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NMR of Enaminones

Part 4†—^{17}O NMR Study of 2,2-Diacylenamines

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Natural abundance ^{17}O NMR spectra of 41 2,2-diacylenamines (enamino diketones and enamino diesters), recorded in acetonitrile solution, are reported. Tertiary enamino diketones show only one ^{17}O signal; primary and secondary derivatives show two ^{17}O signals. The shift difference ($\Delta\delta_{HB}$) between the two carbonyl groups is mainly attributed to intramolecular hydrogen bonding and depends on the donor property of the amino group and the structure of the enamino diketone. The $\delta(^{17}O)$ values correlate well with the pK_a values of amines. Correlations of $\delta(^{17}O\text{-}1)$ values for the chelated carbonyl group with their $\delta(^{13}C\text{-}1)$ and $\delta(^{13}C\text{-}2)$ values are observed. © 1997 by John Wiley & Sons, Ltd.

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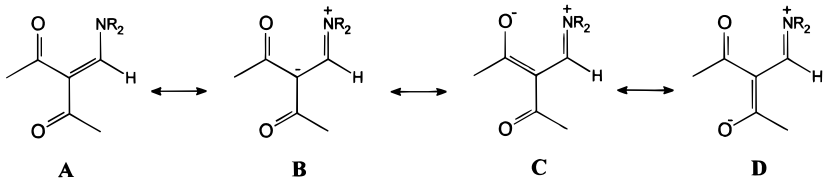
INTRODUCTION

Enaminones are important organic intermediates,[2] and have been reported as potentially biologically active.[3] Enaminone derivatives, diacylenamines,[2a] are useful starting materials for the synthesis of heterocyclic compounds,[2a] the antimalarial drug choroquine and similar products of medicinal interest.[4] The diacylvinyl groups have been used to protect the amino group of amino acids during the synthesis of peptides and penicillin derivatives[5] and amino sugars during Fischer glycosidation.[6] The properties of diacylenamines have been investigated by UV,[7] IR[8] and ^{1}H,[8a,9] ^{13}C[9c,10] and ^{15}N NMR spectroscopy.[9c,11] These studies confirmed that the resonance structures (**B**, **C** and **D**) are important in the ground state of the molecule (Scheme 1).

The resonance interaction of the amino group with the C=C bond, as in enaminones, enamines and amides, reduces the C=C bond order and increases the C—N bond order. The increased C—N bond order in diacylenamines parallels the high barrier of rotation around the C—N bond [13–20 kcal mol^{-1} (1 kcal = 4.184 kJ)],[12] as compared with that in enaminones (9–16 kcal mol^{-1})[13] and enamines (*ca.* 7 kcal mol^{-1}),[14] and is consistent with the results of x-ray analyses. The x-ray crystallographic studies show that in diacylenamines[15] the C—N bond (1.30–1.32 Å) is shorter and the C=C bond (1.39–1.41 Å) is longer than those in enaminones (C—N, 1.32–1.36 Å; C=C, 1.37–1.39 Å)[16] and those in enamines (C—N, 1.38–1.41 Å; C=C, 1.33–1.37 Å).[17]

^{17}O NMR is a particularly useful tool for studying electron distributions[18] and intramolecular hydrogen bonding in molecules.[18,19] Recently, the ^{17}O NMR spectra of enaminones have been investigated.[20] The ^{17}O chemical shifts of enaminones correlated well with their vinylic ^{13}C-2 shifts and with the pK_a values of the amines. As the chemical shift of ^{13}C-2 serves as a characteristic of the electron density, the shielding of the O-atom in enaminones depends on the electron density at the O-atom and reflect the polarization and the degree of n,π-conjugation in the N—C=C—C=O system.[20] In hydrogen-bonded primary and secondary enaminones, the influence of substituents on ^{17}O shift value of the carbonyl O-atom is additive.[20b] The shield-



Scheme 1

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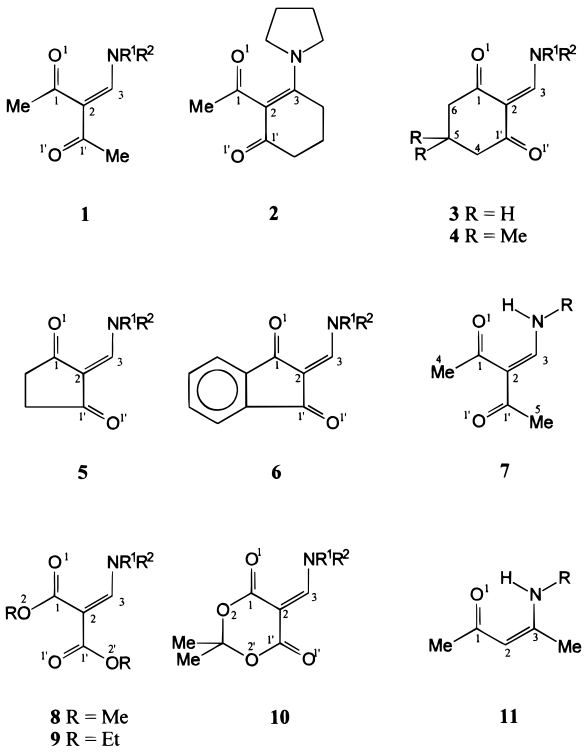
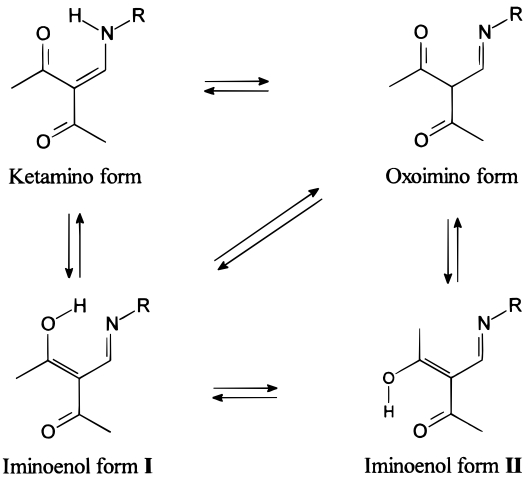


Scheme 2



Scheme 3

ing of the carbonyl O-atom by intramolecular hydrogen bonding ($\Delta\delta_{HB}$), ranging from −14 to −47 ppm, was sensitive to the nature, number and position of the substituents.[20b] It has been demonstrated that the ^{17}O NMR parameters are sensitive to electronic effects, torsional angles, steric interactions and intramolecular hydrogen bonding.[18,19] Therefore, to evaluate the $\Delta\delta_{HB}$ values these factors should be taken into account.

The presence of an intramolecular C=O···HN bond in primary and secondary diacylenamines has been clearly indicated by IR[8a] and ^{1}H NMR spectroscopy[8a] and x-ray crystallography.[15] It has been shown that the hydrogen-bonded diacylenamine systems are essentially planar and that the electron delocalization affects both carbonyl groups almost equally.[15] This makes diacylenamine systems suitable for evaluating the contribution of intramolecular hydrogen bonding in ^{17}O NMR data. ^{17}O NMR investigations of diacylenamines have not been reported. This paper reports the ^{17}O chemical shifts for a variety of 2,2-diacylenamines (**1**–**10**, Scheme 2) in which the effects of the C=O···H—N type of intramolecular hydrogen bonds on the ^{17}O chemical shifts of the hydrogen bonded carbonyl are evaluated.

RESULTS AND DISCUSSION

Structure of enamino diketones

The tautomeric equilibrium of enamino diketones with a primary or secondary amino group is shown in Scheme 3.

The tautomeric iminoenols (**I** and **II**), oxoimino and ketamino forms can be easily distinguished by their ^{1}H NMR data. In the spectra of enaminodiones with a secondary amino group (see Tables 2 and 4), the signals of vinyl proton ^{1}H-3 at δ7.7–8.6 ppm, as a doublet (J = 11–14 Hz), show that the iminoenol forms (**I** and **II**) are not present. The non-equivalence of the two methyl groups and the presence of the strong intramolecular hydrogen bond evidenced by the δ(NH) values (9–13 ppm) indicate that the oxoimino form is not present either. Hence these enamino diketones exist in solution in the ketamino form. In contrast, the structures of enamino diketones with a primary amino group (**3b**, **4b**, and **7a**) were previously assigned as the iminoenol form **I** based on the UV, IR and NMR spectra.[21] In the present case, the ^{1}H NMR spectra of **3b**, **4b** and **7a** show that the vinyl protons (H-3) have a doublet–doublet splitting with coupling constants of 15.6 and 8.7 Hz, and that N-H protons show two broad signals at 5.8–7.3 and 10.3–10.5 ppm, attributed to the non-bonded and bonded N-H, respectively. These data clearly indicate that the enamino diketones (**3b**, **4b** and **7a**) exist in solution in the ketamino form. This is further supported by their ^{17}O NMR data. The ^{17}O signals of the two carbonyls of primary enamino diketones (**3a**, **4b** and **7a**: 445–505 ppm) appear in the region observed for secondary enamino diketones which are known to exist in ketamino form,[7] and there is no signal corresponding to an OH group. The ^{17}O NMR signal for the OH chelated with a C=O group appears at 62–124 ppm,[19,22] and chelated with a C=N (azine) group at *ca.* 95 ppm.[22b] The ^{17}O signals of OH in 2-acylcyclohexane-1,3-diones and 2-acylindan-1,3-diones, in which the structures of the enol forms are very similar to the iminoenol forms **I** and **II**, appear at 120–248 ppm.[22d] Thus the two signals found in compounds **3b**, **4b** and **7a** must belong to the carbonyl groups. This confirms the results of the ^{1}H NMR data, i.e. that primary enamino diketones exist in solution in a ketamino form.

Enamino diketones in the ketamine form can exist in several isomeric forms owing to restricted rotation around the C—CO and C—N single bonds and the C=C double bond. The presence of strong intramolecular hydrogen bonds in enamino diketones with a primary or secondary amino group favours two conformations, the *EZE* and *ZZE* forms (Scheme 4). The ^{1}H chemical shift differences between the two COMe groups in **7** are 0.19–0.24 ppm (Table 4), which is much larger than those (0.04 ppm, Table 2) found between the

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EZE ZZE

Scheme 4

two $COCH_2$ in the fixed *ZZE* conformation **3** and **4**. This can be explained in terms of the anisotropy effect of the non-bonded carbonyl group, which exists in an *s-trans* conformation and causes a deshielding of ^{1}H-4. Therefore, compounds **7** exist in solution in the *EZE* conformation. This is consistent with previous IR, Raman and ^{1}H NMR spectroscopic[8a] and the x-ray crystallographic studies,[15] which show that the chelated enamino diketone systems are essentially planar and that the open-chain enamino diketones adopt the *EZE* conformation and the cyclic enamino diketones the fixed *ZZE* conformation.

Tertiary enamino diketones

The ^{17}O NMR chemical shifts for a series of enamino diketones with tertiary amino groups (**1a–1k**, **2**, **3a–6a**) were recorded at natural abundance in acetonitrile (Table 1). With the exception of the non-symmetric amino group **1e**, the ^{17}O spectra of compounds **1** show only one signal at *ca.* 525 ppm (Table 1). They are shifted to lower field by *ca.* 75 ppm relative to those noted for enaminones (450 ppm).[20a] Similar deshielding was observed for imides (*ca.* 370 ppm)[18] *vs.* amides (*ca.* 330 ppm)[18] and for anhydrides (*ca.* 400 ppm)[18] *vs.* esters (*ca.* 350 ppm).[18] This may result from increased the bond order of the C=O bond due to the second electron-withdrawing carbonyl group which shares the electronic effect coming from the amino group.

Considerable shielding of 62–84 ppm is observed for cyclic enaminone diketones (**3a**, **4a** and **5a**) compared with **1a**. The same effect has been reported previously in enaminone system; 2-(dimethylaminomethylene)cyclohexanone (432 ppm)[20a] and 2-(dimethylaminomethylene)cyclopentanone (410 ppm)[20a] are shielded by 24 and 45 ppm, respectively, relative to 4-dimethylaminobut-3-en-2-one (456 ppm).[20a] The high shielding may be attributed to the reduced double bond character of the carbonyls due to the increased bond polarization and n,π-conjugation of the N—C=C—(C=O)$_2$ system. It has been shown that the ^{13}C shift difference between the two olefinic carbons, which reflects the bond polarization and the degree of the n,π-conjugation, correlated well with the shielding of O in of enaminones.[20a] The ^{13}C shift differences between the C-3 and C-2 for **3a**, **4a** and **5a** (*ca.* 51 ppm) are much larger than that for **1a** (40 ppm).

The existence of only one signal for this type of compound (except for **1e**, **2** and **6a**) can be attributed to the low barriers of rotation around the C=C bond, which makes the isomerization about the C=C double bond fast on the NMR time-scale. The barrier to isomerization about the C=C bond for **1a** is *ca.* 10 kcal mol^{-1}.[12] This result suggests that the dipolar resonance structures **B–D** (Scheme 1) are the main contributors to the ground state of the molecule.

The cyclic compound **2**, with a fixed configuration of the C=C bond, shows two carbonyl ^{17}O signals at 455 and 533 ppm. The former can be assigned to the cyclic carbonyl O-1′, as compared with 3-pyrrolidinylcyclohex-2-en-1-one (443 ppm).[20a] The lower field signals of **2** corresponds to the acetyl O-1. The considerable deshielding of O-1 (79 ppm) relative to the cyclic carbonyl O-1′ can be attributed to the strong steric interaction between the acetyl group and both the cyclic carbonyl group and pyrrolidinyl ring, which twist the acetyl group out of the plane of the enaminone system. The ^{17}O chemical shift of the acetyl O-1 is close to those for ketones (*ca.* 550 ppm),[18] indicating that there is a lack of conjugation between the acetyl group and enaminone system.

Two carbonyl signals (at 424 and 456 ppm) are also observed for compound **6a**. Molecular mechanics calculations show that the molecule **6a** is essentially planar and that the bond angle of O-1—C-1—C-2 (128.6°) is larger than that of O-1′—C-1′—C-2 (125.6°). It has been reported that in planar molecules a bond angle distortion causes deshielding of O.[18,20a] Therefore, the high field signal was assigned to the *trans*-carbonyl O-1′ and the low field signal to the *cis*-carbonyl O-1.

A similar result is observed for compound **1e**, which shows two ^{17}O signals at 502 and 585 ppm. As discussed above, the former is assigned to the *trans*-carbonyl O-1′ which is conjugated with the enamine system, and the latter corresponds to the *cis*-carbonyl O-1 which is twisted out of the plane of the enaminone system due to steric repulsion with the amino group.

The ^{17}O spectra of enamino diesters (**8**, **9** and **10**) are summarized in Table 5. One signal at 293 ppm was observed for cyclic enamino diester **10a**. In the acyclic

Table 1. ^{17}O and ^{13}C data (ppm) for tertiary enamino diketones (1–6)

Compound	R^1	R^2	^{17}O[a,b]	^{13}C-2	^{13}C-3
1a	Me	Me	524.5	115.10	156.59
1b	Et	Et	526.3	115.02	152.85
1c	*i*-Pr	*i*-Pr	525.2	114.28	149.26
1d	$PhCH_2$	$PhCH_2$	536.5	116.78	153.01
1e	Me	Ph	501.7[c]	117.04	151.10
1f	$(CH_2)_4$		524.0	115.68	152.06
1g	$(CH_2)_5$		521.1	113.67	155.60
1h	$(CH_2)_6$		525.9	115.01	155.35
1i	$(CH_2)_7$		526.6	115.41	153.99
1j	$(CH_2)_2O(CH_2)_2$		526.5[d]	114.63	154.47
1k	$(CH_2)_2NMe(CH_2)_2$		525.3	114.63	154.80
2	—	—	454.6[e]	113.64	167.01
3a	Me	Me	457.9	109.36	162.28
4a	Me	Me	462.5	108.22	161.75
5a	Me	Me	440.6[f]	106.72	156.36
6a	Me	Me	424.5[g]	103.10	152.97

[a] 0.5 M acetonitrile solution at 40 °C, δ(O-1) = δ(O-1′), unless indicated otherwise.
[b] Linewidth at half-height: 250–630 Hz (880 Hz for **1f**).
[c] Signal for O-1′; δ(O-1) = 584.7 ppm.
[d] δ(—O—) = 1.2 (100) ppm.
[e] Signal for O-1′; δ(O-1) = 533.3 ppm.
[f] Recorded at 70 °C.
[g] Signal for O-1′; δ(O-1) = 456.3 ppm; measurement at 70 °C gives δ(O-1) = 457.8 ppm and δ(O-1′) = 426.0 ppm.

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enamino diester **8a**, two carbonyl oxygen signals are observed at 372 and 304 ppm; and two ether oxygens are at 149 and 119 ppm. The higher field signals for the carbonyl and methoxy oxygen (304 and 119 ppm) can be assigned to the *trans*-carbonyl group, as compared with methyl 3-dimethylaminoprop-2-enoate (295 and 119 ppm).[20a] The lower field signals (372 and 147 ppm) corresponds to the *cis*-carbonyl group, which is close to those found in methyl acetate (359 and 140 ppm, in acetonitrile solution, new measurement). The deshielding of the *cis*-carbonyl group can be attributed to steric repulsion between the amino and *cis*-carbonyl groups. Previous x-ray studies showed that the *cis*-carbonyl group is twisted out of the enamino ester plane by 67°.[15d]

Primary and secondary enamino diketones

The ^{17}O spectra of enamino diketones (**3–7**) with primary or secondary amino groups (Table 2 and 3) exhibit two carbonyl ^{17}O signals: those at higher field are assigned to the intramolecular hydrogen-bonded carbonyl groups O-1 and the lower field signals to the free carbonyl O-1′. The effects of substituents in these compounds are similar to those noted for the corresponding *N*-substituted enaminones.[20b] It has been shown that the influence of the substituents on ^{17}O chemical shifts of the carbonyl groups in various enaminone systems is additive:[20b]

$$\delta(^{17}\mathrm{O}) = 462.2 + \sum\Delta_i(R_i) \quad (1)$$

where Δ_i is the increment value of substituent R at the *i*-position. The additivity relationship also exists in enamino diketones **7**. The increment value of the hydrogen bonded 2-acetyl group ($\Delta_{Z\text{-}2\text{-}Ac}$) is assigned a value of 53.6 ppm deshielding, and the increment value of non-bonded 2-acetyl group ($\Delta_{E\text{-}2\text{-}Ac}$) is assigned a value of 22.6 ppm deshielding. The calculated ^{17}O chemical shifts for the both carbonyl O-atoms are included in Table 3. The differences between the calculated and the experimental data, $\Delta\delta = \delta(^{17}\mathrm{O}) - \delta(^{17}\mathrm{O})^{calc.}$, are less

Table 2. ^{17}O, ^{1}H and ^{13}C data (ppm) for primary and secondary enamino diketones 3–6

Compound	R^1	R^2	^{17}O-1[a]	^{17}O-1′[a]	$\Delta\delta_{HB}$[b]	^{1}H-N[c]	^{1}H-3	H-4[d]	H-6[d]	^{13}C-1	^{13}C-1′	^{13}C-2	^{13}C-3
3b	H	H	444.5	451.1	−6.6	10.50	8.24 (dd, 15.6, 8.7)	2.47	2.51	200.64	197.57	109.70	158.41
3c	H	Me	436.9[e]	440.8	−3.9	11.07	8.12 (dq, 14.0, 0.7)	2.46	2.48	199.75[f]	196.60[g]	108.77	160.25
3d	H	Ph	451.7	457.3	−5.6	12.93[h]	8.65 (d, 14.0)	2.54	2.58	200.56	196.79	110.07	151.02
4b	H	H	449.8	454.8	−5.0	10.45	8.21 (dd, 15.6, 8.7)	2.36	2.40	200.00	197.09	108.41	157.92
4c	H	Me	440.7	444.8	−4.1	11.01	8.10 (d, 14.0)	2.33	2.37	199.04	196.02	107.52	159.71
4d	H	Ph	458.6	462.9	−4.3	12.88[i]	8.62 (d, 13.8)	2.43	2.47	199.97	196.35	108.84	150.46
5b	H	Me	430.4[j]	430.4	0.0	10.19	7.73 (d, 14.0)	2.52	2.52	206.00	202.03	107.73	156.13
5c	H	Ph	446.0[k]	446.0	0.0	11.94	8.24 (d, 11.5)	2.63	2.63	206.28	202.27	108.94	146.66
6b	H	Me	434.4[l]	434.4	0.0	9.10	7.69 (d, 14.0)	—	—	193.84	188.99	104.45	153.27

[a] 0.5 M acetonitrile solution at 40 °C, unless indicated otherwise; linewidth at half-height: 190–410 Hz.
[b] $\Delta\delta_{HB} = \delta(^{17}\mathrm{O}\text{-}1) - \delta(^{17}\mathrm{O}\text{-}1')$.
[c] Singlet, unless indicated otherwise.
[d] Triplet for **3b**, **3c** and **3d**, J = 6.5 Hz; singlet for **4b**, **4c** and **4d**; multiplet for **5b** and **5c**.
[e] Measurement at 70 °C gives δ(O-1′) = 442.9 ppm and δ(O-1) = 437.4 ppm.
[f] $^3J_{CO,\,H\text{-}3}$ = 7.2 Hz.
[g] $^3J_{CO,\,H\text{-}3}$ = 3.0 Hz.
[h] Broad doublet, J = 14.0 Hz.
[i] Broad doublet, J = 13.8 Hz.
[j] Recorded at 70 °C.
[k] 0.1 M acetonitrile solution at 70 °C.
[l] 0.2 M acetonitrile solution at 70 °C.

Table 3. ^{17}O data (ppm) for 7

Compound	R	^{17}O-1[a]	^{17}O-1$^{calc.}$[b]	$\Delta\delta$[c]	^{17}O-1′[a]	^{17}O-1′$^{calc.}$[b]	$\Delta\delta$[c]	$\Delta\delta_{HB}$[d]
7a	H	484.7	484.8	−0.1	504.5	515.8	−11.3	−19.8
7b	Me	468.5	467.3	0.8	498.1	498.3	−0.2	−29.6
7c	Et	469.6	469.1	0.5	498.5	500.1	−1.6	−28.9
7d	*i*-Pr	469.1	469.3	−0.2	499.5	500.3	−0.8	−30.4
7e	*t*-Bu	466.5	467.1	−0.6	499.8	498.1	1.7	−33.3
7f	CH_2Ph	472.8	474.5	−1.7	502.6	505.5	−2.9	−29.8
7g	*i*-Bu	468.0	466.9	1.2	500.3	497.8	2.5	−31.7
7h	Cyclohexyl	468.5	468.8	−0.3	500.0	499.8	0.2	−31.5
7i	Ph	483.9	491.9	−8.0	518.2	522.9	−4.7	−34.3
7j	2,6-$Me_2C_6H_3$	479.2	—	—	511.3	—	—	−32.1

[a] 0.5 M acetonitrile solution at 40 °C; linewidth at half-height: 150–360 Hz.
[b] Δ_N values were taken from Ref. 20b; for cyclohexylamino group, Δ_N = −16.0 ppm; for hydrogen-bonded 2-acetyl group, $\Delta_{Z\text{-}2\text{-}Ac}$ = 53.6 ppm; for non-bonded 2-acetyl group, $\Delta_{E\text{-}2\text{-}Ac}$ = 22.6 ppm.
[c] $\Delta\delta = \delta(^{17}\mathrm{O}) - \delta(^{17}\mathrm{O})^{calc.}$.
[d] $\Delta\delta_{HB} = \delta(^{17}\mathrm{O}\text{-}1) - \delta(^{17}\mathrm{O}\text{-}1')$.

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Table 4. ^{1}H and ^{13}C data (ppm) for 7

Compound	^{1}H-N[a]	^{1}H-3	H-4[a]	H-5′[a]	^{13}C-1	^{13}C-1′	^{13}C-2	^{13}C-3
7a	10.32	7.89 (dd, 8.6, 15.6)	2.50	2.28	201.26	195.33	112.75	158.40
7b	10.95	7.74 (d, 13.2)	2.48	2.28	200.30	194.31	111.50	161.33
7c	11.04	7.76 (d, 13.4)	2.47	2.26	200.26	194.35	111.30	159.56
7d	11.07	7.80 (d, 13.5)	2.47	2.27	200.15	194.41	111.10	157.79
7e	11.42	7.88 (d, 13.7)	2.47	2.27	200.01	194.44	111.06	155.36
7f	11.33	7.81 (d, 13.3)	2.50	2.26	200.51	194.42	111.86	159.83
7g	11.15	7.71 (d, 13.2)	2.49	2.27	200.30	194.39	111.19	160.38
7h	11.15	7.81 (d, 13.2)	2.48	2.27	200.14	194.36	111.14	157.90
7i	12.76[b]	8.24 (d, 12.8)	2.56	2.38	201.12[c]	194.83[d]	113.27	151.86
7j	12.31[b]	7.82 (d, 12.8)	2.58	2.27	201.30	194.65	112.12	159.14

[a] Singlet, unless indicated otherwise.
[b] Doublet, $J = 12.8$ Hz.
[c] $^{3}J_{CO,\,H\text{-}3} = 7.0$ Hz.
[d] $^{3}J_{CO,\,H\text{-}3} = 4.0$ Hz.

than ± 3 ppm (Table 3) except for **7a** and **7i**. The experimental chemical shift of the non-bonded carbonyl O-1′ of **7a** is much smaller than the calculated value, indicating that there is an additional shielding arising from the contribution of intermolecular hydrogen bonding. The large $\Delta\delta$ values (-8.0 ppm for O-1 and -4.7 ppm for O-1′) for **7i** indicate that the N-Ph ring is twisted out of the plane of enamino diketone system owing to steric repulsion between N-Ph and H-3. Introducing alkyl groups in the two *ortho* positions of **7i**, as in compound **7j**, creates an effect of angular torsion. The slight shielding of the two carbonyl in **7j**, as compared with those in **7i**, demonstrates that the N-Ph ring in **7i** is not coplanar with the enamino diketone moiety. The crystal structure of *N*-(2,2-diacetylvinyl)-*o*-phenylenediamine shows that the aryl ring is rotated out of the plane of enamino diketone by $-145°$.[15a]

The ^{17}O chemical shifts of enaminones have been shown to depend on the donor quality of the amino nitrogen[1,20] and to correlate well with the pK_a values[23] of the corresponding amines. This type of relationship is also found in enamino diketones **7**:

$$\delta(\text{O-1}) = 496.0 - 2.60\ \text{p}K_a \quad (r = 0.983,\ \text{SD} = 1.1,\ n = 8) \quad (2)$$

$$\delta(\text{O-1}') = 532.7 - 3.14\ \text{p}K_a \quad (r = 0.993,\ \text{SD} = 0.8,\ n = 9) \quad (3)$$

The point for **7j** was excluded owing to strong steric interaction [in Eqn (2), the enamino diketone **7a** with a primary amino group was excluded owing to the influence of intermolecular hydrogen bonding].

In the previous paper,[1] the ^{17}O shift values of enaminones correlated well with their $\delta(^{13}\text{C-2})$. In enamino diketones **7**, the $\delta(^{17}\text{O-1})$ values of the hydrogen-bonded carbonyls also correlate with their $\delta(^{13}\text{C-1})$ and $\delta(^{13}\text{C-2})$ values:

$$\delta(^{17}\text{O-1}) = 15.46\,\delta(^{13}\text{C-1}) - 2626.7 \quad (r = 0.985,\ \text{SD} = 1.3,\ n = 9) \quad (4)$$

$$\delta(^{17}\text{O-1}) = 8.40\,\delta(^{13}\text{C-2}) - 465.5 \quad (r = 0.967,\ \text{SD} = 1.9,\ n = 9) \quad (5)$$

(the point for **7j** was excluded). This indicates that the shielding of C-1, C-2 and O-1 is influenced by the same factors.

Intramolecular hydrogen bonding

IR[8a] and x-ray[15] analyses show that hydrogen-bonded open-chain enamino diketone systems exist both in solid form and in solution in the *EZE*-conformation, that the conjugated system is essentially planar and that electron delocalization affects both carbonyl groups almost equally. This demonstrates that the electronic and torsional effects do not contribute to the observed chemical shifts. Therefore, the ^{17}O chemical shift differences ($\Delta\delta_{HB}$) between the carbonyl groups O-1′ and O-1 in enamino diketones with primary or secondary amino

Table 5. ^{17}O, ^{1}H and ^{13}C data (ppm) for enamino diesters (8, 9 and 10)

Compound	R[1]	R[2]	^{17}O-1[a]	^{17}O-1′	^{17}O-2	^{17}O-2′	$\Delta\delta_{HB}$[b]	^{1}H-N	^{1}H-3	^{13}C-1	^{13}C-1′	^{13}C-2	^{13}C-3
8a	Me	Me	372.3	303.9	147.8	118.7	—	—	7.56 (s)	167.78	167.78	92.04	154.18
8b	H	Ph	322.3	328.0	134.6	125.4	−5.7	11.04 (d, 13.9)	8.54 (d, 13.9)	169.36	165.95	92.81	152.27
			323.1[c]	329.6	135.9	124.1	−6.5						
9a	Me	Me	372.5	305.9	178.2	151.1	—	—	7.50 (s)	167.57	167.48	93.06	153.41
9b	H	Ph	321.5	327.0	165.4	154.8	−5.5	11.02 (d, 13.8)	8.54 (d, 13.8)	169.06	165.73	93.49	151.92
			323.2[c]	329.6	165.0	155.8	−6.4						
10a	Me	Me	293.2	293.2	188.9	188.9	0.0	—	8.13 (s)	165.9[d]	165.9[d]	84.02	160.99
10b	H	Ph	314.0	325.5	188.4	188.4	−11.5	11.24 (d, 14.2)	8.65 (d, 14.2)	165.51	163.52	87.23	152.62

[a] 0.5 M acetonitrile solution at 40 °C, unless indicated otherwise; linewidth at half-height: 220–490 Hz.
[b] $\Delta\delta_{HB} = \delta(^{17}\text{O-1}) - \delta(^{17}\text{O-1}')$.
[c] Measurements at 70 °C.
[d] Broad signal.

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groups can be mainly attributed to the intramolecular hydrogen bonding.

The $\Delta\delta_{HB}$ values (Tables 2 and 3), are sensitive to the donor ability of the *N*-substituent and the structure of the compounds. The $\Delta\delta_{HB}$ values, *ca.* −30 ppm for *N*-alkylenamino diketones (**7**), are in good agreement with those obtained previously for the corresponding 4-alkylaminopent-3-en-2-ones **11**.[20b] This indicates that the previous $\Delta\delta_{HB}$ values evaluated for primary and secondary enaminones **11** from the comparison of ^{17}O chemical shifts of the hydrogen-bonded compounds with those non-hydrogen-bonded cyclic analogues are reasonable and acceptable.

For the cyclic enamino diketones **3** and **4**, the $\Delta\delta_{HB}$ values are much smaller than those of the acyclic derivatives **7**. The presence of intramolecular hydrogen bonding in **3** and **4** is clearly indicated by their ^{1}H NMR spectra. The small $\Delta\delta_{HB}$ values for **3** and **4** are consistent with smaller ^{13}C shift differences between the two carbonyl carbons in **3** and **4** (*ca.* 3 ppm), compared with those in **7** (*ca.* 6 ppm). However, this contrasts with the results of x-ray analyses, which show that the conjugated enamino diketone system is strictly planar and that electron delocalization affects both carbonyl groups almost equally.[15b] This may indicate that the conformations of **3** and **4** in solution are not the same as in solid state. In the five-membered ring derivatives **5** and **6**, there is no difference between the two carbonyls; the reasons for this observations are not clear.

Interestingly, the above ring effect was not observed in the cyclic enamino diester **10b** ($\Delta\delta_{HB}$ = −11.5 ppm). It is well known that ester carbonyl groups are less basic than ketones carbonyls,[24] and consequently ester carbonyls are expected to be poorer hydrogen bond acceptors than ketone carbonyls. The $\Delta\delta_{HB}$ values for acyclic enamino diesters **8b** and **9b**, *ca.* −6 ppm, are much smaller than that for the corresponding acyclic enamino diketone **7i** (34 ppm). This is consistent with the lower basicity of the ester carbonyl groups. $\Delta\delta_{HB}$ values of −4 to −13 ppm have been noted previously for hydroxypyridine carboxy esters and benzoates.7[19k]

CONCLUSION

The results of this work confirm that enamino diketones exist in solution in a ketamino form. The ^{17}O spectra of the tertiary enamino diketones show only one signal which is essentially insensitive to substituents (*ca.* 525 ppm). This is attributed to the low barrier of rotation around the C=C double bond and suggests that the dipolar resonance structures (**B**, **C** and **D**) are the main contributors to the ground state of the molecule. The ^{17}O chemical shifts of the two carbonyls in primary and secondary enamino diketones are sensitive to the basicity of the amino groups and depend on the intramolecular hydrogen bonding. Their $\delta(^{17}O)$ values can be calculated by the sum of substituent increments. The large differences between the experimental and calculated data are explained in terms of steric interactions and intermolecular hydrogen bonding. The existence of the strong intramolecular hydrogen bonds in enamino diketones is well evidenced: in alkylamino compounds **7** the chelated carbonyl group is *ca.* 30 ppm more shielded than the non-chelated group ($\Delta\delta_{HB}$ values). Additivity relationships demonstrate that common factors influence the shielding of O-atoms in enaminones and enamino diketones.

EXPERIMENTAL

Compounds

Compounds **1** and **7** were prepared by a known procedure[9a] from a solution of 3-ethoxymethylenepentane-2,4-dione (10 mmol) and the appropriate amine (10 mmol) (in cases of gaseous amines, ammonia or methylamine ethanolic solution or ethylamine aqueous solution was applied) in acetonitrile (10 ml). Enamino diketones **2**,[25] **3a**,[26] **3d**,[27] **4a**,[26] **4d**,[27] **5a**,[26] **5c**,[28] **6a**,[26] **8a**,[12c] **8b**,[9a] **9a**,[29] **9b**,[30] **10a**[8a] and **10b**[8a] were prepared according to literature methods. Transamination[8a] of **3d**, **4d**, **5c** and 2-anilinomethyleneindan-1,3-dione[29] (5 mmol) with an excess of ethanol solution of ammonia (33%, 3 ml) or methylamine (33%, 2 ml) gave **3b**[21] and **4b**[21] or **3c**,[8a] **4c**,[8a] **5b** and **6b**,[31] respectively.

The spectroscopic data (not included in Tables 1–4) of enamino diketones synthesized by the above-mentioned methods are listed below (chemical shifts in ppm; *J* in Hz; IR in cm^{-1}; *m/z* with relative intensity as % of base peak).

1a. M.p. 58.6–59.8 °C (lit.:[26] 59–61 °C). ^{1}H NMR ($CDCl_3$): 7.44 (s, 1H, H-3), 3.00 (br, 6H, NMe_2), 2.33 (s, 6H, 2 COMe). ^{13}C NMR ($CDCl_3$): 197.71 (2 C=O), 156.59, 115.10, 44.84 (NMe_2), 29.94 (2 COMe).

1b. IR (film): 1666, 1620, 1580. ^{1}H NMR ($CDCl_3$): 7.38 (s, 1H, H-3), 3.33 (q, J = 7.0, 4H, 2 NCH_2), 2.33 (s, 6H, 2 COMe), 1.17 (t, J = 7.0, 6H, 2 Me). ^{13}C NMR ($CDCl_3$): 198.24 (2 C=O), 152.85, 115.02, 52.1 and 47.4 (2 NCH_2), 29.72 (2 COMe), 13.27 (2 Me).). MS: 184 ($M + H^+$, 4), 183 (M^+, 11), 168 (26), 140 (11), 136 (16), 127 (14), 126 (100), 124 (30), 112 (12), 108 (14), 98 (42), 96 (21), 94 (14), 84 (31), 82 (19), 72 (14), 70 (22), 69 (22), 68 (24), 56 (66), 53 (22).

1c. IR (film): 1681, 1621, 1574. ^{1}H NMR ($CDCl_3$): 7.48 (s, 1H, H-3), 3.72 (m, 2H, 2 NCH), 2.33 (s, 6H, 2 COMe), 1.28 (d, J = 6.5, 12H, 4 Me). ^{13}C NMR ($CDCl_3$): 198.89 (C=O), 149.26, 114.28, 52.5 and 47.7 (2 NCH), 29.87 (2 COMe), 23.41 (2 Me), 20.36 (2 Me). MS: 212 ($M + H^+$, 15), 211 (M^+, 17), 196 (42), 168 (12), 150 (15), 136 (44), 127 (13), 126 (88), 112 (60), 110 (36), 108 (50), 100 (13), 98 (13), 96 (23), 94 (22), 85 (43), 84 (100), 82 (19), 70 (81), 69 (32), 68 (40), 58 (29), 56 (16), 53 (25).

1d. M.p. 82.4–84.7 °C. IR (film): 1670, 1624, 1590, 1578. ^{1}H NMR ($CDCl_3$): 7.65 (s, 1H, H-3), 7.30–7.40 (m, 6H, 2 Ph), 7.10–7.20 (m, 4H, 2 Ph), 4.44 (br, 4H, 2 NCH_2), 2.10 (s, 6H, 2 COMe). ^{13}C NMR ($CDCl_3$): 198.42 (2 C=O), 153.01, 134.76 (2 C, Ph), 128.98 (4 CH, Ph), 128.17 (2 CH, Ph), 127.56 (4 CH, Ph), 116.78, 61.8 and 55.7 (2 NCH_2), 29.46 (2 COMe). MS: 308 ($M + H^+$, 2), 307 (M^+, 4), 292 (15), 264 (6), 216 (34), 198 (3), 131 (3), 130 (3), 126 (3), 112 (27), 106 (11), 91 (100), 77 (9), 70 (18), 69 (3), 68 (2), 65 (38), 51 (8).

1e. IR (film): 1674, 1631, 1604, 1576. ^{1}H NMR ($CDCl_3$): 7.63 (s, 1H, H-3), 7.38–7.44 (m, 2H, Ph), 7.24–7.29 (m, 1H, Ph), 7.18–7.23 (m, 2H, Ph), 3.25 (s, 3H, NMe), 2.32 (s, 6H, 2 COMe). ^{13}C NMR ($CDCl_3$): 201.6 and 195.56 (2 C=O), 151.10, 147.08 (C, Ph), 129.71 (2 CH, Ph), 126.48 (CH, Ph), 122.26 (2 CH, Ph), 117.04, 42.07 (NMe), 32.2 and 27.1 (2 COMe). MS: 218 ($M + H^+$, 24), 217 (M^+, 35), 202 (49), 184 (46), 174 (64), 160 (75), 140 (3), 132 (86), 130 (40), 126 (43), 117 (55), 106 (26), 104 (46), 103 (20), 102 (10), 91 (47), 90 (22), 84 (23), 77 (100), 65 (18), 63 (18), 55 (10), 53 (18), 51 (60).

1f. M.p. 53.3–54.9 °C. IR (film): 1660, 1620, 1574. ^{1}H NMR ($CDCl_3$): 7.61 (s, 1H, H-3), 3.65 (br, 2H, NCH_2), 2.97 (br, 2H, NCH_2), 2.34 (s, 6H, 2 COMe), 1.97 (m, 4H, 2 CH_2). ^{13}C NMR ($CDCl_3$): 197.55 (2 C=O), 152.06, 115.68, 55.48 and 51.33 (2 NCH_2), 29.77 (2 COMe), 25.87 and 24.59 (2 CH_2). MS: 182 ($M + H^+$, 10), 181 (M^+, 35), 166 (31), 138 (33), 124 (100), 122 (25), 110 (21), 106 (14), 96 (32), 94 (17), 83 (13), 82 (28), 80 (14), 70 (82), 69 (36), 68 (38), 55 (40), 54 (31), 53 (38).

1g. IR (film): 1660, 1621, 1574. ^{1}H NMR ($CDCl_3$): 7.49 (s, 1H, H-3), 3.29 (br, 4H, 2 NCH_2), 2.30 (s, 6H, 2 COMe), 1.69 (m, 6H, 3 CH_2). ^{13}C NMR ($CDCl_3$): 197.99 (2 C=O), 155.60, 113.67, 53.8 (2 NCH_2), 30.00 (2 COMe), 25.80 (2 CH_2), 23.10 (CH_2). MS: 196 ($M + H^+$, 5), 195

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(M^+, 22), 180 (44), 152 (7), 138 (100), 136 (46), 124 (9), 120 (4), 100 (20), 108 (8), 97 (8), 96 (14), 94 (10), 84 (69), 83 (70), 82 (42), 69 (28), 68 (16), 67 (17), 56 (26), 55 (76), 54 (26), 53 (35).

1h. M.p. 63.5–65.3 °C. IR (KBr): 1663, 1610, 1577. IR (film): 1660, 1615, 1574, ^{1}H NMR ($CDCl_3$): 7.50 (s, 1H, H-3), 3.45 (br, 2H, NCH_2), 3.08 (br, 2H, NCH_2), 2.34 (s, 6H, 2 COMe), 1.78 (m, 4H, 2 CH_2), 1.59 (m, 4H, 2 CH_2). ^{13}C NMR ($CDCl_3$): 198.18 (2 C=O), 155.35, 115.01, 56.64 and 53.11 (2 NCH_2), 29.94 (2 COMe), 27.34 (3 CH_2), 26.47 (CH_2). MS: 210 ($M + H^+$, 13), 209 (M^+, 25), 194 (100), 166 (18), 152 (74), 150 (14), 138 (12), 134 (6), 126 (29), 124 (28), 122 (14), 112 (19), 110 (26), 111 (7), 109 (17), 108 (8), 98 (29), 97 (22), 96 (37), 94 (24), 84 (26), 83 (18), 82 (52), 81 (19), 80 (27), 70 (38), 69 (52), 68 (62), 67 (27), 56 (37), 55 (96), 54 (33), 53 (51).

1i. M.p. 126.0–126.8 °C. IR (KBr): 1661, 1610, 1583. ^{1}H NMR ($CDCl_3$): 7.45 (s, 1H, H-3), 3.39 (br, 4H, 2 NCH_2), 2.34 (s, 6H, 2 COMe), 1.50–1.85 (m, 10H, 5 CH_2). ^{13}C NMR ($CDCl_3$): 197.86 (2 C=O), 153.99, 115.41, 58.39 and 50.77 (2 NCH_2), 29.79 (2 COMe), 27.80 (CH_2), 25.51 (3 CH_2), 23.98 (CH_2). MS: 224 ($M + H^+$, 8), 223 (M^+, 14), 208 (59), 180 (7), 166 (10), 164 (4), 152 (5), 140 (7), 139 (8), 138 (18), 136 (8), 126 (19), 124 (41), 122 (11), 112 (23), 110 (21), 98 (18), 97 (12), 96 (30), 84 (35), 83 (38), 82 (54), 81 (12), 80 (23), 70 (42), 69 (42), 68 (36), 67 (23), 56 (35), 55 (100), 54 (24), 53 (40).

1j. M.p. 85.7–87.4 °C. IR (film): 1660, 1622, 1577. ^{1}H NMR ($CDCl_3$): 7.38 (s, 1H, H-3), 3.77 (t, J = 5.0, 4H, 2 OCH_2), 3.33 (t, J = 5.0, 4H, 2 NCH_2), 2.32 (s, 6H, 2 COMe). ^{13}C NMR ($CDCl_3$): 198.24 (2 C=O), 154.47, 114.63, 66.27 (2 OCH_2), 52.36 (2 NCH_2), 30.00 (2 COMe). MS: 198 ($M + H^+$, 7), 197 (M^+, 36), 182 (100), 154 (7), 140 (84), 139 (32), 138 (25), 126 (8), 124 (50), 122 (17), 112 (21), 110 (21), 97 (19), 96 (43), 94 (20), 87 (33), 86 (31), 85 (34), 84 (14), 83 (21), 82 (70), 80 (18), 69 (42), 68 (22), 67 (26), 56 (36), 55 (100), 54 (48), 53 (56).

1k. IR (film): 1660, 1622, 1575. ^{1}H NMR ($CDCl_3$): 7.43 (s, 1H, H-3), 3.35 (t, J = 5.0, 4H, 2 NCH_2), 2.48 (t, J = 5.0, 4H, 2 NCH_2), 2.32 (s, 3H, NMe), 2.31 (s, 6H, 2 COMe). ^{13}C NMR ($CDCl_3$): 198.12 (2 C=O), 154.80, 114.63, 54.45 (2 CH_2, CH_2NMe), 52.26 (2 NCH_2), 45.92 (NMe), 30.01 (2 COMe). MS: 211 ($M + H^+$, 8), 210 (M^+, 14), 138 (4), 124 (15), 100 (24), 98 (33), 97 (21), 96 (13), 86 (13), 83 (14), 82 (30), 71 (37), 70 (100), 69 (14), 68 (11), 67 (16), 58 (63), 57 (37), 56 (45), 55 (22), 54 (19), 53 (16).

2. M.p. 130.8–131.5 °C. IR (KBr): 1662, 1600, 1508. ^{1}H NMR ($CDCl_3$): 3.60 (br, 2H, NCH_2), 2.99 (br, 2H, NCH_2), 2.66 (t, J = 6.6, 2H, CH_2), 2.53 (s, 3H, COMe), 2.32 (m, 2H, CH_2), 1.97 (br, 4H, 2 CH_2), 1.87 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$): 198.96 (C=O), 194.65 (C=O), 167.01, 113.64, 54.91 (NCH_2), 50.45 (NCH_2), 37.78, 31.38 and 19.15 (3 CH_2), 24.73 (CH_2CH_2). MS: 208 ($M + H^+$, 13), 207 (M^+, 33), 192 (100), 190 (34), 178 (15), 164 (20), 151 (8), 138 (11), 136 (34), 123 (48), 108 (45), 96 (17), 95 (13), 94 (19), 82 (29), 80 (28), 70 (96), 68 (31), 67 (33), 66 (28), 55 (55), 54 (19), 53 (32).

3a. M.p. 113.5–114.8 °C (lit.:[26] 118 °C). ^{1}H NMR ($CDCl_3$): 8.05 (s, br, 1H, H-3), 3.39 (s, 3H, NMe), 3.17 (d, J = 0.7, 3H, NMe), 2.46 (t, J = 6.5, 4H, 2 CH_2), 1.95 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$): 196.15 (2 C=O), 162.28, 109.36, 48.53 and 44.66 (NMe_2), 38.18 (C-4 and C-6), 19.56 (C-5).

3b. M.p. 107.5–107.7 °C (lit.:[21] 110 °C). ^{1}H NMR ($CDCl_3$): 7.30 (br, 1H, NH), 1.98 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$): 38.09 (C-6), 37.51 (C-4) and 19.72 (C-5).

3c. M.p. 175.6–176.2 °C. IR (KBr): 3191, 1665, 1605, 1586. ^{1}H NMR ($CDCl_3$): 3.21 (d, J = 5.0, 3H, NMe), 1.96 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$): 37.67 (C-6), 37.33 (C-4) and 19.98 (C-5), 36.60 (NMe). MS: 154 ($M + H^+$, 24), 153 (M^+, 42), 138 (24), 136 (17), 125 (96), 112 (61), 110 (75), 97 (92), 84 (78), 83 (100), 82 (42), 80 (28), 69 (83), 68 (72), 67 (22), 56 (14), 55 (95), 54 (80), 53 (68).

3d. M.p. 120.4–121.7 °C (lit.:[27] 120 °C). ^{1}H NMR ($CDCl_3$): 7.37–7.47 (m, 2H), 7.20–7.30 (m, 3H), 2.00 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$): 138.37 (C, Ph), 129.96 (2 CH, Ph), 126.51 (CH, Ph), 118.16 (2 CH, Ph), 37.98 (C-6), 37.61 (C-4) and 19.70 (C-5).

4a. M.p. 87.0–88.3 °C (lit.:[12a] 83–87 °C; lit.:[26] 93 °C). ^{1}H NMR ($CDCl_3$): 8.01 (s, 1H, H-3), 3.39 (s, 3H, NMe), 3.19 (s, 3H, NMe), 2.36 (s, 4H, 2 CH_2), 1.07 (s, 6H, 2 Me). ^{13}C NMR ($CDCl_3$): 195.60 (2 C=O), 161.75, 108.22, 48.52 and 44.74 (NMe_2), 52.16 (C-4 and C-6), 30.87 (C-5), 28.47 (2 Me).

4b. M.p. 133.4–134.9 °C (lit.:[21] 135 °C). ^{1}H NMR ($CDCl_3$): 6.76 (br, 1H, NH), 1.07 (s, 6H, 2 Me). ^{13}C NMR ($CDCl_3$):51.74 (C-6), 51.19 (C-4), 31.09 (C-5), 28.49 (2 Me).

4c. M.p. 176.3–177.1 °C (lit.:[8a] 171–173 °C). ^{1}H NMR ($CDCl_3$): 3.21 (d, J = 5.0, 3H, NMe), 1.05 (s, 6H, 2 Me). ^{13}C NMR ($CDCl_3$): 51.34 (C-6), 51.01 (C-4), 36.55 (NMe), 31.16 (C-5), 28.52 (2 Me).

4d. M.p. 137.9–138.3 °C (lit.:[8a] 135–136 °C). ^{1}H NMR ($CDCl_3$): 7.37–7.46 (m, 2H), 7.22–7.30 (m, 3H), 1.10 (s, 6H, 2 Me). ^{13}C NMR ($CDCl_3$): 138.39 (C, Ph), 129.96 (2 CH, Ph), 126.46 (CH, Ph), 118.11 (2 CH, Ph), 51.65 (C-6), 51.29 (C-4), 31.16 (C-5), 28.56 (2 Me).

5a. M.p. 91.8–92.6 °C (lit.:[26] 94 °C). ^{1}H NMR ($CDCl_3$): 7.46 (s, 1H, H-3), 3.73 (s, 3H, NMe), 3.37 (s, 3H, NMe), 2.52 (s, 4H, 2 CH_2). ^{13}C NMR ($CDCl_3$): 204.1 (br, CO), 200.7 (br, CO), 48.47 and 33.94 (2 CH_2), 44.36 (NMe_2).

5b. M.p. 205 °C (decomp.). ^{1}H NMR ($CDCl_3$): 3.25 (d, J = 4.5, 3H, NMe). ^{13}C NMR ($CDCl_3$): 33.78 and 33.14 (2 CH_2), 36.70 (NMe).

5c. M.p. 175.6–177.5 °C (lit.:[28] 170 °C). ^{1}H NMR ($CDCl_3$): 7.42–7.48 (m, 2H), 7.26–7.32 (m, 3H), 2.58–2.68 (m, 4H, 2 CH_2). ^{13}C NMR ($CDCl_3$): 137.67 (C, Ph), 130.15 (2 CH, Ph), 127.08 (CH, Ph), 118.00 (2 CH, Ph), 33.98 and 33.40 (2 CH_2).

6a. M.p. 141.9–143.2 °C (lit.:[26] 147 °C). ^{1}H NMR ($CDCl_3$): 7.72–7.78 (m, 2H), 7.58–7.64 (m, 2H), 7.49 (s, 1H, H-3), 3.79 (s, 3H, NMe), 3.37 (s, 3H NMe). ^{13}C NMR ($CDCl_3$): 192.67 (C-1), 188.43 (C-3), 140.81 and 138.66 (2 C, Ar), 133.21, 132.88, 121.51 and 121.34 (4 CH, Ar), 48.00 and 43.69 (NMe_2).

6b. M.p. 250 °C (decomp.). ^{1}H NMR ($CDCl_3$): 7.70–7.78 (m, 2H), 7.58–7.64 (m, 2H), 3.25 (d, J = 5.0, 3H, NMe). ^{13}C NMR ($CDCl_3$): 139.74 (2 C, Ar), 133.29, 133.18, 121.88 and 121.24 (4 CH, Ar), 36.42 (NMe).

7a. M.p. 143.6–145.0 °C (lit.:[21] 146 °C). ^{1}H NMR ($CDCl_3$): 5.87 (br, 1H, NH). ^{13}C NMR ($CDCl_3$): 32.22 (C-4), 27.14 (C-5).

7b. M.p. 107.6–109.2 °C (lit.:[8a] 110–111 °C). ^{1}H NMR ($CDCl_3$): 3.18 (d, J = 5.0, 3H, NMe). ^{13}C NMR ($CDCl_3$): 36.49 (NMe), 31.84 (C-4), 27.26 (C-5).

7c. M.p. 93.4–94.8 °C. IR (KBr): 3182, 1651, 1612, 1584. ^{1}H NMR ($CDCl_3$): 3.41 (dq, J = 7.3, 6.0, 2H, NCH_2), 1.31 (t, J = 7.3, 3H, NCH_2Me). ^{13}C NMR ($CDCl_3$): 45.01 and 15.95 (NCH_2Me),31.89 (C-4), 27.33 (C-4). MS: 156 ($M + H^+$, 7), 155 (M^+, 28), 140 (62), 126 (59), 122 (12), 98 (100), 84 (24), 80 (38), 70 (32), 69 (28), 68 (26), 67 (17), 56 (26), 53 (27).

7d. M.p. 71.4–73.1 °C. IR (KBr): 3183, 1658, 1613, 1581. ^{1}H NMR ($CDCl_3$): 3.49 (m, 1H, NCH), 1.32 (d, J = 6.5, 6H, $NCHMe_2$). ^{13}C NMR ($CDCl_3$): 51.88 and 23.50 ($NCHMe_2$), 31.91 (C-4), 27.36 (C-5). MS: 170 ($M + H^+$, 1), 169 (M^+, 14), 154 (18), 136 (25), 126 (94), 112 (77), 94 (14), 84 (29), 70 (100), 69 (20), 68 (18), 67 (12), 53 (16).

7e. M.p. 88.5–89.9 °C. IR (KBr): 3187, 1663, 1617, 1581. ^{1}H NMR ($CDCl_3$): 1.37 (s, 9H, $NCMe_3$). ^{13}C NMR ($CDCl_3$): 53.64 and 29.75 ($NCMe_3$), 33.87 (C-4), 27.39 (C-5). MS: 184 ($M + H^+$, 4), 183 (M^+, 13), 168 (6), 150 (5), 126 (82), 112 (100), 108 (14), 98 (8), 94 (10), 70 (81), 69 (22), 68 (18), 67 (12), 58 (24), 57 (77), 56 (16), 55 (17), 53 (16).

7f. M.p. 100.5–101.6 °C (lit.:[32] 89–90 °C). IR (KBr): 3168, 1646, 1616, 1575. ^{1}H NMR ($CDCl_3$): 7.30–7.43 (m, 3H), 7.24–7.30 (m, 2H), 4.55 (d, J = 6.0, 2H, NCH_2). ^{13}C NMR ($CDCl_3$): 135.97 (C, Ph), 129.11 (2 CH, Ph), 128.35 (CH, Ph), 127.31 (2 CH, Ph), 53.72 (NCH_2), 31.93 (C-4), 27.29 (C-5). MS: 218 ($M + H^+$, 3), 217 (M^+, 5), 202 (18), 160 (2), 126 (68), 106 (9), 104 (9), 91 (100), 84 (11), 77 (7), 65 (37), 63 (9), 51 (11).

7g. M.p. 54.2–56.0 °C. IR (KBr): 3187, 1653, 1618, 1588. ^{1}H NMR ($CDCl_3$): 3.18 (t, J = 6.5, 2H, NCH_2), 1.87 (m, 1H, CH), 0.97 (d, J = 6.5, 6H, 2 Me). ^{13}C NMR ($CDCl_3$): 58.04, 29.49 and 19.66 (NCH_2CHMe_2), 31.88 (C-4), 27.31 (C-5). MS: 184 ($M + H^+$, 11), 183 (M^+, 36), 168 (38), 150 (4), 140 (34), 126 (100), 122 (97), 112 (33), 108 (9), 98 (18), 95 (18), 94 (17), 86 (24), 84 (33), 80 (46), 70 (70), 69 (59), 68 (26), 67 (20), 57 (39), 56 (26), 55 (32), 53 (39).

7h. M.p. 76.5–78.2 °C. IR (KBr): 3291, 1654, 1619, 1586. ^{1}H NMR ($CDCl_3$): 3.22 (m, 1H, NCH), 1.91–2.02 (m, 2H), 1.74–1.87 (m, 2H), 1.59–1.70 (m, 1H), 1.25–1.50 (m, 5H). ^{13}C NMR ($CDCl_3$): 58.79 (NCH), 33.73 (2 CH_2), 31.92 (C-4), 27.36 (C-5), 24.90 (CH_2), 24.34 (2 CH_2). MS: 213 ($M + H^+$, 3), 209 (M^+, 11), 194 (14), 166 (3), 138 (5), 126 (100), 112 (56), 110 (15), 96 (11), 86 (20), 70 (62), 69 (16), 68 (12), 67 (14), 55 (51), 53 (16).

7i. M.p. 87.7–88.2 °C (lit.:[8a] 89–90 °C). ^{1}H NMR ($CDCl_3$): 7.38–7.44 (m, 2H), 7.20–7.26 (m, 1H), 7.16–7.20 (m, 2H). ^{13}C NMR ($CDCl_3$): 139.04 (C, Ph), 129.97 (2 CH, Ph), 125.79 (CH, Ph), 117.86 (2 CH, Ph), 32.04 (C-4), 27.34 (C-5).

7j. M.p. 74.8–76.1 °C. ^{1}H NMR ($CDCl_3$): 7.14 (s, 3H), 2.33 (s, 6H, 2 Me). ^{13}C NMR ($CDCl_3$): 137.70 (C, Ar), 132.56 (2 C, Ar), 129.10 (2 CH, Ar), 127.35 (CH, Ar), 32.09 (C-4), 27.21 (C-5), 18.53 (2 Me).

Instrumentation

The ^{17}O NMR spectra were recorded on a Bruker-WH-360 spectrometer, equipped with a 10 mm probe, at 48.8

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MHz, in the Fourier transform (FT) mode without lock. System control, data acquisition and data management were performed by an Aspect-2000 microcomputer. The instrumental settings were as follows: spectral width 50 000 Hz (1025 ppm), 2K data points, pulse width 33 μs, acquisition time 20 ms, preacquisition delay 5 μs, 150 000–300 000 scans (1 400 000 scans for **5c** and **6b**), sample spinning (30 Hz). An even number (12–28) 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 $\delta(^{17}O)$, measured in 0.5 M acetonitrile solution at 40 °C at natural isotopic abundance, are reported relative to $\delta(^{17}O)(H_2O)$ (=0.0 ppm); dioxane [$\delta(^{17}O) = 0.0$ 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 ^{1}H 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 Paragon 1000 FT-IR spectrometer and electron impact mass spectra on a Nermag R-10-10C spectrometer. Melting points were observed under a microscope using a Mettler FP-52 instrument.

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