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Adduct formation between phthalate esters and Li^+ in the gas phase: a thermochemical study by FT-ICR mass spectrometry

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Dedicated to Pierre Longevialle.

Abstract

The lithium-cation basicity (LCB = Gibbs energy of adduct dissociation) of methyl benzoate, and the three isomeric dimethyl phthalates (phthalate, iso- and tere-phthalate) has been determined by Fourier transform ion cyclotron resonance (FT-ICR), using the kinetic method. The dimethyl phthalate ester appears to be a relatively strong base toward Li^+, as compared to the other isomers and to methyl benzoate. This is attributed to the chelation effect of the two carboxyl groups. The previously unknown protonic gas-phase basicity of dimethyl phthalate was also determined. Chelation makes also dimethyl phthalate a much stronger base than the two other isomers toward H^+, but its protonated form decomposes readily by loss of a methanol molecule. (Int J Mass Spectrom 217 (2002) 75–79) © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Adduct; Lithium cation; Phthalate; FT-ICR; Basicity

1. Introduction

Phthalate esters are extensively used as plasticizers in the manufacturing of polyvinyl chloride materials. Most often used are the di-ethylhexyl- and di-isononyl-phthalates, DEHP and DINP, respectively, and consequently cited in the analytical chemistry literature [1–3]. Lower alkyl phthalates are also cited in environmental studies [3–5], as well as toxicity studies [6]. Monomers and oligomers, as well as plasticizers, may be leached from PVC wastes. In the past few years, the use of phthalate plasticizers in toy industry and in the fabrication of medical devices (including bags and tubing used for liquids) has been cited as the cause of deficiencies in infants ([7] and references therein).

It is known that the gas-phase basicity (toward H^+) of a molecule is increased by the presence of two basic functions in a position such that the proton may be chelated, e.g., like in diamines [8] and substituted amidines and guanidines [9]. It was shown by Taft et al. that chelation effects are even more efficient when Li^+ interacts with neutral organic bases [10]. This is apparent when lithium basicity is plotted against proton basicity [11]. The lithium cation accommodates the double interaction more easily than the proton does, because of the longer [Li^+–basic center] distances and the more flexible nature of the electrostatic bonding with Li^+. The *ortho* position of the two carboxyl functions in phthalates suggests that a large chelate effect may be observed. This effect could

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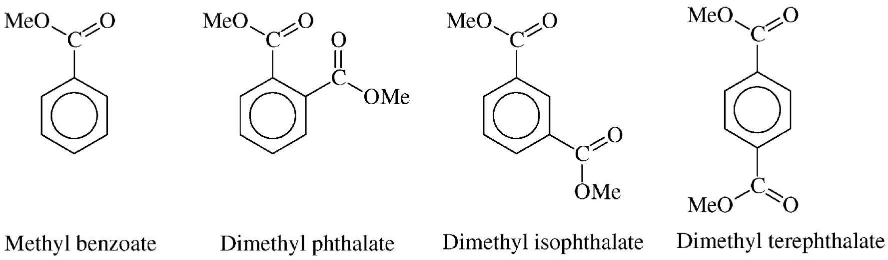


Scheme 1.

be investigated with the aim to differentiate isomers. For example, lithium adducts, obtained by addition of appropriate salts to electrosprayed solutions, may exhibit significant differences in their collision-induced dissociation mass spectra. To determine the efficiency of chelation, we have quantitatively studied the basicity of the three isomeric dimethyl phthalate esters toward Li^+ by Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS), and compared it with their proton basicity. For comparison with the corresponding monofunctional esters, methyl benzoate was studied. The structures of the four esters are given in Scheme 1; note that the conformations shown may not be the most stable.

The corresponding gas-phase properties reported in this work are the Gibbs free energies for the processes:

$$BLi^+ \rightarrow B + Li^+ \tag{1}$$

$$BH^+ \rightarrow B + H^+ \tag{2}$$

defined as lithium-cation basicity, LCB, and gas-phase basicity, GB, respectively.

2. Experimental

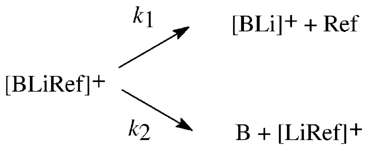
Chemicals were obtained commercially (Aldrich Chemical Co., Fluka Chemical AG) and were used without further purification other than degassing reactants by freeze–pump–thaw cycles in the spectrometer inlet system. The FT-ICR spectrometer, based on an electromagnet (1.6 T) and a Bruker CMS 47 console (Fällanden, Switzerland) [12], has been described previously, as well as its use for LCB determinations, using the kinetic method [13]. Briefly, mixtures of the neutral base to be studied and the reference base (B and Ref, respectively) were introduced in the spectrometer at nominal pressures of 3×10^{-5} to 5×10^{-5} Pa. The lithium cation, generated by laser ablation from a lithium benzoate pellet, was allowed to react with the neutral gases for about 1–2 s. The principal reactions observed were the formation of the simple adducts BLi^+ and $RefLi^+$, and the formation of the dimers $[BLiB]^+$, $[RefLiRef]^+$ and $[BLiRef]^+$. The species of interest, $[BLiRef]^+$, was carefully isolated using a series of ejection pulses, then accelerated by resonant excitation.

After acceleration, the ions were allowed to collide with the neutral gases introduced in the cell (B, Ref, and Ar as the collision gas) at static pressure (5×10^{-4} Pa) during a delay of 12.5 ms. In most cases, the only ionic fragments observed after fragmentation were the lithium-cationized monomers BLi^+ and $RefLi^+$ (Scheme 2).

The kinetic method makes use of the rates of unimolecular dissociation for estimating the relative bond dissociation energies ΔE [14].

In the systems under scrutiny, this will translate into:

$$\ln\left(\frac{k_B}{k_{Ref}}\right) = \ln\left[\frac{I(BLi^+)}{I(RefLi^+)}\right] = \frac{\Delta E}{RT_{eff}} \tag{3}$$



Scheme 2.

where T_{eff} is the effective temperature—not a real thermodynamic temperature but rather a qualitative indication of the degree of excitation of the fragmenting dimer. The rather severe conditions under which the kinetic method applies were discussed in a previous paper [13]. Nevertheless, the empirical validity of Eq. (4):

$$\ln\left(\frac{k_{\text{B}}}{k_{\text{Ref}}}\right) = \ln\left[\frac{I(\text{BLi}^+)}{I(\text{RefLi}^+)}\right] \approx \frac{\Delta\text{LCB}}{RT_{\text{eff}}} \qquad (4)$$

has been verified [15]. The dissociation of the Li^+-bonded dimers, according to Scheme 2, was monitored as a function of the center of mass kinetic energy $E_{\text{k,cm}}$. It was observed that, under our experimental conditions, the dependence of $\ln[I(\text{BLi}^+)/I(\text{RefLi}^+)]$ on $E_{\text{k,cm}}$ was weak (within the collision energy range). Therefore, we use the average of about 10 values of $\ln(k_{\text{B}}/k_{\text{Ref}}) = \ln[I(\text{BLi}^+)/I(\text{RefLi}^+)]$ obtained at different $E_{\text{k,cm}}$. The lower and upper limits of $E_{\text{k,cm}}$ are set by the smallest quantifiable signals for the fragments, and the observation of secondary fragmentations, respectively. The average values of $\ln[I(\text{BLi}^+)/I(\text{RefLi}^+)]$ were translated into ΔLCB, in kJ mol^{-1}, using a $1/RT_{\text{eff}}$ factor of 0.302 [15].

The proton gas-phase basicity of dimethyl phthalate was not found in the literature, and attempts were made to measure its GB using the proton transfer equilibrium method, as described previously [16,17]. This was not completely successful, see discussion, and these measurements were completed by bracketing experiments [17].

3. Results and discussion

The LCB values reported in Table 1 for the four esters were obtained by the kinetic method, from the average of measurements against three reference compounds. The consistency of the overlaps, given by the standard deviation, seems reasonable, and compares well with the precision on individual LCB of references compounds. The proton gas-phase basicity of dimethyl phthalate was not found in the most recent compilation [18]. In fact, during our attempts to determine proton transfer equilibrium constants, we observed a systematic formation of an ion *m*/*z* 163, probably by loss of a methanol molecule. This may explain why there was no report on its gas-phase basicity. Indeed using a series of reference bases, relative basicities could not be obtained with the usual accuracy. Nevertheless, the basicity range was confirmed by bracketing experiments. The GB value of this

Table 1
Lithium-cation basicities (LCBs in kJ mol^{-1}) obtained experimentally by the kinetic method

Compound (B)	Reference (Ref)	LCB(Ref)[a]	ΔLCB[b]	LCB(B)[c]
Dimethyl phthalate	$(\text{EtO})_3\text{PO}$	188.7	+7.67	
	Et_3PO	195.4	+1.65	
	HMPA	198.7	−1.04	197.0 ± 0.8
Dimethyl isophthalate	(*c*-Pr)MeCO	156.5	+1.29	
	$(i\text{-Pr})_2\text{CO}$	156.9	+0.00	
	$(c\text{-Pr})_2\text{CO}$	160.7	−4.22	157.1 ± 0.8
Dimethyl terephthalate	(Et)MeCO	150.6	+1.32	
	$(\text{Et})_2\text{CO}$	153.6	−1.73	
	(*c*-Pr)MeCO	156.5	−4.45	152.0 ± 0.1
Methyl benzoate	$(\text{Et})_2\text{CO}$	153.6	+2.00	
	(*c*-Pr)MeCO	156.5	−1.59	
	$(c\text{-Pr})_2\text{CO}$	160.7	−7.39	154.6 ± 1.4

[a] Literature lithium-cation basicities [11].

[b] Relative lithium-cation basicities obtained using the kinetic method, see text.

[c] Absolute lithium-cation basicities corresponding to the mean of the three experiments carried out for each compound. The uncertainty given is the standard deviation estimated from the range.

Table 2
Gas-phase basicities (GBs in $\mathrm{kJ\,mol^{-1}}$)

Compound (B)	Reference (Ref)	GB(Ref)[a]	ΔGB[b]	GB(B)
Dimethyl phthalate	$MeNH_2$	864.5	$\gg 0$	
	Thiazole	872.1	$\gg 0$	
	i-$PrNH_2$	889.0	$\ll 0$	
	3-Bromopyridine	878.2	$+7.5 \pm 0.3$	
	$(EtO)_3PO$	879.6	-0.9 ± 0.1	
	3-Acetylpyridine	884.3	-2.3 ± 0.4	882.1 ± 4.1[c]
Dimethyl isophthalate				814.3[a]
Dimethyl terephthalate				812.3[a]
Methyl benzoate				819.5[a]

[a] Literature Gibbs energies at 298 K [18], from measurements carried out in our laboratory [19].

[b] Relative GBs at 338 K from proton-transfer equilibrium measurements or bracketing experiments. Reported uncertainties correspond to the standard deviation on two to four determinations of k.

[c] Absolute GBs corresponding to the mean of the three experiments carried out. The given uncertainty is the standard deviation estimated from the range. No temperature correction applied on the ΔGBs measured at 338 K, see text.

compound, along with the already known values for the three other esters, are given in Table 2, and correspond to the protonation of the carbonyl oxygen. The iso- and tere-phthalate molecules have two identical functions, which can be considered independent in first approximation. When proton transfer is realized under equilibrium conditions, the probability for these molecules to be protonated is twice the probability for the monofunctional compound. To estimate the intrinsic substituent effect of the COOMe function, taking methyl benzoate as reference, a statistical correction of $-RT\ln 2 = -1.72\,\mathrm{kJ\,mol^{-1}}$ should be applied to their GB [19]. Therefore, the *meta* and *para* substituent effect of COOMe on the proton basicity of the other COOMe is estimated to be -6.9 and $-8.9\,\mathrm{kJ\,mol^{-1}}$, respectively. This is in good agreement with the electronic effects calculated from the Taft–Topsom equations [20]. On the other hand, the phthalate ester is much more basic than expected, on the ground that *ortho* and *para* substituents exert a roughly similar electronic effe ct. The observed increase in basicity on going from *meta* or *para* isomers to the *ortho* isomer is about $70\,\mathrm{kJ\,mol^{-1}}$. The magnitude of this effect, although approximate owing to experimental difficulties, clearly shows that a chelation effect of the proton is operating here. It will be noted that, within this hypothesis, an entropy decrease upon protonation is expected, which in turn implies a correction to 298 K on ΔGB measured at 338 K. However, such a correction would be well under the experimental uncertainty.

The LCBs were obtained by the kinetic method, and therefore, the statistical correction on symmetrical molecules is not in order. The most stable adducts are supposed to be bonded through a carbonyl–Li^+ interaction. The small range of LCB values and the relative uncertainties make comparisons more uncertain than for GBs. The small decrease of LCB of the terephthalate, relative to methyl benzoate, is expected on the basis of the electronic effects and by analogy with the proton basicities. On the other hand, the isophthalate (*meta* isomer) has a slightly larger LCB than methyl benzoate, although its LCB was expected to be similar to that of terephthalate. The small basicity weakening due to the electron withdrawing substituent effect, may be overcompensated for by some weak unidentified effect. The smallest distance between the two carbonyl oxygens of isophathalate, as in the arbitrary conformation shown on Scheme 2, is not less than 5 Å (0.5 nm). Considering that the distances [Li^+–donor atom] in adducts are usually less than 2 Å, the classical chelation effect seems unlikely. Molecular orbital calculations may help to understand the origin of this irregular behavior. Dimethyl phthalate is a stronger base toward Li^+ than the other esters by 40–$45\,\mathrm{kJ\,mol^{-1}}$. Again, a chelate effect is clearly present. This increase is less than that observed in the case of proton basicity, but corresponds to a larger jump in the relatively compressed LCB scale.

Although a general LCB/GB relationship is not observed [10], linear correlation may be found within homogeneous series of compounds [11]. Even with this restriction, deviations are seen, especially when chelation is possible. When such a linear relationship is established, deviations may be used as an indication for a difference in bonding to Li^+ and H^+. On the basis of our most recent LCB table [11], we have found the following correlation for 1 acid and 11 simple esters, including methyl benzoate, but not the 3 phthalates:

$$\mathrm{LCB} = (0.330 \pm 0.015)\mathrm{GB} - (112.0 \pm 12.1) \qquad (5)$$

data in $\mathrm{kJ\,mol^{-1}}$; correlation coefficient $r = 0.9892$; standard error $s = 2.1\,\mathrm{kJ\,mol^{-1}}$.

The LCB for the three phthalates have been predicted from their GBs using Eq. (3). For the *meta* and *para* isomers, the predicted values, 156.3 and 155.7 $\mathrm{kJ\,mol^{-1}}$, respectively, are close to the experimental data, which seems to indicate a monofunctional behavior toward Li^+. For the *ortho* derivative a value of 178.7 $\mathrm{kJ\,mol^{-1}}$ is obtained. Although there is some uncertainty associated with this estimate, due to the GB uncertainty and the extrapolation out of the range of experimental values used to establish Eq. (3), the difference with the experimental value amounts almost 20 $\mathrm{kJ\,mol^{-1}}$. This is equivalent to the upward deviation in LCB vs. GB plots seen when Li^+ chelation occurs.

In conclusion, dimethyl phthalate is a stronger base in the gas phase than iso- and tere-phthalates on both proton and lithium-cation basicity scales. This is attributed to chelation. The Li^+ cationized phthalate appears to be more kinetically stable than the corresponding protonated form. This observation suggests that cationization by Li^+ or other metal ions would be a promising approach to mass spectrometry studies of the higher phthalate esters homologs of industrial importance and of environmental concern.

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