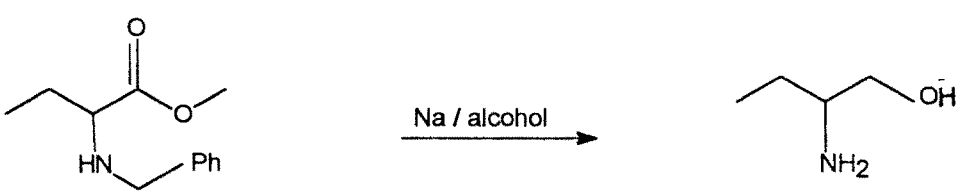
Scheme I.26

1,2-epoxybutane **(67)** and butylene chlorohydrin **(71)** were treated with aqueous ammonia to produce 2-hydroxybutyl amine **(72)**, which underwent dehydration, and cyclisation with sulfuric acid gave 2-ethyl aziridine **(68)**. Cleavage of 2-ethyl aziridine **(68)** with benzyl alochol furnished N-benzyl-2-amino-1-butanol **(73)**, which on hydrolysis yielded (±)-2-amino-1-butanol hydrochloride[30] **(70) (Scheme I.27)**.



Scheme I.27

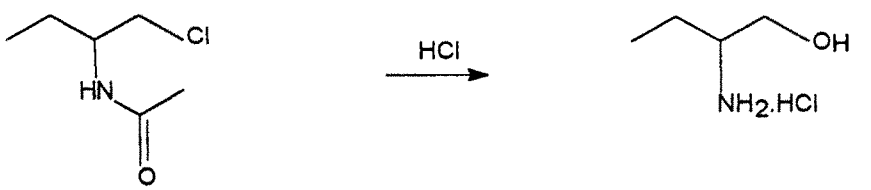
1,2-epoxybutane on treatment with benzyl chloride followed by tosyl chloride and ammonolysis gave (±)-2-amino-1-butanol[31]. Racemic mixture of 2-amino-1-butanol was prepared by reducing the alkyl esters of α-substituted n-butyric acid with sodium in alcohol[32]. For example, N-benzyl-2-aminomethyl butyrate **(74)** on reduction resulted in the formation of (±)-2-amino-1-butanol **(68)** **(Scheme I.28)**.



74 **63**

Scheme I.28

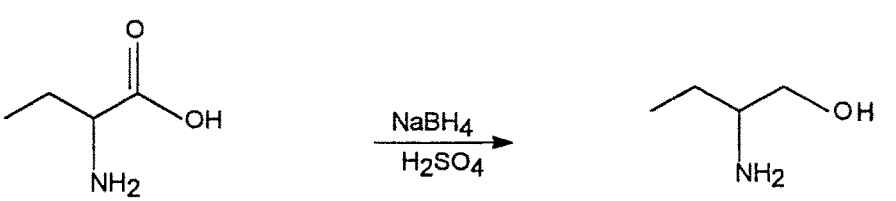
The reduction was also carried out by metal hydride in an organic solvent and subsequent catalytic hydrogenation[33]. (±)-2-amino-1-butanol hydrochloride **(72)** was prepared by the reaction of aqueous 2-(aminoacetyl)-1-chlorobutane **(75)** with methanol in presence of concentrated hydrochloric acid[34,35] **(Scheme I.29)**.



75 **70**

Scheme I.29

α-amino acids on reduction with sodium borohydride - sulfuric acid yielded the corresponding 2-amino alcohols. The operational simplicity, ease of scale up of the reaction without risking explosion and use of inexpensive reagents make this method unique[36]. For example, 2-amino butanoicacid **(76)** on reduction gave (±) 2-amino-1-butanol **(70) (Scheme I.30)**.



76 **70**

Scheme I.30

1.3 RESOLUTION OF AMINO ALCOHOLS

A racemic modification is converted by an optically active reagent into a mixture of diastereomers which can then be separated, and the enantiomers are regenerated by proper chemical treatment.

The amino alcohols were reacted with optically active acids, to form the diastereomers. The diastereomers were separated and treated with a base to regenerate the pure enantiomers of the amino alcohols.

1.3.1 RESOLUTION OF (±)-2-AMINO-1-BUTANOL

(±)-2-amino-1-butanol can be resolved by reacting it with (-) tartaric acid to obtain the corresponding esters, separating the tartarates by fractional crystallization and passing the isomers through a strongly acidic cationic exchange resin bed[37,38].

(±)-2-amino-1-butanol was resolved with (+) mandelic acid in ethanol, the diastereomers were separated and decomposed with sodium ethoxide to get the pure enantiomer[39]. O,O-dibenzoyl D-tartaric acid semi dimethyl amide in aqueous medium was used to resolve (±)-2-amino-1-butanol. The separated diastereomers were reacted with aqueous hydrochloric acid to get the pure enantiomers as hydrochlorides[40].

(±)-2-amino-1-butanol was resolved using di-O-benzoyl tartaric acid and d-4-nitro tartanillic acid as resolving agents[41]. (+) or (-) - N(α-methyl)-5-O,O-pyrrolidinyl aceticacid[42] and (+) or (-) - N-benzoyl-*trans*-2-amino cyclohexane carboxylic acid[43] were used as resolving agents for the resolution of (±)-2-amino-1-butanol.

(±)-2-amino-1-butanol was resolved into its enantiomers by reacting it with (+) tartaric acid in aqueous alcoholic hydrochloric acid, separating the precipitate, and decomposing the salt with alcoholic sodium hydroxide or lime water[44,45]. (±)-2-amino-1-butanol was also resolved with (-) tartaric acid.

Optically active 2-amino alcohols were also produced by selective enzymatic hydrolysis of the corresponding racemic N-alkoxy carbonyl ester derivatives followed by separation and hydrolysis of the ***(R)***-alcohol and ***(S)***-ester derivatives[47-49].

1.3.2 (R) (-) or *(S)*-(+)-2-AMINO-1-BUTANOL AS A RESOLVING AGENT

(±)-N-Carbamoylvaline was resolved using ***(R)***-(-)-or ***(S)***-(+)-2-amino-1-butanol. Both the enantiomers of N-carbamoylvaline were obtained in 95.7% optical purity[50]. ***(R)***-(-) or ***(S)***-(+)-2-amino-1-butanol was used for the resolution of (±)-1,1'-bi-2,2'-naphthyl hydrogen phosphate[51].

Racemic cyclopropane dicarboxylic acids were resolved by salt formation with optically active amines such as (-)-2-(1-naphthyl)ethyl amine or ***(R)***(-) 2-amino-1-butanol[52]. ***(RS)***-(±)-Mandelic acid was resolved with ***(R)***-(-)-2-amino-1-butanol in 95 % ethanol to give the pure enantiomers[53,54]. DL-α-methyl dopa was treated with ***(R)***-(-)-2-amino-1-butanol and the diastereomer obtained was treated with hydrobromic acid to get the corresponding enantiomers[55].

(RS)-(±)-6-methoxy-α-methyl-2-naphthalene aceticacid, ***(RS)***-(±)-N-acetyl-2-phenylglycine were resolved by treatment with ***(R)*** (-)-2-amino-1-butanol[56,57].

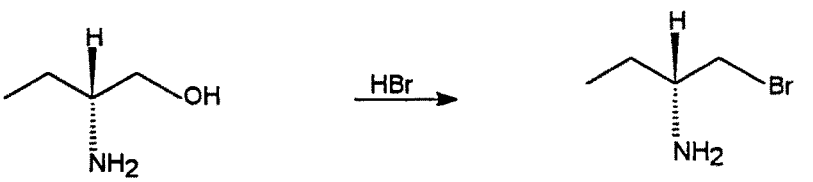
1.4 RACEMISATION OF (R)-(-)-2-AMINO-1-BUTANOL

The treatment of ***(R)***-(-)-2-amino-1-butanol over Raney Co under hydrogen gas at 140° C and 10-50 atmospheric pressure gave 100% racemic 2-amino-1-butanol[58].

(R)-(-)-2-Amino-1-butanol, ammonia and a cobalt catalyst were autoclaved under 50 atmos hydrogen gas for 5 hours at 200°C, gave the racemic 2-amino-1-butanol[59].

1.5 REACTIONS OF 2-AMINO-1-BUTANOL

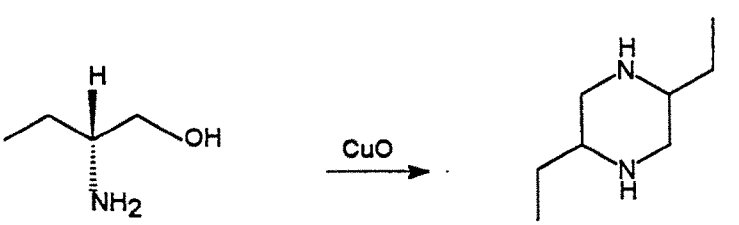
The reaction of ***(R)***-(-)-2-amino-1-butanol **(56)** with hydrobromic acid gave ***(R)*** (-) - 2-amino -1 - bromobutane[60] **(77) (Scheme I.31)**.



56 **77**

Scheme I.31

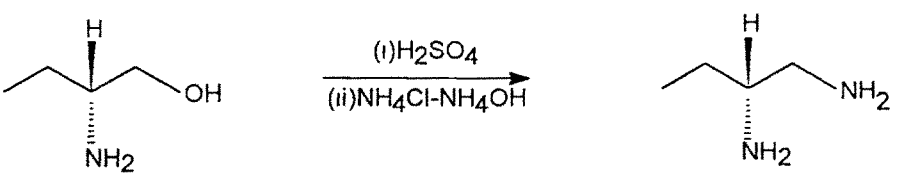
(R)-(-)-2-amino-1-butanol **(56)** on dehydration in presence of copper oxide in dioxane, under high pressure and temperature resulted in the formation of 2,5-diethyl piperazine[60] **(78) (Scheme I.32)**.



56 **78**

Scheme I.32

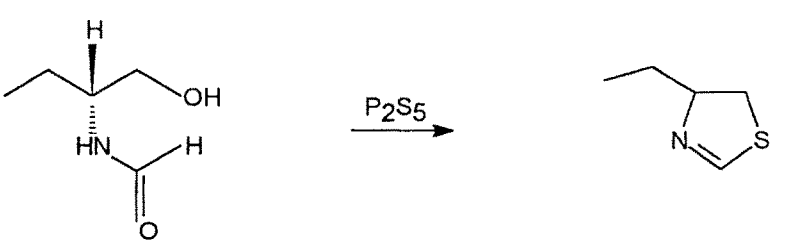
(R)-(-)-2-amino-1-butanol **(56)** on treatment with sulfuric acid followed by stirring with ammonium chloride-ammonium hydroxide produced ***(R)***-(-)-1-ethyl ethylenediamine[60] **(79) (Scheme I.33)**.



56 **79**

Scheme I.33

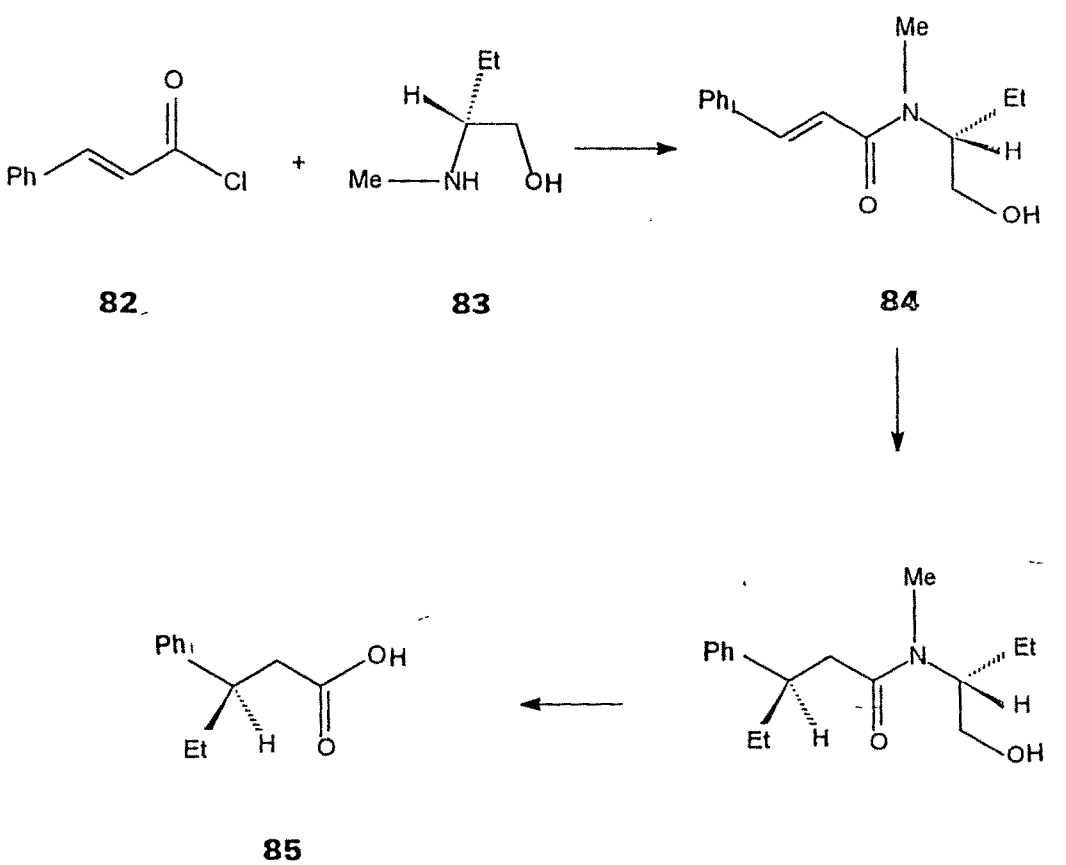
The formyl derivative of ***(R)*** (-)-2-amino-1-butanol **(80)** on reaction with phosphorous pentasulphide furnished 4-ethyl-2-thiazoline[61] **(81) (Schemel.34)**.



80 **81**

Scheme I.34

Reaction of cinnamoylchloride **(82)** with the N-methyl-2-amino-1-butanol **(83)** afforded the corresponding cinnamamides **(84)**. Michael additions of Grignard reagents to the latter followed by acidic hydrolysis, yielded optically active β-phenyl-β-ethyl propanoic acid[62] **(85)** **(Scheme I.35)**.

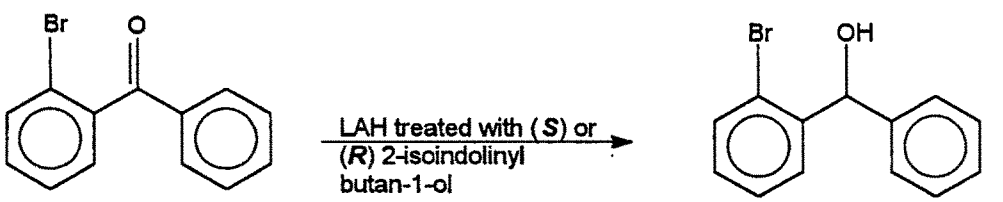


82 **83** **84**

85

Scheme I.35

Lithiumaluminiumhydride treated with ***(S)***-(+) or ***(R)***-(-)-(2-isoindolinyl)butan-1-ol reduced o-bromobenzophenones **(86)** to the corresponding optically active bromobenzhydrols **(87)** with nearly 100 % enantiomeric excess[63] **(Scheme I.36)**.

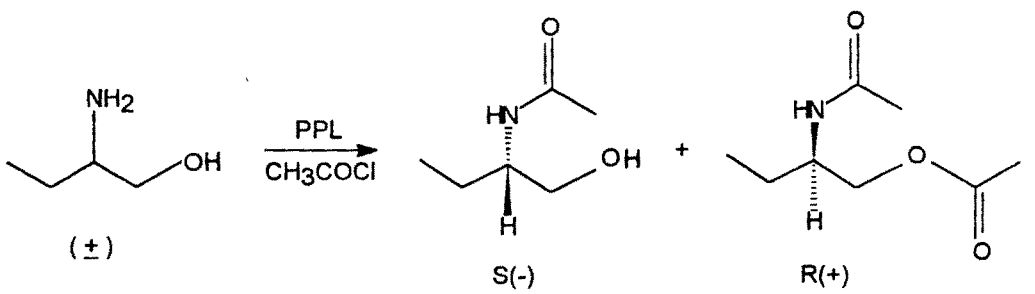


86 **87**

Optically active

Scheme I.36

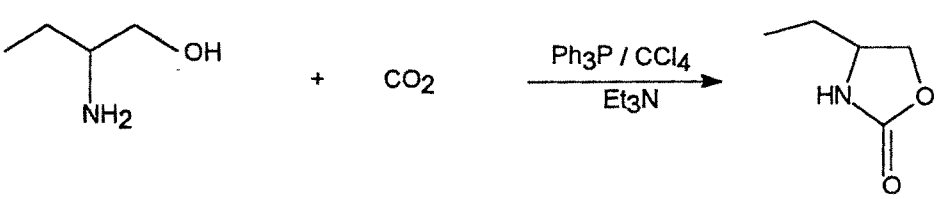
Reaction of DL-2-amino-1-butanol **(63)** with acetyl chloride, in presence of porcine pancreatin lipase (PPL) in ethyl acetate gave the chiral N-acetyl **(88)** and N,O-diacetyl **(89)** derivatives[64] **(Scheme I.37)**.



63 **88** **89**

Scheme I.37

Cyclic urethanes are obtained in good yields under mild conditions from amino alcohols, and carbon dioxide using phosphorous (III) reagents and haloalkanes[65]. For example 2-amino-1-butanol **(63)** on treatment with carbondioxide **(90)** in presence of triphenyl phosphine, carbon tetrachloride and triethyl amine furnished 4-ethyl oxazolidin-2-one **(91) (Scheme I.38)**.



63 **90** **91**

Scheme I.38

1.6 USES OF AMINOALCOHOLS

D-2-Amino-1-butanol was found to be one of the most efficient inhibitor of *plasmodium falciparum* growth '*invitro*'[66]. Ethambutol-2-hydrochloride, is a known antitubercular agent, was prepared by reaction of dichloroethane with ***(S)***-(+)-2-amino-1-butanol[67-71]. In rabbits and rats 2-amino-1-butanol depressed central nervous system activity. In cats 2-amino-1-butanol decreased mean arterial BP by 25-30 %[72].

Some amino alcohols caused larval growth retardation when added to a casein free diet. 2-amino-1-butanol and 2-amino-2-methyl propan-1-ol were most effective, in causing the death of larvae six days after hatching[73-75]. Squarilium derivatives which are useful as non-linear optical materials can be prepared from 2-amino-1-butanol[76]. The lower alkanol amines are used as hardening agents in antiperspirant sticks[77].

N-substituted alkanolamines were tested '*invitro*' against four oral microorganisms; such as *streptococcus mutans, streptococcus sobrinus, actinomyces viscosus* and *actinomyces naeslundii* and found to be effective[78]. 1,2-aminoazides which can be easily converted into unsymmetrical substituted vicinal diamines can be prepared from 1,2-aminoalcohols[79].

Aqueous solution containing water soluble calcium or zirconium compounds 0.1-1.0 %, urea 5-30 %, cysteine 0.1-5 %, and hydroxy carboxylic acids 15 wt %, adjusted to pH 9 - 11 with alkanolamines, is found useful for treatment of hair before wave setting and enhances the wave setting property without damaging the hair[80]. Esters prepared from fatty acids and alkanol amines and salts of the esters with acids such as lactic acid and phosphoric acid are useful as fabric softners which are biodegradable[81]. Cleaning composition prepared by diluting 1-part liquid cleaner containing 0.1 - 10 % alkanolamine with 10 - 150 parts water is useful for cleaning hard surfaces, giving results similar to those obtained with the undiluted cleaner[82]. A series of lipophilic aminoalcohol analogues of the anticholinergic drug **'Vesamicol'** was found to have calcium channel blocking activity[83].

Micro silica slurries containing an aqueous based carrier, microsilica and an aminoalcohol were used as an additive to conventional cement mixes with very low slump, for the manufacture of dry castable concrete pipes, to increase compressive strength and decrease permeability of the hardened concrete[84]. Fatty acid esters of aminoalcohols were found to be inflammation inhibitors[85]. Adhesive compositions are prepared from isocyanate containing polyester- polymethanes, chloroprene rubber polyisocyanate, halogenating agents and amino alcohols[86]. Chiral aminoalcohols react with achiral nitroalkenes in a highly chemoselective manner depending on the amino alcohol, under optimum conditions the reaction is stereospecific[87].

Alkanolamines have been used in urea or phenol-formaldehyde adhesives to improve storage stability[88-90], to increase water dispersability[91] and to improve bond strength and also as a catalyst[92,93]. Alkanolamines are used with methacrylates, hydroperoxides and polymerisation inhibitors to form storage stable mixtures that form strong bonds rapidly between plastic sheets[94-96] and, or metal sheet or parts under anaerobic conditions. The alkanolamines have been used as intermediates in molluscicides, herbicides, algaecides and fungicides[97-101]. Low levels of triethanol amine or one of its salts are added to cement clinkers, the efficiency of grinding is increased by reducing the agglomeration of the cement particles. The resulting cement is more free flowing and the pack set is reduced[102]. When added to concrete, triethanolamine reduces the set time by 50 %, it is believed that the hygroscopicity of the alkanolamine enables it to remove the excess of water from hydrated cement[103].

Alkanolamines can be used as a component of polymeric coatings on glass to prevent breakage[104]. The alkanolamines have been used exclusively as salts, amides, and free amines in providing antifogging, anti frosting and dirt repellent films[105-108] on glass for automobiles and plastic films. Alkanolamines were used in a variety of corrosion inhibiting formulations [109-111]. The alkanolamines were used in formulations for cutting fluids, lubricating oils and cleaning and etching solutions[112-113]. In epoxy resin, the alkanolamine acts as a cross linker or hardner or hardner accelerator[114,115].

The alkanolamines are useful intermediates in preparation of pharmaceutical compounds. Some specific uses of these products are as anti tumour agents and anti convulsants. Tris-(2-hydroxy ethyl)amine-o-cresoxy acetate has been patented as an antitumour agent for several carcinomas and sarcomas in laboratory animals. Tris-(mono ethanolamine) cobalt and organyl substituted silatranes show similar activity[116-118]. Ethanolamine-O-sulfate is an anticonvulsant in animal testing[119]. Ethanolamine N-(6-purinyl) anthranillate acts as an anti inflammatory agent[120].

1.7 TOXICOLOGICAL INFORMATION ON ALKANOL AMINES

Alkanolamines are of low acute oral toxicity. However serious toxic effects may result if they are swallowed in substantial quantities. Toxicological data have indicated that the alkanolamines present low hazards from vapour inhalation at ordinary temperatures. However when heated, vapour in high concentration may be generated which are irritating to eyes and nose. Alkanol amines have a severe irritating and injurious effect on the eyes.

1.8 THE PRESENT WORK

Enantiomerically pure aminoalcohols can be used as chiral building blocks. In the present study ***(R)*** and ***(S)*** 2-amino-1-butanol were used since both the enantiomers were readily and cheaply available.

Secondary aminoalcohols uncontaminated by tertiary and quarternary derivatives are of special importance. The direct arylation of the 2-amino-1-butanol involves the risk of producing the tertiary or quarternary derivative along with the derivatized product at both $-NH_2$ and -OH groups. To produce the N-mono substituted derivative of 2-amino-1-butanol a method has been developed.

N-Tosyl-1,3-Oxazolidines are used as chiral auxiliaries. N-benzenesulfonyl, N-Tosyl and N-benzyloxycarbonyl derivatives of 2-amino-1-butanol were reacted with various aldehydes, furnished the corresponding 1,3-oxazolidines with diastereoselectivity.

An isoindolin-1-one molecule has been synthesised by the reaction of 2-amino-1-butanol with o-phthalaldehyde. A new chiral ten membered heterocyclic ring is also synthesised from the 2 (1-hydroxybutyl) phthalimide.

1.9 REFERENCES

1. '*The alkanol amines Hand Book*', The Dow Chemical Co. 1981.
2. Chaudhury Aditya N & Chatterjee A, ***J. Ind. Chem. Soc.***, **36** (1959) 585.
3. Cherbuliez E, Yazgi A & Rabinowitz J, ***Helv.***, **44** (1961) 1164.
4. Lapporte SJ & Ferstandig LL, ***J. Org.Chem.***, **26** (1961) 3681.
5. Colclough T, Cunneen J F & Moore C G, ***Tetrahedron.***, **15** (1961) 187.
6. Cairns T L. ***J.Org.Chem.***, **17** (1952) 751.
7. Burger A & Hornbaker E D, ***J.Am.Chem.Soc.***, **74** (1952) 5514.
8. Dornow A & Bruncken K, ***Chem.Ber.***, **83** (1950) 189.
9. Tschoubar B, ***Bl*** (1949) 160; ***Th*** **6**, 80.
10. Bergmann E D & Sulzbacher M, ***J.Org.Chem.***,**16** (1951) 84.
11. Chang Yen tsai & Hartung Will, ***J.Am.Chem.Soc.***, **75** (1953) 89.
12. Singaram Bakthan, Fisher Gary B, Goralski Christian T & Nicholson Lawrence W, ***U.S.Pat.***, 5,367,073(1994);***CA*** **122** (1995) 290871x.
13. Inui Satoyuki, Baba Hideyuki, Morya Atsushi & Tsuneki Hidegaki, ***Jap. Kokai.***, 07,337,18(1995); ***CA*** **122** (1995) 314162j.
14. Delair P, Einhorn C, Einhorn J & Luche J L, ***J.Org.Chem.***, **59** (1994) 4680.

15. Reetz Manfred T, Roelfin Karin, Griebenow Nils, ***Tetrahedron Lett.***, **35** (1994) 1969.

16. Goralski Christian T, Hash Dennis L, Nicholson Lawrence W, Zakett Donald, Fisher Gary B & Singaram Bakthan, ***Tetrahedron Lett.***, **35** (1994) 3251.

17. Moody Harold M, Kaptein Bernard M, Broxterman Quirinus B, Boesten Wilhelmus H J & Kamphius Johan, ***Tetrahedron Lett.***, 35 (1994) 1777.

18. Berlin A Y & Sycheva T P; ***Th*** **6**, 34; ***CA*** **44** (1950) 7853f.

19. Cheney L C, ***J.Am.Chem.Soc.***, **73** (1951) 685.

20. Clinton R O, Salvador V J & Laskowski S C, ***J.Am.Chem Soc.***, **71** (1949) 3366; ***Th*** **6**, 482.

21. Vaughan W R, Klonowski R S, Elhinney M C & Millward B B, ***J.Org.Chem.***, **26** (1961) 138; ***Th*** **17**, 74.

22. Narasaka Koichi & Ukaji Yutaka, ***Chem.Lett.***, **1** (1984) 147.

23. Avison A W D, ***J.Applied Chem.***, **1** (1951)469; ***Th*** **9**,114.

24. Zahn S H & Gleissner A, ***Ang.Ch.***, **72** (1960)269; ***Th*** **16**, 114.

25. Bevinakatti H S, Newadkar R V, ***Tetrahedron : Asymmetry***, 1 (1990) 583.

26. Wilkinson R G, Shepherd R G, Thomas J P & Baughn C, ***J.Am.Chem.Soc.***, **83** (1961) 2212.

27. Cook Chacho, Cho Youngsang, Jew Sangsup & Park Minsoo, ***Soul Taehakkyo Yakhak Non munjip***, **8** (1983) 20; ***CA*** 101 (1984) 151368f.

28. Zee Shing Hsu, Wang Chun Mei & Yang Chung Heng, ***K'o Hsuch Fa Chan Yuch K'an***, **10(7)** (1982) 602; ***CA*** **98** (1983) 71438h.

29. Agarwal K C, Patel D, Khanna Jagmohan & Jain Padamchand, ***Indian Pat.***,149,953 (1979); ***CA*** **92** (1980) 41335f.

30. Belzecki Czeslaw, Tomasik Wiltold & Trojnas Jerzy, ***Pol.Pat.***, 86457 (1977); ***CA*** **90** (1979) 86723f.

31. Oppici Ernesto, ***Fr.Demande*** 2,253,009 (1975); ***CA*** **84** (1976) 43293z.

32. Nargund P K, Mehra R K, Fulwadiwala P B S & Mehta S C R, ***Indian Pat.***,139,104 (1976); ***CA*** **92** (1980) 163566c.

33. Nargund P K, Mehra R K, Fulwadiwala P B S & Mehta S C R, ***Indian Pat.***, 139,103 (1976); ***CA*** **92** (1980) 163565b.

34. Singh Balwant. ***Brit. Pat.***, 1,541,290(1978); ***CA*** **91** (1979) 157248q.

35. Singh Balwant. ***US.Pat.***, 3,944,617 (1976); ***CA*** **84** (1976) 164154p.

36. Abiko Atsushi & Masamune Satorn, ***Tetrahedron Lett.***, **33** (1992) 5517.

37. Vaidya S V, Malshe V C & Shirodkar S S, ***Indian. Pat.***, 166,781 (1991); ***CA*** **116** (1992) 6152m.

38. Samant R N & Chandalia S R B. ***Ind.Eng.Chem.Process.Des.Dev.***, **24** (1985) 426; ***CA*** **102** (1985) 138507y.

39. Krajicek Alois, Spicak Edward, Immer Adolf, Cerny Antonia & Semonsky Miroslav, ***Czech.Cs.*** 208913 (1982); ***CA*** **99** (1983) 5191s.

40. Magdanyi Laszlo & Kovaes Lagos, ***Hung Teljes.***, **19** (1981) 369; ***CA*** **95** (1981) 97030g.

41. Qi Jianzhong & Wang Qizhuo, ***Yiyao Gongye.***, **17** (1986) 241.

42. Sailo Masahiko, Kato Yoshiki, Watanabe Kenzo & Wakabayashi Toshio, ***Jap.Kokai.***, 77,139,001 (1977); ***CA*** **88** (1978) 89089y.

43. Nohira Hiroyuki & Takiguchi Daigaku, ***Ger. Offen.***, 2,514,653 (1975); ***CA*** **84** (1976) 16742p.

44. Rakhneva Ya, Mutafchieva E & Yanakova M, ***Tr. Nanchnoizsled. Khim Farm Inst.***, **9** (1974) 193; ***CA*** **83** (1975) 42764w.

45. Mutafchieva E, Rakhneva Ya & Aleksandrov N, ***Farmatsiya***. **25** (1975) 7; ***CA*** **83** (1975) 163561m.

46. Halmos Imre A & Ricketts Thomas E, ***Brit. Pat.***, 1,188,185 (1973); ***CA*** **82** (1975) 86073d.

47. Franclanci Franco, Cesti Pietro, Foa Marco & Martinengo Tiziano, ***Eur. Pat.***, 239,122 (1987); ***CA*** **108** (1988) 166129x.

48. Franclanci Franco, Cesti Pietro & Foa Marco , ***J. Org. Chem.***, **52** (1987) 23.

49. Franclanci Franco, Cesti Pietro, Foa Marco & Martinengo Tiziano, ***Eur. Pat.***, 222,561 (1987); ***CA*** **107** (1987) 216176x.

50. Nohira Hiroyuki & Kurogami Akesuna, ***Jap. Kokai.*** 6150,956 (1986); ***CA*** **105** (1986) 97946k.

51. Xu Zunle, Huang Wenhong, Wu Liang & Xie Song Kai, ***Yonji Huaxue.***, **6** (1985) 475; ***CA* 105** (1986) 60244d.

52. Fanshawe W J, Epstein J P, Crawley L S, Hoffmann C M & Safir S R, ***Aus. Pat.***, 534,404 (1984); ***CA* 101** (1984) 230031.

53. Kazan John & Yu Chen S, ***US Pat.***, 4,259,521 (1981); ***CA* 95** (1981), 6842j.

54. Dannen Berg Wolfgang & Schmand Horst, ***Eur. Pat.***, 0518 (1979); ***CA* 92** (1980) 6259n.

55. Mutak Stejpan, Gaspert Branko & Djoki Slobodan, ***Aus. Pat.***, 334,345 (1977); ***CA* 86** (1977) 190466a.

56. Kessels Gerard, ***Eur. Pat.***, 468,592 (1992); ***CA* 116** (1992) 193944f.

57. Miyazaki Hideya, Shiraiwa Tadashi & Kurawaka Hidemoto, ***Technol. Rep. Kansai Univ.***, **34** (1992) 91.

58. Harsy Stephen G. ***US. Pat.***, 4,990,666 (1991); ***CA* 114** (1991) 184790j.

59. Ichikawa Yataro, Nakagawa Koji & Yoshisato Eishin, ***Jap. Kokai.***, 76,06,911 (1976); ***CA* 84** (1976) 164151k.

60. Sei Tsuboyama, Kaoru Tsuboyama & Masaya Yunagita, ***Rika Gaku Kenkyusho Hokoku.***, **41** (1965) 194; ***CA* 64** (1966) 14079g.

61. Jean Roggero & Jaques Metzger, ***Compt .Rend.***, **253** (1961) 2704; ***CA* 56** (1962) 8679e.

62. Joel Touet, Sylvie Baudouin & Eric Brown, ***Tetrahedron: Asymmetry.***, **3** (1992) 587.

63. Joel Touet, Leze Antoine & Eric Brown, ***Tetrahedron: Asymmetry.***, **3** (1992) 841.

64. Susana Fernandez, Rosario Brieva, Francisca Rebolledo & Vicente Gotor, ***J. Chem. Soc. Perkin Trans I.***, **21** (1992) 2885.

65. Kubota Tasuhiko, Kodaka Masato, Tomohiro Takenari & Okuno Hiroaki, ***J. Chem. Soc. Perkin Trans I.***, **22** (1993) 5.

66. Vial Henri J, Theut Monique J, Ancehin Marie Laurie, Philippot Jean R & Chavis Claude, ***Biochem. pharmacol***, **33** (17) (1984) 2761; ***CA* 101** (1984) 183463z.

67. Han Ju on & Choe I Ryong., ***Tongbo.***, **27(2)** (1979) 88; ***CA* 91** (1979) 140265n.

68. Singh Balwant, ***US. Pat.***, 3,944,618 (1976); ***CA* 84** (1976) 164155q.

69. Singh Balwant, ***US. Pat.***, 3,944,608 (1976); ***CA* 84** (1976) 164204e.

70. Singh Balwant, ***US. Pat.***, 3,944,619 (1976); ***CA* 84** (1976) 179657d.

71. Zoja Giorgio, ***Brit. Pat.***, 1,198,923 (1970); ***CA* 73** (1970) 76648v.

72. Boyadzhiev Tsu & Verizarov At, ***Eksp. Med. Morfol.***,**11(3)** (1972) 157; ***CA* 79** (1973) 212b.

73. Bridges R G & Ricketts J, ***Biochem. J.***, **102(1)** (1967) 4; ***CA* 66** (1967) 73598y.

74. Bridges R G & Ricketts J, ***Insect Physiol***, **13(6)** (1967) 835; ***CA* 67** (1967) 61891w.

75. Bridges R G & Price Gareth M, ***Comp. Biochem. Physiol.***, 34(1) (1970) 47; ***CA* 73** (1970) 22601f.

76. Fu Ryuju, ***Jap. Kokai.***, 03,112,950 (1991); ***CA* 116** (1992) 62238u.

77. Schebece Frank, ***Eur. Pat.***, 448,278 (1991); ***CA* 116** (1992) 27845e.

78. Murata Yushifumi, Miyamoto Etsuko, Uede Michihiro & Kawashima Susuma, ***Bokin Bobai.*, 19(7)** (1991) 343.

79. Benalil Aziza, Carboni Bertrand & Vawtier Michel, ***Tetrahedron.*, 47** (2991) 8177.

80. Minagawa Motoi, Niikura Maho & Hanesaka Yuji ***Jap. Kokai.*, 03,251,519** (1991); ***CA* 116** (1992) 91138d.

81. Ploog U, Pousati O, Sandkuehler P, Trins A U, Guenter V T, Wahle B & Waltenberger P. ***Ger. Offen DE.***, 4,111,966 (1992); ***CA* 118** (1993) 41227c.

82. Alam Farooq, Strickland Wilbur Cecil Jr, Dewaele John Karel Emma & Scott Louise Gail. ***Eur. Pat.***, 503,219 (1992); ***CA* 118** (1993) 41234c.

83. Sipahimalani Anil S, Werth John L, Michelson Robert H, Dutta Aloke K, Efange Mbua N & Thayer Stanley A. ***Biochem pharmacol.*, 44(10)** (1993) 2039.

84. Scheiner Paul, ***US. Pat.***, 5,176,752 (1993); ***CA* 118** (1993) 108543y.

85. Bockstergel B, Emling F, King A, Jessel B & Janessen B, ***Ger. offen DE.***, 4,120,917 (1993); ***CA* 118** (1993) 161053q.

86. Murachi T, ***Jap. Kokai.***, 04,288,384 (1992); ***CA* 119** (1993) 170673u.

87. Morris M L & Sturgers M A, ***Tetrahedron Lett.*, 34** (1993) 43.

88. BASF AG, ***Fr. Demande.***, 2,163,578 (1973); ***CA* 80** (1974) 71673 j.

89. United Merchants & Manufacturers Inc, ***US. Pat.***, 3,962,166 (1976); ***CA* 85** (1976) 110037e.

90. Tesson G, ***US. Pat.***, 4,182,839 (1980); ***CA* 92** (1980) 130758p.

91. Hendrick H & Lumley N, ***US. Pat.***, 3,624,246 (1971); ***CA* 76** (1972) 86624k.

92. BASF AG, ***Ger. offen.***, 2,401,544 (1975); ***CA* 84** (1976) 77669s.

93. Klyarski S, ***USSR. Pat.***, 544,663 (1977); ***CA* 86** (1977) 122384z.

94. Kusayama S, ***Jap. Kokai.***, 74,121,886 (1976); ***CA* 82** (1975) 157239s.

95. Rabas V, Rosicky J & Novotny Jiri, ***Czech. Pat.***, 170,325 (1977); ***CA* 88** (1978) 153670k.

96. Nakenishi T, ***Jap. Kokai.***, 7455,733 (1974); ***CA* 81** (1974) 136967a.

97. Balasubramanian G, ***Cheiron.***, **6(1)** (1977) 24.

98. Imamura K & Suzuki S, ***Jap. Kokai.***, 78,86,028 (1978); ***CA* 90** (1979) 34984x.

99. Sakurai K, ***Shinkin to Shinkinsho.***, **16(1)** (1975) 35.

100. Lada A, Petrocci A N, Green H A & Merianos J J, ***US. Pat.*** 4,061,750 (1977); ***CA* 88** (1978) 70484b.

101. Rusay R, ***US. Pat.***, 4,202,685 (1980); ***CA* 93** (1980) 132150d.

102. W R Greece & Co, ***US. Pat.***, 3,443,976 (1969); ***CA* 71** (1969) 24515p.

103. William Kellet H, ***Ger. offen.***, 2,820,067 (1978); ***CA* 90** (1979) 75699b.

104. Kawabata T, Asai K, Saito T & Nagahisa S, ***Jap. Kokai.***, 78,139,662 (1978); ***CA* 90** (1979) 139142z.

105. Hoshima T & Ishihara H, ***Jap. Kokai.***, 74,116,180 (1974); ***CA* 82** (1975) 172712t.

106. Okhara A, ***Jap. Kokai.***, 77,141,873 (1977); ***CA* 88** (1978) 154497w.

107. Ukihahi H & Hara A, ***Jap. Kokai.***, 75,35,035 (1975); ***CA* 84** (1976) 137402m.

108. Uda T, Ishii M, Kawaji S & Kuroda Y, ***Jap. Kokai.***, 79,118,404 (1977); ***CA* 88** (2978) 50256a.

109. Tanimoto F, Kitano H, Aizawa Y & Kashiwagi H, ***Jap. Kokai.***, 7544,946 (1976); ***CA* 84** (1976) 34455b.

110. Suzuki T & Maeda A, ***Jap. Kokai.***, 75,109,841 (1975); ***CA* 84** (1976) 154100d.

111. Maga B F & West C W, ***US. Pat.***, 3,959,170 (1976); ***CA* 85** (1976) 128587u.

112. Hacias K J, ***S. African Pat.***, 77,06,814 (1978); ***CA* 90** (1979) 57722z.

113. Teeter F C, Sheldahl D B & Creech B C, ***US. Pat.***, 3,630,898 (1971); ***CA* 76** (1972) 74561z.

114. Wadwill H, ***US. Pat.***, 3,943,104 (1976); ***CA* 85** (1976) 6668a.

115. Rach V, Tekhno. ***Organ. Proivod.***, **46** (1979)1.

116. Voronkov M G, D´yakov V M, Semenova N V, Stetsenko N A, Prokhoda E F, Platonova A T & Simbritsev N L, ***Can. Pat.***, 1,036,618 (1978); ***CA* 90** (1979) 103645b.

117. Chemov O, ***Farmakol. Toshihot (Kiev).***, **8** (1973) 86.

118. Luhevics E, ***Latv PSR Zinat .Ahad Vestis Kim Ser.***, **42** (1978) 338.

119. Anlezark G, ***Br. J. Pharmacol.***, **56 (3)** (1976) 383.

120. Bobranski B, ***Arch. Immuncol. Ther. Exp.***, **22 (3)** (1974) 419.