Host-guest chromatographic behaviour of ketones in micellar paper chromatographic separation

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Separation of 14 ketone compounds by paper chromatography using pure water micellar solution of hexadecyltrimethyl ammonium bromide (CTAB) and/or sodium dodecyl sulphate (SDS) as the mobile phase has been reported. Based on the calculated molecular structural factors (e.g. length, width and height, etc.) and the cavities of micelles, the ketones can be divided into three molecular groups. Each group has its own characteristics and all the groups show the suitability between the solute molecules (guest) and micelles (host). The suitability is the main driving force of chromatographic migration and reveals the relationship between solutes' molecular structures and the cavities of surfactants. Furthermore, the suitability can be directly used to explore molecular structure such as sizes and geometry.

Host-guest chemistry is one of the most spectacular fields for chemists. Spectrofluorimetry, spectral methods and ion-molecule probe techniques have mainly been used to study this field. While liquid chromatography does not give information about molecular structures, host-guest chromatography (HGC), which is based on recognition, can be used directly to explore molecular structures, such as size, geometry, etc. Several studies have been reported to explain the relationship between the guest and host in explain terms of the suitability of the molecular structures of solutes (guest) for the micellar shapes and sizes (host).

We can study the relationship between molecular structures of solutes and micellar shapes and sizes with normal micellar paper chromatography besides separation. Several types of organic compounds for example, alcohols, phenols, vitamin B and amino acids have been studied with this method in our laboratory. This note reports the separation of 14 ketone compounds by micellar paper chromatography (MPC). Their HGC behaviours have also been described.

Materials and Methods

p-Phenylacetophenone, p-phenoxyacetophenone, p-methoxyphenyl ethylketone, 2,5-cyclohexadienyl ketone and 2-pentyl-2-cyclopentenyl ketone were prepared and purified in our laboratory. The other reagents were purchased from Lanzhou University and used as received. SDS was washed five times with absolute ethyl alcohol before use. Distilled water was used to make the stock surfactant solutions. Traditional methods of paper chromatography were applied. Spot visualization was performed with 2,4-dinitrophenylhydrazine. All compounds showed yellow to red colour spots after spraying with the reagent. Retardation factors ($R_f$) were calculated from four data points for every compound in two experiments with two pieces of paper used each time.

Results and Discussion

According to the basic tendency the ketones be divided into three groups. There are many factors influencing the solute’s migration novel concept has been introduced to compare better the relationship between molecular structures and micellar shapes and sizes; \( \Delta R_f=R_{f2}-R_{f1} \) where \( R_{f1} \) is \( R_f \) value obtained when the concentration of surfactant is equal to its CMC, and \( R_{f2} \) is the value at concentration higher than CMC. So, all the influential factors can be considered relatively, and \( \Delta R_f \) value expresses only the “net contribution” for “net micellar increasing”. According to Armstrong’s equation:

\[
R_f = \frac{1}{1 - R_f} + \frac{K_s C_m}{K_p [A]_0}
\]

where \( K_s \) and \( K_m \) are binding constants of the stationary phase and pseudophase respectively, \([A]_0\) is the concentration of the stationary phase binding sites.
0 is the phase ratio, $C_m$ is the micelle concentration, and $R_f$ is the retardation factor. Equations 2 and 3, derived from Eq. 1 are used to discuss the suitability between the solute molecules and micelles.

$$\Delta R_f = \frac{K_r[A]_0}{K_r[A]_0 + K_m} \frac{K_m \Delta C_m}{K_m \Delta C_m + 1} \quad \ldots (2)$$

or

$$\Delta R_f = \frac{K_r[A]_0}{K_r[A]_0 + 1} \frac{K_m \Delta C_m}{K_m \Delta C_m + 1} \quad \ldots (3)$$

where $\Delta C_m = C_{m2} - C_{m1}$.

According to Eq. 2, when $\Delta R_f > 0$, $K_m > 0$ and the solute is binding type, micelles give "net positive contribution" to solute; when $\Delta R_f = 0$, $K_m = 0$ and solute is non-binding, the micelles are non-contributing. According to Eq. 3, when $\Delta R_f < 0$, $K_m < 0$, the solutes belongs to an antibinding type and micelles have a "net negative contribution". The solutes have been classified by the molecular length, width, height and micellar size as small, medium, big and super molecules. Plots of $\Delta C_m$ vs $R_f$ showed different curve tendencies for different kinds of solutes indicating different molecular groups.

The HGC behaviours of phenols, amino acids and diphenylmethyl alcohols (DPMA) showed the regularity as above. In order to have a clear view about suitability, the authors distinguished TLC and HPLC methods used in their laboratory from other works. Data showed that the relationship was applicable to any type of liquid chromatography such as PC, TLC and HPLC. It was observed that adding organic additives improved the separation by micellar chromatography, however, the micelles changed their shapes and sizes in this case. Hence, for all further studies we used the pure water system.

Since there are no authoritative data on molecular structural factors (length, width, height, etc.) available at present, we have calculated the molecular structural factors and the longest possible length of surfactant's longest chain (LPLS) for knowing the biggest possible size of micellar 'cavity'. All the three dimensional organic molecules were grouped with atoms. The structural factors of the three dimensional ketone molecules can be calculated with different parameters, such as bond distance, atomic radius and hybridization of atomic orbitals. The length, width and height of the ketones, LPLS, molecular structures and the water solubilities related to discussion are listed in Table 1.

Table 2 gives the $R_f$ of ketones with paper chromatography using different concentrations of CTAB and/or SDS aqueous solutions as mobile phase. Data show that all the ketones can be separated by CTAB and/or SDS micellar solutions in pure water as mobile phase at suitable concentrations, or at different concentrations being combined with different surfactants. All the plots of $C_m$ versus $R_f/(1 - R_f)$ were sawtoothed curves, conforming to the early results. This is because of migration of ketones due to the static electricity, hydrophobic and stereo effects between solutes and micelle, as well as the dynamic equilibrium of micellar cavities, etc. This conformed to the results of Fu et al., and illustrated that the suitability between the solutes' molecular structures and micellar cavities is the main driving force in the separation of ketones.

On the basis of comparison of the calculated molecular structural factors (Table 1) with the 'cavities' of micelles, the ketones can be divided into three groups, A, B and C. All these suitabilities showed excellent regularity. The order of stereo effect is $A_1 > A_2 > B > C$. We noticed that the length of 2-octanone is much longer than that of m-nitroacetophenone, but, the stereo effect of m-nitroacetophenone is much stronger than that of the others. This may be because of m-nitroacetophenone being a planar molecule, is more rigid than linear 2-octanone.

**HGC behaviour of molecular Group A**

According to the molecular structural factors of ketones in Table 1, the molecules in Group A are big molecules (longer length) in CTAB and show very strong stereo effect, namely, $\Delta R_f >> 0$, $K_m >> 0$. However, the LPLS of SDS is shorter than that of CTAB. Group A shows mainly the super molecular characteristics and some big molecular characteristics in SDS, hence, the plots of $\Delta C_m$ versus $\Delta R_f$ are almost parallel, though a little above the line of $\Delta R_f = 0$. An example is shown in Fig. 1; the others are similar. The molecular factors of sub-group A1 are a little different from sub-group A2, the curves show the difference between A1 and A2. Lengths of A1 are longer than that of A2, the $\Delta R_f$ of A1 grows more rapidly than that of A2 and the curves of A1 are generally higher than those of A2 (Fig. 1).
The shapes and sizes of micelles are in a continuous equilibria system in aqueous solution. In an aqueous micellar solution, there are several kinds of micelles with different shapes and sizes. These micelles are spherical, rod-shaped, disk-shaped, etc. The cores (cavities) change with these shapes. The shapes and cavities of micelles are in dynamic equilibria. However, Eq. 2 or Eq. 3 arise from a special condition in which there is only one type of micelles and the stoichiometry between the pseudophase and solute is 1:1. For 2:1 complexes the correct pseudophase retention equation is:

\[
\frac{R_f}{1 - R_f} = \frac{1}{K[A]} + \frac{K_1 C_m}{K[A]0} + \frac{K_1 K_2 C_m^2}{K[A]0}
\]

where \(K, K_1\) and \(K_2\) are the binding constants to the stationary phase, first pseudophase and second pseudophase respectively. \(\Delta R_f\) can be expressed as follows:

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**Table 1—Molecular structural factors of ketones**

<table>
<thead>
<tr>
<th>Group</th>
<th>Comp.</th>
<th>L (nm)</th>
<th>W (nm)</th>
<th>H (nm)*</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(p)-Tolyl phenyl ketone</td>
<td>1.106</td>
<td>0.431</td>
<td>0.192</td>
<td><img src="image1" alt="Structure" /></td>
</tr>
<tr>
<td>2</td>
<td>(p)-Isopropylphenyl ethyl ketone</td>
<td>1.101</td>
<td>0.431</td>
<td>0.371</td>
<td><img src="image2" alt="Structure" /></td>
</tr>
<tr>
<td>A</td>
<td>3 (p)-Phenylacetophenone</td>
<td>1.079</td>
<td>0.431</td>
<td>0.262</td>
<td><img src="image3" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>4 (p)-Phenoxyacetophenone</td>
<td>1.014</td>
<td>0.431</td>
<td>0.261</td>
<td><img src="image4" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>5 (p)-Pentyl-2-cyclopentenyl ketone</td>
<td>1.013</td>
<td>0.443</td>
<td>0.161</td>
<td><img src="image5" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>6 (p)-Methoxylphenyl ethyl ketone</td>
<td>0.965</td>
<td>0.431</td>
<td>0.360</td>
<td><img src="image6" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>7 Phenyl ketone</td>
<td>0.935</td>
<td>0.431</td>
<td>0.392</td>
<td><img src="image7" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>8 (p)-Nitroacetophenone</td>
<td>0.740</td>
<td>0.431</td>
<td>0.247</td>
<td><img src="image8" alt="Structure" /></td>
</tr>
<tr>
<td>B</td>
<td>9 (p)-Methylacetophenone</td>
<td>0.732</td>
<td>0.431</td>
<td>0.255</td>
<td><img src="image9" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>10 (p)-Aminoacetophenone</td>
<td>0.726</td>
<td>0.431</td>
<td>0.255</td>
<td><img src="image10" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>11 (m)-Nitroacetophenone</td>
<td>0.666</td>
<td>0.564</td>
<td>0.253</td>
<td><img src="image11" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>12 Cyclohexanone</td>
<td>0.505</td>
<td>0.319</td>
<td>0.273</td>
<td><img src="image12" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>13 2,5-Cyclohexadienyl ketone</td>
<td>0.443</td>
<td>0.445</td>
<td>0.178</td>
<td><img src="image13" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>14 2-Octanone</td>
<td>1.070</td>
<td>0.234</td>
<td>0.178</td>
<td><img src="image14" alt="Structure" /></td>
</tr>
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</table>

LPLS*: L, W and H express length, width and height respectively.

LPLS express the longest possible length of surfactant’s chain.

Either $K_1$ or $K_2$ or both can be negative, $\Delta R_f$ shows synthesis of $K_1$ and $K_2$. For a more complex system (or real system), the equation will include $K_3$, $K_4$, ... etc. As above, the shapes and sizes of micelles can change with increase in the concentration of surfactant solution, and the cavities of micelles are in dynamic equilibria. This means that $K_1$ and $K_2$ (even $K_3$, $K_4$, etc.) are dependent on different solutes which may or may not be suitable for a certain cavity (or cavities) of micelles.

In CTAB the curves of $A$ become flat when $C_m$ is higher than 0.04 mol/L, because the second micellar phase ($K_2$ area in Fig. 1) emerges and has become the main phase. The main driving force of chromatographic migration, in this case, is the suitability between ketone and the second micellar phase. The second micellar cavity is bigger than the first one, so ketone becomes relatively smaller and shows the medium molecular characteristics. Fig. 1 also shows that molecular Group A has different characteristics in $K_1$ (first micellar phase) area and "$K_1 + K_2$" (first, second mixed micellar phase) areas.

### Table 2—$R_f$ values of Ketones in CTAB/SDS Micellar Solution

<table>
<thead>
<tr>
<th>Ketone</th>
<th>CTAB (mol/L)</th>
<th>SDS (mol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.00</td>
<td>0.01</td>
</tr>
<tr>
<td>1</td>
<td>0.00</td>
<td>0.01</td>
</tr>
<tr>
<td>2</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>3</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>4</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>5</td>
<td>0.00</td>
<td>0.06</td>
</tr>
<tr>
<td>6</td>
<td>0.88</td>
<td>0.87</td>
</tr>
<tr>
<td>7</td>
<td>0.00</td>
<td>0.01</td>
</tr>
<tr>
<td>8</td>
<td>0.60</td>
<td>0.59</td>
</tr>
<tr>
<td>9</td>
<td>0.72</td>
<td>0.71</td>
</tr>
<tr>
<td>10</td>
<td>0.85</td>
<td>0.90</td>
</tr>
<tr>
<td>11</td>
<td>0.77</td>
<td>0.88</td>
</tr>
<tr>
<td>12</td>
<td>0.00</td>
<td>0.87</td>
</tr>
</tbody>
</table>

\[ \Delta R_f = \frac{K[A]0K_1[2(C_2 + C_1) + 1]D C_m}{(K[A]0 + 1)^2 + (K[A]0 + 1)K_1K_2(C_2^2 + C_1^2) + (C_2 + C_1)[K_1K_2(C_2^2 + C_1^2) + 1 + K_2^2C_1C_2]} \]

... (5)

When $K_2$ is zero and $C_i$ is zero, this equation reduces to Eq. 2 or Eq. 3.
In $K_1$ area, $\Delta R_f$ increases very fast, because the ketones are big molecules which are suited to the cavity of the first micellar phase completely. In "$K_1 + K_2$" area, although the second micellar phase has emerged, the first micellar phase is still the main phase. An interesting phenomenon appears in the mixed phase; the curves show a crisscross plot indicating that different ketones show different suitabilities in this case.

**HGC behaviour of molecular Group C**

Figure 2 shows the behaviour of molecular Group C. It clearly illustrates that all the ketones of Group C are small molecules, both in CTAB and in SDS micellar solutions. All the curves are around the line $\Delta R_f = 0$. However, the curves in SDS are higher than those in CTAB because LPLS of SDS is smaller and the ketones show larger stereo effects.

**HGC behavior of molecular Group B**

Ketones of Group B are very close to medium size molecules in CTAB; their curves are below the curves of Group A (Figs 1 and 3).

All the ketones of Group B become close to super size molecules in SDS micellar solutions for short LPLS; their curves are higher than that in CTAB and are almost parallel to the line of $\Delta R_f = 0$ (Fig. 3). All the curves show excellent regularity in SDS, the curves from top to bottom are in direct ratio to their length for the super size (Table 1, Fig. 3). However, $p$-nitroacetophenone shows typical super molecular characteristics.

**Solubility and stereo factors of solutes and their contribution to $\Delta R_f$ values**

Under certain conditions, some factors such as molecular inner hydrogen bond and/or solubility of solutes influence the HGC behaviour of ketones. Since the micellar cavities are hydrophobic, the solubility and stereo factors of solute will compete with each other. The characteristics of super and big molecules are dependent on the stereo effect, and those of small or medium sized solutes on the polarity, hydrophobicity or hydrophilicity. The stereo effects are less significant for small molecules but increase in significance for medium sized molecules. It was observed that the hydrophilic - hydrophobic equilibria influence the suitabilities on certain conditions.

The water solubilities of Group B are different (Table 1). In CTAB, the stereo effect of Group B becomes smaller and hydrophilinocity becomes more important. The substituted methyl on benzene ring is a hydrophobic group, so, $p$-methylacetophenone shows higher molecular $\Delta R_f$ values (Fig. 1) and its curve is below the curves of Group A. Group B shows medium sized molecules' characteristics (Fig. 3), and the curves show the competition between stereo effect and hydrophilicity. $p$-Nitroacetophenone shows typical super molecular characteristics for both stereo effect and high hydrophilicity in SDS (Fig. 3).
The same regularity is also shown in Fig. 1. In \( K_2 \) area of CTAB, the values of \( \Delta R_f \) ketones are in the order: \( p \)-phenylacetophenone > phenyl ketone > \( p \)-methylacetophenone in comparison with their lengths (Table 1) for their medium molecular characteristics. However, phenyl ketone shows more super molecular characteristics for its double benzene ring structure which is much more rigid and shows more stereoscopic effect in smaller cavities of SDS micellar solution (Fig. 1).

**Conclusion**

Liquid chromatography, although simple and effective, does not give information about the molecular structures. However, HGC, a novel technique combining the host-guest chemistry and chromatographic methods, gives more structural information on the molecules. Results show that the suitability between the molecular structures of solutes (guest) and the cavities of micelles (host) is the main driving force of chromatographic migration.

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**References**