Hydrogen-Bonding in Cyclic 2-(3-Oxo-3-phenylpropyl)-Substituted 1,3-Diketones: ^{17}O-NMR Spectra and X-Ray Structure Determination

by **Jin-Cong Zhuo***[1])

Institute of Organic Chemistry, University of Lausanne, BCH, CH-1015 Lausanne-Dorigny

and **Kurt Schenk**

Institute of Crystallography, University of Lausanne, BSP, CH-1015 Lausanne-Dorigny

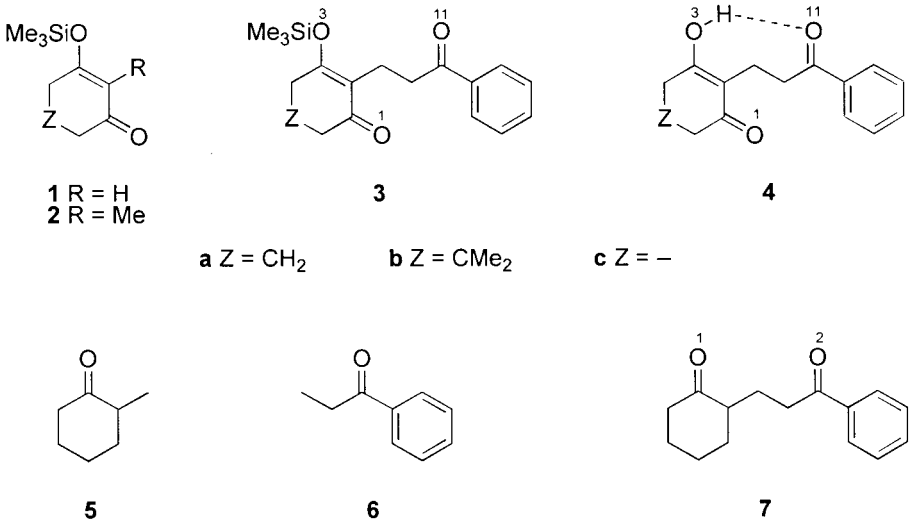
Structures of cyclic 2-(3-oxo-3-phenylpropyl)-substituted 1,3-diketones **4a**–**c** were determined by ^{17}O-NMR spectroscopy and X-ray crystallography. In $CDCl_3$ solution, compounds **4a**–**c** form an eight-membered-ring with intramolecular H-bonding between the enolic OH and the carbonyl O(11)-atom of the phenylpropyl group, as demonstrated by increased shielding of specifically labeled **4a**–**c** in the ^{17}O-NMR spectra ($\Delta\delta(^{17}O(11)) = 36$ ppm). In solid state, intermolecular H-bonding was observed instead of intramolecular H-bonding, as evidenced by the X-ray crystal-structure analysis of compound **4b**. Crystals of compound **4b** at 293 K are monoclinic with $a = 11.7927(12)$ Å, $b = 13.6230(14)$ Å, $c = 9.8900(10)$ Å, $\beta = 107.192(2)^\circ$, and the space group is $P2_1/c$ with $Z = 4$ (refinement to $R = 0.0557$ on 2154 independent reflections).

Introduction. – Hydrogen bonding plays an important role in organic and biological molecules, and has been widely studied [1]. ^{17}O-NMR Spectroscopy is a particularly useful tool to investigate the bonding state of O-atoms and intramolecular H-bonding in organic compounds [2]. Intramolecular H-bonding in a molecule generally causes shielding of the O-atom [2–10]. Shielding of the O-atom by intramolecular H-bonding ($\Delta\delta_{HB}$ value) ranging from -5 to -50 ppm has been reported for various compounds including enaminones [3][4], ketones [5], aldehydes [6], amides [7], and esters [8].

We previously observed eight-membered-rings formed by intramolecular H-bonding between the side chain enolic OH and the uracil C(4)=O in 1,3-dimethyl-5-(3-cyano-3-hydroxypropan-3-en-1-yl)uracil [10]. *Gellman* and co-workers [11] have reported intramolecularly H-bonded eight-membered rings for diamides. This paper reports such H-bonding in triketones **4a**–**c**.

Results and Discussion. – *^{17}O-NMR Spectra*. The ^{17}O-NMR spectra of cyclic 3-(trimethylsilyl)oxy (TMSO) enones **1**–**3** and triketones **4** were recorded in $CDCl_3$ (*Table 1*). 3-[(Trimethylsilyl)oxy]cyclohex-2-en-1-one (**1a**) shows two signals in the ^{17}O-NMR spectrum, one at 493.5 and the other at 124.5 ppm. The former is assigned to the carbonyl O-atom, and the latter corresponds to the TMSO O-atom. The signal of the carbonyl O-atom appears at higher field than in case of cyclohex-2-en-1-one (544.3 ppm, in MeCN) [12]. This is attributed to the n-donation of the TMSO group. The n-donating ability of the TMSO group is very similar to that of the EtO group, but

[1]) Correspondence to: J.-C. Zhuo, ArQule, Inc., 19 Presidential Way, Woburn, MA 01801, USA. E-mail: jzhuo@arqule.com.



it is significantly smaller than that of Me_2N group, as demonstrated by 3-ethoxyhex-2-en-1-one (493.2 and 123.9 ppm, in $CDCl_3$ at 40°, new measurement) and 3-(dimethylamino)cyclohex-2-en-1-one (446.2 ppm in MeCN) [12]. The ^{17}O chemical-shift values of 5,5-dimethyl-3-[(trimethylsilyl)oxy]cyclohex-2-en-1-one (**1b**) are very close to those of **1a**. The C=O signal of the five-membered-ring enone **1c** is shielded by 38 ppm compared with that of the six-membered-ring enone **1a**. The difference is

Table 1. *^{17}O-NMR Chemical Shifts* ($CDCl_3$, 40°; δ [ppm]) *of Compounds* **1**–**7** *with Line-Width* [Hz] *at Half-Height in Parentheses.* ^{17}O-Enriched groups are marked by *.

Compound	O(1)	O(2) or O(11)	–O–
1a	493.5 (610)		124.5 (425)
1b	498.4 (530)		122.6 (450)
1c	455.7 (200)		126.8 (340)
2a	497.5 (350)		118.5 (410)
2b	503.8 (460)		115.8 (490)
2c	450.5 (206)		115.3 (350)
3a	500.8 (590)	536.5 (820)	120.6 (660)
3b	504.9 (970)*		116.4 (850)*
	506.9 (990)	536.2 (660)	116.2 (650)
	503.3* (680)	537.1* (980)	116.8* (920)
3c	452.7 (800)	537.7 (1050)	116.7 (1140)
	453.7 (800)*	536.1 (1010)*	116.4 (730)*
4a	472.5 (820)	498.4 (1070)	121.3 (660)
4b	483.1 (850)	498.5 (1020)	117.8 (950)
	483.9* (1040)	498.8* (1200)	117.3* (890)
	483.9* (1200)		117.3* (740)
4c	272.8* (1550)	503.7* (1460)	272.8* (1550)
5	541.1 (230)		
6	532.7 (280)		
7	543.6 (860)	533.7 (770)	

similar to that of cyclic enones ($\Delta\delta \approx 36-42$ ppm) [13], and larger than that observed for cyclic 2-(phenylmethylene) ketones ($\Delta\delta = 28$ ppm) [14], cyclic 2-(*N*,*N*-dimethylmethylene) ketones ($\Delta\delta = 22-25$ ppm) and saturated cyclic ketones ($\Delta\delta = 13$ ppm) [12]. The additional Me group at C(2) of these compounds, as in **2a** and **2c**, causes a slight shielding of the TMSO O-atom (4–7 ppm), indicating that the conjugation of the O–C=C–C=O system is reduced due to the steric interactions between the Me and the TMSO groups and/or the C=O group. As a result, the C=O signals were shifted to higher field (*ca.* 4 ppm). Interestingly, the Me group at C(2) in compound **2b** causes a slight shielding of both O-atoms, the basis for which is not very clear.

In compound **3a**, three signals were observed at 536.5, 500.8, and 120.6 ppm. To assign these, ^{17}O-NMR spectra of compounds **5**–**7** were recorded. 2-(3-Oxo-3-phenylpropyl)cyclohexanone (**7**) shows two signals in the ^{17}O-NMR spectrum, one at 543.6 and the other at 533.7 ppm, comparable to those of 2-methylcyclohexanone (**5**; 541.1 ppm) and 1-phenylpropan-1-one (**6**; 432.7 ppm). Thus, the higher-field signal (533.7 ppm), attributed to extended conjugation of the C=O group with the unsaturated system, is assigned to the benzoyl O(11), and the signal at 543.6 ppm corresponds to the carbonyl O(1). The signal at 536.5 ppm of compound **3a** is assigned to the benzoyl carbonyl O(11) on the basis of the ^{17}O-NMR spectra of **2a**, **6**, and **7**. The other two signals (at 500.8 and 120.6 ppm) correspond to the carbonyl O(1) and TMSO O-atoms of the cyclic moiety, respectively. The specfically labelled derivatives **3b** and **3c** further confirm these assignments. Comparison of the chemical-shift values of the compounds **3a**–**c** with those of 2-Me analogues **2a**–**c** show that the 3-oxo-3-phenylpropyl group does not affect the conjugation system O–C=C–C=O.

The three ^{17}O signals for 2-(3-oxo-3-phenylpropyl)cyclohex-2-ene-1,3-dione (**4a**) were observed at 498, 472, and 121 ppm. The lowest-field signal (498 ppm) is assigned to the carbonyl O(11) of the phenylpropyl group, and the signals at 472 and 121 ppm were assigned to the carbonyl O(1) and enolic O-atoms of the cyclic moiety. The assignments were confirmed by the investigation of the ^{17}O-enriched compound **4b**, in which both O-atoms in the six-membered ring are enriched in ^{17}O, which shows only two signals at 483 and 117 ppm. Both unlabelled and fully labelled **4b** show three signals at 498, 483, and 117 ppm. Thus, the signal at 498 ppm is assigned to the carbonyl O(11) of the phenylpropyl group, and the signals at 483 and 117 ppm are assigned to the carbonyl O(1) and enolic O-atoms of the cyclic moiety. Interestingly, in the five-membered-ring derivative **4c**, the carbonyl O(1)- and enolic O-atoms in the ring display the same chemical shift at 273 ppm, which may be attributed to rapid tautomerization [15][16].

In the cyclic 2-(3-oxo-3-phenylpropyl) 1,3-diketones **4a**–**c**, the signals for the carbonyl O(11) of the phenylpropyl group appears at *ca.* 500 ppm. They are at *ca.* 36 ppm higher field than those of the corresponding silyl ethers **3a**–**c**. The shielding due to H-bonding is well-known [2–10], thus, the shielding effect on the O(11) of **4a**–**c** is interpreted as the result of a H-bond between the enolic OH and O(11).

Whether the H-bond between the enolic OH and O(11) is inter- or intramolecular was tested by a dilution experiment with **4b** by ^{1}H-NMR: the ^{1}H-NMR signal at 10.00 ppm (in $CDCl_3$) did not change its position between 0.01M and 0.25M, confirming the intramolecular character of the H-bond. Furthermore, changing the solvent to one that is a better H-bond acceptor only slightly affected the signal in **4b** ((D_6)acetone: 9.40 ppm, (D_6)benzene: 10.19 ppm, (D_6)DMSO: 10.43 ppm), demonstrating that the

intramolecular H-bonding is rather strong and is not replaced by an intermolecular bridge to a solvent molecule.

X-Ray Crystallography. To test whether the eight-membered ring formed by intramolecular H-bonding exists also in the solid state, the X-ray crystal-structure determination was carried out for **4b** at 293 K (*Table 2*). An ORTEP view of compound **4b** is shown in *Fig. 1*[2]).

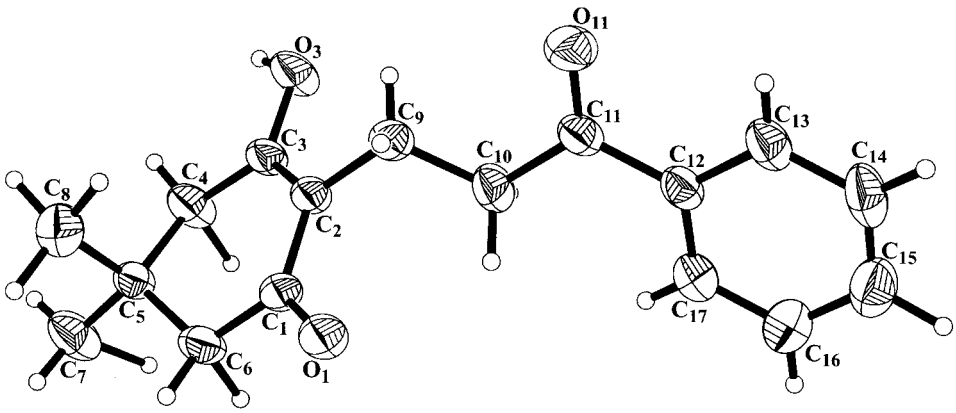


Fig. 1. *ORTEP View of triketone* **4b**. Arbitrary numbering.

X-Ray analysis of the structure of **4b** shows that the cyclic diketone moiety exists as an envelope conformation: C(1)–C(4), C(6), C(9), O(1), and O(3) atoms are strictly coplanar, and the C(5)-atom sticks out of the plane. The Ph group is virtually planar and is twisted out of the mean plane of the HO–C=C–C=O system by 121.9°. The dihedral angle between the plane C(10)–C(11)–O(11)–C(12) and the mean plane of the HO–C=C–C=O system is 123.3°, and that between the plane C(10)–C(11)–O(11)–C(12) and the Ph ring is 5.5°.

Fig. 2 shows the packing arrangement for compound **4b**. It is clear that compound **4b** does not exhibit intramolecular H-bonding in the solid state. The molecules are linked consecutively into chains of intermolecular H-bonds between carbonyl O(1) in one molecule and OH proton in the other. According to the nomenclature for β-diketone enols [17], the intermolecular H-bonds have an *anti-anti* conformation with distances O(1)···H–O(3) of 1.83 Å and O(1)···O(3) of 2.62 Å. The O(1)···O(3) distance can be compared with inter- and intramolecular H-bonded O···O distances. Acyclic β-diketones with strong intramolecular hydrogen-bonds have O···O distances of 2.42–2.55 Å [16][18], and cyclic β-diketones with intermolecular H-bonds have O···O distances of 2.55–2.59 Å [16][17][19]. The O(1)···O(3) distance of 2.62 Å observed for compound **4b** indicates strong intermolecular H-bond in solid state.

---

[2]) Supplementary crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* (deposition number: CCDC 171429) and can be obtained on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

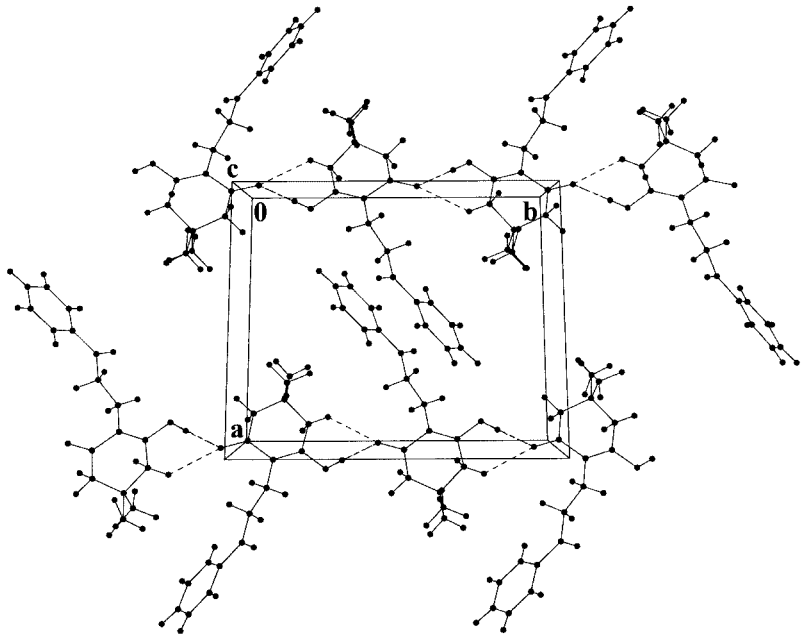


Fig. 2. *The unit-cell packing arrangement for triketone* **4b**. The H-Bonds are represented by – – –.

In the packing arrangement (*Fig. 2*), O(1)···H–C(4) intermolecular H-bonds were also observed between the carbonyl O(1) in one molecule and the H–C(4) in the other, evidenced by a distance for O(1)···H–C(4) of 2.54 Å. O···H–C H-bonds have been observed in various compounds and play an important role in determining crystal packing and molecular conformation [1f][20]. Surprisingly, this type of O···H–C intermolecular H-bonding has not been observed for other of β-diketones in solid state [17–19][21].

We thank Prof. *Hugo Wyler* for valuable comments and the *Swiss National Science Foundation* for financial support.

Experimental Part

General. M.p.: *Mettler FP-52* (microscope). ^{1}H- and ^{13}C-NMR Spectra: *Bruker DPX-400* spectrometer at 400.13 and 100.62 MHz, resp.; $CDCl_3$ solns. at 20°; δ in ppm rel. to Me_4Si (= 0 ppm), J in Hz.

^{17}O-NMR Spectroscopy. The ^{17}O-NMR spectra were recorded on a *Bruker WH-360* spectrometer, equipped witha 10-mm probe, at 48.8 MHz, in the *Fourier* transform (FT) mode without lock. System control, data acquisitions, and data management were performed by an *Aspect-2000* microcomputer. Instrumental settings: spectral width 50000 Hz (1025 ppm), 2-K data points, pulse width 33 μs, acquisition time 20 ms, preacquisition delay 5 μs, 150000–1000000 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 8-K words and exponentially multiplied with a 100-Hz line-broadening factor (LB) before being subjected to the FT. The chemical shifts δ_O, measured in 0.4–0.6M $CDCl_3$ soln. at 40° at natural isotopic abundance, are reported relative to $\delta_O(H_2O)$ (= 0.0 ppm); dioxane (δ_O = 0 ppm) was used as an external standard; downfield shifts are positive. The general reproducibility of chemical-shift values is *ca.* ±1 ppm.

Structure Determination for **4b**. Crystal properties and details of the data collection, which was carried out on a *Bruker Smart 1000* equipped with Mo radiation, are given in *Table 2*. The data were corrected for the

variation of exper. conditions as well as for *Lorentz* and polarization effects. For the structure solution, refinement, and representation, the SHELXTL system was used [22]. All non-H-atoms were refined anisotropically. Ideal positions were imposed on the H-atoms, but their isotropic displacement parameters were refined.

Table 2. *Crystal Data and Structure Refinements for Compound* **4b**

Formula	$C_{17}H_{20}O_3$
M_r	272.33
Temp.	293 (2) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1/c$
a [Å]	11.7927 (12)
b [Å]	13.6230 (14)
c [Å]	9.8900 (10)
β [deg]	107.192 (2)
V [$Å^3$]	1517.9 (3)
Z	4
d [g/cm]	1.192
Absorption coefficient, mm^{-1}	0.081
$F(000)$	584
θ Range for data collection	1.81 to 23.30°
Index ranges	$-12 \le h \le 13$ $-15 < k \le 14$ $-9 \le l \le 10$
Reflections collected	5626
Independent reflections	2154 ($R_{int} = 0.0391$)
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2154/0/187
Goodness-of-fit on F^2	0.760
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0557, wR2 = 0.1859
R Indices (all data)	$R1 = 0.0702$, $wR2 = 0.02091$
Extinction coefficient	0.019 (5)
Largest diff. peak and hole	0.311 and −0.235 eÅ^{-3}

Materials. The known compounds **1a**–**c** and **2a**–**c** were prepared from the corresponding β-diketones according to the method in [23]. Compounds **3a**–**c** were prepared from triketones **4a**–**c** by reaction of trimethysilyl cyanide with the corresponding β-diketones according to the method in [23]. ^{17}O-Enriched compounds, cyclopentane-1,3-[$^{17}O_2$]dione and 5,5-dimethylcyclohexane-1,3-[$^{17}O_2$]dione, were prepared by exchange from the corresponding unlabeled 1,3-diketones and $H_2{}^{17}O$ (2.272%; *Yeda R&D Co. Ltd.*) according to the method in [24].

2-(3-Oxo-3-phenylpropyl)-3-[(trimethylsilyl)oxy]cyclohex-2-en-1-one (**3a**): ^{1}H-NMR ($CDCl_3$): 7.97–8.01 (m, 2 arom. H); 7.51–7.56 (m, 1 arom. H); 7.43–7.47 (m, 2 arom. H); 2.97–3.02 (m, 2 H–C(2′)); 2.62–2.68 (m, 2 H–C(1′)); 2.40 (t, $J = 6.5$, 2 H–C(4)); 2.36 (t, $J = 6.7$, 2 H–C(6)); 1.86–2.00 (m, H–C(5)); 0.26 (s, Me_3Si). ^{13}C-NMR ($CDCl_3$): 200.36 (C(1)); 199.30 (C(3′)); 169.80 (C(3)); 136.92 (arom. C); 132.77 (1 arom. CH); 128.46 (2 arom. CH); 128.24 (2 arom. CH); 121.35 (C(2)); 37.59 (C(2′)); 36.82 (C(6)); 31.20 (C(4)); 21.04 (C(5)); 18.65 (C(1′)); 0.91 (3 Me).

5,5-Dimethyl-2-(3-oxo-3-phenylpropyl)-3-[(trimethylsilyl)oxy]cyclohex-2-en-1-one (**3b**): ^{1}H-NMR ($CDCl_3$): 7.96–8.01 (m, 2 arom. H); 7.51–7.56 (m, 1 arom. H); 7.42–7.47 (m, 2 arom. H); 2.97–3.02 (m, 2 H–C(2′)); 2.62–2.68 (m, 2 H–C(1′)); 2.27 (s, 2 H–C(4)); 2.23 (s, 2 H–C(6)); 1.06 (s, 2 Me); 0.26 (s, Me_3SiO). ^{13}C-NMR ($CDCl_3$): 200.39 (C(1)); 199.16 (C(3′)); 168.03 (C(3)); 136.83 (arom. C); 132.82 (1 arom. CH); 128.50 (2 arom. CH); 128.25 (2 arom. CH); 120.04 (C(2)); 50.72 (C(6)); 45.19 (C(4)); 37.49 (C(2′)); 32.21 (C(5)); 28.35 (2 Me); 18.60 (C(1′)); 0.99 (Me_3Si).

2-(3-Oxo-3-phenylpropyl)-3-[(trimethylsilyl)oxy]cyclopent-2-en-1-one (**3c**): ^{1}H-NMR ($CDCl_3$): 7.94–7.98 (*m*, 2 arom. H); 7.52–7.57 (*m*, 1 arom. H); 7.42–7.47 (*m*, 2 arom. H); 3.11–3.16 (*m*, 2 H–C(2′)); 2.48–2.55 (*m*, 2 H–C(4), 2 H–C(1′)); 2.41–2.45 (*m*, 2 H–C(5)); 0.31 (*s*, Me_3Si). ^{13}C-NMR ($CDCl_3$): 206.18 (C(1)); 199.87 (C(3′)); 182.30 (C(3)); 136.81 (arom. C); 132.94 (1 arom. CH); 128.53 (2 arom. CH); 128.13 (2 arom. CH); 122.42 (C(2)); 36.16 (C(2′)); 33.83 (C(5)); 29.02 (C(4)); 16.77 (C(1′)); 0.85 (Me_3Si).

2-(3-Oxo-3-phenylpropyl)cyclohexane-1,3-dione (**4a**). A mixture of cyclohexane-1,3-dione (4 mmol) and 3-(dimethylamino)-1-phenylpropan-1-one hydrochloride (2 mmol), and Et_3N (3 mmol) was heated at 160° for 15 min. After cooling, the mixture was purified by flash chromatography (AcOEt) to give **4a** (0.41 g, 84%). IR (KBr): 2200–3200*m* (br), 1686v*s*, 1568v*s*, 1375v*s*, 1364v*s*, 1163*s*, 1138v*s*, 1070v*s*, 734*s*, 699*s*, 683*s*. ^{1}H-NMR ($CDCl_3$): 10.07 (br., OH); 7.98–8.02 (*m*, 2 arom. H); 7.57–7.63 (*m*, 1 arom. H); 7.44–7.50 (*m*, 2 arom. H); 3.29–3.33 (*m*, 2 H–C(2′)); 2.64–2.68 (*m*, 2 H–C(1′)); 2.46 (*t*, *J* = 6.3, 2 H–C(4)); 2.31 (*t*, *J* = 6.5, 2 H–C(6)); 1.87–1.95 (*m*, 2 H–C(5)). ^{13}C-NMR ($CDCl_3$): 204.57 (C(1)); 198.99 (C(3′)); 173.67 (C(3)); 135.77 (arom. C); 134.15 (1 arom. CH); 128.75 (2 arom. CH); 128.53 (2 arom. CH); 114.85 (C(2)); 38.34 (C(2′)); 36.69 (C(6)); 29.17 (C(4)); 20.48 (C(5)); 15.19 (C(1′)). EI-MS: 244 (7, M^+), 226 (2), 139 (87), 120 (41), 105 (100), 91 (8), 77 (39).

5,5-Dimethyl-2-(3-oxo-3-phenylpropyl)cyclohexane-1,3-dione (**4b**): Prepared from cyclohexane-1,3-dione as described for **4a**. IR (KBr): 2200–3200*m* (br.), 1685v*s*, 1638*m*, 1596*s*, 1562v*s*, 1378v*s*, 1311v*s*, 1281v*s*, 1248v*s*, 1175*s*, 1147v*s*, 1064v*s*, 1050v*s*, 742v*s*, 693v*s*. ^{1}H-NMR ($CDCl_3$): 9.97 (br., OH), 7.97–8.01 (*m*, 2 arom. H); 7.57–7.63 (*m*, 1 arom. H); 7.44–7.49 (*m*, 2 arom. H); 3.27–3.01 (*m*, 2 H–C(2′)); 2.65–2.69 (*m*, 2 H–C(1′)); 2.33 (*s*, 2 H–C(4)); 2.19 (*s*, 2 H–C(6)); 1.03 (*s*, 2 Me). ^{13}C-NMR ($CDCl_3$): 204.34 (C(1)); 198.55 (C(3′)); 171.73 (C(3)); 135.79 (arom. C); 134.10 (1 arom. CH); 128.73 (2 arom. CH); 128.49 (2 arom. CH); 113.59 (C(2)); 50.53 (C(6)); 42.86 (C(4)); 38.39 (C(2′)); 31.43 (C(5)); 28.30 (2 Me); 15.35 (C(1′)). EI-MS: 272 (11, M^+), 254 (2), 167 (75), 137 (6), 133 (8), 120 (57), 111 (38), 105 (100), 91 (6), 83 (24), 77 (34).

5,5-Dimethyl-2-(3-oxo-3-phenylpropyl)cyclohexan-1,3-[$^{17}O_2$]dione ([$^{17}O_2$]-**4b**). Prepared from cyclohexane-1,3-[$^{17}O_2$]dione in a similar way.

5,5-Dimethyl-2-{3-[^{17}O]oxo-3-phenylpropyl}cyclohexane-1,3-[$^{17}O_2$]dione ([$^{17}O_3$]-**4b**). A soln. of 5,5-dimethyl-2-(3-oxo-3-phenylpropyl)cyclohexane-1,3-[$^{17}O_2$]dione (**4b**) in MeCN containing 2% H_2O was left at r.t. for 24 h. Evaporation of the solvents afforded the totally ^{17}O-enriched compound **4b**.

2-{3-[^{17}O]oxo-3-phenylpropyl}cyclopentane-1,3-[$^{17}O_2$]dione ([$^{17}O_3$]-**4c**). A mixture of cyclopentane-1,3-[$^{17}O_2$]dione (4 mmol), 3-(dimethylamino)-1-phenylpropan-1-one hydrochloride (2 mmol), and Et_3N (3 mmol) was heated at 160° for 15 min. After cooling, the mixture was purified by flash chromatography (AcOEt) to give **4c**, which was dissolved in MeCN containing 2% H_2O. The soln. was left at r.t. for 24 h. Evaporation of the solvents afforded the totally ^{17}O-enriched compound **4c** (0.40 g, 87%). IR (KBr): 2200–3200*m* (br.), 1686v*s*, 1583v*s*, 1375v*s*, 1160*s*, 742*s*, 689*s*, 667*s*. ^{1}H-NMR ($CDCl_3$): 10.37 (br., OH); 7.97–8.01 (*m*, 2 arom. H); 7.59–7.64 (*m*, 1 arom. H); 7.45–7.51 (*m*, 2 arom. H); 3.24–3.28 (*m*, 2 H–C(2′)); 2.53–2.57 (*m*, 2 H–C(1′)); 2.48 (br. *s*, 2 H–C(5), 2 H–C(4)). ^{13}C-NMR ($CDCl_3$): 203.77 (C(3′)); 196.06 (br., C(1)); 135.91 (arom. C); 134.10 (1 arom. CH); 128.76 (2 arom. CH); 128.42 (2 arom. CH); 117.12 (C(2)); 37.78 (C(2′)); 30.22 (C(5), C(4)); 14.22 (C(1′)). EI-MS: 230 (6, M^+), 212 (1), 125 (100), 120 (10), 105 (60), 91 (4), 77 (27).

2-(3-Oxo-3-phenylpropyl)cyclohexan-1-one (**7**) [25]. A mixture of cyclohexanone (4 mmol) and 3-(dimethylamino)-1-phenylpropan-1-one hydrochloride (2 mmol), and Et_3N (3 mmol) was heated at 160° for 20 min. After cooling, the mixture was purified by flash chromatography (AcOEt) to give **7** (0.43 g, 93%). ^{1}H-NMR ($CDCl_3$): 7.96–8.00 (*m*, 2 arom. H); 7.52–7.58 (*m*, 1 arom. H); 7.43–7.48 (*m*, 2 arom. H); 3.13 (*ddd*, *J* = 17.0, 8.5, 5.8, 1 H); 2.97 (*ddd*, *J* = 17.0, 8.4, 6.5, 1 H); 2.40–2.49 (*m*, 1 H); 2.37–2.40 (*m*, 1 H); 2.26–2.36 (*m*, 1 H); 2.02–2.20 (*m*, 3 H); 1.82–1.92 (*m*, 1 H); 1.63–1.75 (*m*, 3 H); 1.40–1.52 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 213.23 (C(1)); 200.27 (C(3′)); 136.82 (arom. C); 132.98 (1 arom. CH); 128.55 (2 arom. CH); 128.10 (2 arom. CH); 49.98 (C(2)); 42.26 (C(2′)); 36.33 (C(6)); 34.61; 28.14; 25.09; 24.51.

REFERENCES

[1] a) F. Hibbert, *Adv. Phys. Org. Chem.* **1986**, *22*, 113; b) 'The Hydrogen Bond. Recent Developments in Theory and Experiments', Eds. P. Schuster, G. Zundel, C. Sandorfy, North Holland, Amsterdam, 1976; c) J. Emsley, *Struct. Bonding (Berlin)*, **1984**, *57*, 147; d) J. Emsley, *J. Chem. Soc. Rev.* **1980**, *9*, 91; e) F. Hibbert, J. Emsley, *Adv. Phys. Org. Chem.* **1991**, *26*, 255; f) G. A. Jeffrey, W. Saenger, 'Hydrogen Bonding in Biological Structures', Springer, Berlin, 1991; g) G. A. Jeffrey, 'An Introduction to Hydrogen Bonding',

Oxford University Press, Oxford, 1997; h) G. R. Desiraju, T. Steiner, 'The Weak Hydrogen Bond in Structural Chemistry and Biology', Oxford University Press, Oxford, 1999.
[2] 'O-17 NMR Spectroscopy in Organic Chemistry', Ed. W. D. Boykin, CRC Press, Boca Raton, FL, 1991.
[3] a) J.-C. Zhuo, *Magn. Reson. Chem*. **1997**, *35*, 21; b) J.-C. Zhuo, *Magn. Reson. Chem.* **1997**, *35*, 311; c) J.-C. Zhuo, *Magn. Reson. Chem*. **1997**, *35*, 432.
[4] a) J.-C. Zhuo, *Magn. Reson. Chem*. **1998**, *36*, 565; b) J.-C. Zhuo, *Helv. Chim. Acta* **1997**, *80*, 2137; c) J.-C. Zhuo, *Molecules*, **1997**, *2*, 31.
[5] a) D. W. Boykin, A. L. Baumstark and M. Beeson, *J. Org. Chem*. **1991**, *56*, 1969; b) A. L. Baumstark, D. W. Boykin, *New J. Chem*. **1992**, *16*, 357.
[6] D. W. Boykin, S. Chandrasekaran, A. L. Baumstark, *Magn. Reson. Chem*. **1993**, *31*, 489.
[7] B. Nowak-Wydra, L. W. Allison, A. Kumar, D. W. Boykin, *J. Chem. Res., Synop.* **1991**, 490.
[8] D. W. Boykin, A. Kumar, *J. Heterocycl. Chem*. **1992**, *29*, 1.
[9] a) G. Jaccard, J. Lauterwein, *Helv. Chim. Acta* **1986**, *69*, 1469; b) G. Jaccard, P.-A. Carrupt, J. Lauterwein, *Magn. Reson. Chem*. **1988**, *26*, 239; c) E. Liepins, M. V. Petrova, E. Gudriniece, J. Paulins, S. L. Kuznetsov, *Magn. Reson. Chem*. **1989**, *27*, 907; d) A. L. Baumstark, S. S. Grahan, D. W. Boykin, *Tetrahedron Lett*. **1990**, *31*, 957; e) A. M. Orendt, R. R. Biekofsky, A. B. Pomilio, R. H. Contreras, J. C. Facelli, *J. Phys. Chem*. **1991**, *95*, 6179; f) A. L. Baumstark, S. S. Grahan, D. W. Boykin, *J. Chem. Soc.*, *Chem. Comm*. **1989**, 767; g) D. W. Boykin, A. Kumar, *J. Mol. Struct.* **1993**, *298*, 121.
[10] J.-C. Zhuo, H. Wyler, P. Péchy, H. Dahn, *Helv. Chim. Acta* **1994**, *77*, 317.
[11] a) G.-B. Liang, J. M. Desper, S. H. Gellman, *J. Am. Chem. Soc*. **1993**, *115*, 925; b) G. P. Dado, S. H. Gellman, *J. Am. Chem. Soc*. **1994**, *116*, 1054.
[12] J.-C. Zhuo, *Magn. Reson. Chem*. **1996**, *34*, 595.
[13] D. W. Boykin, A. L. Baumstark, A. Mehdizadeh, M. K. Venkatramanan, *Magn. Reson. Chem*. **1990**, *28*, 305.
[14] J.-C. Zhuo, *Magn. Reson. Chem*. **1997**, *35*, 717.
[15] P. Gilli, V. Bertolasi, V. Ferretti, G. Gilli, *J. Am. Chem. Soc*. **1994**, *116*, 909.
[16] 'The Chemistry of Enols', Ed. Z. Rappoport, John Wiley & Sons, Chichester, England, 1990.
[17] M. C. Etter, Z. Urbanczyk-Lipkowska, D. A. Jahn, J. S. Frey, *J. Am. Chem. Soc*. **1986**, *108*, 5871.
[18] V. Bertolasi, P. Gilli, V. Ferretti, G. Gilli, *J. Am. Chem. Soc*. **1991**, *113*, 4917.
[19] A. Katrusiak, *J. Mol. Struct.* **1992**, *269*, 329.
[20] a) T. Steiner, W. Saenger, *J. Am. Chem. Soc*. **1992**, *114*, 10146; b) K. N. Houk, S. Menzer, S. P. Newton, F. M. Raymo, J. F. Stoddart, D. J. Williams, *J. Am. Chem. Soc*. **1999**, *121*, 1479; c) R. Vargas, J. Garza, D. A. Dixon and B. P. Hay, *J. Am. Chem. Soc*. **2000**, *122*, 4750; d) M. Felemez, P. Bernard, G. Schlewer, B. Spiess, *J. Am. Chem. Soc*. **2000**, *122*, 3156; e) E. S. Meadows, S. L. De Wall, L. J. Barbour, F. R. Fronczek, M.-S. Kim, G. W. Gokel, *J. Am. Chem. Soc*. **2000**, *122*, 3325.
[21] a) J. Emsley, L. Y. Y. Ma, S. C. Nyburg, A. W. Parkins, *J. Mol. Struct.* **1990**, *240*, 59–67; b) J. Emsley, L. Y. Y. Ma, S. A. Karaulov, M. Motevalli, M. B. Hursthouse, *J. Mol. Struct.* **1990**, *216*, 243; c) J. Emsley, L. Y. Y. Ma, P. A. Bates, M. Motevalli, M. B. Hursthouse, *J. Chem. Soc., Perkin Trans. 2* **1989**, 527; d) J. Emsley, L. Y. Y. Ma, P. A. Bates, M. B. Hursthouse, *J. Mol. Struct*. **1988**, *178*, 297; e) J. Emsley, N. J. Freeman, P. A. Bates, M. B. Hursthouse, B. Michael, *J. Chem. Soc., Perkin Trans. 1* **1988**, 297; f) J. Emsley, N. J. Freeman, M. B. Hursthouse, P. A. Bates, *J. Mol. Struct*. **1987**, *161*, 181.
[22] SHELXTL 5.05, Siemens Analytical X-Ray Systems, Madison, WI 53719.
[23] J.-C. Zhuo, *Molecules* **1999**, *4*, 310.
[24] M. Gorodetsky, Z. Luz, Y. Mazur, *J. Am. Chem. Soc*. **1967**, *89*, 1183.
[25] N. S. Cf. Gill, K. B. Jamas, F. Lions, K. T. Potts, *J. Am. Chem. Soc*. **1952**, *74*, 4923.

Received July 26, 2001