CHAPTER V

CONCLUSION

Two different types of six valproic acid derivatives using pyridoxine as pro-moiety were synthesized. Since they are the derivatives of the existing antiepileptic drug, they are believed to possess antiepileptic activity.

The six-membered ring cyclic acetal of pyridoxine, 5-hydroxymethyl-8-methyl-2-(1-propylbutyl)-*4H*-dioxino[4,5-*c*] pyridine or α^4,3-O-(2-propylpentanylidene)pyridoxine was obtained in quantitative yield by saturating the hydrogen chloride on 2-propylpentanal suspension of pyridoxine hydrochloride.

The mono-, di- and trivalproate esters of pyridoxine were successfully prepared by selective esterification of pyridoxine using valproyl chloride as acylating agent. Two monovalproate esters, two divalproate esters and a trivalproate esters were synthesized in the yield of 50-70 %.

3-Hydroxy-4-hydroxymethyl-2-methyl-5-(2-propylpentanoyl)oxy methylpyridine or pyridoxine-5-valproate was obtained by the interaction of α^4,3-O-isopropylidenepyridoxine with valproyl chloride to yield the corresponding ester, followed by hydrolysis of the isopropylidene group.

4-Hydroxymethyl-5-hydroxymethyl-2-methyl-3-(2-propylpentanoyl)oxypyridine or pyridoxine-3-valproate was obtained by the reaction of 1 mole of pyridoxine with 1 mole of valproyl chloride in the presence of sodium carbonate as an acid accepter.

4-Hydroxymethyl-2-methyl-3-[(2-propylpentanoyl)oxy]-5-[(2-propyl pentanoyl)oxymethyl]pyridine or pyridoxine-3,5-divalproate was obtained by monoesterification of pyridoxine-5-valproate with 1 mole of valproyl chloride in the presence of pyridine.

2-Methyl-3-[(2-propylpentanoyl)oxy]-4-[(2-propylpentanoyl)oxy methyl]-5-hydroxymethylpyridine or pyridoxine-3,4-divalproate could be obtained by the interaction of 1 mole of pyridoxine hydrochloride with 2 moles of valproyl chloride in the presence of pyridine.

2-Methyl-3-[(2-propylpentanoyl)oxy]-4,5-di[(2-propylpentanoyl) oxymethyl]pyridine or pyridoxine trivalproate could be obtained by treating pyridoxine hydrochloride with an excess of valproyl chloride in the presence of pyridine.

An attempt to synthesize 9-hydroxy-8-methyl-3-(1-propylbutyl)-4*H*,9*H*-dioxepino[5,6-*c*]pyridine or α^4,α^5-O-(2-propylpentanylidene) pyridoxine, the seven-membered ring cyclic acetal of pyridoxine from the Diels-Alder reaction of 4-methyl-5-ethoxyoxazole and 2-(1-propylbutyl)-1,3-dioxep-5-ene was completely unsuccessful at temperature ranging from 180 °c for 48 hours to room temperature for 240 hours. It is probable that the failure is due to the low reactivity of 2-(1-propylbutyl)-1,3-dioxep-5-ene.