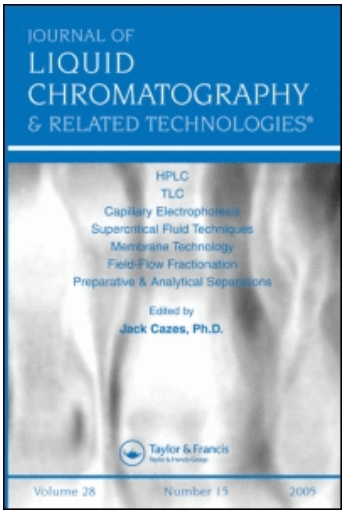

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Computational Chemical Analysis of the Retention of Saccharides on Amino Phase

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COMPUTATIONAL CHEMICAL ANALYSIS OF THE RETENTION OF SACCHARIDES ON AMINO PHASE

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SUMMARY

A model adsorbent of primary amino bonded phase was constructed by molecular design and the structure was optimized by molecular mechanics (MM2) of the CAChe™ program. The properties of standard molecules were calculated by MOPAC-BlogP of the CAChe™. Furthermore, the capacity ratios of saccharides measured on a primary amino bonded phase in aqueous acetonitrile was analyzed by the molecular interaction energies calculated by MM2. The capacity ratios were basically related to summation of calculated van der Waals and hydrogen bonding energies.

INTRODUCTION

Primary amino bonded phases and quaternary amine ion-exchange resins have been used for the separation of saccharides in liquid chromatography. The retention mechanism however has not been well discussed, and it was suggested that the number and the steric position of hydroxy groups are important [1]. The recovery from amino bonded phases was however poor for some saccharides such as mannose, ribose, arabinose and galactose. The reason for the poor recovery may be due to the in-column glycation of saccharides with the amino phase. The reaction mechanism of glycation was analyzed by comparison of the reactivity of saccharides with p-toluidine and computational chemical analysis. The reactivity could be related to the hydrogen bonding energy of the amino group of aromatic amines and hydroxy groups of saccharides as calculated by MM2 of the CAChe™ program [2]. On the other hand, the calculation of molecular interaction made it possible to explain the alkyl chain length effect on hydrogen bonding of alkanols and the chiral recognition mechanism [3]. The retention mechanism of saccharides on the amino phase was further analyzed by computational chemical analysis of molecular interaction between a saccharide and a model amino phase constructed by a computational chemical method

EXPERIMENTAL

The molecular design and computational chemical calculation were performed by the CAChe™ program from Sony-Techtronix (Tokyo-Beaverton(OR)). The computer used was a Macintosh IIfx.

RESULTS AND DISCUSSION

A honeycomb type layer was first constructed, and the two layers were bonded together in parallel to diminish the flexibility

of the hydrocarbon phase. The selectivity of the hydrocarbon phase was examined by the energy value of molecular interaction calculated by molecular mechanics (MM2) of the CAChe™ program, then one surface of the hydrophobic phase was hydroxylated. The hydroxylated phase demonstrated properties similar to those of a vinylalcohol copolymer gel in liquid chromatography and an ethylene glycol phase in gas chromatography where polyaromatic hydrocarbons were retained more than expected from their Van der Waals volumes calculated by MOPAC-Blog P of the CAChe™ program. This may be due to weak hydrogen bonding [4]. The basic hydrocarbon phase was modified by bonding amino groups on one surface as shown in Fig. 1. The dark of circles decreases in order of nitrogen > carbon > hydrogen atoms.

The molecular weight of the amino phase was 5,154 which was constructed of 368 carbons, 30 nitrogens and 318 hydrogens. The basic selectivity of the modified bonded phase having amino

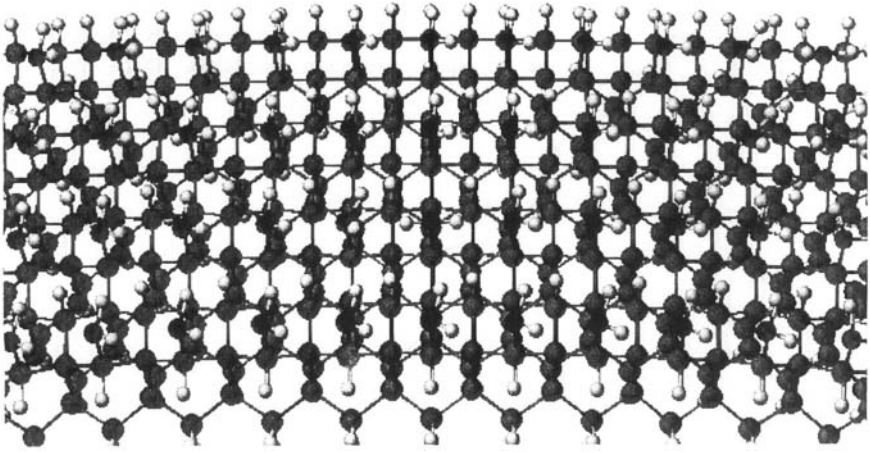

Fig. 1 Computer designed amino phase

Table 1 Molecular interaction energies of standard compounds with amino phase

chemicals	VWV Å^3/mole	TE Kcal/mole	HB Kcal/mole	ES Kcal/mole	VW Kcal/mole
amino phase		1507.85	-40.12	-1.56	376.78
benzene	83.79	1489.94	-47.81	-1.36	372.27
naphthalene	127.60	1473.60	-52.94	-1.32	370.63
anthracene	171.49	1457.24	-58.32	-1.20	369.46
hexane	112.79	1498.46	-40.20	-1.56	366.76
decane	180.01	1496.51	-40.55	0.62	361.64
tetradecane	247.26	1491.06	-40.50	0.11	356.01
pentanol	104.06	1495.49	-45.53	-1.49	368.59
nonanol	171.44	1490.51	-45.43	-1.43	363.10
tridecanol	238.62	1485.40	-45.26	-1.50	357.12
cyclohexane	101.40	1504.50	-40.18	-1.51	370.72
perhydronaphthalene	157.27	1503.55	-40.13	-1.52	367.21
perhydroanthracene	212.88	1516.67	-40.25	-1.51	367.49

VWV: van der Waals volume, TE: total energy, HB: hydrogen bonding energy, ES: electro static energy, VW: van der Waals energy

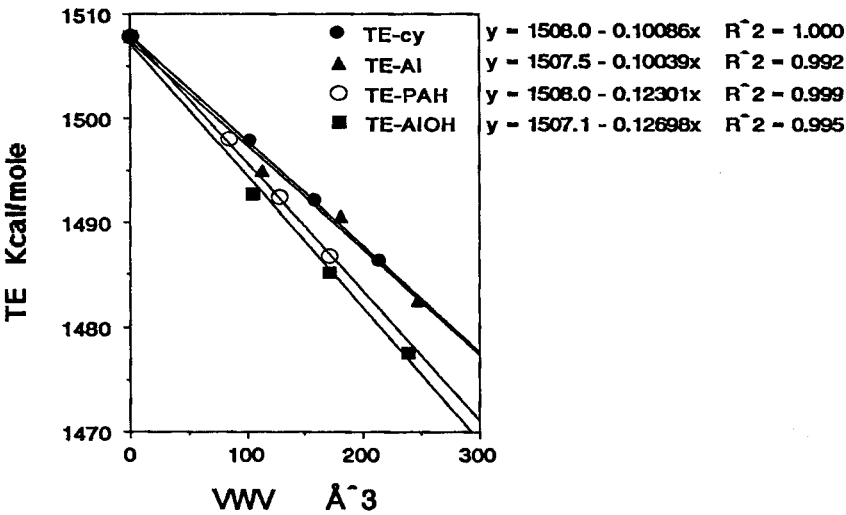

Fig. 2 Selectivity of amino phase based on total energy and van der Waals volume

groups was first examined from the molecular interaction between this phase and standard compounds used for the evaluation of the model hydrophobic adsorbent. The chemicals are given in Table 1 with their van der Waals volumes calculated by MOPAC-BlogP of the CAChe™ program and their molecular interaction energies calculated by MM2 of the CAChe™ program.

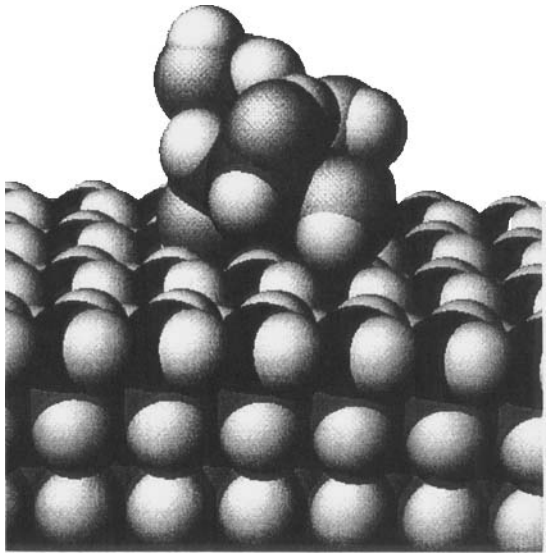

Fig. 3 Adsorption of glucose on the amino phase

The selectivity of this amino phase was examined by comparison of slopes between their van der Waals volumes and calculated energy values as shown in Fig. 2.

The selectivity was enhanced in the order: alkanes ≈ alkanols > cyclic hydrocarbons > aromatic compounds from van der Waals energy calculated by MM2, and alkanols ≈ aromatic compounds > cyclic hydrocarbons ≈ alkanes from total energy calculated by MM2. The selectivity was similar to those for the hydroxylated phase as compared to the result obtained on two hydrophobic phases. The order of selectivity was: alkanes ≈ alkanols > aromatic compounds ≈ cyclic hydrocarbons by van der Waals energy and : aromatic compounds > alkanols > alkanes ≈ cyclic hydrocarbons by total energy.The selectivity was different from that of hydrophobic phases on which aromatic compounds demonstrated the most selectivity by van der Waals energy and the least selectivity by total energy [4].

Amino groups are usually bonded on silica gels, vinylalcohol gels and methyl silicone phase coated on silica gels. The molecular interaction between this amino phase and saccharides was therefore directly examined by MM2 calculation of the CAChe™ program.

The optimized form, a saccharide adsorbed on the amino phase, indicated that the number of hydrogen bonds between a saccharide and the amino phase can be related to their capacity ratios measured by liquid chromatography on a propylamine bonded vinylalcohol copolymer gel in 70% aqueous acetonitrile.

The adsorption form of glucose on the amino phase is shown in Fig. 3. The dark of circles decreases in order of nitrogen > carbon > oxygen > hydrogen atoms. The hydroxy groups of carbon 1 and 2 of glucose made hydrogen bonding with the amino groups of surface, and that of carbon 6 of glucose protruded toward space as seen in Fig. 3. The hydroxy groups of carbon 2, 3 and 4 of mannose made hydrogen bonding with the amino groups of surface, and that of carbon 1 of manose protruded toward space. The capacity ratio was further related to total, hydrogen bonding, electrostatic and van der Waals energies as calculated by MM2.

After subtracting the individual energy of saccharides from the molecular interaction energy listed in Table 2, the capacity ratio demonstrated a good relation with the summation of van der Waals energy and hydrogen bonding energies as given in Fig. 4. Hence, a smaller van der Waals energy means stronger steric forces, and a larger hydrogen bonding energy means strongerhydrogen bonding. An exception was ribose. These saccharides may be adsorbed by their reversed form, therefore, the molecular interaction energy was calculated. The molecular interaction energy of the reversed-form was generally less than that of normal form that was first calculated and listed in Table 2. The smaller value of summation of van der Waals energy and hydrogen bonding energy calculated first and that done later was also related to the capacity ratio. The

Table 2 Molecular interaction energy of saccharides with amino phase

saccharide	k'	TE*	HB*	ES*	VW*	NH2/TE#	NH2/HB#	NH2/ES#	NH2/VW#
Arabinose	0.93	16.66	-3.04	5.83	2.32	1507.00	-51.35	3.90	370.75
Fructose	1.03	19.81	-3.30	10.60	2.24	1509.65	-51.17	8.46	369.18
Galactose	1.28	18.99	-2.28	9.03	5.11	1503.99	-58.63	8.75	372.20
Glucose	1.38	15.36	-3.94	8.24	4.62	1501.84	-64.90	9.07	374.12
Mannose	1.25	31.93	-3.18	9.11	8.27	1512.58	-53.36	7.37	373.14
Ribose	0.83	16.12	-2.65	5.94	1.89	1505.64	-60.29	3.64	373.36
Xylose	1.01	15.99	-3.36	5.07	2.30	1508.91	-51.23	4.26	370.27

unit: Kcal/mole, * energies of saccharides , # energies of molecular interaction

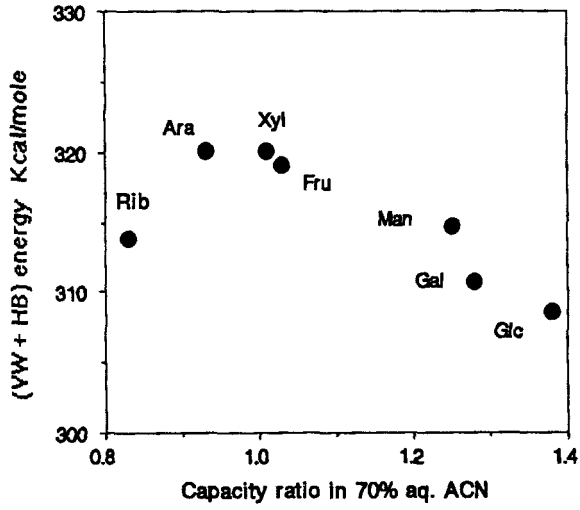

Fig. 4 Capacity ratio related to calculated energy

smaller energy showed a good relation with the capacity ratio, however glucose was an exception in this case.

If the retention form in chromatography and the surface structure of adsorbent are known, the difference of retentiontime, hence that of molecular interaction can be related to energy values calculated by computational chemistry.

References

1 M. D'Amboise, T. Hanai and D. Noel, Carbohydr. Res., **79**, 1 (1980).

2 T. Kinoshita, M. Miyayama, M. Miyamasu, Y. Kamitani, N. Nimura and T. Hanai, Biomedical Chromatography, **7**, 64 (1993).

3 T. Hanai, H. Hatano, N. Nimura and T. Kinoshita, presented at 7th International Symposium on Molecular Recognition and Inclusion, July 26-31, 1992, Kyoto Japan.

4 T. Hanai, H. Hatano, N. Nimura and t. Kinoshita, submitted for publication.

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