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Intramolecular hydrogen bonding in conformationally semi-rigid α-acylmethane derivatives: a theoretical NMR study†

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Conformational mobility is a core property of organic compounds, and conformational analysis has become a pervasive tool for synthetic design. In this work, we present experimental and computational (employing Density Functional Theory) evidence for unusual intramolecular hydrogen bonding interactions in a series of α-acylmethane derivatives, as well as a discussion of the consequences thereof for their NMR spectroscopic properties.

Introduction

Conformational flexibility is an intrinsic trait of most organic compounds.[1] The remarkable ability of molecules to adopt multiple possible conformations is usually accompanied by a defined preference for certain of those conformations, a property that resides at the core of molecular interactions and molecular recognition.[2] Although the distribution of conformational states can be strongly influenced by solvent effects,[3] intramolecular attractive or repulsive interactions are often decisive factors that lead molecules to "choose" a specific spatial arrangement of atoms.[4] Much, if not all, of the chemical machinery that sustains life as we know it hinges on subtle interactions of small thermodynamic value but enormous structural importance. Such interactions are deployed in multidirectional fashion and can on occasion result in robust, macroscopic 3D molecular scaffolds. Often, unforeseen attractive interactions can become important design elements with applications ranging from synthesis[5] to catalysis[6] and, ultimately, biology.[7]
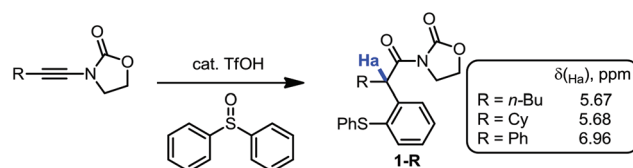
N-Acyloxazolidinones, popularized through the seminal, textbook work of Evans and others[8] remain, even in the 21st century, as cornerstone reagents for aldol- and related transformations. This is largely due, as in most cases of successful asymmetric induction (be it stoichiometric or catalytic), to

their adoption of predictable conformations in solution as governed (at a given temperature) by either chelation or dipole attraction/repulsion effects.

Herein, we present experimental and computational evidence for an unusual intramolecular hydrogen bonding interaction in a series of *N*-acyloxazolidinones and other α-acylmethane derivatives, with striking consequences to their NMR spectroscopic properties. The study also includes theoretical (density functional theory, DFT) ^{1}H- and ^{13}C-NMR determinations. Theoretical NMR determinations are often used in cases of problematic and dubious NMR assignments[9] and should be more frequently used as a tool to enable correct NMR analyses.

Results and discussion

During our recent studies on redox-neutral reactions of *N*-alkynyloxazolidinones (ynamides),[10] leading to the preparation of various α-arylated acyloxazolidinone products (**1**, Scheme 1), we noted the consistently and unusually low field ^{1}H-NMR shifts of the hydrogen marked in blue as Ha. For instance, in product **1-*n*Bu** (R = *n*Butyl) the signal for Ha appeared at δ = 5.67 ppm, at 5.68 ppm for **1-Cy**

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Scheme 1 Redox-neutral arylation of ynamides and unusual chemical shifts of Ha.

	δ(Ha), ppm
R = *n*-Bu	5.67
R = Cy	5.68
R = Ph	6.96

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(R = Cyclohexyl), and for **1-Ph** (R = Phenyl), the signal goes to 6.96 ppm, lying practically within the aromatic region.

In order to eliminate any possible effect of the sulfur residue on the aromatic ring, we compared the known compound **1-Dec** (R = Decyl) with its desulfurated analogue **2-Dec**. A decrease in chemical shift of 0.64 ppm (from 5.66 to 5.02 ppm, respectively) was found, whereas an equally high chemical shift value of δ = 5.11 ppm has been reported[11] for the desulfurated methyl derivative **2-Me** (cf. Fig. 1a).

This far exceeds, for instance, the predicted value for this structure obtained by simple NMR-predicting software (the ChemOffice 13.0 suite,[12] for example, predicts a chemical shift, δ, of just 3.52 ppm). The value is all the more striking if one compares the acyloxazolidinone **2-Me** with other carbonyl analogues (cf. Fig. 1b). Indeed, the aldehyde **3-Me** (which could be expected to exert a comparable electron-withdrawing effect on the C–H bonds in α-position with respect to an acyloxazolidinone moiety), the ethylester **4-Me**, the methyl-thioester **5-Me** or the N-methylcarboxamide **6-Me** are all

known compounds reported to have chemical shifts for Ha inside a narrow window not exceeding a δ value of 3.92 ppm (vide infra Table 1).

Detailed analysis of the structure of acyloxazolidinones **1-R**/**2-R** revealed the possible intervention of an intramolecular hydrogen bonding interaction through a 6-membered ring ranging from the electron-rich oxazolidinone (Oxaz) carbonyl oxygen to the methinic hydrogen Ha, giving rise to the conformer shown in Fig. 2. We recognised that this structure-specific interaction might lie at the heart of the unusually high chemical shift observed for this particular compound (which is absent in the other derivatives, cf. Fig. 1b).

To validate this assumption, we required a tool to accurately model the two extreme conformational situations where this hydrogen bond is present and absent, compare their relative stability and simulate the NMR spectrum of both forms. We resorted to high-level DFT calculations since it is well-known that general purpose, theoretical ^{1}H-NMR spectra could be reliably covered by this level of theory.[13] This required accuracy aims not only at reliably reproducing the already known experimental data but also predict new values for unknown derivatives or non-detectable conformers. The latter is a crucial requirement as we need to compare experimentally assessed H-bonded situations with non-measurable conformers for which no H-bonding is operative and experimental quantification by NMR is not accessible.

We will initially focus on desulfurated α-acylmethane derivatives, i.e., the known compounds **2-Me–6-Me** (cf. Fig. 1c). We further added an unknown compound, the N-methylimidazolidinone (Imid) **7-Me**, to enlarge the predictability test of our model, and resynthesized **5-Me** to ascertain the ^{1}H-NMR chemical shift for Ha, since calculations found a discordant value with that reported in literature (see below in ref. 24).

Fig. 1 (a) Evaluation of the influence of an arylsulfur residue on the chemical shift of Ha, and on its desulfurated version, for oxazolidinone compounds. (b) Comparative analysis of analogous desulfurated carbonyl derivatives. (c) The different experimentally known α-acylmethane derivatives studied in this work, with the exception of **7-Me** that has been prepared by us for the first time.

Fig. 2 Possibility of six-membered intramolecular hydrogen bonding in **2-Me**.

Table 1 Experimental and calculated ^{1}H-NMR chemical shifts (in ppm) of Ha for derivatives **2-Me–7-Me** in chloroform

^{1}H-NMR chemical shifts	2-Me (R^1 = Oxaz)	3-Me (R^1 = H)	4-Me (R^1 = OEt)	5-Me (R^1 = SMe)	6-Me (R^1 = NHMe)	7-Me (R^1 = Imid)
B3LYP	5.23	3.69	3.68	3.88	3.26	5.43
B3LYP-D3	5.02	3.70	3.68	3.91	3.33	5.17
CAM-B3LYP	5.16	3.62	3.63	3.85	3.21	5.36
M06-2X	5.12	3.79	3.82	4.22	3.48	5.20
LC-ωPBE	5.10	3.64	3.64	3.92	3.30	5.29
Experimental	5.11 (ref. 11)	3.64 (ref. 23)	3.72 (ref. 24)	3.92[a] (ref. 25)	3.55 (ref. 26)	5.28[a]

[a] This work (see ESI).

Computational details

Calculations were performed using the GAUSSIAN09 suite of programs.[14] Initial lowest-energy conformations were optimized by density functional theory (DFT) using the well-known hybrid B3LYP functional[15] with the Pople's diffuse, polarized, split-valence, double-zeta 6-31+G* basis set.[16] From these geometries, the corresponding ^{1}H-NMR isotropic magnetic shielding values were calculated reoptimizing them with the larger triple-zeta 6-311+G(d,p) basis set[17] (necessary to get a high accuracy in the determination of chemical shifts,[13] see the ESI,† for geometries) combined with different functionals. These include the hybrids B3LYP, which gives reliable ^{1}H-NMR chemical shifts for the most common compounds, their empirical dispersion, B3LYP-D3,[18] and long-range corrected, CAM-B3LYP,[19] versions, and the Minnesota M06-2X functional,[20] which accounts for non-covalent interactions. We have also included for comparison the non-hybrid GGA-functional LC-ωPBE,[21a] the long range corrected version of PBE[21b] (another widely used functional for general purposes). All the calculations have been carried out including implicit solvent (in which the corresponding experimental spectra have been recorded, see below) through a Polarizable Continuum Model (PCM).[22] Results obtained from these calculations for the chemical shift (in ppm) of the Ha hydrogen of the selected, lowest-energy conformers for compounds **2-Me–7-Me** (Fig. 1c) are summarized in Table 1.

It should be noted that the precision in the ^{1}H-NMR chemical shift determination is fairly high along the different methods employed. Yet, for this set of molecules, the LC-ωPBE functional performs extremely well, achieving δ values in very close agreement to the experimental ones (see the ESI† for details), therefore we elected the LC-ωPBE functional for further analyses.

Interestingly, the calculated lowest-energy conformations for **2-Me** and **7-Me** correspond to that depicted in Fig. 2, in which a 6-membered hydrogen bond[27] is established between Ha and the carbonyl group of the heterocyclic moiety. We had originally postulated that this was at the origin of the unusual chemical shift values for Ha. With the help of DFT calculations, we are able to consider conformations in which the hydrogen bonding event is absent and recalculate the chemical shift associated to Ha in the same solvent (chloroform). Results for the two limiting conformations in each case (hydrogen bonded, **2-Me** and **7-Me**, and non-hydrogen bonded, **2b-Me** and **7b-Me**) are presented in Table 2. An important drop (about 1.5 ppm to high field) is observed affecting the δ value of Ha of the conformer in which the hydrogen bonding is not operating with respect to the one in which the hydrogen bond is established (lowest-energy conformer).

Since the free-energy difference (ΔG) between the two limiting conformations (B3LYP/6-31+G(d)) is 4.46 kcal mol^{-1} for **2-Me** and 5.44 kcal mol^{-1} for **7-Me**, a conformational equilibrium of conformers **2b-Me** and **7b-Me** (without hydrogen bonding) can be excluded. This means that, besides other possible, energetically accessible conformations, the apparent

Table 2 Calculated ^{1}H-NMR chemical shift (in ppm) of Ha in conformers including and excluding hydrogen bonding for derivatives **2-Me** and **7-Me**, in chloroform, at the LC-ωPBE/6-311+G(d,p) level of theory

^{1}H-NMR chemical shifts	**2-Me** hydrogen bonding	**2b-Me** non-hydrogen bonding	**7-Me** hydrogen bonding	**7b-Me** non-hydrogen bonding
LC-ωPBE	5.10	3.64	5.29	3.53
Experimental	5.11[11]	—^{a}	5.28^b	—^{a}

^{a} Non applicable. ^{b} This work (see ESI).

chemical shifts of Ha for **2-Me** and **7-Me** should be very close to the theoretical calculated values, as it is evidenced in Table 2.

At this juncture, we wished to dive into simulated spectra, with the aim to modulate the strength of the intramolecular H-bond by the calculated value for Ha. Accordingly, we elected several *ad hoc* unreported derivatives: the permethylated **8-Me** and the perfluorinated **9-Me** oxazolidinone analogues, and the acylcarbamate **10-Me**, which constitutes the ring-strainless open-chain version of the oxazolidinone derivative **2-Me** (Fig. 3). Calculations made on these compounds were performed for the conformations for which the 6-membered, intramolecular hydrogen bond is expected to be operative and gave rise to the set of δ values for Ha collected in Table 3 along with the calculated O⋯Ha distances.

From Table 3, it could be pointed out that, concerning the deshielding of Ha, the ureido derivative **7-Me** and the open acylcarbamate **10-Me** appear to be the more effective compounds establishing the intramolecular hydrogen bond, given the enhanced Lewis basicity (and hence stronger hydrogen bond-donor ability) of the carbonyl oxygen interacting with Ha. Contrarily to this, the fluorinated **9-Me** derivative leads to a less electron-rich carbonyl, weakening the hydrogen bond and observing the corresponding δ value of Ha at higher field (by about 0.6 ppm, see Table 3). Interestingly, the incorporation of four methyl groups in **8-Me** did not substantially affect the chemical shift of Ha with respect to the pure oxazolidinone moiety (**2-Me**). On the other hand, the hydrogen bonds (if available) expected to be stronger when presenting a higher δ value for Ha, also present, in general, shorter distances (Table 3).

Additionally, the LC-ωPBE chemical shifts correlate fairly well with the O⋯Ha equilibrium distances in compounds **2-Me** and **7-Me–10-Me** (see Fig. 4), with some small variations for shorter distances.[28]

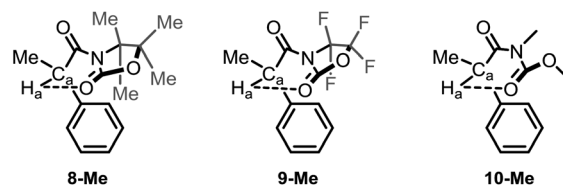**Fig. 3** *Ad hoc* structures created for the study of the 6-membered, intramolecular hydrogen bond in this series of compounds.

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Table 3 Calculated ^{1}H-NMR chemical shifts of Ha for known structures **2-Me** and **7-Me** and unknown **8-Me–10-Me** and O···Ha distances

Parameters	2-Me (R^1 = Oxaz)	7-Me (R^1 = Imid)	8-Me (R^1 = Oxaz(Me$_4$))	9-Me (R^1 = Oxaz(F$_4$))	10-Me (R^1 = open Oxaz)
δ (in ppm)	5.10	5.29	5.21	4.75	5.31
Distance (in Å)^a	2.243	2.198	2.201	2.295	2.173

^{a} O···Ha distances were extracted from the corresponding ^{1}H-NMR calculations (LC-ωPBE/6-311+G(d,p) in chloroform (PCM)).
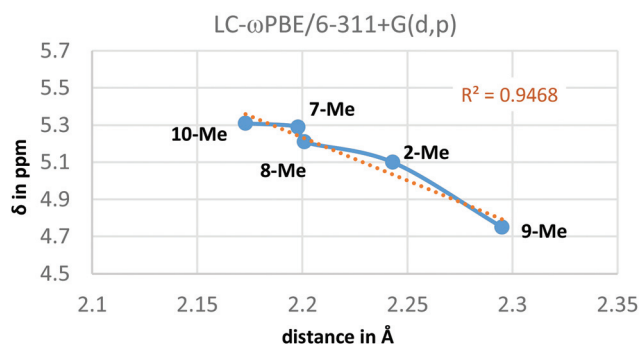
Fig. 4 Calculated ^{1}H-NMR chemical shifts *vs.* O···Ha distance for derivatives **2-Me** and **7-Me–10-Me**.

A comparison of these distances with the sum of the corresponding van der Waals radii for hydrogen and oxygen atoms, that is, 2.70 Å,[29] constitutes another observation pointing to the presence of intramolecular hydrogen bonding because its short distance,[30] as the oxazolidinone carbonyl group establishes another weak C=O···H–Ph interaction in **2-Me** at 2.777 Å, a distance slightly higher than the sum of the corresponding van der Waals radii. Interestingly, the remaining carbonyl group establishes three different close interactions: at 2.589 (C=O···CH$_2$), 2.644 (C=O···Me) and 2.792 Å (C=O···H–Ph) (Fig. 5), all them around the expected van der Waals distance.

In order to characterize this special interaction and evaluate its strength, we applied the quantum theory of atoms in molecules (QTAIM)[31] over derivatives **2-Me** and **7-Me–10-Me** (from the corresponding LC-ωPBE/6-311+G(d,p) calculations) using the Multiwfn suite.[32] This theory is a topological analysis able to identify bonding interactions within a molecule by means of the gradient vector field of the charge density, $\rho(\mathbf{r})$. Typical $\rho(\mathbf{r})$ values in shared interactions are 0.722, 0.551, and 0.252 a.u. for N$_2$, O$_2$, and C–C bond in ethane molecules, respectively, whereas in closed-shell interactions they are 0.046 and 0.036 a.u.

for LiCl molecules and NaCl molecules, respectively.[31a,33] These bonding interactions can be classified in terms of the properties of the Laplacian of the electron density, $\nabla^2\rho(\mathbf{r})$, into two broad general classes: shared ($\nabla^2\rho(\mathbf{r}) < 0$, *i.e.* covalent bonds) and closed-shell ($\nabla^2\rho(\mathbf{r}) > 0$, *i.e.* hydrogen bonds) interactions.[34] Concerning our study, the well-known criteria of the hydrogen bonding on the basis of AIM theory at the bond critical point (BCP), where the gradient vector field, $\nabla\rho(\mathbf{r})$, vanishes, are: (i) $\rho(\mathbf{r})$ between 0.002 and 0.034 a.u., and (ii) $\nabla^2\rho(\mathbf{r})$ between +0.024 and +0.139 a.u.[35] Mata *et al.*[36] correlated the hydrogen-bonding energy, E_{HB}, with the Lagrangian kinetic energy, $G(\mathbf{r})$, at the BCP as $E_{HB} = 0.429 \times G(\mathbf{r})$.

Therefore, we calculated the BCPs and searched for those with a positive value of $\nabla^2\rho(\mathbf{r})$, finding a BCP in all cases in between the C=O···Ha path (**2-Me**, as an example, in Fig. 6). Laplacians of the electron density, $\nabla^2\rho(\mathbf{r})$, charge densities, $\rho(\mathbf{r})$, and Lagrangian kinetic energies, $G(\mathbf{r})$, at each C=O···H$_a$ BCP, Ha chemical shifts, C=O···Ha equilibrium distances, and calculated E_{HB} energies are summarized in Table 4.

The data in Table 4 corroborates the presence of hydrogen bonds in the C=O···Ha paths for oxazolidinone- (**2-Me** and **8-Me–9-Me**), imidazolidinone-based (**7-Me**) and the open-chain **10-Me** compounds. The strongest hydrogen bond can be found in the latter structure **10-Me**, with a rather short O···H distance, whereas the weakest one, as expected, appeared in the fluorinated derivative **9-Me**.

Based on both the energy (E_{HB}) and the O···Ha distances, these hydrogen bonds are positioned in the limit in between medium and weak and, hence, they present a bond contribution mostly electrostatic.[27b,37] As a reference, the calculated CCSD(T) interaction energy for a water dimer, a HF dimer, or a

Fig. 6 Interatomic bond critical points (orange circles) identified by QTAIM and the corresponding paths between the concerned atoms. Circles in yellow correspond to ring critical points.

Fig. 5 Close interactions in the two carbonyl groups present in **2-Me**.

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Table 4 Laplacians of the electron density, $\nabla^2\rho(\mathbf{r})$, charge densities, $\rho(\mathbf{r})$, and Lagrangian kinetic energies, $G(\mathbf{r})$, at each C=O···Ha BCP, Ha chemical shifts, O···Ha equilibrium distances, and calculated E_{HB} energies for derivatives **2-Me** and **7-Me–10-Me**

Parameters	**2-Me** (R^1 = Oxaz)	**7-Me** (R^1 = Imid)	**8-Me** (R^1 = Oxaz(Me$_4$))	**9-Me** (R^1 = Oxaz(F$_4$))	**10-Me** (R^1 = open Oxaz)
$\nabla^2\rho(\mathbf{r})$ (in a.u.)	0.06209	0.06791	0.06790	0.05658	0.07821
$\rho(\mathbf{r})$ (in a.u.)	0.01745	0.01899	0.01878	0.01586	0.02069
$G(\mathbf{r})$ (in a.u.)	0.01359	0.01493	0.01484	0.01234	0.01712
δ (in ppm)	5.10	5.29	5.21	4.75	5.31
distance (in Å)	2.243	2.198	2.201	2.295	2.173
E_{HB} (in kcal mol^{-1})	3.66 (4.46)[a]	4.02 (5.44)[a]	3.99	3.32	4.61 (5.14)[a]

[a] In parenthesis, the B3LYP/6-31+G(d) calculated energy difference between the limiting conformations (those following an intramolecular C=O··· Ha hydrogen bonding scheme and those that does not). Note that most part of this energy difference corresponds to the hydrogen bonding event.

HCl dimer is 4.92, 4.52 and 1.90 kcal mol^{-1}, respectively.[38] Although the hydrogen-bond energy (E_{HB}) could be well correlated with the O···Ha distance (Fig. 7a), the best correlating descriptor with E_{HB} is the corresponding charge density ($\rho(\mathbf{r})$) at the BCP,[39] as it is showed in Fig. 7b.

Solvent is usually an important parameter in NMR theoretical calculations and must be considered in order to accurately reproduce experimental NMR spectra.[3,40] In hydrogen bonding, the election of the solvent for spectroscopic properties is not innocent, since high-polar solvents can theoretically disrupt or even break these types of interactions.[41] Thus, expecting that we could achieve different chemical shifts for Ha in polar solvents and have access to other molecular conformations than those stabilized by hydrogen bonding, we experimentally and theoretically (LC-ωPBE/6-311+G(d,p))

Fig. 7 Correlation between the calculated energy of the hydrogen bond (E_{HB}) and either the O···Ha distance (a) or the charge density (b).

studied the corresponding ^{1}H-NMR spectra for **7-Me** (R^1 = Imid) in deuterated methanol and dimethylsulfoxide (Table 5).

Nevertheless, the conclusion that is drawn from Table 5 is that no solvent effect is observed in the chemical shift of Ha, even in the presence of methanol, a polar protic solvent. Therefore, since in Table 2 was clearly shown that the non-hydrogen bonded form of **7-Me** (**7b-Me**) presented a chemical shift of 3.53 ppm, we must conclude that, even with polar solvents, the conformational equilibrium at room temperature keeps this specially stabilized conformation the most part of the time, avoiding the expected shielding of the chemical shift of Ha.

Traditionally, organic chemists rely mostly on ^{1}H-NMR spectra, with relatively little attention being paid to ^{13}C-NMR analysis. However, ^{13}C-NMR constitutes a crucial axis to determining and ascertaining structures mainly due to the fact that it presents a much larger window allowing the appreciation of even small variations and rendering the collapsing of two different signals unlikely. In addition, H–H coupling often leading to broad/multiplet bands and often complicating assignment is absent in ^{13}C-NMR. Therefore, ^{13}C-NMR provides, from a theoretical point of view,[13d,42] an ideal ground where many organic products could be unambiguously characterized by a unique fingerprint. We thus set out to complete our findings and reinterpret the problem at hand based on ^{13}C-NMR data for the Ca carbon (the methinic carbon to which Ha is bonded), see Fig. 1 and 3.

Table 6 compiles the chemical shift values for Ca for compounds **2-Me** and **2b-Me**, **3-Me–6Me**, and **7-Me** and **7b-Me**, using the five functionals initially considered (Table 1). Nevertheless, the basis set used was Pople's polarized split-valence double-zeta 6-31G(d,p),[16] since it is known that Pople's double-zeta basis sets perform better than the triple-zeta ones

Table 5 Theoretical and experimental solvent effects on the ^{1}H-NMR chemical shift of Ha for compound **7-Me**

^{1}H-NMR chemical shifts	CDCl$_3$	MeOD	DMSO-d_6
Theoretical[a]	5.29	5.31	5.30
Experimental[b]	5.28	5.26	5.24

[a] LC-ωPBE/6-311+G(d,p). [b] This work (see ESI).

Table 6 Experimental and calculated values of the ^{13}C-NMR chemical shifts (in ppm) of Ca for derivatives **2-Me–7-Me** (along with **2b-Me** and **7b-Me**) in chloroform

^{13}C-NMR chemical shifts	B3LYP	B3LYP-D3	CAM-B3LYP	M06-2X	LC-ωPBE	Experimental
2-Me	45.86	46.16	44.33	48.59	43.08	42.6 (ref. 11*a*)
						42.8[a] (ref. 11*b*)
2b-Me	51.18	51.17	49.38	53.20	47.55	–[b]
3-Me	57.22	56.91	55.23	58.89	52.94	53.2 (ref. 23*a*)
						53.11 (ref. 23*b* and *c*)
4-Me	49.15	48.82	47.39	50.03	45.46	45.59 (ref. 24*a*)
						45.5 (ref. 24*b*)
5-Me	58.00	57.75	55.75	60.32	53.46	54.23[c]
6-Me	51.61	50.73	49.72	51.68	47.23	47.2 (ref. 26*a*)
7-Me	45.45	45.67	43.91	47.83	42.61	42.69[c]
7b-Me	50.63	50.71	48.91	52.47	47.14	–[b]

[a] Carbon non-assigned in the experimental spectrum. [b] Non-applicable. [c] This work (see ESI).

for ^{13}C-NMR calculations, probably due to some cancellation errors.[43]

Table 6 also reflects a traditional problem associated with the theoretical determination of ^{13}C-NMR chemical shifts, namely that the obtained values are very sensitive to the functional used. This variability is perhaps the main reason why theoretical calculations on ^{13}C-NMR spectra are less common. In this case, although CAM-B3LYP and LC-ωPBE are again the more reliable functionals, LC-ωPBE clearly outperforms, delivering chemical shifts very close to the experimental values.

Furthermore, it is important to highlight the difference of *ca.* 11 ppm between the chemical shifts calculated for Ca in the imidazolidinone (**7-Me**) and the methylthio (**5-Me**) derivatives. This showcases the large spectral window made possible by ^{13}C-NMR.

Calculations for the *ad hoc* structures **8-Me–10-Me** led to the results collected in Table 7. Owing to the fact that ^{13}C-NMR is quite sensitive to steric factors (about an order of magnitude more than ^{1}H-NMR)[44] the reported δ values calculated for Ca do not correlate with any property treated in this text. This is in the line presented just above, for which ^{13}C-NMR determinations are better oriented to the unambiguous assignment of spectroscopic data and, hence, the accurate prediction of spectra for unknown products.

Finally, and as expected given the results achieved for ^{1}H-NMR, solvent effects on compound **7-Me** were almost negligible, as it could be drawn from Table 8, indicating that the hydrogen-bonded conformer should be largely favoured within the timescale of the experiment.

Table 8 Theoretical and experimental solvent effects on the ^{13}C-NMR chemical shift (in ppm) of Ca for compound **7-Me**

^{13}C-NMR chemical shifts	CDCl$_3$	MeOD	DMSO-d_6
Theoretical[a]	42.61	43.58	43.60
Experimental[b]	42.69	43.78	42.13

[a] LC-ωPBE/6-31G(d,p). [b] This work (see ESI).

Conclusions

In summary, we have presented experimental and computational evidence for an unusual intramolecular hydrogen bonding interaction in a series of *N*-acyloxazolidinones and other α-acylmethane derivatives, with striking consequences to their NMR spectroscopic properties. In the course of this study, theoretical (DFT) ^{1}H- and ^{13}C-NMR determinations, along with QTAIM analysis, were employed to clearly identify the nature of such special interaction, among others found in these structures. Of special interest is the finding of the reliability and accuracy of the LC-ωPBE functional, which works fairly well in this domain, at least for this kind of derivatives. Crucial has been the possibility to calculate conformers not accessible by synthesis and that emphasize the stronger interaction involved in this series of compounds. Therefore, results presented here hint at possible general applications to the prediction of highly accurate NMR spectral properties for organic compounds.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Table 7 Calculated ^{13}C-NMR chemical shifts (in ppm) of Ca for known structures **2-Me** and **7-Me** and unknown **8-Me–10-Me**[a]

^{13}C-NMR chemical shifts	**2-Me**	**7-Me**	**8-Me**	**9-Me**	**10-Me**
δ (in ppm)	43.08	42.61	44.63	45.57	45.44

[a] Structures referred here were calculated at the LC-ωPBE/6-31G(d,p) level of theory and using chloroform as solvent (PCM).

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Notes and references

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