

CHROM. 14,179

LIQUID CHROMATOGRAPHY OF ADAMANTANES ON CARBON ADSORBENTS

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(Received July 13th, 1981)

SUMMARY

The retention behaviour of various adamantanes has been investigated on carbon adsorbents with methanol–water and acetonitrile–water mobile phases. The relationships between the molecular connectivity and the rate of change of the capacity ratio with the mobile phase composition, and between the surface area of contact between the adsorbent and the molecular structure, indicate that the retention mechanism is better explained in terms of adsorption than in terms of hydrophobicity. Although methanol generally yields greater selectivities than acetonitrile for a given water content, acetonitrile gives much shorter analysis times for an equivalent selectivity. The influence of various substituents of the adamantanes on the contact surface area has been investigated, and the results explained on the basis of a change in the adsorption energy of one or several adsorption positions.

INTRODUCTION

Adamantane derivatives are very important compounds encountered in pharmacy, biochemistry, medicine, chemistry of plastics, synthesis of special lubricants, etc. The chromatographic behaviour of these compounds has only recently been systematically studied^{1–3}. It has been shown that in normal-phase chromatography^{1,2} there are two contributions to the adsorption energy, related respectively to the type of functional groups and to the arrangement of these groups. Normal-phase chromatography gives good separations of adamantane derivatives having the same number of polar functional groups. However, it is difficult to use this technique for solutes with different numbers of polar groups since the differences in retention times are too large and it is not possible to use gradient elution with this group of compounds because of the necessity for a refractive index detector.

Reversed-phase chromatography with octadecyl-modified silica gel has proved to be very successful for such compounds³. However, this type of stationary phase is sometimes unable to resolve solutes of similar structures. Therefore, it is attractive to use carbon adsorbents as it is often possible to obtain very different selectivities with these materials than with the usual reversed-phase packings⁴.

The purpose of this work was to investigate the retention of adamantane derivatives on carbon adsorbents. The retention mechanism was studied as well as the effects of the mobile phase composition and of various substituents.

EXPERIMENTAL

A Model 6000A pumping system (Waters Assoc., Milford, MA, U.S.A.) was employed. Sample injection was performed with a Rheodyne 7020 sampling valve (Rheodyne, Berkeley, CA, U.S.A.) and solutes were detected with a Waters Model R-401 differential refractometer.

The carbon adsorbents were prepared as described previously⁵. The basic carbon materials were Black Pearls L and Sterling FT-FF (Cabot, Boston, MA, U.S.A.). Particle hardening was carried out by pyrolysis of benzene at 850 C. The particle size used was in the range 20–30 μm . The columns were packed at 200 bar using suspensions of carbon particles in acetonitrile–dibromomethane mixtures.

The mobile phases were prepared by pipetting appropriate volumes of methanol and acetonitrile (pro-analysis grade; E. Merck, Darmstadt, G.F.R.) or water (twice distilled). The compositions are given in v/v. Experiments were performed at room temperature (19–20 C).

The structures of the adamantane and diamantane molecules are shown in Fig. 1. All standards of adamantane derivatives were provided by the Laboratory of Synthetic Fuels, Institute of Chemical Technology, Prague.

RESULTS AND DISCUSSION

Retention mechanism

The retention mechanism on carbon surfaces is often pure adsorption⁶, and the chromatographic behaviour of systems based on carbon materials can generally be explained using Snyder's approach developed for normal-phase adsorption chromatography⁷. It is clear, however, that the solvophobic effect associated with the use of aqueous mobile phases cannot always be neglected. This is particularly true for com-

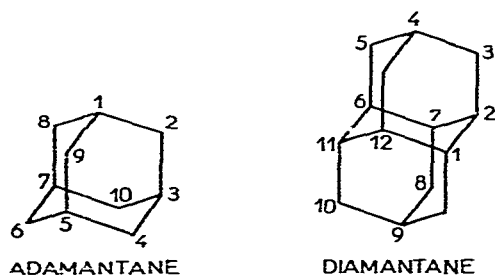


Fig. 1. Structures of adamantane and diamantane.

pounds of large molecular size (large molar volume) which leads to a greater solvophobic contribution, and spherical shape (small surface area of contact with a flat surface) which reduces the adsorption contribution. In such cases, the retention mechanism may become mixed. This situation may occur with the adamantane derivatives.

The study of possible relationships or correlations between retention, *i.e.*, capacity ratio, k' , and the molecular connectivity or the contact surface area can give information on the retention mechanism and helps in determining which one of the two contributions (hydrophobic and adsorption) is predominant.

The molecular connectivity, χ , which is easy to calculate, gives a good estimate of the surface area of the cavity created in the solvent to accommodate the solute⁸. When the retention mechanism is governed by the solvophobic effect, the rate of variation of $\log k'$ with the mobile phase composition (volume fraction) is linearly related to the molecular connectivity. This assumes that $\log k'$ is also linearly related to the solvent composition. As will be seen below, this assumption does not hold exactly for all the adamantanes eluted on carbon materials; the curvature of the plots is small, however. It was thus assumed that over a limited range of solvent composition the plots $\log k'$ vs. water content were linear. The slopes of these straight lines were determined and then plotted *versus* the molecular connectivity for 27 adamantane and diamantane derivatives, Fig. 2 (methanol-water mixtures). The values of χ for the adamantanes are given in Table I. The results clearly indicate that retention cannot simply be explained in terms of hydrophobicity as the correlation is, at best, very weak.

It is more difficult to evaluate the contact surface area, CSA, between the adsorbent and the adsorbate molecule as this requires knowledge of the position of the molecule on the surface of the adsorbent. However, in some cases it is quite easy to estimate the CSA, *e.g.* when the adsorbate molecule is flat (*i.e.*, benzene) or when it

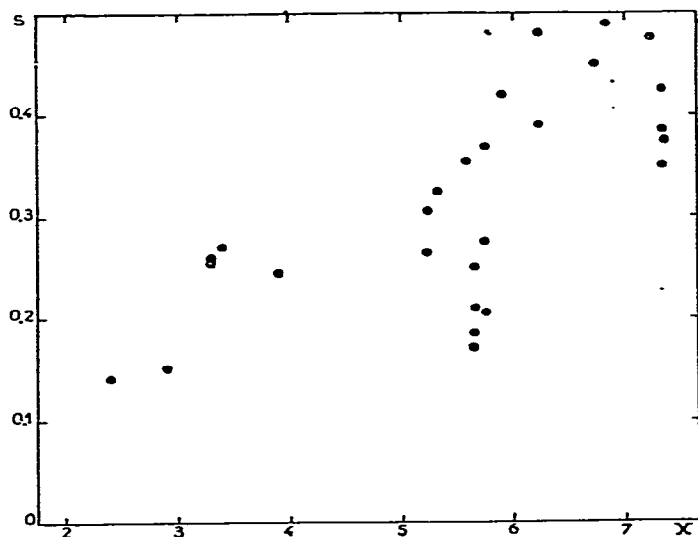


Fig. 2. Relationship between the molecular connectivity, χ , and the slope, S , of the $\log k'$ vs. solvent composition plots (methanol-water mixtures).

TABLE I

MOLECULAR CONNECTIVITY, χ , AND CONTACT SURFACE AREA, CSA, OF THE ADAMANTANE DERIVATIVES STUDIED

CSA = 1.00 for benzene

<i>Solute</i>	χ	CSA*	CSA**
Adamantane	4.900	—	1.00
Diamantane	6.899	—	1.48
Adamantan-1-ol	5.235	0.83	0.82
Adamantan-2-ol	5.326	1.01	1.04
Adamantanone	5.235	0.76	0.78
3-Methyladamantan-1-ol	5.571	1.05	1.03
3,5-Dimethyladamantan-1-ol	5.907	1.27	1.25
3,5,7-Trimethyladamantan-1-ol	6.243	1.50	1.46
3-Ethyl-5-methyladamantan-1-ol	6.468	1.44	1.40
3-Ethyl-5,7-dimethyladamantan-1-ol	6.596	1.66	1.61
2-Methyladamantan-1-ol	5.747	0.92	0.93
1-Methyladamantan-2-ol	5.747	1.09	1.09
2-Methyladamantan-2-ol	5.747	—	1.09
2-Ethyladamantan-2-ol	6.220	1.30	1.28
2-Propyladamantan-2-ol	6.720	1.48	1.48
2-Butyladamantan-2-ol	7.220	1.70	1.67
2-Isobutyladamantan-2-ol	7.078	1.63	1.62
Adamantane-1,4-diol	5.662	0.58	—
Adamantane-2,4-diol	5.662	0.78	—
Adamantane-2,6-diol	5.662	0.63	—
1-Hydroxyadamantan-4-one	5.662	0.58	—
2-Hydroxyadamantan-4-one	5.754	0.74	—
Diamantan-1-ol	7.256	1.27	1.24
Diamantan-3-ol	7.326	1.34	1.30
Diamantan-4-ol	7.235	1.19	1.11
Diamantanone	7.326	0.98	1.00
Cyclohexane	3.000	0.97	—
Cyclohexanol	3.394	0.81	—
Hexane	2.914	1.150	—
Decane	4.914	1.953	—

* Calculated from retention data in methanol-water mixtures.

** Calculated from retention data in acetonitrile-water mixtures.

is highly symmetrical (*i.e.*, carbon tetrachloride). It is clear from the structure of the adamantane molecule that there are four stable adsorption positions on the carbon surface, each of which corresponds to the contact of a cyclohexane ring with the adsorbent.

This indicates that, if the main contribution to the retention is adsorption, the rate of change of $\log k'$ with the mobile phase composition should be similar for adamantane and benzene and identical for adamantane and cyclohexane. This is indeed observed with methanol-water and acetonitrile-water mixtures.

The values of CSA for the adamantane derivatives investigated are given in Table I. The reference compound is benzene (CSA = 1.00). It can be seen that the

average relative CSA for adamantane is equal to that of benzene. It has already been shown that the CSA of cyclohexane is very close to that of benzene⁶.

The values of CSA for the other compounds will be discussed in detail below. However, the results obtained with benzene, adamantane and methyladamantanol suggest that the retention mechanism is mainly adsorption.

Rôle of the water content of the mobile phase

As previously reported⁴, the eluotropic strength of methanol-water and acetonitrile-water mixtures is approximately linearly related to the volume composition on carbon adsorbents, the linearity being greater with methanol than with acetonitrile. This results in almost linear plots of $\log k'$ vs. composition of the eluent. A significant curvature of these plots would indicate that the system is not governed by a pure adsorption process. It must be noted, however, that a non-linear behaviour can sometimes be observed with pure adsorption systems. This happens when the contact surface area between the solute molecule and the adsorbent changes with the solvent composition. In the case of carbon adsorbents, this should presumably occur with highly polar compounds containing conjugated benzene rings, but does not seem very likely with the adamantane derivatives.

Non-linear plots are observed for some solutes. As expected, the curvature of

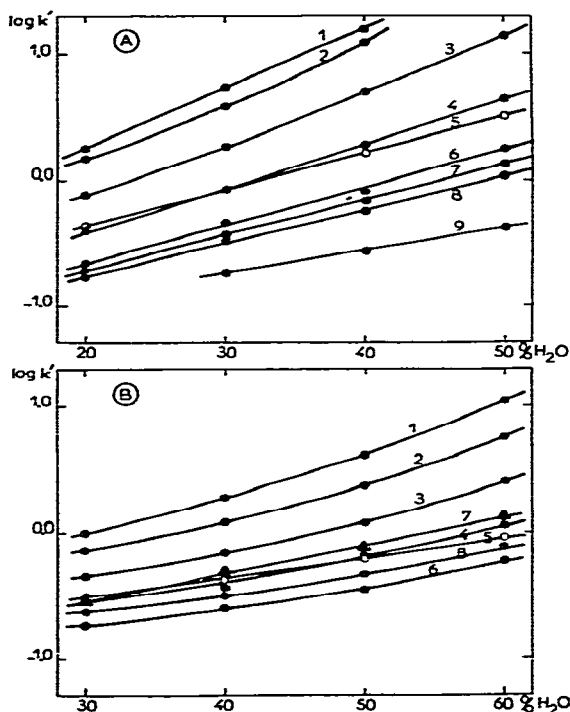


Fig. 3. Variation of $\log k'$ with the mobile phase water content (% v/v). A. Methanol-water mixtures; B. acetonitrile-water mixtures. Solutes: 1 = 2-*n*-butyladamantan-2-ol; 2 = 3,5,7-trimethyladamantan-1-ol; 3 = 3,5-dimethyladamantan-1-ol; 4 = 3-methyladamantan-1-ol; 5 = 2-methyladamantan-1-ol; 6 = adamantan-1-ol; 7 = benzene; 8 = adamantanone; 9 = 1-hydroxyadamantan-4-one.

the plots is greater for acetonitrile than for methanol where the plots are quasi-linear. Some results are given in Fig. 3. In the case of acetonitrile the shape of the plots indicates that with increasing water content the solutes are more strongly retained than expected assuming a pure adsorption mechanism. It must be noted that the curvature of the plots becomes significant only at high water contents (> 50%). Because acetonitrile has a higher eluotropic strength than methanol, it has to be mixed with larger amounts of water to provide similar k' values. This partly explains why greater curvatures are observed for acetonitrile than for methanol. The curvature is probably the result of an increasing hydrophobic contribution to the retention.

The examination of the curves $\log k'$ vs. mobile phase composition reveals that inversions in the elution order occur for a few compounds, e.g., 2-methyl- and 3-methyladamantan-1-ol in methanol-water and acetonitrile-water mixtures. The 3-methyl isomer is the more strongly retained at high water contents. This can simply be explained by the fact that the CSA for the 3-methyl isomer is larger than for the other one (see below). At low water contents, 2-methyladamantan-1-ol is eluted last (although close to the other isomer) because it interacts less with the solvent. With increasing water content, however, the contribution due to the solvent strength is larger for 3-methyladamantan-1-ol, the k' of which increases more rapidly than that of 2-methyladamantan-1-ol. This results in an inversion in the elution order.

Rôle of the organic modifier

Changing the organic solvent can result in a change in both the absolute and relative retentions. As far as the absolute retention is concerned, acetonitrile has a stronger eluting power than methanol: for a given water content the k' values are smaller with acetonitrile than with methanol. The change in absolute retention can be accompanied by a change in selectivity if the solutes studied have different CSA values. This happens with the adamantanes. It is difficult to determine *a priori* what is the best organic modifier for a given separation as this depends on the compounds investigated. Moreover, it also depends on what the analyst is interested in: maximum selectivity, minimum time of analysis, etc.

This is illustrated with a few examples showing some of the separation problems that can be encountered with the adamantanes:

(i) separation of positional isomers containing

- polar substituents (adamantan-1-ol and -2-ol)
- non-polar substituents (3-methyl- and 2-methyladamantan-1-ol)
- non-polar and polar substituents (2-methyladamantan-1-ol and 1-methyladamantan-2-ol)

(ii) separation of compounds with different degrees of substitution (non-polar substituents: 3-methyl- and 3,5-dimethyladamantan-1-ol)

These examples do not represent all the possible separation problems, but the conclusions that will be drawn give a good impression of the differences between the behaviours of acetonitrile and methanol.

The variations of the selectivity, α , with the water content of the eluent are indicated in Table II for two pairs of solutes in methanol-water and acetonitrile-water mixtures. Similar results are obtained for other pairs.

Two observations can be made from Table II. First, α increases with increasing water content. This stems from the fact that the solutes in each pair have different

TABLE II

INFLUENCE OF THE WATER CONTENT ON THE SELECTIVITY, α

A = 1-Methyladamantan-2-ol and 2-ethyladamantan-1-ol; B = 3-methyl- and 2-methyladamantan-1-ol.

Pair of solutes	Modifier	Water content (%)		
		30	40	50
A	Methanol	0.99	1.16	1.40
	Acetonitrile	0.93	—	1.05
B	Methanol	1.30	1.47	1.90
	Acetonitrile	1.26	1.33	1.46

CSA values, the most strongly retained solute having the largest CSA. Secondly, for a given water content, the selectivity is larger with methanol-water mixtures than with acetonitrile-water ones. This suggests that methanol is a better modifier if high selectivities are expected, regardless of the time of analysis.

It is also interesting to compare the two modifiers in terms of the time necessary to obtain a given selectivity. The corresponding data are reported in Table III. The time of analysis is accounted for by $1 + k'$, k' being the capacity ratio of the most strongly retained solute in each pair. The results indicate that acetonitrile is generally more "efficient" than methanol, on a time basis. This is particularly true when high α values are required (although, for a given water content, methanol yields higher selectivities). In some cases (low α values or compounds with very different CSA values) methanol becomes more efficient than acetonitrile. This corresponds, however, to low k' values (< 1) for which both modifiers are equivalent.

From these examples, and from other data not discussed here, it can be concluded that although methanol can potentially give larger selectivities than acetonitrile, it is generally better to use acetonitrile because, for a given selectivity, it requires shorter analysis times.

TABLE III

INFLUENCE OF THE ORGANIC SOLVENT ON THE ANALYSIS TIME FOR A GIVEN SELECTIVITY

A = 3-Methyl- and 2-methyladamantan-1-ol; B = adamantan-2-ol and -1-ol; C = 1-methyladamantan-2-ol and 2-methyladamantan-1-ol; D = 3,5-dimethyl- and 3-methyladamantan-1-ol.

Pair solutes	Methanol			Acetonitrile		
	α	$1 + k'$	Water content (%)	α	$1 + k'$	Water content (%)
A	1.40	5.48	50	1.40*	3.30*	70*
B	1.47	3.42	40	1.46	1.89	50
C	1.43	3.55	50	1.42	1.85	60
D	1.84	1.70	20	1.89	2.21	50

* Extrapolation.

Rôle of the solute structure

This has been investigated by studying the change in retention with the solvent composition. The relevant parameter is the contact surface area, as previously mentioned. CSA values (relative to benzene) are given in Table I. They have been calculated from the retention data obtained with acetonitrile–water and methanol–water mixtures. The CSA value for a given solute is the value of the slope of the plot of $\log k'$ vs. composition for that compound, divided by the corresponding slope for benzene. For these calculations it was assumed that the plots were linear (see above). The results in Table I show an excellent agreement between the values obtained in the two solvent systems. This does not mean, however, that methanol and acetonitrile are equivalent, as it has already been shown.

The examination of CSA values gives information on the rôle of the adamantane skeleton. The relative CSA values of benzene, adamantane and cyclohexane have been discussed above.

As for diamantane, it is clear from the structure of this molecule that its CSA is larger than that of adamantane, but not twice as large. The experiments give a value of 1.48, in good agreement with that (1.41) derived from a geometrical projection of the molecule onto a flat surface. On the other hand, it is remarkable that diamantane is much more strongly retained than adamantane [the relative retention is about 9 in acetonitrile–water (60:40)]. This is the result of the greater hydrophobic effect in the case of diamantane, in addition to the contribution of the extra four carbon atoms to the adsorption energy on the carbon surface.

The effect of a substituent on the adamantane molecule on the dependence of the retention on the mobile phase composition is related to the position and the nature of this group. Before discussing the effect on the CSA, it must be recalled that, because of its shape, adamantane has four stable and equivalent positions on the carbon surface. Depending on the location of the substituent, different adsorption positions will be affected. Moreover, according to the chemical nature of the substituent, the value of the contact surface area of a given adsorption can be increased or decreased. For instance, a methyl group increases the contact area whereas a polar group (such as –OH) decreases it because the molecule is partly shifted from the carbon surface in order to maximize specific polar interactions with the mobile phase. The situation is in fact more complex in the case of polar substituents because two opposite effects may occur. Indeed, the polar group can either come close to the surface of the adsorbent if its energy of adsorption is large enough, but it can also be pushed away from the surface if its interactions with the polar mobile phase are larger than its interactions with the adsorbent. This can result in a decrease or an increase of the CSA, the actual situation depending on the polar group and on the mobile phase composition.

The effect of non-polar substituents was examined with two groups of solutes: (i) polymethyladamantan-1-ols and (ii) 2-*n*-alkyladamantan-2-ols. The substitution of a tertiary carbon by a methyl group increases the CSA by 0.22 units, independently of the organic modifier. This appears in the series adamantan-1-ol, 3-methyl-, 3,5-dimethyl- and 3,5,7-trimethyladamantan-1-ol, and 3-methyl-, 5-methyl- and 3-ethyl-5,7-dimethyladamantan-1-ol. If the methyl substitution is made on a secondary carbon, the effect on the CSA is smaller: an increase of about 0.10 units in the series adamantan-1-ol, 2-methyladamantan-1-ol. The smaller effect in this case can be ex-

plained in terms of modified adsorption positions. In tertiary substitution, three adsorption positions are modified (and the corresponding CSA values are increased), whereas only two positions are modified for secondary substitutions.

As far as alkyladamantanes are concerned, the addition of a CH_2 group increases the CSA by about 0.20 units, slightly less than that for a methyl substitution on the basic skeleton. This is in agreement with other results obtained with carbon materials⁶, showing that the effect on retention of the substitution of a CH_3 group on a ring is slightly larger than that of the addition of a CH_2 group to a chain. As can be seen in Table I, the CSA increase due to a CH_2 group calculated from the retention data of hexane and decane is also very close to 0.20 units (0.194). As is well known for both adsorption and hydrophobic effects, branching decreases the effect of the alkyl chain: isobutyladamantan-2-ol is less strongly retained than *n*-butyladamantan-2-ol and its retention is less dependent on the mobile phase composition.

From the previous results it follows that a linear plot of $\log k'$ vs. carbon atom number, n_c , should be obtained in the different series discussed, as in a given series the adsorption energy is proportional to the contact surface area. Such linear plots are shown in Fig. 4.

In the case of polar substituents, the effect is more complex because, as previously mentioned, the mobile phase might play a rôle. Moreover, the intensity of solute-solvent interactions is also related to the position of the polar group in the solute molecule (charge density and steric hindrance of the group). It is thus difficult to predict the effect of a given substituent on the CSA.

The comparison of the CSA values of adamantane, adamantan-1-ol and -2-ol indicates that the addition of an OH group on a tertiary carbon decreases the CSA by

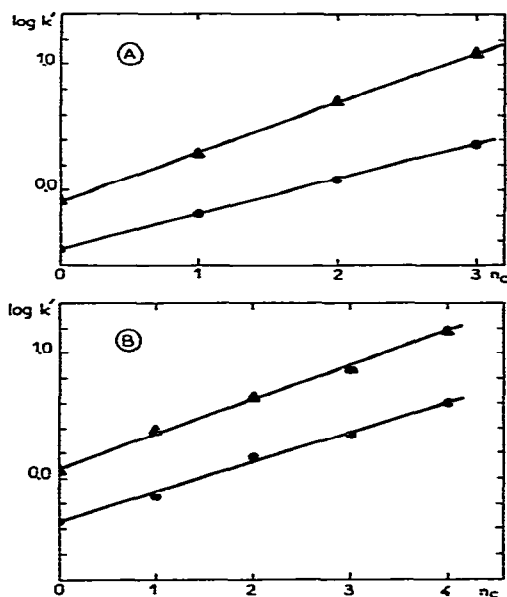


Fig. 4. Variation of $\log k'$ with the number of carbon atoms, n_c . A. Polytertiary methyladamantan-1-ols; B. 2-*n*-alkyladamantan-2-ols. \blacktriangle , Methanol-water (60:40); \bullet , acetonitrile-water (50:50).

0.18 units, but no significant effect if it is added at a secondary carbon. The result is similar to that obtained with a methyl group; the greater effect of tertiary substitution and the smaller CSA value for tertiary OH-substituted adamantanes can be explained by a smaller contact surface area for three adsorption positions. It must be noted that the CSA value of adamantan-1-ol is very similar to that of cyclohexanol (0.82 and 0.81 respectively). The negligible effect of a secondary OH group on the CSA is probably due to the compensation between adsorption of the OH group and interaction with the mobile phase (the charge density on the oxygen atom is larger in adamantan-1-ol than in -2-ol). The comparison between the values obtained for adamantanone 1-hydroxy- and 2-hydroxyadamantan-4-one indicates that the effect of a tertiary OH group is to decrease the CSA by 0.12 units and that of a secondary OH group to decrease it by 0.03 units. These values are very close to those obtained with the adamantanols.

The data obtained with adamantanediols show that, as it could be predicted, increasing the number of polar groups significantly decreases the CSA (*i.e.*, the CSA value for adamantane-1,4-diol is only about 50% of that of adamantane). The effect of the position of the groups is difficult to explain as the different groups may interact with each other. It can be noted, however, that the difference between the CSA values of adamantan-2-ol and -1-ol (0.18 units) is similar to that between those of adamantane-2,4-diol and -1,4-diol (0.20 units). The CSA value of adamantane-2,6-diol is close to that of adamantane-1,4-diol although there is no tertiary OH group in the first molecule. This result can perhaps be explained by the fact that, for these two compounds, all the four adsorption positions are affected instead of only three for adamantane-2,4-diol.

The contribution of a keto group can be calculated from the data for the adamantanone derivatives. The comparison between adamantane and adamantanone gives a decrease in CSA of 0.23 units; the corresponding decrease from adamantan-1-ol to 1-hydroxyadamantan-4-one and from adamantan-2-ol to 2-hydroxyadamantan-4-one is in both cases 0.25 units. Although there is a good agreement between these values, the result is nevertheless surprising as experiments with different types of solutes have indicated that: (i) the adsorption of a keto group is stronger than that of an OH group on carbon surfaces; and (ii) the keto group is generally less polar (and less hydrophobic) than the OH group⁶. We have no explanation for this behaviour.

As far as diamantanols are concerned, it is more difficult to interpret the results as the geometry of the molecule is not as simple as that of the adamantanols. If it can be assumed that the molecule has six stable adsorption positions, three are affected by the presence of a substituent on a tertiary carbon, independently of the position of this carbon. Only two positions are affected in the case of a secondary carbon. This is in agreement with experimental results (diamantan-3-ol has the largest CSA).

The tertiary carbon atoms are not equivalent and can be classified in two groups: the central carbons (1,2,6,7,11 and 12) and the extremity carbons (4,9) (*cf.*, Fig. 1). It is observed that the effect of substitution is larger for the extremity carbons: diamantan-4-ol has a smaller CSA than diamantan-1-ol. The difference between the effects associated with the two groups of tertiary carbons is rather large. The average decrease in CSA is 0.24 units for a central tertiary OH group, 0.36 units for an extremity tertiary OH group and 0.14 units for a secondary OH group.

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