against one definite boundary, namely the one which separates zones of carrier substances of slightly higher and slightly lower affinity. As an illustration the following cases studied so far, using homogloous alcohols as carriers, may be quoted.

Valine: *tert.* butanol/water
Leucine: *sec.* butanol/*tert.* butanol
Methionine: *sec.* butanol/*tert.* butanol
Leucyl-glycyl-glycine: *iso*amyl/*n*-butylalcohol
Phenylalanine: *n*-amyl/*iso*-amylalcohol
Glycyl-tryptophan: benzylalcohol/*n*-amylalcohol

The procedure, for which we suggest the name »carrier displacement chromatography» has several advantages. The zones are sharp and of appreciable concentration, and the degree of separation can be predicted from the known behaviour of the carrier system. The spacing between the zones can be varied at will, by chosing suitable amounts of carriers and varying their proportions, provided that the adsorption column is large enough to give complete separation in the carrier system. Obviously it should be possible to apply the same principle to ionic exchange and displacement partition columns.

This type of separation can easily be demonstrated by a very simple arrangement. If the outlet of a small column (for example about 1 ml of a mixture of charcoal and Super-Cel 1 : 5) is allowed to touch the centre of a large circular filter paper between two glass plates, and an experiment similar to that described above is carried out (with correspondingly smaller volume), the filter paper will take up the effluent. After drying and spraying with ninhydrin, it will show a number of concentric rings corresponding to the amino acids and peptides present at the alcohol boundaries.

The work is continued with particular attention to peptide separations. A more detailed report will appear elsewhere.

The Use of Ethyl α-Thienylcyanoacetate in the Synthesis of Substituted α-Thienylacetic Acids

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The preparation of substituted thienylacetic acids has been a rather cumbersome problem. This can be illustrated by the synthesis of benzylthienylacetic acid, which has been obtained by the following steps [1]: Ethyl α-thienylglyoxylate was prepared from thiophene and ethyl oxalyl chloride. The free acid was prepared and converted to benzylthienylhydroxyacetic acid by means of benzylmagnesium chloride. This acid was reduced with stannous chloride yielding benzylthienylacetic acid.

The same acid has now been prepared from ethyl α-thienylcyanoacetate by benzylation with the aid of anhydrous potassium carbonate and benzyl chloride [2]. The ethyl benzylthienylcyanoacetate was then converted to benzylthienylacetic acid. The method is very useful for preparing other substituted thienylacetic acids, especially if the corresponding halogen compound cannot be converted to the Grignard compound.

We are indebted to the Swedish Natural Science Research Council for financial support.

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Received March 20, 1950

Ethyl α-thienylcyanoacetate was prepared from thienylacetonitrile with the aid of sodium amide and diethylcarbonate by a general method[3]. Thienylacetonitrile has been prepared by Blicke and Zienty[4], who refluxed thenyl chloride with sodium cyanide dissolved in dilute alcohol. Using this method, however, I have obtained a considerable quantity of ethyl thenyl ether. This complication is to be expected as benzyl bromide, when refluxed with dilute alcohol, yields ethyl benzyl ether[5]. The complication can be avoided by using acetone as solvent instead of alcohol.

Thienylacetonitrile. In a 500 ml, three-necked roundbottom flask, fitted with a reflux condenser, a mercury-sealed stirrer and a dropping funnel were placed 9.0 g (0.18 moles) of sodium cyanide dissolved in 100 ml of water and 100 ml of acetone. The mixture was refluxed and stirred on an oil bath. 21.0 g (0.16 moles) of thenyl chloride dissolved in 50 ml of acetone was added during one hour and the mixture refluxed with stirring for three hours. The acetone was removed by distillation and the nitrile was extracted from the residue with ether. The ether solution was dried with anhydrous sodium sulphate, the ether removed by distillation and the residue fractionated *in vacuo*. The fraction boiling at 110—113°/ 13 mm was collecte das pure nitrile. Yield 14.0 g(70 %).

Ethyl α-thienylcyanoacetate was prepared from 0.11 moles of sodium amide, 12.3 g (0.10 moles) of thienylacetonitrile and 15.4 g (0.13 moles) of diethyl carbonate according to the general process[3]. Yield 8.0 g (41 %) of ethyl α-thienylcyanoacetate boiling at 156—160°/14 mm.

Analysis:

$C_9H_9O_2NS$	C	H	N	S
Calc.	55.36	4.65	7.17	16.42
Found	55.57	4.54	7.20	16.42

Ethyl α-thienylbenzylcyanoacetate. 3.0 g (0.015 moles) of ethyl α-thienylcyanoacetate, 4 g (0.03 moles) of benzyl chloride, 4.5 g (0.033 moles) of anhydrous potassium carbonate and 30 ml of acetone were refluxed on an oil bath for 12 hours[2]. The acetone was removed by distillation and the residue treated with water and extracted with ether. After drying with anhydrous sodium sulphate, the ether was removed by distillation and the residue fractionated in vacuo. The fraction boiling at 206—210°/13 mm was collected as pure ethyl thienylbenzylcyanoacetate. Yield 2.6 g (60 %).

α-Thienylbenzylacetic acid. 2.6 g (0.009 moles) of ethyl thienylbenzylcyanoacetate was treated for ten minutes on a water bath with 1.1 g (0.02 moles) of potassium hydroxide dissolved in 10 ml of alcohol. The precipitated potassium carbonate[6] was removed by filtration and washed with alcohol. To the filtrate was added a solution of 1.0 g (0.018 moles) of potassium hydroxide dissolved in 10 ml of water and the mixture was refluxed until no more ammonia escaped (12 hours). The alcohol was removed by distillation. The residue was acidified with diluted hydrochloric acid, and the precipitated acid was extracted with ether. After removing the ether, 1.8 g (86 %) of thienylbenzylacetic acid was obtained. The crude acid was recrystallized from dilute formic acid and finally from petrol. Melting point 74.5—75.5°. A mixture of the acid obtained by this method and the acid obtained by the method described earlier[1] showed no melting point depression.

Equiv. wt.	Calc. 231.3	Found 230.8

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Received February 24, 1950.