

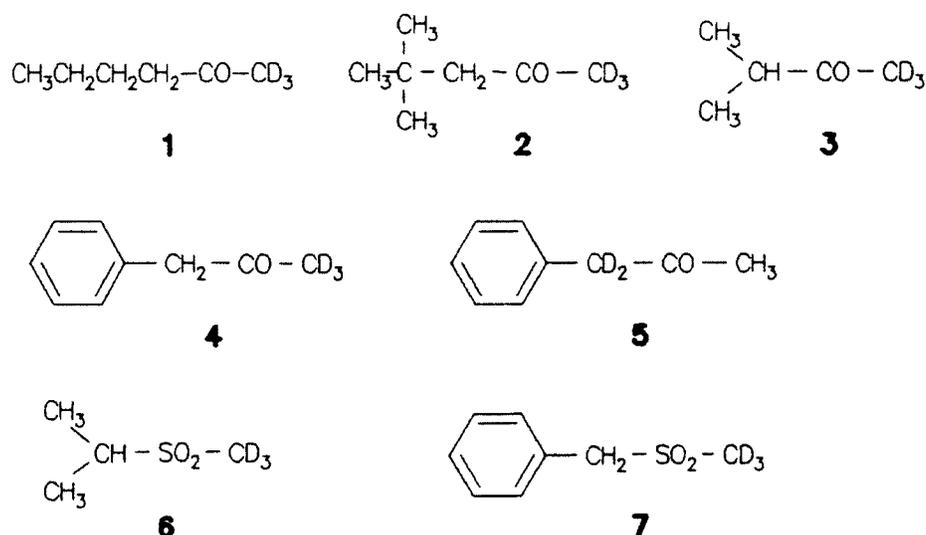
# OMS Letters

Dear Sir,

## REGIO-SPECIFICITY OF THE DEPROTONATION OF SOME ALIPHATIC KETONES AND SULFONES BY NCI

The investigation of negative ions in the gas phase has found considerable interest over the last 15 years<sup>1</sup>, in particular with respect to the  $[M-H]^-$  ions of ketones and sulfones (enolate ions). Unsymmetrical ketones and sulfones with C-H bonds at both  $\alpha$ -positions form two isomeric  $[M-H]^-$  ions which do not isomerize in the gas phase.<sup>1</sup> For an understanding of the gas phase chemistry of these enolate ions, it is important to know the factors influencing the formation of the isomeric ions. The  $[M-H]^-$  ions are easily generated in the gas phase by a deprotonation via chemical ionization by  $HO^-$  or  $NH_2^-$ , and the relative abundances of the isomeric enolates in the mixture can be determined by using specifically deuterated substrates. It has been shown for 2-pentanone-1,1,1-d<sub>3</sub>, that the  $H^+$ - and  $D^+$ -abstraction are observed in a statistical ratio<sup>2</sup>. However, it is not known whether a statistical deprotonation will always occur during NCI and whether special kinetic or thermodynamic effects will determine the relative abundances of the isomeric  $[M-H]^-$  ions.

We have studied the regioselectivity of the deprotonation of some ketones and sulfones during NCI using a VG ZAB-2F mass spectrometer<sup>3</sup> and the deuterated compounds shown in Scheme 1. The results are represented in Table 1, where the ratio  $q$  is statistically corrected for the deprotonation at the two acidic sites of the keto and sulfone group, respectively, relative to a deprotonation at the  $CD_3$  group but neglecting isotope effects.



Scheme 1

*A priori* thermodynamic control of the deprotonation under CI conditions is expected, and the relative abundances of the isomeric  $[M-H]^-$  ions should be determined by the heats of formation,  $\Delta H_f([M-H]^-)$ , and the local gas phase acidities of the  $\alpha$ -C-H groups. Some thermodynamic data pertinent to this are given in the Tables 2 and 3.

**Table 1:** Relative abundances of isomeric  $[M-H]^-$  ion by deprotonation with  $NCI(OH^-)$

comp.	$[M-H]^-/[M-D]^-$	q	comp.	$[M-H]^-/[M-D]^-$	q
<b>1</b>	1 : 1.7	1.1	<b>2</b>	1 : 1.3	0.9
<b>3</b>	1 : 31.3	10.4	<b>5</b>	1 : 2.3	3.5
<b>4</b>	2.5 : 1	3.8	<b>7</b>	1.5 : 1	2.2
<b>6</b>	1 : 4.3	1.4			

MNDO favours the secondary enolates over the primary ones by c. 40 kJ. mol<sup>-1</sup> in the case of 2-hexanone and of 4,4-dimethyl-2-pentanone. Similarly, the tertiary enolate generated from 3-methyl-2-butanone is more stable than the primary isomer by c. 70 kJ.mol<sup>-1</sup> (Table 2). However, both 2-butanone and 3-pentanone are more acidic than acetone by only c. 8 kJ.mol<sup>-1</sup> (Table 3) although 3-pentanone forms only a secondary enolate. 3-Methyl-2-butanone may form a tertiary enolate and shows a further increase in the gas phase acidity by merely c. 2 kJ.mol<sup>-1</sup>. In fact, these small effects may be due to an increased stability of the anions due to an increased polarizability of the larger ions, even if primary enolates are formed in each case. Hence, it is difficult to predict correctly thermodynamic effects on the generation of isomeric enolates in the gas phase, although it has been claimed that methyl substitution at the acidic C-H groups of ketones increases the gas phase acidity whereas a decrease is observed for the  $\alpha$ -methylation of sulfones.<sup>4</sup>

The q-value for the 2-hexanone **1** corresponds within the limits of error to a statistical abstraction of H<sup>+</sup> and D<sup>+</sup>, in agreement with the results of Donnelly et al.<sup>2</sup> This agrees with the expectations derived from the gas-phase acidities of ketones (Table 2) and, obviously, the formation of isomeric enolate ions from ketones with primary and secondary  $\alpha$ -C-H-bonds is thermodynamically controlled. This is corroborated by the deprotonation of the deuterated 4,4-dimethyl-2-pentanone **2** exhibiting again a statistical abstraction of H<sup>+</sup> and D<sup>+</sup> to form primary and secondary enolates. A steric effect of the tert.butyl group at the  $\alpha$ -position expected for a *kinetic* control of the deprotonation is *not* observed. Furthermore, identical results are obtained for the deprotonation of **2** by  $NCI(OH^-)$ ,  $NCI(F^-)$  and  $NCI(NH_2^-)$  showing that the strength of the base has no influence on an exothermic deprotonation in accord with a thermodynamically controlled reaction. However, these experimental results are in conflict with the MNDO calculations. Clearly, MNDO can not be used reliably to calculate the stability of enolate ions.

**Table 2:**  $\Delta H_f([M-H]^-)$  [kJ.mol<sup>-1</sup>] calculated by MNDO<sup>5</sup> of the isomeric enolates of ketones 1 - 5 and sulfones 6 - 7.

enolate ion	$\Delta H_f$	enolate ion	$\Delta H_f$
$[\text{CH}_3(\text{CH}_2)_2\text{CH}_2\text{-CO-CH}_3]^-$	-247.7	$[\text{CH}_3(\text{CH}_2)_2\text{CH-CO-CH}_3]^-$	-287.9
$[(\text{CH}_3)_3\text{C-CH}_2\text{-CO-CH}_2]^-$	-213.0	$[(\text{CH}_3)_3\text{C-CH-CO-CH}_3]^-$	-253.5
$[(\text{CH}_3)_2\text{CH-CO-CH}_2]^-$	-213.0	$[(\text{CH}_3)_2\text{C-CO-CH}_3]^-$	-283.3
$[\text{C}_6\text{H}_5\text{-CH}_2\text{-CO-CH}_2]^-$	-75.3	$[\text{C}_6\text{H}_5\text{-CH-CO-CH}_3]^-$	-164.0
$[(\text{CH}_3)_2\text{CH-SO}_2\text{-CH}_2]^-$	+322.2	$[(\text{CH}_3)_2\text{C-SO}_2\text{-CH}_3]^-$	+259.0
$[\text{C}_6\text{H}_5\text{-CH}_2\text{-SO}_2\text{-CH}_2]^-$	+486.2	$[\text{C}_6\text{H}_5\text{-CH-SO}_2\text{-CH}_3]^-$	+396.6

**Table 3:** Gas phase acidities<sup>6</sup> [kJ.mol<sup>-1</sup>] of some ketones and sulfones.<sup>4</sup>

ketone/sulfone	$\Delta H_{\text{acid}}$	ketone/sulfone	$\Delta H_{\text{acid}}$
$\text{CH}_3\text{COCH}_3$	1548.3	$\text{CH}_3\text{CH}_2\text{COCH}_3$	1540.8
$\text{CH}_3\text{CH}_2\text{COCH}_2\text{CH}_3$	1540.8	$\text{C}_6\text{H}_5\text{CH}_2\text{COCH}_3$	1476.7
$\text{C}_6\text{H}_5\text{SO}_2\text{CH}_3$	1517.5	$\text{C}_6\text{H}_5\text{SO}_2\text{CH}_2\text{CH}_3$	1525.1

For the ketone 3 producing primary as well as tertiary  $[M-H]^-$  ions, the abstraction of  $\text{H}^+$  from the terminal methyl group is preferred by a factor of 10. In the absence of any steric effects this result establishes a distinctly *decreased* acidity of the *tertiary*  $\alpha\text{-C-H}$  group. This is again largely at variance with the MNDO calculation predicting the tertiary enolate to be more stable than the primary one by as much as 70 kJ.mol<sup>-1</sup>. R. R. Squires has generated both isomeric enolate ions of 3-methyl-2-butanone in an elegant experiment via a decarboxylation of the corresponding keto carboxylate ions under CID conditions<sup>7</sup>. Subsequently, the enolate ions have been equilibrated by a reaction with methanol, and a strong predominance of the primary enolate in the equilibrium mixture is observed<sup>7c</sup> in agreement with our results. Clearly, a tertiary enolate is less stable than a primary one, and the 10 kJ.mol<sup>-1</sup> difference of the gas-phase acidities<sup>5</sup> of acetone and 3-methyl-2-butanone reflect the increase of the polarizability with the size of the  $[M-H]^-$  ion stabilizing also the primary enolate.

However, the preferred formation of the secondary enolate from the isotopomeric phenylacetones 4 and 5 is undoubtedly due to the exceptional stability of a benzyl anion, although this effect is again certainly exaggerated by the MNDO calculations (Table 2). The results agree with the increase of the gas phase acidity of benzyl methyl ketone (Table 3). Note that a rather small isotope effect of  $k_{\text{H}}/k_{\text{D}} = 1.1$  is obtained for the deprotonation by a comparison of 4 and 5 as expected for a thermodynamical control of the reaction. In the case of acetone-d<sub>3</sub> an isotope effect of 1.5 was observed.<sup>8</sup>

The gas phase acidities of ketones and sulfones are rather similar, but an increasing  $\alpha$ -methyl substitution at the acidic site of a sulfone decreases its acidity.<sup>4b</sup> In our experiments the corresponding sulfones and ketones **6** and **3** and **7** and **4**, respectively, behave in a qualitatively similar manner, but the regiospecificity of the deprotonation is distinctly less for the sulfones (Table 1). In particular, the dramatic discrimination of the tertiary enolate of the ketone **3** is not found for the sulfone **6** exhibiting only a moderate preference for the formation of the primary  $\alpha$ -sulfonyl carbanion. Very likely the (thermodynamic) stability of the ketone enolates is mostly due to a  $\pi$ -conjugative effect forcing the enolate into a planar configuration at the  $\alpha$ -C atom whereas the stabilization of an  $\alpha$ -sulfonyl carbanion has less stringent steric requirements. The resonance structure of the tertiary enolate of **3** corresponds to a tetrasubstituted ethen, and it is possible that this sterically unfavourable situation prohibits a planar configuration at the  $\alpha$ -C atom and diminishes the resonance stabilization of the tertiary [M-H]<sup>-</sup> ion in the case of the ketone **3** much more than in the case of the sulfone **6**.

Yours sincerely

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