CHAPTER V

CONCLUSIONS

N-acylurea has been known to possess anticonvulsant activity for more than 40 years. In addition, at the Faculty of Pharmaceutical Sciences, Chulalongkorn University, N-2-propylpentanoylurea and some acylurea derivatives have also been evaluated for their favorable anticonvulsant activity compared to the known valproic acid. In order to further explore structure modification of this compound, focus has been on the variation of N-3 substitution since the N, N′-diarylureas have recently been reported to possess potent anticonvulsant activity. Therefore a series of N-acyl-N′-arylurea has been initiated and synthesized. Two pathways of synthesis were used as follows :

1. The isothiocyanate pathway

In this method, valproic acid was converted into acid chloride and was subsequently reacted with potassium thiocyanate in dry acetone. The acylisothiocyanate obtained was then reacted with the aniline or arylamine derivatives to give the N-acyl-N′-arylthiourea with moderately high yield. The thiourea derivatives were easily converted to the corresponding ureas by oxidation of their thio carbonyl group with

alkaline hydrogen peroxide. The yield of this step was high. Eight compounds in both ureide and thioureide types were prepared by this pathway namely N-(2-propylpentanoyl)-N′-phenylthiourea, N-(2-propylpentanoyl)-N′-(4-methylphenyl)thiourea, N-(2-propylpentanoyl)-N′-(2-methylphenyl)thiourea, N-(2-propylpentanoyl)-N′-(4-nitrophenyl) thiourea, N-(2-propylpentanoyl)-N′-phenylurea, N-(2-propylpentanoyl)-N′-(4-methylphenyl)urea, N-(2-propylpentanoyl)-N′-(2-methylphenyl) urea and N-(2-propylpentanoyl)-N′-(4-nitrophenyl)urea.

2. The isocyanate pathway

In this method , 2-propylpentanoyl chloride was allowed to react with potassium thiocyanate in dry dioxane, in the presence of catalytic amount of stannic chloride, and then reacted with 4-aminopyridine to obtain the product. By this method, N-(2-propylpentanoyl)-N′-(4-pyridinyl)urea which can not be synthesized by the first pathway has been successfully prepared with 30 % yield.