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^{17}O chemical shifts and deuterium isotope effects on ^{13}C chemical shifts of intramolecularly hydrogen-bonded compounds

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ABSTRACT: ^{17}O chemical shifts were measured in 40 enamines activated in the β-position by C=O, COO, NO_2, SO and SO_2 groups. Data for the oxygen-containing series of *o*-hydroxyacyl aromatics are also included for comparison. Intramolecular hydrogen bonding in the enamines is discussed in terms of the acceptor and donor groups and the separating link. ^{17}O chemical shifts, the two-bond deuterium isotope shifts on C-α ^{13}C shifts and ^{1}H NH or OH chemical shifts are correlated to show the interrelations of these parameters in elucidating intramolecular hydrogen bonds and their strength in a wide variety of compounds. ^{17}O chemical shifts in open-chain compounds are shown to reflect intramolecular hydrogen bonding by a change to lower frequency whereas for five-membered rings steric effects cause higher frequency chemical shifts. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: ^{17}O chemical shifts; intramolecular hydrogen bonding; isotope effects; enamino ketones; enamino esters; enamino lactones; β-nitroenamines; β-sulfinylenamines; β-sulfonylenamines

INTRODUCTION

Intramolecular hydrogen bonding (RAHB, resonance-assisted hydrogen bonding)[1,2] (Fig. 1) as discussed in this paper can be described by three factors, the acceptor, the donor and the link (the double bond).[3] For systems in which oxygen is the acceptor, it is relevant to study ^{17}O chemical shifts to add to the information available from OH ^{1}H chemical shifts,[4] $^{n}\Delta$C(YD) (Y = O),[2,3,5–8] $^{1}\Delta$N(D)[2] (Y = N) and $^{1}\Delta^{13}$C(^{18}O) (X = C) isotope effects.[9]

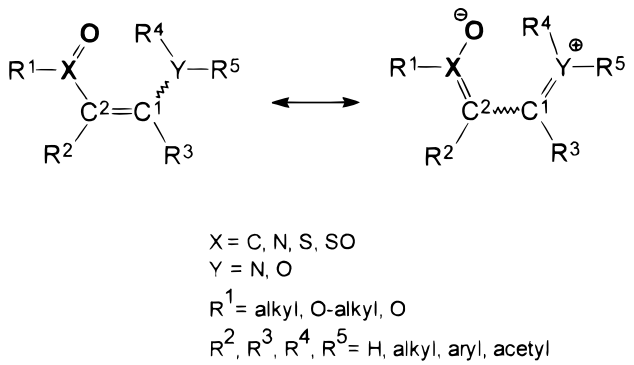

Figure 1. Resonance-assisted hydrogen bonding (RAHB). For alkyl chains of R[1] the carbons are numbered α', β', γ', etc. Olefinic carbon atoms are numbered 1 and 2 from the nitrogen substituent.

Hydrogen bonding has been shown to influence C=^{17}O chemical shifts,[10–25] and the effect has been described in terms of the acidity of the donor,[23] the basicity of the acceptor,[23] a twist of the acceptor group[16] and in-plane distortions.[17,18] The OH chemical shifts of intramolecularly hydrogen-bonded phenols vary somewhat,[14,17,19–21] and recent data for indane-1, 3-diones show larger variations in enols.[22] Steric effects could also play a role.[9] ^{17}O chemical shifts show a large dispersion[10] in general and have therefore been used to estimate equilibrium constants of tautomeric systems such as β-diketones.[26–28] One problem in using ^{17}O chemical shifts in tautomeric systems is to obtain proper limiting ^{17}O chemical shifts.[28]

Hydroxyl ^{1}H chemical shifts and $^{2}\Delta$C(OD) isotope effects may be used to describe the strength of hydrogen bonds.[5–9] A first goal of this work was to establish a quantitative relationship between hydrogen bond strength and ^{17}O chemical shifts.

Comparatively little has been done to investigate C=^{17}O chemical shifts in intramolecularly hydrogen-bonded systems in which this group is an acceptor and NH groups are donors. Studies of *o*-aminoacetophenone[16] and 1-aminoanthraquinone and 1-aminofluorenone[18] revealed very small hydrogen bond effects. Very recently effects have been studied in a series of *N*-phenyl-substituted enamino ketones.[24,25] Enamino ketones and enamino esters are good model

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systems in such studies as some of them can exist both as the hydrogen-bonded *Z*-isomers and non-hydrogen-bonded *E*-isomers.

^{17}O chemical shifts have so far not been investigated to any large extent for sulfoxides.[29] The *β*-sulfinylenamines seem a very good choice as they too in some instances can exist as both *E*- and *Z*-isomers.[30,31]

RESULTS AND DISCUSSION

A number of enamino ketones, nitroenamines, enamino lactones, sulfinylenamines and sulfonylenamines (Fig. 1) were investigated. As stated above, they exist as both *E*- and *Z*-isomers.

The characterization of *E*- and *Z*-isomers was based on NH chemical shifts and $^{2}\Delta$(ND) isotope effects[2,3] and these characterizations were used to assign ^{17}O resonances for those cases in which one isomer clearly dominates over the other, taking into account variations caused by different concentrations or different temperature (Table 1).

The stereochemistry of *β*-sulfinylenamines has been much debated,[30,31] but recent studies have revealed that they exist as the *E*-isomers[31] and the later discussion of substituent effects is based on this assumption.

Assignment of ^{17}O resonances

It was previously reported that the carbonyl oxygen resonance is narrower when hydrogen bonded.[12] This is also seen for a number of compounds in this study (**5**, **6**, **12**, **16** and **19**), meaning that the oxygen resonance of the *Z*-isomer is narrower than that of the *E*-form. This feature was used to make tentative *E*/*Z* assignments of the ^{17}O resonances in compounds which existed as a 1:1 mixture of *E*- and *Z*-isomers. For **1**–**4** the ^{17}O linewidths of the hydrogen-bonded and non-hydrogen-bonded isomer are comparable but for **4** the hydrogen-bonded form exhibits a broader line. Compounds **4** and **7** have the *N*-phenyl group in common. The *N*-substituent is in this case the benzyl group. *tert*-Butyl and benzyl groups show very broad resonances for the *β*-sulfinylenamines (**18**, **24**, **27** and **31** in Table 1). For the benzyl analog of **33** the resonances were so broad that they could not be detected. Hence for these compounds with large substituents at nitrogen the bulk effect may in some instances overshadow the hydrogen bond effect and make the use of linewidths for the assignment of ^{17}O resonances of hydrogen-bonded resonances less useful.

For **1**, **2** and **4** the hydrogen bond is relatively strong, judging from *δ*NH in Table 1 and the hydrogen-bonded carbonyl ^{17}O resonance which is shifted to higher frequencies.

For the nitro compound **15**, no assignments of the two closely lying resonances have been made. For the sulfones **39**–**40** no attempt was made to assign the signals because the resonances have comparable linewidths and very similar resonance frequencies.

The majority of the ^{17}O NMR spectra were recorded at 300 K despite the fact that in most cases this leads to broad ^{17}O resonances. The reason was the instability of the sulfinylenamines at higher temperatures. As judged from a comparison at 300 and 337 K (see **2**, **5** and **10**), the chemical shifts are different, but so are the solvents. The comparisons made in the following are at identical temperatures. Concentration also has an effect, as seen for **33** and **2**.

^{17}O chemical shift correlations for *o*-hydroxyacyl aromatics

An objective of this work was to study effects of intramolecular hydrogen bonding on chemical shifts and related parameters [$^{2}\Delta$C(OD)] of nuclei in the neighbourhood of the hydrogen bond.

There were precedences in the literature showing that changes induced by hydrogen bonding on ^{17}O chemical shifts [$\Delta\delta(C{=}^{17}O)$] correlated with YH chemical shifts[12,24] but no studies of such correlations have been presented with two-bond isotope effects [$^{2}\Delta$C(OD)].

Therefore, we gathered from the recent literature[7,11,12,14,19] relevant data for intramolecularly hydrogen-bonded carbonyl groups with a hydroxy group as donor, in *o*-hydroxyacyl aromatic compounds, including 2-acylindane-1,3-diones, combined them with our own data and searched for correlations. The correlation equations and related statistics are given below from linear regression analysis of the data.

$$\delta(C{=}^{17}O)(\pm 10.8) = 694.1(\pm 33.2) - 16.7(\pm 2.7)\delta(OH) \quad (1a)$$

$R_{18} = -0.838$ (for ketones and aldehydes)

$$\delta(C{=}^{17}O)(\pm 13.9) = 590.4(\pm 30.0) - 13.9(\pm 2.3)\delta(0H) \quad (1b)$$

$R_{6} = -0.944$ for (2-acylindane-1,3-diones)

$$\delta(C{=}^{17}O)(\pm 11.7) = 554.1(\pm 12.0) - 214.1(\pm 39.4)^{2}\Delta C(OD) \quad (2a)$$

$R_{18} = -0.806$ (for aldehydes and ketones)

$$\delta(C{=}^{17}O)(\pm 13.1) = 477.9(\pm 13.1) - 130.9(\pm 24.1)^{2}\Delta C(OD) \quad (2b)$$

$R_{6} = -0.953$ for (2-acylindane-1,3-diones)

^{17}O chemical shifts of *o*-hydroxyacetophenones, measured in this work and included in the above correlations, are as follows: $\delta(C{=}^{17}O)$, $\delta\,^{17}OH$, $\delta\,^{17}OR$ for 2-hydroxy-5-methoxyacetophenone = 487, 75, 35 ppm, for 5-fluoro-2-hydroxyacetophenone = 493, 79 ppm and for 2-hydroxy-3-methoxyacetophenone = 485, 71, 32 ppm. A correlation between the parameter $^{2}\Delta$C(OD) [defined as the difference between $\delta(C{=}^{17}O)$ of a deriv-

Table 1 .^{17}O NMR chemical shifts (δ) and line halfwidth ($w_{1/2}$, Hz) of enamines R^1—X(=O)—CR^2=CR^3—NR^4R^5 [a]

No.	R^1	X	R^2	R^3	R^5	C[b]	δ_E	w_E	δ_Z	w_Z	δ_{NH}	$^2\Delta$C(ND)	t(°C)	Solvent
1	Me	C	Ac	H	H	2.5	502.7	484	482.7	497	10.3/6.4		60	$CDCl_3$ + MeCN[c]
2	Me	C	Ac	H	Me	1.5	491.0	705	457.0	666	9.5		27	$CDCl_3$
2	Me	C	Ac	H	Me	2.5	497.7	484	467.0	432			60	$CDCl_3$ + MeCN[c]
3	Me	C	Ac	H	Et	2.5	494.0	340	464.0	365			60	$CDCl_3$ + MeCN[c]
4	Me	C	Ac	H	Ph	2.5	516.8	587	482.4	649	12.8	0.324	60	$CDCl_3$ + MeCN[c]
5	Et	C	Me	H	Me	2.8	446.0	543	421.0	200	9.5/4.3	0.280/0.100	27	$CDCl_3$
5	Et	C	Me	H	Me	2.5	460.4	800	433.4	420			60	$CDCl_3$ + MeCN[c]
6	Et	C	Me	H	Et	2.5	442.0	569	418.0	200	9.7/4.5	0.272/0.104	27	$CDCl_3$
6	Et	C	Me	H	Et	2.5	462.2	795	433.8	560			60	$CDCl_3$ + MeCN[c]
7	Et	C	Me	H	Ph	2.5	464.2	637	436.1	697			60	$CDCl_3$ + MeCN[c]
8	Me	C	Me	H	Bn	2.5	472.4	501	444.2	647			60	MeCN
9	Et	C	H	H	Et	2.8			421.0[d]	530			27	$CDCl_3$
10	Me	C	H	Me	*n*-Pr	2.7			401.0[d]	528	9.5	0.259	27	$CDCl_3$
10	Me	C	H	Me	*n*-Pr	2.5			412.0	484			60	$CDCl_3$ + MeCN[c]
14	O	N	Me	H	2′-$C_4H_3N_2$	0.3			551.0[d]	1200	10.7	0.215	27	$CDCl_3$
15	O	N	Me	H	Ph	2.5	535.8		544.7				60	MeCN
16	EtO	C	H	Me	Me	2.5			296.9	439			60	$CDCl_3$ + MeCN[c]
16	EtO	C	H	Me	Me	2.5			289.0[d]	442	8.5	0.165	27	$CDCl_3$
17	EtO	C	H	H	Ph	2.5			299.0	622			60	$CDCl_3$ + MeCN[c]
18	EtO	C	H	Me	Bn	0.9			292.0[d]	704	9.0		27	$CDCl_3$
23	Me	S	H	H	Me	0.6	45.0	350					27	$CDCl_3$
24	Me	S	H	H	Bn	0.8	50.0	860			4.8		27	$CDCl_3$
25	Me	S	Me	H	*t*-Bu	0.5	30.0	680			4.0		27	$CDCl_3$
26	Et	S	Me	H	Me	0.6	23.0	403					27	$CDCl_3$
27	Ph	S	H	H	Bn	0.4	37.0	3000			4.8		27	$CDCl_3$
28	Ph	S	Me	H	*t*-Bu	0.4	16.0	750			4.0	0.097	27	$CDCl_3$
29	*t*-Bu	S	H	H	*t*-Bu	0.7	24.0	950			6.2/4.5	0.111/0.091	27	$CDCl_3$
30	*t*-Bu	S	Me	H	*t*-Bu	0.6	4.0	720			3.8		27	$CDCl_3$
31	*t*-Bu	S	H	Me	Bn	0.5	20.0	1000			4.4	0.083	27	$CDCl_3$
32[e]	CH_2	S	H	CH_2	Et	0.8	62.0	790			4.4		27	$CDCl_3$
33[e]	CH_2	S	CH_2CH_2	H	*t*-Bu	0.8	48.0	590			3.9		27	$CDCl_3$
33[e]	CH_2	S	CH_2CH_2	H	*t*-Bu	0.4	46.0	600			3.9		27	$CDCl_3$
39[f]	Me	S=O	H	Me	Bn	0.5	165.7[g]	190	164.0[g]	190	7.7/5.7	0.110/0.090	27	MeCN
40[f]	Me	S=O	H	Me	*i*-Pr	0.5	166.1[g]	190	164.0[g]	190	7.7/5.2	0.100/0.070	27	MeCN

[a] R^4 = H, except for **23** and **26**, where R^4 = CH_3 . Bn = benzyl; 2′-$C_4H_3N_2$ = 2-pyrimidyl.
[b] mol dm^{-3}.
[c] Mixture 1 : 1 (v/v).
[d] The *Z*- and *E*-isomers were assigned on the basis of δ_{NH} and $^2\Delta$C(ND) isotope effects.
[e] CH_2 groups are connected to form a five-membered ring.
[f] Imines were found at 160 ppm.
[g] Not assigned. It can be interchanged with another isomer.

ative lacking OH in the *ortho* position to the carbonyl group (reference compound) and the chemical shift of a compound *ortho*-substituted with an OH group] and δOH revealed that for 2-hydroxy-1-acetylnaphthalene the data points falls severely off the correlation line because of the conformational difference in the carbonyl group between the hydrogen-bonded compound and the reference compound.

Although the correlation coefficients are not very high, nevertheless, the above equations indicate an interrelationship of the NMR parameters in the environment of the hydrogen bond.

Enamino ketones and enamino esters

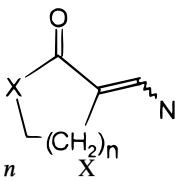
The conformational difference between the intramolecular hydrogen-bonded compounds and the reference compounds is a problem when the effect of hydrogen bonds is discussed. Such a situation occurs for the hydrogen-bonded enamines if, e.g., α,β-unsaturated ketones were used as a reference, as the carbonyl groups of these typically would be in an *s-trans* position to the double bond. Therefore, for the enamines **1**–**4** we used the non-hydrogen-bonded carbonyl oxygen as a reference and, for those compounds existing as both *Z*- and *E*-isomers, the ^{17}O chemical shifts of the latter were used as references in the determination of hydrogen bonding.

The data in Table 1 show that $\Delta\delta\,^{17}O_{HB}$ for **2**, **5** and **9** are much larger in the open system than in the *o*-aminoacetophenone derivatives ($\Delta\delta\,^{17}O_{HB}$ is estimated to be 5 ppm to lower frequency in 2-methylaminoacetophenone[16]), in accordance with the stronger hydrogen bonding in the olefinic systems.[3]

A comparison of **5-*Z*** and **9-*Z*** shows that the γ-effect for the 2-CH_3 group is close to zero whereas a comparison of **6-*Z*** and **9-*Z*** gives a γ-effect 3 ppm to lower frequency. γ-Effects of aliphatic ketones are 5 ppm to higher frequency. A comparison of the ^{17}O chemical shifts of **5-*Z*** and **10-*Z*** measured in $CDCl_3$ gives a difference of 20 ppm. This could in principle be due to a γ-effect caused by the extra methyl group at the β'-position of **5** but, judging from simple ketones[32] and α,β-unsaturated ketones,[33] this effect should be in the opposite direction. The difference cannot be ascribed to a stronger hydrogen bond [δNH and $^2\Delta$C(ND) are similar] but can probably be ascribed to a smaller twist[14,34] of the carbonyl group in **10-*Z***. A comparison of ^{17}O chemical shifts of **6** and **8**, measured under the same experimental conditions, gives a γ-effect of -10 ppm to lower frequency, regardless of the configuration, a value similar to the -13 ppm found for aliphatic ketones.[32]

The data for cyclic compounds are given in Table 2. The cyclohexanone derivative **13** exists only in the *Z*-form, judging from the two-bond isotope effect, $^2\Delta$C(ND). The cyclopentanone derivative **11** exists as a mixture of *E*- and *Z*-isomers in the ratio 1:1. A difference in ^{17}O chemical shifts of 17 ppm between the two isomers was observed. As the isomers occur in equal proportions, the assignment of the ^{17}O signals had to be estimated by internal comparison. As the five-membered ring leads to weaker hydrogen bonding,[3] the smaller difference found compared with the open-chain compounds seems reasonable. For the lactone **19** the ^{17}O resonance of the *E*-isomer is also shifted to higher frequency than the *Z*-isomer, as found for the five-membered cyclic ketones. This can be ascribed to

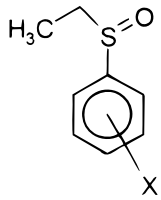
Table 2. Chemical shifts of cyclic enaminones and enaminoesters in $CDCl_3$–CH_3CN (1:1)



No.	*n*	X	R	^{17}O=C chemical shifts (ppm)	^{17}O linewidths (Hz)	N*H* chemical shifts (ppm)	$^2\Delta$C(ND) (ppm)
11-*Z*	1	CH_2	CH_3	414	240	8.48[a]	0.224[a]
11-*E*	1	CH_2	CH_3	397	375	5.20[a]	0.127
12-*Z*	1	CH_2	Ph	449	614	10.75[b]	0.270
12-*E*	1	CH_2	Ph	434	921	7.5[b]	0.140
13-*Z*	2	CH_2	Ph	457	827		
						11.9[a]	0.361[a]
				453[c]	650[c]		
19-*Z*	1	O	CH_3	288	200	8.2[a]	0.162[a]
19-*E*	1	O	CH_3	265	280	4.92[a]	0.117[a]
20-*E*	1	O	Ph	283 (163[d])	922 (666[d])	8.1[b]	0.156[a]
21-*E*	1	O	CH_2Ph	272 (160[d])	639 (466[d])	5.8[b]	0.120
22-*E*	1	O	$CH(CH_3)$Ph	278 (158[d])	424	4.95[a]	0.111[a]

[a] NH chemical shifts and $^2\Delta$C(ND) are taken from Ref. 3.
[b] Solvent CH_3CN, temperature 333 K.
[c] Solvent $CDCl_3$, temperature 300 K.
[d] Alkoxy oxygen atom.

Table 3. ^{17}O chemical shifts of aromatic sulfoxides in $CDCl_3$ (relative to external water)



No.	X	^{17}O=S chemical shifts (ppm)[a]	^{17}O linewidths (Hz)
34	*p*-$NH(CH_3)$	1 (−2)	479
35	*o*-$NH(CH_3)$	−1 (2)	446
36	*p*-$N(CH_3)_2$	0	329
37	*o*-$N(CH_3)_2$	−21 (−17)	471
38	H	−4[b]	420[b]

[a] Numbers in parentheses refer to C_6D_6 as solvent.
[b] Compound **38** was measured in CH_2Br_2. Taken from Ref. 29.

poorer intramolecular hydrogen bonding of the carbonyl on the ring for the *Z*-isomer. The hydrogen bond effect is thus overshadowed by steric effects, as also seen for **26** (see below).

β-Sulfinylenamines

^{17}O chemical shifts of aromatic sulfoxides are given in Table 3. A comparison of the data for **34**, **36** and **38** indicates that little electronic effect is transmitted from the NR_2 groups to the sulfoxide oxygen atom. Twist angles for **34**, **35** and **37** were obtained from MMX calculations[35] (Table 4). These show two low-energy conformations of a sulfinyl group of **34**, **35** and **37** [*p*-$NHCH_3$, *o*-$NHCH_3$ and *o*-$N(CH_3)_2$ isomers, respectively]. The $N(CH_3)_2$ group is twisted *ca.* 64° out of the plane of the benzene ring, but the twisting of the $NHCH_3$ group is negligible. It can be assumed that the −21 ppm chemical shift in **37** relative to **36** results primarily from steric interaction between sulfinyl and $N(CH_3)_2$ moieties through space rather than through the aromatic ring. This conclusion is reached from comparison of the ^{17}O shift in **38** with that in **34** or **36**, showing that conjugation of the $NHCH_3$ or $N(CH_3)_2$ group does not change the ^{17}O chemical shift much. Steric interaction should be much smaller for the $NHCH_3$ group because of a much smaller twist. A comparison of the chemical shifts of **34** and **35** reveals no effect of hydrogen bonding.

The acyclic sulfoxide **29** exists as *E*- and *Z*-isomers, with no discernible difference in ^{17}O chemical shifts between the two forms (most probably due to overlap of the weak signal of the *Z*-form with that of the *E*-form), indicating that the weak hydrogen bond of the latter (see deuterium isotope effects, Table 1) has no effect, as also observed for the aromatic compounds in Table 3.

A comparison of the ^{17}O chemical shifts of **29** and **30** gives a γ-effect caused by the β-methyl group of 20 ppm to lower frequency (Table 1). Similar effects are found by comparing the data for **24** and **25** or **27** and **28**. Based on these comparisons, it is also seen that substituents on nitrogen play a similar role.

Comparison of the ^{17}O chemical shifts of **23** and **24** revealed that going from an NHR group to an $N(CH_3)_2$ group caused a high-frequency shift of 5 ppm (Table 1), in contrast to the *ca.* 1 ppm for aromatic compounds (**34** *vs.* **36**, Table 3).

A comparison of the ^{17}O chemical shifts for **26** and **33** gives a 25 ppm shift to higher frequency upon ring formation. This is opposite to the shift to lower frequency for ketones.

A comparison of the data for **24** and **29** gives a shift of 26 ppm to lower frequencies from three methyl groups in the γ′-position. This γ-effect is of opposite sign for ketones and sulfoxides (see above), whereas the γ-effect caused by methyl substitution at C-2 is large and negative for the sulfoxides (−20 ppm) compared with *ca.* −3 ppm for ketones. The explanation of the above marked differences in the ketone and sulfoxide series is not clear.

Hydrogen bonding

As can be seen in Fig. 2(a), δNH and δC=^{17}O correlate for a broad range of intramolecularly hydrogen-bonded compounds (*Z*-) including ketones, esters, nitro com-

Table 4. MMX parameters for aromatic sulfoxides[a]

No.	Energy (kcal/mol)	O···HN (Å)	O—S—C^2—C^1 (°)	LP—S—C^2—C^1 (°)	H—N—C^1—C^2 (°)
34	0.41		−139.8	−10.6	−1.0
	0.39		31.7	161.3	0.1
35	3.70		−149.4	−14.5	3.3
	2.99	2.05	33.8	163.2	−4.3
37	9.74		−144.8	−15.3	64.3
	11.86		23.5	153.7	83.7

[a] Total strain energy (kcal/mol) and torsion angles along given bonds are cited. Numbering of aromatic carbons conforms with that in the enamine chain (see Fig. 1).

pounds, sulfoxides and sulfones. The correlations for *Z*- and *E*-compounds are described by Eqns (3) and (4), respectively:

$$\delta(\mathrm{C{=}^{17}O})(\pm 149) = -620.5(\pm 104.5) + 107.3(\pm 11.7)\delta(\mathrm{NH})$$
$$R_{11} = = 0.946 \quad (3)$$
$$\delta(\mathrm{C{=}^{17}O})(\pm 150) = -337.7(\pm 219.9) + 114.6(\pm 43.4)\delta(\mathrm{NH})$$
$$R_{16} = 0.591 \quad (4)$$

The data for the *E*-forms, which do not have hydrogen bonds, clearly fall on a separate line. The spread is more marked, possibly because the NH chemical shifts of the non-hydrogen-bonded NH proton are prone to solvent and concentration effects, in contrast to the *Z*-derivatives. On the other hand, the effect of intermolecular hydrogen bonding on ^{17}O chemical shifts is small (see below). Comparison of the two plots shows that changes in the electron-withdrawing power of an acceptor (**R—S=O < R—SO$_2$ < O=C(OR)— < O=C(R)— < O=N(O)—** induces changes in the strength of hydrogen bonding, reflected in chemical

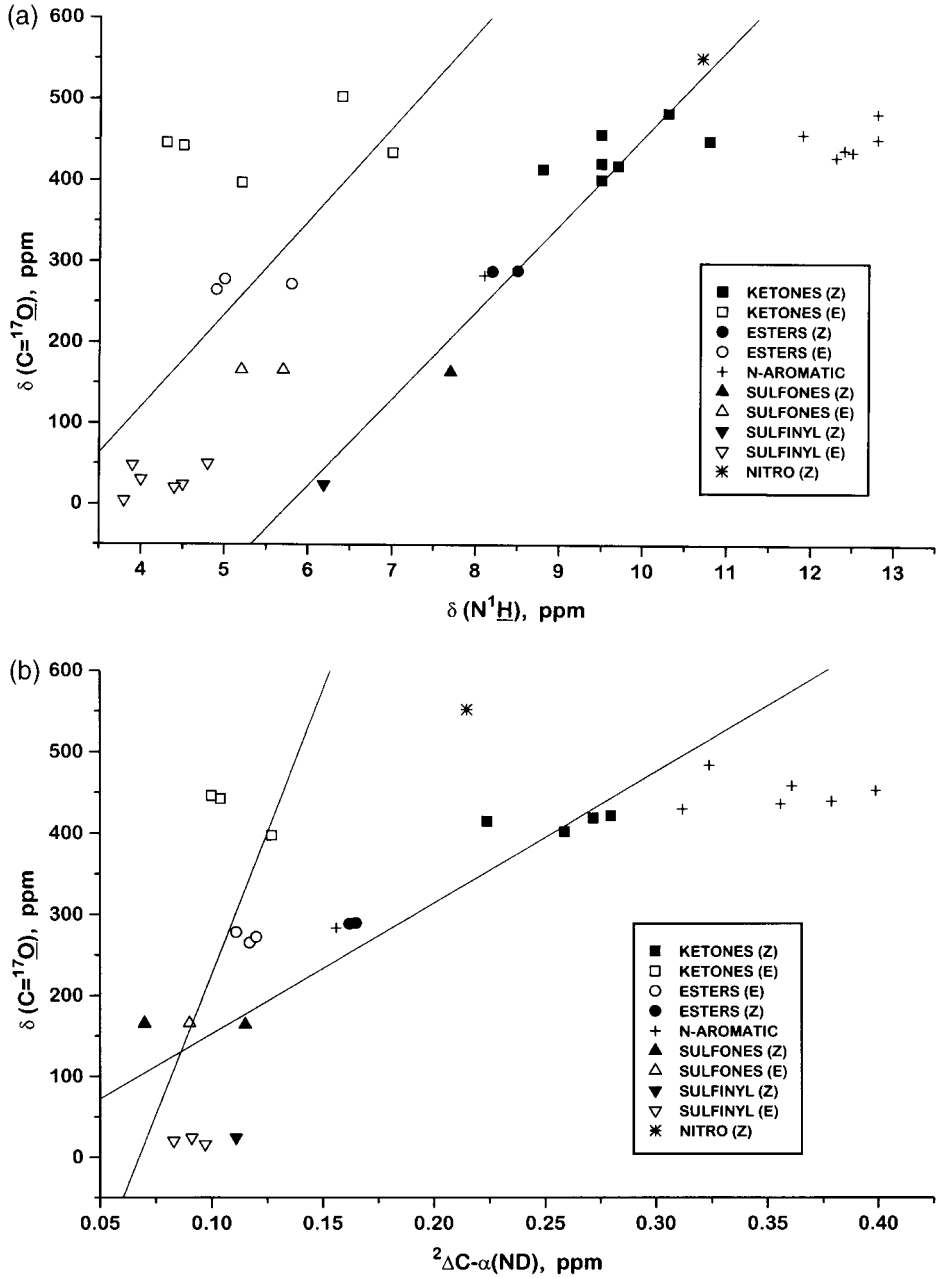


Figure 2. Plots of ^{17}O chemical shifts in the enamines studied *vs.* (a) NH chemical shift and (b) deuterium isotope effect on ^{13}C NMR chemical shifts $^{2}\Delta$C-1 (ND). The NH chemical shifts and isotope effects of *N*-aromatic enamino ketones were taken from Ref. 43. ^{17}O chemical shifts were taken from Ref. 25. Data for *N*-phenyl derivatives were not included in correlations (5) and (6).

shifts of the NH proton. The ^{17}O data of Zhuo[24,25] are included and, as for other *N*-phenyl derivatives, these data fall below the correlation line for *Z*-derivatives (indicated with a plus sign). This feature is also found for the ester **20**.

A plot of $^{2}\Delta$C-1 (ND) *vs.* δC=^{17}O [Fig. 2(b)] shows similar features, although a combination of data for sulfoxides, sulfones and nitroenamines together with those of ketones and esters may be questionable. The correlation equations for the *Z*- and *E*-series are given as Eqns (5) and (6), respectively:

$$\delta(\mathrm{C{=}^{17}O})(\pm 54.8) = -8.3(\pm 46.3) + 1609.9(\pm 223.7)\,[^{2}\Delta C - 1(\mathrm{ND})]$$
$$R_9 = 10.931 \qquad (5)$$

$$\delta(\mathrm{C{=}^{17}O})(\pm 153.1) = -469.7(\pm 368.1) + 6963.1(\pm 3523.6)[^{2}\Delta\mathrm{C} - 1(\mathrm{ND})]$$
$$R_{10} = 0.550 \qquad (6)$$

Zhuo[24,25] established hydrogen bonding effects of 27 ppm to lower frequency in *N*-alkylenaminones and 33 or 45 ppm to lower frequency in *N*-phenylenaminones, but he obtained the values by comparison with the conformationally different *trans-s-trans* cyclic enamino ketones. The present study also reveals clearly that, as inferred from the plot in Fig. 2(a), *N*-phenyl and *N*-alkyl derivatives do not fall on the same correlation line. It is most probable that phenyl groups influence δNH, δOH and $^{2}\Delta$C-1(ND) but apparently not δC=^{17}O.

The correlation within comparable groups of compounds is of interest but is often difficult to interpret, as seen for the $^{1}\Delta^{13}$C(^{18}O) one-bond isotope effect of acyl derivatives.[9,36]

Intermolecular effects

CH_3SOCH_3 gave chemical shifts relative to external water[37] of 18.7 (neat), 12 (CH_2Cl_2), 10 ($CDCl_3$) and 8 ppm (CH_3OH), giving a hint that intermolecular hydrogen bonding in this case gives a negligible shift to lower frequency. The previously discussed difference between **23** and **24** gives a 5 ppm effect in the opposite direction for intermolecular hydrogen bonding in the sulfoxides studied here. This trend is consistent if one compares the values for **33**, showing a high frequency shift accompanying the increase in concentration.

CONCLUSION

^{17}O chemical shifts are susceptible to influences from electronic, including conjugation effects, in-plane angle distortions and hydrogen bonding. For strong hydrogen bonds the latter effect dominates, and the C=^{17}O chemical shifts become good gauges for the existence of hydrogen bonding. As the intermolecular effects on ^{17}O chemical shifts are small, ^{17}O chemical shifts may in favorable cases (absence of strongly electron withdrawing or electron-donating substituents) be used to gauge weak intramolecular hydrogen bonds, as both δO*H*, δN*H* and $^{2}\Delta$C(YD) start to vary depending on YH exchange for such weak hydrogen bonds.

The changes in ^{17}O chemical shifts upon hydrogen bond formation are so large that this has to be taken into account for C=^{17}O chemical shifts when these are extrapolated or estimated from non-hydrogen-bonded or weakly hydrogen-bonded models.

The effect of hydrogen bonding in open-chain enamino ketones can be estimated to cause a 20 ppm shift to lower frequency, whereas for enamino lactones the effect is 23 ppm to higher frequency. This reversal for five-membered rings possibly occurs because strain or steric effects are more important. The 20 ppm shift to lower frequency can be compared with a 50 ppm shift found for *o*-hydroxyacyl aromatics.[23]

For β-sulfinylenamines, no difference could be observed between hydrogen-bonded and non-hydrogen-bonded species in the derivatives studied. The ^{17}O chemical shift of the sulfoxide group is dominated by substituent effects and possibly to a minor extent by steric effects.

EXPERIMENTAL

The compounds were synthesized and purified according to published procedures for enamino ketones,[38] nitroenamines,[39] enamino lactones,[40] sulfinylenamines[41] and sulfonylenamines.[42]

The compounds were purified just before use and the samples were allowed to equilibrate to reach the steady-state population of *Z*- and *E*-forms. The δ values of the NH resonances were measured in the solutions used for ^{17}O experiments, which, for solutions in $CDCl_3$, were performed on a Bruker 500 MHz AMX spectrometer at ambient temperature. The δ^{17}O values were calibrated against an external H_2O sample and usually FIDs from 100 000 scans were obtained using a 40 ms acquisition time and a 30° pulse over an 11 kHz spectral window, with a 120 μs delay before the start of acquisition; 4K data points and 100 Hz line broadening were used for processing the data.

All other ^{17}O NMR spectra were acquired as described below on a Varian VXR-400 spectrometer equipped with a 10 mm broadband probe. Spectra were acquired at natural abundance at 60 °C in acetonitrile or chloroform–acetonitrile (1:1, v/v) (Aldrich, anhydrous gold label under nitrogen) containing 1% butan-2-one as an internal standard. The concentration of the compounds employed in these experiments was 0.5 M. The signals were referenced to external deionized water at 60 °C. The butan-2-one resonance was used as an internal control for the chemical shift measurements for these compounds. The instrumental settings were: spectral width 35 kHz, 2K data points, 90° pulse angle (40 μs pulse width), 100 μs acquisition delay and 29 ms

acquisition time. Typically 40 000–80 000 scans were required. The spectra were recorded with sample spinning and without a lock. The signal-to-noise ratio was improved by applying a 25 Hz exponential broadening factor to the FID prior to Fourier transformation. The data point resolution was improved to ± 0.1 ppm by zero filling to 8K data points. The reproducibility of the chemical shift data is estimated to be better than ± 1 ppm.

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