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SYNTHESIS OF AMINO ACID BONDED SILICA GEL VIA ACTIVE ESTER WITH N-HYDROXYSUCCINIMIDE

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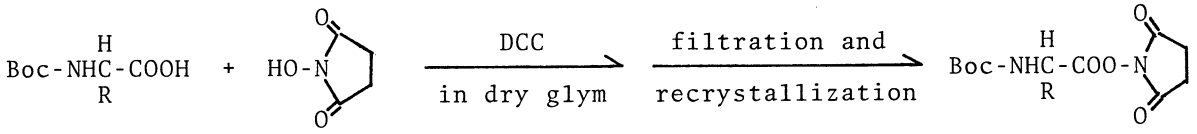
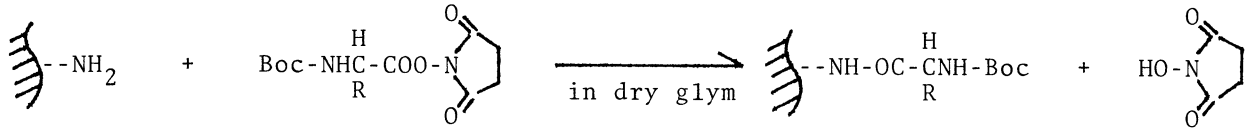
The surface of silica gel was chemically modified by amino acid via active ester with N-hydroxysuccinimide. The formations of insoluble by-product and fine particle coming from silica gel, which occur in DCC method were avoided. The amounts of amino acid coupling to silica gel were about twice larger than that by DCC method.

Surface chemical modification of silica gel has wide variety of applications in many fields. The usage in high-performance liquid chromatography is one of the branches being attacked most intensively. In recent few years, the derivatization of silica gel with amino acid has been challenged with the intention to prepare the gel having an ability to resolve enantiomeric amino acids[1)-4)]. The techniques of peptide synthesis have been vastly utilized for the amino acid bonding to silica gel. The condensation reaction by DCC(dicyclohexylcarbodiimide) has been employed in many cases because of its simplicity. However, the DCC method gives a severe problem to the washing by filtration, which takes long time. One is coming from the formation of insoluble by-product and the other is caused by the breakage of silica gel to fine particles. So, alternatives to the DCC coupling are required. Foucault et al. prepared chiral silane(N-(3-(triethoxysilylpropyl))-L-prolineamide), then attached it onto silica gel[1)]. The idea, in which the amino-acidized silane is coupled directly onto silica gel, is very attractive because of its large amount of amino acid bonding and no residue of unreacted amino functionality left on the gel, but the procedure was rather complicated. Recently, a method via active ester with N-hydroxysuccinimide(HOSu) was briefly mentioned in two articles[5),6)]. But, neither detail of the synthesis nor a description with regard to remarkable features connoted in this method were presented. So, it is worthwhile to present detail of the synthesis in this letter and to emphasize its advantages. It is well-established that the preparation of active ester with HOSu is carried out without racemization. The active ester can be isolated and purified. The isolated active ester is fairly stable. Furthermore, the coupling of active ester to amino-silica gel proceeds under mild condition. Procedures are schematized as follows;

1. preparation of amino-silica gel,
2. preparation of active ester,



3. coupling reaction of the active ester to the amino-silica gel,



Amino-silica gel was prepared from silica gel(Toyo Soda, LS310, 5μ) and 3-aminopropyltriethoxysilane. The amounts of aminopropyl functionality bonded on the silica gel were determined as 1.15mmole/g-dry gel from nitrogen analysis. The active esters of Boc-aspartic acid-β-benzyl ester, Boc-phenylalanine and Boc-tryptophan with HOSu were prepared according to the method by Anderson et al.[7]. They were recrystallized twice from isopropanol. Their purities were checked from measurements of melting point and ^{13}C NMR. Boc-amino acid-OSu(3mmole) was dissolved in 10 ml of dried 1,2-dimethoxyethane(dry glym). This solution was added to the suspension of amino-silica gel(3g) in 15 ml of dry glym. The mixture was gently stirred for 48 hours at ambient temperature. After the reaction, the gel was filtered off and washed thoroughly with glym, DMF, and methanol, until the droplet of filtrate did not leave any residue after evaporation of solvent. Finally, the gel was washed with dichloromethane and dried under vacuum at room temperature. The above-mentioned problem as encountered in DCC method did not occur in this method. The amounts of coupling were determined by nitrogen analysis as 0.40, 0.30 and 0.42mmole/g-dry gel for Boc-aspartic acid, Boc-phenylalanine and Boc-tryptophan-amino-silica gel, respectively. These values were about twice larger than that obtained by the DCC method. Another importance is that the active ester method offers the clear evidence of covalent bonding to silica gel not just adsorption, from a disappearance of the characteristic spectrum due to the leaving moiety of active ester by using spectroscopic means for modified silica gel. The investigations along these lines are being carried out. Boc-group can be removed from Boc-amino acid silica gel by the treatment with trifluoroacetic acid solution in dichloromethane. The silica gel modified by L-phenylalanine could resolve D,L-histidine with high efficiency by ligand-exchange high-performance liquid chromatography. Experiments by the tryptophan bonded silica gel are under investigations. The details of these results will be given elsewhere.

References

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