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Conformations of vicinal-triketones. A theoretical and ^{17}O NMR approach

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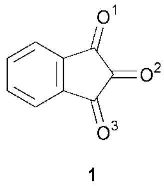
The conformations of a representative group of vicinal triketones have been studied by ^{17}O NMR spectroscopy and, for some of them, DFT calculations have been performed in order to rationalize the results and gain an insight into their geometry; ^{17}O NMR chemical shifts have also been computed by the GIAO method. A dependence of chemical shifts on intercarbonyl dihedral angles, like that observed for α-dicarbonyl systems, has been observed. A constraint to changing conformation, which overrides steric destabilization, has also been observed.

Introduction

Vicinal triketones (vic-triketones), and polycarbonyl compounds in general, are a class of organic compound that, although known for more than one hundred years, is still fascinating and intriguing for chemists.[1] The interest in them has recently further increased due to isolation of biologically important substances[2,3] possessing masked α,β-diketoamide moieties, and the exploitation of α,β-diketoesters in organic synthesis.[4] Due to the juxtaposition of carbonyl groups, the structure of polycarbonyl compounds is of particular interest from the theoretical, as well as from the experimental, point of view.[5] An interesting feature observed for α-dicarbonyl compounds is the dependence of some physical properties on the OCCO intercarbonyl dihedral angle ϑ.[6] Whereas a clear relationship has been observed between this angle and ^{17}O NMR chemical shifts for α-diketones,[7a,8] a less clear-cut dependence has been observed for α-diamides.[7b] It was thus of interest to study vic-triketones in order to obtain a better comprehension of this relationship, possibly extend its validity to vic-triketones, and have a detailed knowledge of their conformations. Following on from our previous studies on α-dicarbonyl derivatives by ^{17}O NMR spectroscopy,[7] we present here an ^{17}O NMR and theoretical study of some model vic-triketones, **1**–**8**. Also, such a study can serve as a closer starting point for studies of α,β-diketoamides and esters and tetra- and pentaketones.



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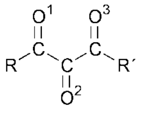

2: R = R′ = C_6H_5, **3**: R = R′ = 4-$MeOC_6H_4$,
4: R = R′ = 4′-$O_2NC_6H_4$,
5: R = R′ = Me, **6**: R = R′ = ^{t}Bu,
7: R = Me, R′ = ^{t}Bu, **8**: R = Me, R′ = C_6H_5

Results and discussion

The structures and oxygen numbering of the eight compounds studied (**1**–**8**) are as shown, and the spectroscopic data are given in Table 1. The $\delta(^{17}O)$ O^1, O^3 values are at 524–608 ppm, and triketones with terminal aliphatic substituents are the most deshielded. $\delta(^{17}O)$ O^2 is at 531–610 ppm, compound **6** being the most shielded and **1** the most deshielded.

In order to rationalize the exceptional shift of its central ^{17}O, compound **6** was investigated, together with the related compounds **5** and **7**, both experimentally and by DFT calculations. The geometries were optimised by B3LYP calculations[9] using a 6-31G(d,p) basis set. Significant geometric parameters are given in Table 2. The angles are defined as follows: ϑ_1 and ϑ_2 are the O^1CCO^2 and O^2CCO^3 dihedral angles, respectively, and β_1 and β_2 are the RCO^1 and the $R'CO^3$ bending angles, respectively. The agreement with the experimental structural data available in the literature[1] for other vicinal triketones is good. Indeed, the range of our C–O bond lengths, 1.214–1.218 Å, which is within the range found for other open chain vicinal triketones,[5] is narrow in comparison with that of cyclic triketones. Likewise, the range of the computed ϑ values includes the values found for similar unconstrained triketones.

^{17}O chemical shifts were calculated by the GIAO method at the B3LYP/6-31G(d,p) and B3LYP/6-311G++(2d,2p) levels of theory. The calculated ^{17}O chemical shifts, relative to the gaseous H_2O shift calculated at the same level of theory, are also reported in Table 2. We note that although the trend is correct and the $\delta(^{17}O)$ values are lower for **6** than for the (similar) values of **5** and **7**, in contrast with expectation the $\delta(^{17}O)$ values calculated at the lower level are closer to the measured values. The reason for this is unknown.

In the study of the influence of variation of the intercarbonyl dihedral angles, ϑ_1 and ϑ_2, on the ^{17}O chemical shifts, the central oxygen, O^2, in the vic-triketones is the most interesting, since it is influenced by both angles, while the other two oxygens, O^1 and O^3, can be regarded as a special case of α-dicarbonyls. This latter point is demonstrated by the near identity of the shifts

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Table 1 ^{17}O NMR shifts (δ, ppm) and half-height line widths ($\nu_{\frac{1}{2}}$, Hz) of vic-triketones in MeCN

Compound	R	R′	δ O^1,O^3	$\nu_{\frac{1}{2}}$	δ O^2	$\nu_{\frac{1}{2}}$
1	Indanetrione		533	245	610	230
2	C_6H_5	C_6H_5	546	350	573	270
3[a]	4-$MeOC_6H_4$	4-$MeOC_6H_4$	524	700	578	860
4[b,c]	4-$O_2NC_6H_4$	4-$O_2NC_6H_4$	580	800	580	800
5	Me	Me	589	153	568	100
6	^{t}Bu	^{t}Bu	608	770	531	480
7	Me	^{t}Bu	587, 613	*ca.* 150	569	180
8	Me	C_6H_5	590, 550	270, 335	569	300
1·H_2O[d]			510	285	55	325
2·H_2O[d]			512	490	56	310

[a] OMe resonance: $\delta = 69$, $\nu_{\frac{1}{2}} = 555$ Hz. [b] NO_2 resonance: $\delta = 580$. [c] Isochronism of all the three oxygen signals is discussed in the text. [d] Hydrates at O^2 of **1** and **2**

for **2** and benzil and for **3** and 4-methoxyphenyl phenyl α-diketone.[7a]

The measured difference in the $\delta(^{17}O)$ values for O^1, O^3 of **1** and **2** is −12.1 ppm, a value identical, but of the opposite sign, to that observed for α-diketones. Annulation (as observed, *e.g.*, for indan-1-one and acetophenone, where a $\Delta\delta = -46$ has been measured[10]) can contribute significantly to the observed chemical shifts, overwhelming the effect of the dihedral angle and leading to an apparently opposite effect. The relatively small $\Delta\delta$ observed is indicative that this might be the case for **1** and **2**.

A further comparison can be made for compound **1** with some indane-1,3-diones.[11] While a comparable geometry is assured for both systems by sp^2 hybridisation of all the carbons of the five-membered ring, a rough deshielding of $\Delta\delta = 25$ is observed for O^1, O^3 compared with the shifts for the corresponding oxygens of the indane-1,3-diones.[11] This finding is in good agreement with the known influence of the dihedral angle in α-diketones[7a,8] and indicates that substitution of a carbonyl group by a vinylic group will modify the ^{17}O NMR chemical shifts, which are dependent on the dihedral angles. To our knowledge, an ^{17}O NMR study of this important feature for carbonyl groups conjugated with vinylic groups has not been reported, so our observations could be regarded as a preliminary study related to this phenomenon.

While most $\delta(^{17}O)$ O^2 values are observed in the narrow range 568.7–580 ppm, two values are significantly different from all the other values, namely 610.1 ppm for **1** and 531 ppm for **6**. The large deshielding ($\Delta\delta = 36.7$) observed for **1** relative to **2** is qualitatively easily understood, if $\vartheta_1 = \vartheta_2 = ca.\ 90°$ for **2**. Indeed, for the aromatic α-diketones[7a] benzil ($\vartheta = ca.\ 90°$) and 9,10-phenanthrenequinone ($\vartheta = ca.\ 0°$), a $\Delta\delta$ value of 12 ppm was measured. Hence, the $\Delta\delta$ difference between **1** and **2** is approximately three-times, rather than two-times, larger than that for α-diketones, as naively expected. Part of this discrepancy may be due to the uncertain knowledge of the exact ϑ, ϑ_1 and ϑ_2 values and/or to actual small deviations of these angles from the exact 0 and 90° values. An X-ray study of **1** reported the values $\vartheta_1 = \vartheta_2 = 0°$, within the experimental error,[12] but the solution values of the various ϑ angles that we use, *e.g.*, 90° for **2**, unless a geometrical constraint is present as in **1**, necessarily involve a severe approximation. Our DFT calculations *in vacuo* (see Table 2) estimate these angles for the aliphatic derivatives **5**–**7** to vary from 112 to 152°. Note, however, that the observed $\Delta\delta$ of 16.0 ppm for aliphatic α-diketones[8] for an angle ϑ varying from 0 to 82°, is closer to half of the value of 36.7 ppm.

Another contributing feature in the aromatic vic-triketones is possible conjugation between the outer carbonyl groups and an adjacent aromatic ring. The influence of conjugation on the ^{17}O NMR carbonyl shifts has been studied extensively[13] and a comparison of the difference in $\delta(^{17}O)$ O^1 and O^3 between **1**–**4** and **5**–**8** immediately enables us to recognise its presence in our systems. This is clearly reflected in the different δ values for O^1 and O^3 of **8**. The degree of conjugation is a function of the angle between the carbonyl group and the aromatic ring. For carbonyl-bearing aromatic systems, such as acetophenones[10,14] and benzaldehydes,[10,14] the role of steric inhibition of resonance is firmly established and quantitative relationships have been developed to measure the dihedral angles between several different types of carbonyl groups and aromatic rings.[13] In both acetophenone and benzaldehyde, this angle is 0° within the experimental error. Since the effects of *para*-substituents on the ^{17}O NMR carbonyl shifts are very similar for our system and for acetophenone, benzaldehyde and α,α,α-trifluoroacetophenones,[15] it is reasonable to assume that this dihedral angle is also close to 0° in the vic-triketones. Further evidence is deduced from the ^{17}O NMR shifts of the substituents. The OMe shift is in good agreement with those measured for anisoles substituted by *p*-electron-withdrawing groups (EWGs)[16] and for 4-methoxy-α,α,α-trifluoroacetophenone.[15] The data for compound **4** can be misleading because of apparent isochronism. All three expected signals have sufficiently similar chemical shifts that, due to the relatively large line width of ^{17}O NMR signals, apparently merge to one observed signal. Substitution by EWGs in position 4 of aryl ketones causes deshielding of the C=O group, with $\delta(^{17}O)$ CO values ranging from 543 to 573 ppm.[7a,15] The chemical shift range for analogous aromatic nitro groups is very narrow and the signals are almost coincident, varying from *ca.* 578 to *ca.* 586 ppm.[17] The shift of the central carbonyl (O^2) is relatively insensitive to the structure, except in **1** and **6**, and is again in the same region of the spectrum. Since the estimated half-height line width of the observed signal is 800 Hz, *i.e.*, *ca.* 20 ppm, this "isochronism" becomes understandable and both $\vartheta_1 = \vartheta_2 = 90°$ and Ar–CO dihedral angle close to 0° are most probable. These results are in complete agreement with those obtained by Horner and Maurer by UV spectroscopy.[18]

The chemical shifts of the external oxygen atoms of the aliphatic derivatives **5**–**7** and of the carbonyl adjacent to the methyl group of **8** are deshielded compared with those of **1**–**4**, for the reasons discussed above. These shifts resemble more those of aldehydes than those of ketones.[19] This is suggestive of a small electronic and steric interaction between the external and the central carbonyl groups, as already noted for the two halves of α-diketones.[7a] A further reason can be the deshielding effect caused by strong EWGs, as shown by the >20 ppm difference observed between acetone and α,α,α-trifluoroacetone.[15] The reason for the deshielding observed for the carbonyl adjacent to the ^{t}Bu group is discussed below. It is noteworthy that the chemical shift differences between O^1, O^2 and O^3 of **6** are large and comparable but in the opposite direction to those observed for **1**. The conformationally important result is given by the shift differences observed for the central oxygens O^2. However, the $\Delta\delta_{5-6} = 37.7$ may indicate that the dihedral angles $\vartheta_1 = \vartheta_2$ in **6** are closer to 90° than are those in **5**. This experimental observation is in agreement with the computed shifts

Table 2 GIAO B3LYP/6-31G(d,p) and B3LYP/6-311G++ (2d,2p) ^{17}O NMR chemical shifts and relevant B3LYP/6-31G (d,p) optimised geometry data

		5	6	7
δ^a	O^2 centr 6-31G (d,p)	566.12	551.08	568.25
	6-311G++ (2d,2p)	601.98	591.54	606.91
	O^1 6-31G (d,p)	638.49	598.77	633.68
	6-311G++ (2d,2p)	674.47	635.40	672.44
	O^3 6-31G (d,p)	638.50	598.77	603.34
	6-311G++ (2d,2p)	674.76	635.39	639.71
ϑ	ϑ_1	138.01	126.97	152.05
	ϑ_2	138.02	126.99	112.31
β	β_1	125.38	124.92	125.26
	β_2	125.38	125.21	125.21
$R_{C=O}$/Å	O^1	1.214	1.218	1.216
	O^2	1.215	1.215	1.215
	O^3	1.214	1.218	1.216
R_{C-C}/Å	C1–C2	1.542	1.544	1.544
	C2–C3	1.542	1.544	1.541

[a] Chemical shift value respect to gaseous water.

(Table 2). In fact, while the absolute values of the experimental and computed shifts are different, the $\Delta\delta_{5-6}(\text{exp}) = 37.7$ compares reasonably with a $\Delta\delta_{5-6}(\text{calc})$ of 16 ppm. This agreement is particularly satisfactory taking into account that computed values are *in vacuo*, while the measured shifts are in the polar solvent MeCN.

Further support for this interpretation of the influence of ϑ variation on ^{17}O NMR shifts is given by the experimental and computed data of **7**. The dihedral angles ϑ_1 and ϑ_2 in **7** are different and one of them is higher and the other lower compared with the computed $\vartheta_1 = \vartheta_2$ value for **5**. The two effects should operate in opposite directions and compensate one another. Both the experimental and the computed values of $\delta(^{17}O)$ O^2 of **5** and **7** are nearly identical.

^{17}O NMR shifts for aldehydes and ketones do not change monotonously on introducing alkyl groups in juxtaposition to the carbonyl group. For example, shieldings of 27.5 and 7.5 ppm have been observed on going from acetaldehyde to pivaldehyde, and from acetone to *tert*-butyl methyl ketone, respectively; a slight deshielding (3.0 ppm) is observed for the change from diisopropyl ketone to *tert*-butyl isopropyl ketone.[19] This is probably due to the superposition of several effects, such as γ effects (shielding), van der Waals interactions (deshielding), and slight changes of angles and other structural parameters.

The high deshielding observed for the external carbonyl groups of **6** has been viewed as a strong indication of van der Waals interactions between the *tert*-butyl groups and the adjacent carbonyl. ^{17}O NMR downfield shifts in hindered carbonyl systems can result from two distinctly different reasons, as discussed by Boykin *et al.*[20] These are (a) that an increase of the dihedral angle between the carbonyl group and a conjugated system will reduce the extent of conjugation or (b) repulsive van der Waals interactions, when a physical constraint is such that the steric interaction cannot be avoided. In the case of **6** only the latter can operate. This observation seems to indicate the presence of a constraint to changing conformations in these systems, which overrides to the steric destabilization caused by the bulkiness of the ^{t}Bu group on the carbonyl. While *normal* aldehydes and ketones can enlarge their R(CO)R angles in order to minimize this crowding, as discussed,[21] *e.g.*, for acetone and di-*tert*-butyl ketone, it seems that vic-triketones cannot, as shown by the near invariance of their β values (Table 2).

In two cases, **1** and **2**, we also measured the spectra of the mixtures of the tricarbonyl form and its hydrates at the central carbonyl. The carbonyl ^{17}O NMR shift of **1**·H_2O compares well with those reported for some indane-1,3-diones,[11] while a slight shielding can be observed when comparing **2**·H_2O with most aryl ketones.[13] Most probably, this shielding is due to (internal) hydrogen bonding between the carbonyl and the hydroxy groups. A comparison of our results with those observed[22] in other hydrogen-bonded systems seems to indicate a weak hydrogen bond. The geminal OH groups also show an ^{17}O NMR shift in the normal range[23] observed for the hydroxy groups of alcohols. Further studies in different solvents and with variable concentrations would help us to better understand this point.

Experimental

All compounds studied are known. Compound **1** is commercially available, **2** and **3** were a gift from Professor H. Dahn (Lausanne University) and **4**–**8** were prepared either by the Saba procedure,[24] *via* the reaction of diazodiketones with dimethyldioxirane, or through the monobromodicarbonyls, following the Dahn procedure.[25] All compounds have physical properties consistent with their structures and with the literature data.

^{17}O NMR spectra were recorded, in the Fourier transform mode, on a Varian VXR 300 spectrometer equipped with a Sun 3/60 computer and with a 10 mm broad band probe at 65 °C (probe temperature = 338 K) at natural isotopic abundance. The instrumental settings were: 40.662 MHz frequency, spectral width 36 kHz, acquisition time 10 ms, preacquisition delay 100 µs, pulse angle 90° (pulse width 28 µs). The number of scans varied largely (10^5–10^6) as a function of solubility. The spectra were recorded with sample spinning and without lock. The signal-to-noise ratio was improved by applying a 30 Hz exponential broadening factor (l.b.) to the FID prior to Fourier transformation. Half-height line widths are computer estimated after line broadening factor application. The data point resolution was improved by zero filling to 16K data points. Chemical shifts are expressed in ppm and referred to external tap water by the substitution method. The chemical shift is obtained by taking the peak maximum. The reproducibility of the chemical shift data is estimated to be ±1 ppm.

All samples were prepared in dry MeCN and a few molecular sieves (4 Å, pellets) were left in the bottom of the NMR tube throughout the recording of the spectra for all samples except **1**·H_2O and **2**·H_2O, thus giving solutions free of the hydrated triketone.

All the calculations have been carried out on a DEC alpha personal workstation 500 au, using the GAUSSIAN 94[26] quantum mechanical package.

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