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NMR of Enaminones

Part 2*—^{17}O NMR Spectra of Primary and Secondary Enaminones: Evaluation of Substituent Increments and Intramolecular Hydrogen Bonding

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Natural abundance ^{17}O NMR spectra of 55 primary and secondary enaminones with various substituents at the C-1, C-3 and N-positions are reported. Analyses of the ^{17}O chemical shifts of these enaminones give the values of the increments for the substituents at these positions. The influence of the substituents on the ^{17}O chemical shifts of the carbonyl groups of the enaminones is additive. It is found that the ^{17}O chemical shifts of the enaminones can be calculated by the sum of the substituent increments. The differences between the calculated and the experimental data are generally less than ±2 ppm. The large deviations observed for the enaminones with a primary amino group are explained in terms of the formation of intermolecular hydrogen bonds. The chemical shift differences between the *E*- and *Z*-forms of enaminones is mainly attributed to intramolecular hydrogen bonding. The contribution coming from intramolecular hydrogen bonding ($\Delta\delta_{HB}$), ranging from −14 to −47 ppm, depends on the donor properties of the amino groups and the type of substituents. The ^{17}O chemical shifts of these enaminones correlate well with each other and with the pK_a values of the corresponding alkylamines. Fair correlations of the ^{17}O data of carbonyl groups with the ^{1}H-2 chemical shifts are observed, suggesting that the change of electron density on the carbonyl O atom parallels that on C-2.

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INTRODUCTION

^{17}O NMR spectroscopy has proved to be a particularly useful method for the study of intramolecular hydrogen bonding in organic compounds.[2,3] The shielding in ^{17}O NMR by the hydrogen bonding components ($\Delta\delta_{HB}$ values, ranging from −5 to −50 ppm) has been shown to depend on the H-donor and H-acceptor groups.[3] $\Delta\delta_{HB}$ values of −50, −30, −19 and −10 ppm have been reported for ketone,[3f,g] aldehyde[3h] and amide,[3a,j] nitro and ester[3k] carbonyl oxygens, respectively.

The properties and synthetic applications of enaminones have been studied extensively.[4] The intramolecular hydrogen bonding in enaminones with primary or secondary amino groups has been demonstrated by ^{1}H and ^{15}N NMR.[5,6] Recently, the ^{17}O NMR spectra of some tertiary enaminones have been investigated and the ^{17}O chemical shifts have been shown to be sensitive to the nature, number and position of the substituents.[1] However, the effects of the substituents are not additive. In order to evaluate the substituent increments and the contribution coming from intramolecular hydrogen bonding ($\Delta\delta_{HB}$ values), the ^{17}O NMR spectra of primary and secondary enaminones with various substituents groups have been investigated.

RESULTS

The ^{17}O chemical shifts and linewidths for a series of cyclic and aliphatic enaminones (**1** and **11**), obtained at natural abundance in acetonitrile solution (0.5 M) at 40 °C, are listed in Tables 1–8.

Enaminones with primary or secondary amino groups can exist in both *E*- and *Z*-forms.[4b] They can be easily distinguished by their ^{1}H NMR spectra: the N-H signals of the *E*-form (4–8 ppm) appear at much higher field than those of the *Z*-form (9–13 ppm), indicating the presence of strong intramolecular hydrogen bonding in the latter. Furthermore, the ^{1}H chemical shifts of H-2 and H-3 of the *E*-form are displaced to low field, *ca.* 0.3 and 0.8 ppm lower than those of the corresponding *Z*-form, respectively. The chemical shift differences between the *E*- and *Z*-forms have been previously observed in their ^{13}C[5,7] and ^{15}N NMR[5,6] spectra. That enaminones **1a**–**h** (Table 1) exist in the mixture of the two stereoisomers, *E*- and *Z*-forms, is clearly shown by their ^{17}O NMR spectra. The assignments of ^{17}O chemical shifts in both isomers are based on the shielding effects of intramolecular hydrogen bonding upon ^{17}O NMR.[2,3]

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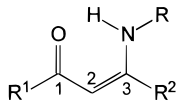

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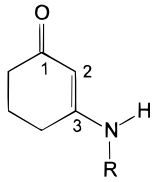

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	R^1	R^2		R^1	R^2
1	Me	H	**7**	Et	H
2	Ph	H	**8**	i-Pr	H
3	Me	Me	**9**	t-Bu	H
5	Ph	Me	**10**	CF_3	H
6	Ph	Ph	**11**	CO_2Et	H

	a	b	c	d	e	f	g	h	i
R	H	Me	Et	i-Pr	i-Bu	t-Bu	CH_2Ph	Ph	Ac

The ^{17}O carbonyl signal for cyclic and aliphatic enaminones appears between 385 and 517 ppm. They are upfield of those of α,β-unsaturated ketones (*ca.* 540 ppm[2]) and downfield of those of *N*-substituted acetamides (*ca.* 330 ppm[2]).

The results in Tables 1–8 show that the $\delta(^{17}O)$ values are influenced by the nature of the nitrogen substituents. The shift values of enaminones with *N*-alkyl substituents are very similar. A benzyl group at N causes a marked deshielding (*ca.* 7 ppm) of the carbonyl O atom, compared with the corresponding N-Me analogue. The enaminones with anilino or acetamido groups show strong deshielding. This can be interpreted as a result of delocalization of the nitrogen electron lone pair and as a result of the electron-withdrawing effect to the nitrogen atom.

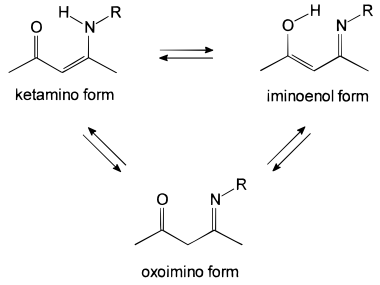
In all cases, substituents at C-1 and C-3 positions cause shielding of the carbonyl O atoms. These effects are different from those previously noted for tertiary enaminones[1] in which C-1 substituents cause shielding, whereas C-3 substituents cause deshielding.

DISCUSSION

Structures of enaminones

Theoretically, enaminones can exist in the tautomeric iminoenol form, oxoimino form and ketamino form, as shown in Scheme 1.

These forms can be easily distinguished by their ^1H NMR spectra. The absence of the methylene proton signal and the presence of a vinylic proton signal in ^1H NMR spectra of this type of compound suggest that the oxoimino form is not present. From the splitting pattern of protons on the carbon adjacent to the enaminone nitrogen, it has been shown that the enaminones exist in the ketamino form.[8] This conclusion can be further supported by ^{17}O NMR data. The ^{17}O NMR spectra for cyclic enaminones show only one signal at 443–516 ppm, which cannot be assigned to the iminoenol form and oxoimino form: the ^{17}O NMR signal for the OH chelated with a C=O group appears at



Scheme 1.

Table 1. ^1H and ^{17}O data (ppm) for 1a–h

Compound	$\delta(^{17}O)^{exp.a}$	$\delta(^{17}O)^{calc.}$	$\Delta\delta^b$	$\Delta\delta_{HB}{}^c$	$\delta(^1H\text{–}N)^d$	$\delta(^1H\text{-}2)$	$\delta(^1H\text{-}3)$
(*Z*)-**1a**	462.2 (90)	462.2	0.0	−6.2	9.20	5.08 (d, 7.6)	6.75 (dt, 7.6, 11.0)
(*E*)-**1a**	468.4 (150)				5.18	5.42 (d, 13.2)	7.45 (dt, 13.2, 11.0)
(*Z*)-**1b**	444.4 (90)	444.7	−0.3	−16.7	9.66	4.99 (d, 7.2)	6.62 (dd, 13.0, 7.2)
(*E*)-**1b**	461.1 (240)				5.02	5.22 (d, 13.2)	7.56 (dd, 13.2, 8.0)
(*Z*)-**1c**	446.4 (90)	446.5	−0.1	−14.5	9.78	4.97 (d, 7.0)	6.66 (dd, 13.0, 7.0)
(*E*)-**1c**	460.9 (290)				4.88	5.24 (d, 13.2)	7.50 (dd, 13.2, 8.0)
(*Z*)-**1d**	446.5 (90)	446.7	−0.2	−14.9	9.78	4.96 (d, 7.0)	6.71 (dd, 13.0, 7.0)
(*E*)-**1d**	461.4 (290)				4.58	5.25 (d, 13.3)	7.45 (dd, 13.3, 9.5)
(*Z*)-**1e**	444.9 (140)	444.2	0.7	−16.0	9.91	4.97 (d, 7.0)	6.62 (dd, 13.0, 7.0)
(*E*)-**1e**	460.9 (290)				4.93	5.25 (d, 13.0)	7.51 (dd, 13.0, 8.0)
(*Z*)-**1f**	445.0 (140)	444.5	0.5	−14.0	10.15	4.99 (d, 7.5)	6.82 (dd, 13.2, 7.5)
(*E*)-**1f**	459.0 (190)				4.90	5.30 (d, 13.0)	—
(*Z*)-**1g**	451.8 (170)	451.9	−0.1	−16.0	10.05	5.05 (d, 7.3)	6.70 (dd, 13.0, 7.3)
(*E*)-**1g**	467.8 (300)				5.08	5.32 (d, 13.3)	7.57 (dd, 13.3, 8.3)
(*Z*)-**1h**	471.4 (240)	469.3	2.1	−17.1	11.59	5.30 (d, 7.7)	7.23 (dd, 12.5, 7.7)
(*E*)-**1h**	488.4 (240)				6.84[e]	5.67 (d, 13.3)	7.90 (t, 13.3)

[a] Acetonitrile solution at 40 °C; linewidth (±10 Hz) at half-height in parentheses.
[b] $\Delta\delta = \delta(^{17}O)^{exp.} - \delta(^{17}O)^{calc.}$.
[c] $\Delta\delta_{HB} = \delta(^{17}O)(Z\text{-form}) - \delta(^{17}O)(E\text{-form})$.
[d] Singlet unless indicated otherwise.
[e] Doublet, $J = 13.3$ Hz.

Table 2. ^{1}H and ^{17}O NMR data (ppm) for 2a–h

Compound	$\delta(^{17}O)^{exp.a}$	$\delta(^{17}O)^{calc.}$	$\Delta\delta^{b}$	$\Delta\delta_{HB}{}^{c}$	$\delta(^{1}H–N)^{d}$	$\delta(^{1}H\text{-}2)$	$\delta(^{1}H\text{-}3)$
(*Z*)-**2a**	430.9 (240)	428.4	2.5	−12.4[e]	9.58	5.80 (d, 7.8)	7.05 (dt, 13.5, 7.8)
(*E*)-**2a**	443.3 (220)				4.87	6.14 (d, 13.0)	—
(*Z*)-**2b**	411.3 (190)	410.9	0.4	−21.9	10.19	5.69 (d, 7.3)	6.93 (dd, 12.7, 7.3)
(*Z*)-**2c**	413.0 (340)	412.7	0.3	−20.0	10.34	5.69 (d, 73)	6.97 (dd, 12.8, 7.3)
(*Z*)-**2d**	412.9 (390)	412.9	0.0	−20.6	10.35	5.72 (d, 7.3)	7.02 (dd, 13.0, 7.3)
(*Z*)-**2f**	410.5 (390)	410.4	0.1	−20.6	10.72[f]	5.72 (d, 7.4)	7.13 (dd, 13.0, 7.4)
(*Z*)-**2g**	417.6 (440)	418.1	−0.5	−22.3	10.60	5.77 (d, 7.4)	7.01 (dd, 12.8, 7.4)
(*Z*)-**2h**	436.3 (540)	435.5	0.8	−24.2	12.15[g]	6.04 (d, 8.0)	7.54 (dd, 12.6, 8.0)

[a,b] See Table 1.
[c] $\Delta\delta_{HB} = \delta(^{17}O)[(Z)\text{-}\mathbf{2}]\text{-}\delta(^{17}O)[(E)\text{-}\mathbf{1}]\text{-}(-27.9)$.
[d] Singlet unless indicated otherwise.
[e] $\Delta\delta_{HB} = \delta(^{17}O)[(Z)\text{-}\mathbf{2}]\text{-}\delta(^{17}O)[(E)\text{-}\mathbf{2}]$.
[f] Doublet, $J = 13.0$ Hz.
[g] Doublet, $J = 12.7$ Hz.

Table 3. ^{1}H and ^{17}O NMR data (ppm) for 3a–i

Compound	$\delta(^{17}O)^{exp.a}$	$\delta(^{17}O)^{calc.}$	$\Delta\delta^{b}$	$\Delta\delta_{HB}{}^{c}$	$\delta(^{1}H\text{-}N)^{d}$	$\delta(^{1}H\text{-}2)^{d}$
(*Z*)-**3a**	439.2 (110)	435.2	4.0	−12.3	9.70	5.03
(*Z*)-**3b**	418.2 (130)	417.7	0.5	−27.3	10.72	5.00
(*Z*)-**3c**	419.3 (120)	419.5	−0.2	−30.9	10.76	4.95
(*Z*)-**3d**	419.2 (140)	419.7	−0.5	−30.1	10.84	4.91
(*Z*)-**3e**	416.6 (170)	417.2	−0.6	−28.3	11.00	4.96
(*Z*)-**3g**	424.7 (240)	424.9	−0.2	−28.7	11.18	5.05
(*Z*)-**3h**	435.3 (190)	442.3	−7.0	−37.6	12.48	5.19
(*Z*)-**3i**	483.6 (160)	485.6	−2.0	−32.8	12.33	5.33

[a,b] See Table 1.
[c] $\Delta\delta_{HB} = \delta(^{17}O)[(Z)\text{-}\mathbf{3}]\text{-}\delta(^{17}O)[(E)\text{-}\mathbf{4}]$.
[d] Singlet.

Table 4. ^{1}H and ^{17}O NMR data (ppm) for 4a–i

Compound	$\delta(^{17}O)^{exp.a}$	$\delta(^{17}O)^{calc.}$	$\Delta\delta^{b}$	$\delta(^{1}H\text{-}N)^{c}$	$\delta(^{1}H\text{-}2)^{c}$
(*E*)-**4a**	451.5 (180)	464.0	−12.5	5.08	5.23
(*E*)-**4b**	445.5 (220)	446.5	−1.0	5.99	5.04
(*E*)-**4c**	450.2 (290)	448.3	1.9	4.84	5.11
(*E*)-**4d**	449.3 (340)	448.5	0.8	4.35	5.14
(*E*)-**4e**	444.9 (240)	446.0	−1.1	4.72	5.12
(*E*)-**4g**	453.4 (440)	453.7	−0.3	4.85	5.19
(*E*)-**4h**	471.2 (240)	471.1	0.1	6.27	5.59
(*E*)-**4i**	516.4 (300)	514.4	2.0	8.08	6.62

[a,b] See Table 1.
[c] Singlet.

Table 5. ^{1}H and ^{17}O NMR data (ppm) for 5a–h

Compound	$\delta(^{17}O)^{exp.a}$	$\delta(^{17}O)^{calc.}$	$\Delta\delta^{b}$	$\Delta\delta_{HB}{}^{c}$	$\delta(^{1}H–N)^{d}$	$\delta(^{1}H\text{-}2)^{d}$
(*Z*)-**5a**	408.0 (190)	401.4	6.6	−15.6	10.21	5.74
(*Z*)-**5b**	384.7 (290)	383.9	0.8	−32.9	11.33	5.69
(*Z*)-**5c**	385.2 (340)	385.7	−0.5	−37.1	11.37	5.66
(*Z*)-**5g**	391.6 (290)	391.1	0.5	−33.9	11.75	5.76
(*Z*)-**5h**	398.4 (480)	408.5	−10.1	−46.6	13.10	5.90

[a,b] See Table 1.
[c] $\Delta\delta_{HB} = \delta(^{17}O)[(Z)\text{-}\mathbf{5}]\text{-}\delta(^{17}O)[(E)\text{-}\mathbf{4}]\text{-}(-27.9)$.
[d] Singlet.

Table 6. ^{1}H and ^{17}O NMR data (ppm) for 6a–h

Compound	$\delta(^{17}O)^{exp.}$ [a]	$\delta(^{17}O)^{calc.}$	$\Delta\delta$[b]	$\delta(^{1}H\text{–}N)$[c]	$\delta(^{1}H\text{-}2)$[c]
(*Z*)-**6a**	416.6 (540)	414.4	2.2	10.42	6.15
(*Z*)-**6b**	396.7 (530)	396.9	−0.2	11.34	5.78
(*Z*)-**6c**	398.4 (530)	398.7	−0.3	11.37	5.76
(*Z*)-**6g**	403.4 (680)	404.1	−0.7	11.71	5.84
(*Z*)-**6h**	420.9 (680)	421.5	−0.6	12.90	6.09

[a,b] See Table 1.
[c] Singlet.

62–124 ppm[3,9a–d] and with a C=N (azine) group at *ca.* 95 ppm,[9d] the ^{17}O NMR signal for the C=O of ketones appears at *ca.* 550 ppm[2] and the keto-form of *β*-diketones[9e] and *β*-keto esters[9d] at *ca.* 560 ppm. Hence the iminoenol form is not present at least in solution and the signal at 443–516 ppm must belong to the ketamino form.

Correlations of δ(^{17}O) data with δ(^{1}H-2) data and the pK_a values of the amines

^{17}O shift values for 1-amino-substituted anthraquinones,[3d,e] amide-analogous *N*-acyl derivatives[10] and *N*-nitrosamines[11] have been found to depend on the pK_a of the donor NH group. The ^{17}O chemical shifts of enaminones with tertiary amino groups have been previously correlated with the pK_a values of the corresponding amines.[1] Comparison of the present $\delta(^{17}O)$ values with the pK_a values[12] of the substituted amines indicates such a relationship. Excellent linear relationships between the $\delta(^{17}O)$ values of the carbonyl groups in enaminones with a secondary amino group and the pK_a values[12] of the corresponding substituted amines were observed (Table 9). In these relationships, the enaminones with primary amino groups were excluded owing to the influence arising from intermolecular hydrogen bonding.

As linear correlations of the ^{17}O chemical shifts of the carbonyl groups of enaminones **1–11** with the pK_a values of amines, these data also correlate linearly with

Table 9. Correlations of δ(^{17}O) data with the pK_a values of the amines[a]

Series	Slope	Intercept	n[b]	r	S.D.
(*E*)-**1**	−4.64	510.2	8[c]	0.995	1.0
(*Z*)-**1**	−4.32	491.4	7	0.995	1.1
(*Z*)-**2**	−4.04	455.0	6	0.996	1.0
(*Z*)-**3**	−4.99	470.0	7	0.973	6.3
(*E*)-**4**	−5.49	504.4	8[c]	0.989	3.8
(*Z*)-**5**	−2.15	408.9	4	0.956	2.3
(*Z*)-**6**	−3.85	438.8	4	0.997	1.0
(*Z*)-**11**	−6.34	477.5	6	0.966	1.0

[a] The pK_a value for acetamide (−1.59) from Ref. 12a and the other alkylamines from Ref. 12b are used for the regression analyses.
[b] NH_2 group was excluded unless otherwise indicated.
[c] NH_2 group was included.

Table 7. ^{1}H and ^{17}O NMR data (ppm) for 7b–10g

Compound	$\delta(^{17}O)^{exp.}$ [a]	$\delta(^{17}O)^{calc.}$	$\Delta\delta$[b]	$\delta(^{1}H\text{–}N)$[c]	$\delta(^{1}H\text{-}2)$	$\delta(^{1}H\text{-}3)$
(*Z*)-**7b**	436.3 (120)	436.5	−0.2	9.67	4.99 (d, 7.4)	6.64 (dd, 13.0, 7.4)
(*Z*)-**7g**	443.9 (200)	443.7	0.2	10.04	5.05 (d, 7.3)	6.72 (dd, 12.7, 7.3)
(*Z*)-**8b**	428.8 (140)	429.0	−0.2	9.70	5.07 (d, 7.0)	6.76 (dd, 12.6, 7.0)
(*Z*)-**8g**	436.4 (220)	436.2	0.2	10.08	5.07 (d, 7.3)	6.76 (dd, 12.5, 7.3)
(*Z*)-**9b**	433.0 (120)	432.4	0.6	9.77	5.17 (d, 7.5)	6.72 (dd, 12.6, 7.5)
(*Z*)-**9g**	438.9 (180)	439.6	−0.7	10.11	5.23 (d, 7.6)	6.80 (dd, 12.6, 7.6)
(*Z*)-**10f**	390.3 (190)	391.5	−1.2	10.65	5.37 (d, 7.0)	7.27 (dd, 14.0, 7.0)
(*Z*)-**10g**	400.1 (240)	398.9	1.2	10.47	5.41 (d, 7.0)	7.17 (dd, 13.0, 7.0)

[a,b] See Table 1.
[c] Singlet.

Table 8. ^{1}H and ^{17}O NMR data (ppm) for 11b–g

Compound	$\delta(^{17}O)^{exp.}$ [a]	$\delta(^{17}O)^{cal.}$	$\Delta\delta$[b]	$\delta(^{1}H\text{-}N)$[c]	$\delta(^{1}H\text{-}2)$	$\delta(^{1}H\text{-}3)$
(*Z*)-**11b**	409.6 (290)	409.9	−0.3	10.37	5.83 (d, 7.0)	7.07 (dd, 13.4, 7.0)
(*Z*)-**11c**	410.6 (290)	411.7	−1.1	10.52	5.82 (d, 7.0)	7.11 (dd, 13.0, 7.0)
(*Z*)-**11d**	411.6 (290)	411.9	−0.3	10.60	5.81 (d, 7.0)	7.16 (dd, 13.4, 7.0)
(*Z*)-**11e**	410.5 (360)	409.4	1.1	10.65	5.83 (d, 7.0)	7.07 (dd, 13.3, 7.0)
(*Z*)-**11f**	409.3 (310)	409.7	−0.4	11.01	5.85 (d, 7.0)	7.26 (dd, 13.7, 7.0)
(*Z*)-**11g**	418.4 (390)	417.1	1.3	10.74	5.89 (d, 7.0)	7.16 (dd, 13.0, 7.0)

[a,b] See Table 1.
[c] Singlet.

Table 10. Correlations between the δ(^{17}O) data of enaminones

Type of correlation	Slope	Intercept	n[a]	r	S.D.
(*E*)-**1** *vs.* (*Z*)-**1**	1.06	−13.6	7	0.996	1.0
(*Z*)-**2** *vs.* (*Z*)-**1**	0.99	36.7	7[b]	0.993	1.3
(*Z*)-**2** *vs.* (*E*)-**1**	0.88	8.6	6	0.998	0.7
(*E*)-**4** *vs.* (*E*)-**1**	0.92	21.0	7[b]	0.975	2.3
(*E*)-**4** *vs.* (*Z*)-**3**	1.07	1.58	7	0.993	3.4
(*Z*)-**11** *vs.* (*Z*)-**1**	1.22	−133.3	6	0.981	0.7

[a] NH_2 group was excluded unless indicated otherwise.
[b] NH_2 group was included.

each other (Table 10). For secondary amino groups, an excellent correlation is obtained between ^{17}O chemical shifts of cyclic enaminones [(*E*)-**4b**–(*E*)-**4i**] and those of aliphatic enaminones [(*Z*)-**3b**–(*Z*)-**3i**]. The near-unity values of the slope (1.07) of the correlation line indicate that the steric and electronic effects of the substituents on δ(^{17}O) are essentially similar in the two series of enaminones.

The ^{1}H chemical shifts of the H-2 protons of enaminones have been shown to be dependent on the electron density at C-2, which is affected by inductive and mesomeric effects.[4] They also reflect the polarization and the degree of n,π-conjugation. In Part 1,[1] it was shown that the ^{1}H chemical shifts of the H-2 protons of the enaminones with tertiary amino groups correlate with the pK_a values of the corresponding amines. In enaminones with primary and secondary amino groups (**1**–**6** and **11**), good correlations of the ^{1}H chemical shifts of H-2 protons with the pK_a values of the substituted amines (Table 11), and also with the ^{17}O shifts of their carbonyl O atoms (Table 12), were observed. This indicates that the shielding of the carbonyl O atom is influenced by the factors which affect the base strength of the amines RNH_2 and the ^{1}H chemical shifts of the H-2 protons. The relationship between δ(^{17}O) and δ(^{1}H-2) suggests that the electron density at the carbonyl O-atom parallels that at the C-2 atom.

Evaluation of the values of the substituent increments

The influence of the substituents at C-1, C-3 and N on the ^{17}O chemical shifts of enaminones was analyzed by using 4-aminobut-3-en-2-one [(*Z*)-**1a**] as a reference. The influence of a substituent at the *i*-atom on the ^{17}O chemical shift is defined as the value of substituent increment Δ_i. The value of the increment of the C-1 substituent ($\Delta_{C\text{-}1}$) for a phenyl group was obtained by statistical analysis of the chemical shift differences between C-1 phenyl-substituted enaminones (**2b–h**) and the corresponding analogues (**1b–h**) and between 3-amino-1-phenylbut-2-en-1-ones (**5b–h**) and 4-aminopent-3-en-2-ones (**3b–h**). The values of the substituent increments for C-3 substituents ($\Delta_{C\text{-}3}$) were obtained in a similar way. The Δ_{cyclo} value for cyclic enaminone systems (**4a–i**) is 1.8 ppm. The value of the increment for a substituent at the N atom (Δ_N) was deduced by statistical analysis from the $\Delta_{C\text{-}1}$, $\Delta_{C\text{-}3}$ and a base value of 462.2 ppm [(*Z*)-**1a** as a reference]. The additive influence of the substituents on the ^{17}O chemical shifts of the enaminones (*Z*)-**1**–(*Z*)-**11** and (*E*)-**4** can be represented by the following relationship:

$$\delta(^{17}O) = 462.2 + \sum\Delta_i(R_i)$$

where the Δ_i is the value of the increment of substituent R at the *i*th position (Table 13), and the constant 462.2 ppm is the ^{17}O chemical shift of (*Z*)-**1a**. The ^{17}O chemical shifts calculated [$\delta(^{17}O)^{calc.}$] by the above equation are included in Tables 1–8. The differences (in ppm) between the experimental and calculated values, $\Delta\delta = \delta(^{17}O)^{exp.} - \delta(^{17}O)^{calc.}$, are also given in these tables. It must be pointed out that the influences of intermolecular hydrogen bonding between solutes on the ^{17}O chemical shifts should be taken into account for

Table 11. Correlations of δ(^{1}H-2) data with the pK_a values of the amines

Series	Slope	Intercept	n	r	S.D.
(*E*)-**1**	−0.07	6.00	8	0.970	0.04
(*Z*)-**1**	−0.05	5.55	8	0.990	0.02
(*Z*)-**2**	−0.05	6.30	7	0.993	0.02
(*Z*)-**3**	−0.03	5.30	8	0.969	0.04
(*E*)-**4**	−0.12	6.33	8	0.985	0.10
(*Z*)-**5**	−0.04	6.07	5	0.979	0.02
(*Z*)-**6**	−0.05	6.33	4[a]	0.999	0.01
(*Z*)-**11**	−0.05	6.32	6[b]	0.887	0.01

[a] Point for (*Z*)-**6a** was excluded.
[b] A better correlation was obtained (r = 0.990) when the point for (*Z*)-**11f** was excluded.

Table 12. Correlations of the δ(^{17}O) with δ(^{1}H-2) data of enaminones

Series[a]	Slope	Intercept	n	r	S.D.
(*E*)-**1**	62.2	134.3	8	0.963	2.8
(*Z*)-**1**	82.9	33.7	8	0.944	3.5
	79.1	52.0	7[b]	0.987	1.7
(*Z*)-**2**	71.9	2.1	6[b]	0.988	1.7
(*E*)-**4**	46.7	214.8	8	0.996	2.4
(*Z*)-**5**	59.1	49.9	4[b]	0.982	1.5
(*Z*)-**6**	57.6	66.3	5	0.961	3.5
	72.2	−18.9	4[b]	0.993	1.6

[a] δ(^{17}O) *vs.* δ(^{1}H-2).
[b] Point for NH_2 derivative was excluded.

Table 13. Values of substituent increments Δ (in ppm) for the calculation of δ(^{17}O) of enaminones $R^1COCH{=}C(R^2)NHR$ in MeCN[a]

Substituent	$\Delta_{C(1)}$	$\Delta_{C(3)}$	Δ_N
H	—	0.0	0.0
Me	0.0	−27.0	−17.5
Et	−8.2	—	−15.7
i-Pr	−15.7	—	−15.5
i-Bu	—	—	−18.0
t-Bu	−12.3	—	−17.7
Bn	—	—	−10.3
Ph	−33.8	−14.0	7.1
CF_3	−53	—	—
CO_2Et	−34.8	—	—
Ac	—	—	50.4

[a] The increment for cyclic enaminones (**4a–i**) is 1.8 ppm.

more precise calculations. However, since the strength of the intermolecular hydrogen bonding depends on several factors, such as concentration, temperature, solvent and the structure of the molecule investigated, and is not easy to determine, this term was not included in the equation. It has been shown that the torsion angle and van der Waals repulsion caused by steric interaction can have considerable influence on the ^{17}O chemical shift.[3]

Comparison of the experimental data with those from calculations shows that in the cases of enaminones with primary amino groups (R = H) the $\Delta\delta$ values have a considerable deviation. This may arise from the formation of intermolecular hydrogen bonds in these enaminones. Generally, the influence of the intermolecular hydrogen bonds on ^{17}O chemical shift shielding is weaker than that of intramolecular hydrogen bonds. Therefore, the experimental chemical shifts are larger than the calculated ones. In cyclic enaminone systems [(*E*)-**4a**–(*E*)-**4i**], the formation of intramolecular hydrogen bonds is not possible. The experimental chemical shift of (*E*)-**4a** is much smaller than the calculated value, indicating that there is shielding resulting from the contribution of intermolecular hydrogen bonding. In the N-Ph substituted enaminones, the large $\Delta\delta$ values may arise from the steric repulsion between N-Ph and C-3 substituent or H-3, as a result of the Ph group twisted out of the plane of the enaminone system. For **3h** and **5h** the $\Delta\delta$ values (−7.0 and −10.1 ppm, respectively) indicate that the N-Ph ring is considerably twisted, which leads to enhancement of the donating ability of the nitrogen electron lone pair to the C=C—C=O system and shielding of the O atom. The crystal structure of (*Z*)-4-(*p*-nitrophenylamino)pent-3-en-2-one shows that the aryl ring is rotated out of the plane of N—C=C—C=O by 17.3°.[13d]

Intramolecular hydrogen bonding

^{17}O NMR data have been shown to be sensitive to intramolecular hydrogen bonding, which causes a shielding −5 to −50 ppm, previously reported for various compounds.[2,3] The existence of both *E*- and *Z*-isomers of the enaminones **1a**–**h** is clearly shown by their ^{1}H and ^{17}O NMR spectra. The ^{17}O signal of the *Z*-form appears at higher field than that of the *E*-form. This shift difference, *ca.* −16 ppm, can be attributed to intramolecular hydrogen bonding. The presence of intramolecular hydrogen bonding in the *Z*-form is clearly evidenced by the signal of N-H, which is found at low field (9.2–10.0 ppm, Table 1). Although the influence of the configuration on ^{17}O shift value should be taken into account for the evaluation of intramolecular hydrogen bonding, the previous results from the ^{15}N shift values of enaminones showed that the effect of the configuration is much smaller than that of intramolecular hydrogen bonding.[6a] This conclusion is also applicable to the ^{17}O shift values of enaminones.

The secondary enaminones (*Z*)-**3b**–(*Z*)-**3i** show considerable shielding of the carbonyl O atoms, $\Delta\delta_{HB} \approx -30$ ppm, compared with the same *N*-substituted cyclic enaminones, (*E*)-**4b**–(*E*)-**4i**, where intramolecular hydrogen bonds cannot exist. These shielding effects can be attributed to intramolecular hydrogen bonding for the following reasons:

(a) The N-H signal for the enaminones (*Z*)-**3b**–(*Z*)-**3i** appears at low field, $\delta(^{1}H\text{-}N) = 10.5$–12.5 ppm (Table 3), whereas those for cyclic analogues are at 4.3–8.0 ppm (Table 4). This shows clearly that there is a strong intramolecular hydrogen bonding in the former.

(b) The intramolecular hydrogen bonding which causes a significant shielding of the carbonyl O atom has been noted for various carbonyl compounds.[2,3] The ^{17}O signals for the intramolecular hydrogen bonded *Z*-form of enaminones **1b**–**h** are noted to be upfield of those of the corresponding *E*-form by *ca.* 16 ppm.

(c) The results of x-ray structures[13] and of theoretical calculation[14] of enaminones demonstrate that the carbonyl group, the C=C double bond and the C—N single bond are in an almost coplanar conformation. This indicates that torsional effects, which should be taken into account for the evaluation of intramolecular hydrogen bonding, are negligible in the present system.

(d) In the absence of hydrogen bonding, the shielding effect is absent. The previous results show that the ^{17}O signal of 3-dimethylaminocyclohex-2-en-1-one (446 ppm) appears even at higher field than that of 4-dimethylaminopent-3-en-2-one (454 ppm).[1]

(e) The additive influences of the substituents are also present in the cyclic enaminones (*E*)-**4b**–(*E*)-**4i**, in which intramolecular hydrogen bonding is absent, indicating that the effects of the substituents in two series are identical. This was also supported by the excellent linear relationship between ^{17}O shift values of cyclic enaminones (*E*)-**4** and those of aliphatic enaminones (*Z*)-**3** with a near-unity value of the slope. Hence the chemical shift differences between (*E*)-**4** and (*Z*)-**3**, $\Delta\delta_{HB} \approx -30$ ppm, must be attributed to intramolecular hydrogen bonding between the N-H proton and carbonyl oxygen.

The shift difference between (*E*)-**4a** and (*Z*)-**3a**, which have a primary amino group, $|\Delta\delta_{HB} = -12.3$ ppm$|$, is smaller than those of the compounds which have a secondary amino group, $|\Delta\delta_{HB} \approx -30$ ppm$|$. It is possible that there is an additional influence due to intermolecular hydrogen bonding.

In the C-1 Ph enaminones (*Z*)-**5a**–(*Z*)-**5h**, the contribution of the phenyl group to the observed carbonyl ^{17}O shift value should be taken into account. The effect of the phenyl group for estimating $\Delta\delta_{HB}$ value for (*Z*)-**5** is assigned a value of 27.9 ppm shielding, based on the chemical shifts of 3-dimethylamino-1-phenylbut-2-en-1-one (426.2 ppm)[1] and 4-dimethylaminopent-3-en-2-one (454.1 ppm).[1] It has been shown that the torsional effects can considerably influence the ^{17}O shift values. The x-ray analyses of 3-pyrrolidino-1-phenylbut-2-en-1-one[13a] and 4-pyrrolidinopent-3-en-2-one[13b] show that both molecules are virtually planar and that the C=O, C=C and C—N bond lengths and the relevant bond angles are identical. Therefore, the torsional effects can be reasonably negligible. The $\Delta\delta_{HB}$ values for (*Z*)-**5**, *ca.* −33 ppm, corrected the effect of phenyl, are estimated from the chemical shift differences between (*Z*)-**5a**–(*Z*)-**5h** and the corresponding (*E*)-**4a**–(*E*)-**4h**. Similarly, the $\Delta\delta_{HB}$ values for (*Z*)-**2a**–(*Z*)-**2h**, *ca.* −21 ppm, are estimated on the basis of the above effect of the phenyl group and the ^{17}O data of the *E*-form of the enaminones (*E*)-**1a**–(*E*)-**1h**. Again the $|\Delta\delta_{HB}|$ values for (*Z*)-**2a**

(−12.4 ppm) and (*Z*)-**5a** (−15.6 ppm) are smaller than those for the corresponding analogues which have the secondary amino group.

The $\Delta\delta_{HB}$ values for enaminones (*Z*)-**6**–(*Z*)-**11** are not estimated, owing to the lack of a suitable reference system. However, the $\Delta\delta_{HB}$ values for (*Z*)-**6** should be close to those for the enaminones (*Z*)-**5a**–(*Z*)-**5h**. The $\Delta\delta_{HB}$ values for (*Z*)-**7b**–(*Z*)-**11** should be close to those for enaminones (*Z*)-**1b**–(*Z*)-**1g**.

The shielding effects of intramolecular hydrogen bonding of the type NH···C=O have been reported previously.[3d,e] In *o*-acetamido- and *o*-trifluoroacetamidoacetophone the shielding effects $\Delta\delta_{HB} = -4.1$ and −21.0 ppm are noted relative to the corresponding *para*-isomer,[3e] and in 1-aminoanthraquinones[3d] the shielding effects $\Delta\delta_{HB}$ are −5.2, −15 and −29 ppm for amino, acetamido and trifluoroacetamido derivatives, respectively. It is generally admitted that $\Delta\delta_{HB}$ values indicate the strength of the hydrogen bond.[3] The high value of −30 ppm found in the present system indicates a strong hydrogen bond.

CONCLUSION

The results of this work confirm that the enaminones studied exist in solution mainly in a ketamino form. The ^{17}O shift values of enaminones in the *Z*-form can be calculated by the sum of substituent increments. Steric interactions and intermolecular hydrogen bonding result in large deviations between the experimental and calculated data. The ^{17}O shift values for enaminones are dependent on the basicity of the amine groups and correlate well with the pK_a values of the corresponding amines. The existence of strong intramolecular hydrogen bonding in aliphatic enaminones is demonstrated by the shielding of the chelated carbonyl groups: $\Delta\delta_{HB}$ values range from −14 to −47 ppm, depending on the character, number and position of the substituents in the N—C=C—C=O system.

EXPERIMENTAL

Materials

β-Diketones, alkylamines, 4-methoxybut-3-en-2-one and 3-aminocyclohex-2-en-1-one were purchased from Fluka. Enaminones **1a–d**,[15] **1e**,[16] **1f**,[15] **1g**[17] and **1h**[18] were prepared from 4-methoxybut-3-en-2-one and **11b–g** from ethyl 4-ethoxy-2-oxobut-3-enoate,[19] **10f**[20] and **10g**[21] from 4-ethoxy-1,1,1-trifluorobut-2-en-2-one[22] and the appropriate amine in THF according to the known procedures.[19,21] Enaminones **2a**[18], **2b**,[23] **2c**,[23] **2d**, **2f**, **2g**[24] and **2h**[24] were prepared from the sodium salt of benzoylacetaldehyde and the appropriate amine according to the literature method.[24] Compounds **3a**,[25] **5a**[25] and **6a**[26] were prepared from the corresponding β-diketone and ammonium acetate according to the literature method.[25] The acetylation of **3a** and **4a** afforded the corresponding **3i**[27] and **4i**,[28] respectively. Compounds **3b**,[8] **3c**,[8] **3d**,[29] **3e**,[30] **3g**,[8] **3h**,[24] **4b**,[31] **4e**, **4g**,[32] **4h**,[33] **5b**,[34] **5c**,[34] **5g**,[24] **5h**,[24] **6b**,[34] **6c**,[35] **6g**[8] and **6h**[36] were prepared from the corresponding β-diketone and the appropriate amine according to Greenhill's procedure.[37] Transamination[38] of 1-dimethylaminopent-1-en-3-one,[1] 1-dimethylamino-4-methylpent-1-en-3-one[1] and 4,4-dimethyl-1-dimethylaminopent-1-en-3-one[1] with excess of an ethanolic solution of methylamine (5.6 M) or benzylamine gave the corresponding **7b**,[6a] **8b**[6a] and **9b**[6a] and **7g**, **8g** and **9g**, respectively.

3-Ethylaminocyclohex-2-en-1-one (**4c**):[25,39] a solution of 3-ethoxycyclohex-2-en-1-one[40] (5 mmol) and ethylamine (70% aqueous solution, 2 ml) in acetonitrile (5 ml) was kept at room temperature for 5 h. The volatiles were evaporated under vacuum. The residue was shown to be pure **4c** (quantitative).M.p. 66.3–67.7 °C (lit.:[25] 66–67 °C).

3-(1-Methylethylamino)cyclohex-2-en-1-one (**4d**):[39] a mixture of 3-ethoxycyclohex-2-en-1-one (5 mmol) and isopropylamine (8 mmol) contained in a sealed tube was heated at 120 °C for 6 h. After cooling, the mixture was flash chromatographed on a silica gel column with methylene chloride to afford **4d**, 0.66 g (86%). M.p. 103.5–104.6 °C (lit.:[39] 105–106 °C).

The spectroscopic data of some enaminones synthesized by the above-mentioned methods are listed below (chemical shifts in ppm; *J* in Hz; IR in cm^{-1}; *m/z* in % of base peak).

(*Z*)-**1e**.[16] IR (film), 3260, 3040, 1630, 1570, 1545; ^{1}H NMR ($CDCl_3$), 9.91 (br, 1H, H-N), 6.62 (dd, *J* = 13.0, 7.0, 1H, H-3), 4.97 (d, *J* = 7.0, 1H, H-2), 2.99 (t, *J* = 6.5, 2H, NCH_2CHMe_2), 2.06 (s, 3H, Me), 1.78 (m, 1H, NCH_2CHMe_2), 0.92 (d, *J* = 6.5, 6H, NCH_2CHMe_2); ^{13}C NMR ($CDCl_3$), 197.24 (C-1), 153.07 (C-3), 93.31 (C-2), 56.93, 29.87 and 19.73 (NCH_2CHMe_2), 28.93 (COMe); EI-MS, *m/z* 141 (M^+, 29), 126 (24), 98 (100), 80 (29), 70 (30), 56 (24).

(*E*)-**1e**. ^{1}H NMR ($CDCl_3$), 7.51 (dd, *J* = 13.0, 8.0, 1H, H-3), 5.25 (d, *J* = 13.0, 1H, H-2), 4.93 (br, 1H, H-N), 2.91 (t, *J* = 6.5, 2H, NCH_2CHMe_2), 2.10 (s, 3H, Me), 1.85 (m, 1H, NCH_2CHMe_2), 0.94 (d, *J* = 6.5, 6H, NCH_2CHMe_2).

(*Z*)-**2d**. IR (film), 3260, 3050, 1625, 1580; ^{1}H NMR ($CDCl_3$), 10.35 (br, 1H, H-N), 7.85–7.90 (m, 2H, Ph), 7.37–7.44 (m, 3H, Ph), 7.02 (dd, *J* = 13.0, 7.3, 1H, H-3), 5.69 (d, *J* = 7.3, 1H, H-2), 3.51 (m, 1H, $NCHMe_2$), 1.30 (d, *J* = 6.5, 6H, $NCHMe_2$); ^{13}C NMR ($CDCl_3$), 189.63 (C-1), 152.29 (C-3), 139.83 (C, Ph), 130.78 (CH, Ph), 128.22 (2 CH, Ph), 126.98 (2 CH, Ph), 89.78 (C-2), 50.30 and 23.78 ($NCHMe_2$); EI-MS, *m/z* 189 (M^+, 19), 174 (7), 146 (10), 112 (13), 105 (87), 77 (100), 70 (51), 58 (17), 51 (28).

(*Z*)-**2f**. M.p. 47.6–48.8 °C; IR (KBr), 3250, 1625, 1580; ^{1}H NMR ($CDCl_3$), 10.72 (d, *J* = 13.0, 1H, H-N), 7.84–7.90 (m, 2H, Ph), 7.36–7.44 (m, 3H, Ph), 7.13 (dd, *J* = 13.0, 7.4, 1H, H-3), 5.72 (d, *J* = 7.4, 1H, H-2), 1.36 (s, 9H, $NCMe_3$); ^{13}C NMR ($CDCl_3$), 189.44 (C-1), 149.93 (C-3), 139.91 (C, Ph), 130.72 (CH, Ph), 128.21 (2 CH, Ph), 126.97 (2 CH, Ph), 89.85 (C-2), 52.20 and 30.08 ($NCMe_3$); EI-MS, *m/z* 203 (M^+, 37), 188 (48), 146 (65), 105 (99), 91 (16), 77 (100), 70 (91), 57 (75), 51 (38).

(*Z*)-**3e**.[31] IR (film) 3220, 3060, 1610, 1580, 1565; ^{1}H NMR ($CDCl_3$), 11.00 (br, 1H, H-N), 4.96 (s, 1H, H-2), 3.06 (t, *J* = 6.5, 2H, NCH_2CHMe_2), 2.01 (s, 3H, COMe), 1.91 (s, 3H, Me), 1.83 (m, 1H, NCH_2CHMe_2), 0.98 (d, *J* = 6.6, 6H, NCH_2CHMe_2); ^{13}C NMR ($CDCl_3$), 194.60 (C-1), 163.31 (C-3), 95.07 (C-2), 50.67, 29.12 and 20.11 (NCH_2CHMe_2), 28.72 (COMe), 18.94 (Me).

(*E*)-**4d**.[39] IR (film), 3240, 3060, 1660, 1625, 1565, 1545, 1530; ^{1}H NMR ($CDCl_3$), 5.14 (s, 1H, H-2), 4.35 (br, 1H, H-N), 3.60 (m, 1H, $NCHMe_2$), 2.27–2.36 (m, 4H, 2 CH_2), 1.97 (m, 2H, CH_2), 1.20 (d, *J* = 6.3, 6H, $NCHMe_2$); ^{13}C NMR ($CDCl_3$),197.22 (C-1), 163.81 (C-3) , 96.52 (C-2), 44.06 and 22.08 ($NCHMe_2$), 36.37, 29.97 and 21.98 (3 CH_2); EI-MS *m/z* 153 (M^+, 13), 138 (12), 125 (18), 110 (38), 97 (33), 96 (100), 83 (34), 82 (44), 68 (28), 55 (23).

(*E*)-**4e**. IR (film), 3240, 3060, 1660, 1580, 1545, 1530; ^{1}H NMR ($CDCl_3$), 5.12 (s, 1H, H-2), 4.72 (br, 1H, H-N), 2.90 (dd, *J* = 6.5, 6.0, 2H, NCH_2CHMe_2), 2.35 (t, *J* = 6.3, 2H, CH_2), 2.32 (t, *J* = 6.5, 2H, CH_2), 1.97 (m, 2H, CH_2), 1.91 (m, 1H, NCH_2CHMe_2), 0.95 (d, *J* = 6.6, 6H, NCH_2CHMe_2); ^{13}C NMR ($CDCl_3$), 197.16 (C-1), 165.47 (C-3), 96.17 (C-2), 50.55, 27.42 and 20.11 (NCH_2CHMe_2), 36.43, 29.69 and 22.03 (3 CH_2); EI-MS, *m/z* 167 (M^+, 21), 124 (100), 112 (83), 97 (78), 96 (89), 84 (72), 83 (48), 67 (46), 55 (38).

(*Z*)-**6c**. IR (film), 3230, 3060, 1655, 1590, 1565, 1550; ^{1}H NMR ($CDCl_3$), 11.37 (br, 1H, H-N), 7.88–7.93 (m, 2H, Ph), 7.38–7.50 (m, 8H, Ph), 5.76 (d, *J* = 7.0, 1H, H-2), 3.27 (qd, *J* = 7.1, 6.0, 2H, NCH_2Me), 1.24 (t, *J* = 7.1, 3H, NCH_2Me);^{13}C NMR ($CDCl_3$), 188.21 (C-1), 166.73 (C-3), 140.30 and 135.71 (2 C, Ph), 130.62 (CH, Ph), 129.41 (CH, Ph), 128.51 (2 CH, Ph), 128.17 (2 CH, Ph), 127.58 (2 CH, Ph), 126.98 (2 CH, Ph), 93.16 (C-2), 39.53 and 16.13 (NCH_2Me); EI-MS, *m/z* 251 (M^+, 41), 250 (43), 235 (19), 234 (73), 222 (8), 221 (7), 174 (5), 146 (4), 105 (43), 104 (23), 103 (22), 91 (20), 77 (100), 51 (35).

(*Z*)-**7g**. IR (film), 3280, 3060, 3030, 1655, 1635, 1570, 1550; ^{1}H NMR ($CDCl_3$), 10.04 (br, 1H, H-N), 7.24–7.40 (m, 5H, Ph), 6.72 (dd, *J* = 12.7, 7.3, 1H, H-3), 5.05 (d, *J* = 7.3, 1H, H-2), 4.37 (d, *J* = 6.0, 2H,

CH_2Ph), 2.33 (q, $J = 7.5$, 2H, CH_2Me), 1.10 (t, $J = 7.5$, 3H, CH_2Me); ^{13}C NMR ($CDCl_3$), 201.43 (C-1), 152.30 (C-3), 138.00 (C, Ph), 128.77 (2 CH, Ph), 127.65 (CH, Ph), 127.17 (2 CH, Ph), 93.36 (C-2), 52.46 (NCH_2Ph), 34.93 and 9.63 (CH_2Me); EI-MS, m/z 189 (M^+, 30), 160 (46), 132 (11), 130 (9), 104 (11), 92 (37), 91 (100), 77 (13), 65 (45).

(*Z*)-**8g**. IR (film), 3280, 3060, 3030, 1658, 1632, 1570, 1550; ^1H NMR ($CDCl_3$): 10.08 (br, 1H, H-N), 7.22–7.40 (m, 5H, Ph), 6.76 (dd, $J = 12.5$, 7.3, 1H, H-3), 5.07 (d, $J = 7.3$, 1H, H-2), 4.36 (d, $J = 6.0$, 2H, CH_2Ph), 2.50 (m, 1H, $CHMe_2$), 1.10 (d, $J = 6.7$, 6H, $CHMe_2$); ^{13}C NMR ($CDCl_3$), 204.77 (C-1), 152.79 (C-3), 137.91 (C, Ph), 128.77 (2 CH, Ph), 127.66 (CH, Ph), 127.25 (2 CH, Ph), 92.21 (C-2), 52.50 (NCH_2Ph), 39.63 and 19.57 ($CHMe_2$); EI-MS, m/z 203 (M^+, 6), 160 (21), 130 (3), 98 (9), 91 (100), 77 (3), 65 (11).

(*Z*)-**9g**. IR (film), 3280, 3060, 3030, 1660, 1632, 1567, 1550; ^1H NMR ($CDCl_3$), 10.11 (br, 1H, H-N), 7.20–7.37 (m, 5H, Ph), 6.80 (dd, $J = 12.6$, 7.6, 1H, H-3), 5.23 (d, $J = 7.6$, 1H, H-2), 4.36 (d, $J = 6.0$, 2H, CH_2Ph), 1.14 (s, 9H, CMe_3); ^{13}C NMR ($CDCl_3$), 206.52 (C-1), 152.99 (C-3), 137.93 (C, Ph), 128.77 (2 CH, Ph), 127.67 (CH, Ph), 127.33 (2 CH, Ph), 89.72 (C-2), 52.55 (NCH_2Ph), 41.63 and 27.67 (CMe_3); EI-MS, m/z 217 (M^+, 12), 160 (40), 130 (10), 98 (75), 91 (100), 77 (9), 65 (22).

(*Z*)-**11b**. M.p. 75.8–76.9 °C; IR (KBr), 3220, 1720, 1632; ^1H NMR ($CDCl_3$), 10.37 (br, 1H, H-N), 7.07 (dd, $J = 13.4$, 7.0, 1H, H-3), 5.83 (d, $J = 7.0$, 1H, H-2), 4.29 (q, $J = 7.1$, 2H, OCH_2Me), 3.14 (d, $J = 5.2$, 3H, NMe), 1.36 (t, $J = 7.1$, 3H, OCH_2Me); ^{13}C NMR ($CDCl_3$), 178.61 (C-1), 163.63, 61.67 and 14.14 (CO_2CH_2Me), 158.30 (C-3), 91.44 (C-2), 35.97 (NMe); EI-MS, m/z 157 (M^+, 2), 111 (2), 84 (100), 55 (5).

(*Z*)-**11c**. IR (film), 3240, 1725, 1628; ^1H NMR ($CDCl_3$), 10.52 (br, 1H, H-N), 7.11 (dd, $J = 13.0$, 7.0, 1H, H-3), 5.82 (d, $J = 7.0$, 1H, H-2), 4.29 (q, $J = 7.1$, 2H, OCH_2Me), 3.37 (qd, $J = 7.1$, 6.0, 2H, NCH_2Me), 1.36 (t, $J = 7.1$, 3H, OCH_2Me), 1.29 (t, $J = 7.1$, 3H, NCH_2Me); ^{13}C NMR ($CDCl_3$), 178.50 (C-1), 163.68, 61.62 and 14.14 (CO_2CH_2Me), 156.68 (C-3), 91.19 (C-2), 44.33 and 16.05 (NCH_2Me); EI-MS, m/z 171 (M^+, 3), 125 (2), 98 (100), 80 (36), 70 (9), 68 (8).

(*Z*)-**11d**. IR (film), 3240, 1725, 1627; ^1H NMR ($CDCl_3$), 10.60 (br, 1H, H-N), 7.16 (dd, $J = 13.4$, 7.0, 1H, H-3), 5.81 (d, $J = 7.0$, 1H, H-2), 4.29 (q, $J = 7.1$, 2H, OCH_2Me), 3.56 (m, 1H, $NCHMe_2$), 1.36 (t, $J = 7.1$, 3H, OCH_2Me), 1.30 (d, $J = 6.6$, 6H, $NCHMe_2$); ^{13}C NMR ($CDCl_3$), 178.34 (C-1), 163.71, 61.58 and 14.13 (CO_2CH_2Me), 154.92 (C-3), 91.01 (C-2), 50.93 and 23.51 ($NCHMe_2$); EI-MS, m/z 185 (M^+, 5), 139 (3), 112 (100), 96 (25), 94 (20), 82 (4), 70 (67).

(*Z*)-**11e**. IR (film), 3250, 1725, 1630; ^1H NMR ($CDCl_3$), 10.65 (br, 1H, H-N), 7.07 (dd, $J = 13.3$, 7.0, 1H, H-3), 5.83 (d, $J = 7.0$, 1H, H-2), 4.29 (q, $J = 7.1$, 2H, OCH_2Me), 3.14 (t, $J = 6.6$, 2H, NCH_2CHMe_2), 1.85 (m, 1H, NCH_2CHMe_2), 1.36 (t, $J = 7.1$, 3H, OCH_2Me), 0.96 (d, $J = 6.6$, 6H, NCH_2CHMe_2); ^{13}C NMR ($CDCl_3$), 178.49 (C-1), 163.65, 61.65 and 14.14 (CO_2CH_2Me), 157.53 (C-3), 91.11 (C-2), 57.48, 29.57 and 19.61 (NCH_2CHMe_2); EI-MS, m/z 199 (M^+, 5), 126 (100), 110 (3), 108 (3), 82 (31), 70 (53), 57 (19), 55 (20).

(*Z*)-**11f**. IR (film), 3250, 1725, 1628; ^1H NMR, 11.01 (br, 1H, H-N), 7.26 (dd, $J = 13.7$, 7.0, 1H, H-3), 5.85 (d, $J = 7.0$, 1H, H-2), 4.29 (q, $J = 7.1$, 2H, OCH_2Me), 1.36 (t, $J = 7.1$, 3H, OCH_2Me), 1.35 (s, 9H, $NCMe_3$); ^{13}C NMR ($CDCl_3$), 177.98 (C-1), 163.76, 61.55 and 14.13 (CO_2CH_2Me), 152.80 (C-3), 91.04 (C-2), 53.23 and 29.82 ($NCMe_3$); EI-MS, m/z 199 (M^+, 4), 126 (45), 110 (10), 82 (10), 70 (100), 57 (22).

(*Z*)-**11g**. IR (film), 3240, 1725, 1630; ^1H NMR ($CDCl_3$), 10.74 (br, 1H, H-N), 7.22–7.40 (m, 5H, Ph), 7.16 (dd, $J = 13.0$, 7.0, 1H, H-3), 5.89 (d, $J = 7.0$, 1H, H-2), 4.50 (d, $J = 5.7$, 2H, NCH_2), 4.29 (q, $J = 7.1$, 2H, OCH_2Me), 1.36 (t, $J = 7.1$, 3H, OCH_2Me); ^{13}C NMR ($CDCl_3$), 179.06 (C-1), 163.45, 61.71 and 14.11 (CO_2CH_2Me), 156.91 (C-3), 136.51 (C, Ph), 128.98 (2 CH, Ph), 128.12 (CH, Ph), 127.23 (2 CH, Ph), 91.83 (C-2), 53.09 (NCH_2Ph); EI-MS, m/z 233 (M^+, 5), 160 (19), 130 (6), 104 (3), 91 (100), 77 (5), 65 (19).

Melting points were observed under a microscope using a Mettler FP-52 instrument.

Spectroscopy

The ^{17}O NMR spectra were recorded on a Bruker WH-360 spectrometer, equipped with a 10 mm probe, at 48.8 MHz, in the Fourier transform (FT) mode without lock. System control, data acquisitions and data management were performed with an Aspect-2000 microcomputer.

The instrumental settings were as follows: spectral width 50 kHz (1025 ppm), 2K data points, pulse width 33 μs, acquisition time 20 ms, preacquisition delay 5 μs, 2×10^5–5×10^5 scans, sample spinning (28 Hz). An even number (12–28) of left shifts (LS) were applied to the FID signal; the latter was zero-filled to 8K words and exponentially multiplied with a 100 Hz line-broadening factor (LB) before being subjected to FT. The chemical shifts δ_0, measured in 0.5 M acetonitrile solution at 40 °C at natural isotopic abundance, are reported relative to $\delta_0(H_2O)$ (=0.0 ppm); dioxane ($\delta_0 = 0$ ppm) was used as an external standard; downfield shifts are positive. The general reproducibility of chemical shifts values is *ca.* ±1 ppm (±0.2 ppm within the same series).

The ^1H and ^{13}C NMR spectra (δ, in ppm relative to internal TMS in $CDCl_3$ solution at 20 °C) were recorded on Bruker WH-250 and Bruker Advance DPX-400 spectrometers, IR spectra on a Perkin-Elmer 1420 spectrophotometer and electron impact (EI) mass spectra on a Nermag R-10-10C spectrometer.

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