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HIGHLY STABLE TAUTOMERS OF β-KETOESTER: CONFORMATIONS OF 9-OXO-8,9,10,11-TETRAHYDRO- AND 9-HYDROXY-10,11-DIHYDRO-7*H*-CYCLOOCTA-[*de*]NAPHTHALENE-8-CARBOXYLIC ESTERS

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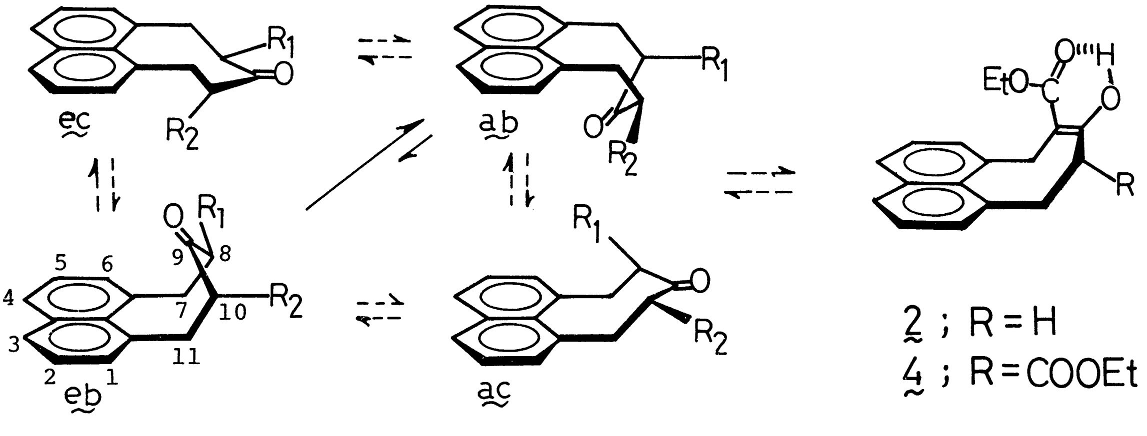
Tautomers of the titled β-ketoester, both keto (**1**) and enol (**2**), are obtained, which are unusually stable in the solid state as well as in solution. NMR studies revealed that **1** exists as an equilibrium mixture of axial-boat (**ab**) and equatorial-boat (**eb**) conformers in solution, whereas **2** exists in only one conformation.

In a preceding paper, we reported that tautomers of β-ketodiester, **3** and **4** are unusually stable compared to those reported so far.[1] In our continuing studies of 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene system, we have further found that the titled β-ketomonoester affords both keto (**1**) and enol (**2**) isomers of high stability, and found that the former isomer assumes two different forms in solution, in sharp contrast to the ketodiester compound (**3**).[1] Here, we report the preferred conformations of tautomers **1** and **2** based on the NMR spectra.

The keto form (**1**)[2] was prepared by treatment of **3**[1] with EtONa in EtOH and a subsequent neutralization with hydrobromic acid. Treatment of **1** with EtONa in EtOH followed by hydrochloric acid resulted in the enol form (**2**).[2]

The proton-decoupled ^{13}C-NMR spectrum[3] of **1** exhibits a sharp line for each of the peri ring carbons at 30°C, which is split into two lines of different peak hights below -40°C. On the other hand, the room-temperature ^{1}H-NMR spectrum[4] of **1** shows a sharp triplet for the methyl group, which is split into two triplets of different intensities at low temperature. Thus, it is evident that **1** exists in two different conformations interchanging to each other by the inversion of the peri ring. One of these conformations, which exists dominantly in **1**, is possibly to be a boat with COOEt axial (**ab**), because the lower-field signal of the C_7-methylene group of **1** has a large vicinal coupling constant (J=12.9 Hz), which can be explained only by a spin interaction between the interior benzyl and adjacent equatorial protons of the boat conformation as described before.[5] A strong vicinal coupling ($J_{11in,10eq}$=13 Hz) together with the long-range spin interaction ($J_{8eq,10eq}$=1 Hz) also suggests the **ab** conformation (Table 2). This is consistent with IR spectra,[6]



2 ; R = H
4 ; R = COOEt

1 ; R_1 = COOEt, R_2 = H
3 ; R_1 = R_2 = COOEt
5 ; R_1 = R_2 = H

where the C=O frequency shifts (Δν) of 1 are very small in both the ketone ($+6cm^{-1}$) and the ester ($-2cm^{-1}$) carbonyl vibrations[7] as compared to those of the ketodiester compound (3) (+16 and +7 cm^{-1}, respectively).[1]

On the other hand, the minor conformation of 1 cannot be obtained directly in the ^1H spectra, because all the signals except for the methyl group are hidden under those of the major conformer (ab). However, it is observed that the ring inversion in 1 causes an exchange of the benzyl protons between $H_{in} \rightleftharpoons H_{ex}$ and the magnitude of the vicinal coupling constant, $J_{7in,8eq}$, is decreased with the elevation of the temperature. Thus, by considering the conformational changes in the peri-8-membered ring of 8,9,10,11-tetrahydro-7*H*-cycloocta[*de*]naphthalene,[5] it is suggested that the minor isomer of 1 assumes an equatorial conformation (eb).

This result is consistent with ^{13}C chemical shifts in Table 2. Thus, a high-field shift of the C-10 signal in the axial isomer (ab) relative to that in the equatorial (eb) results from the γ-gauche effect.[8] A marked shielding of C-8 carbon in eb compared to that in ab should be caused by the eclipsed interaction between the ketone and the equatorial COOEt.[9] Moreover, the C-7 in eb resonates at a higher field than that in ab as a result of the gauche interaction between the equatorial COOEt and the peri bond.

Consequently, 1 exists as an equilibrium mixture of axial-boat (ab) and equatorial-boat (eb) conformers in solution. The isomer ratio (eb/ab) in 1 is then calculated from the high-temperature averaging spectra in a usual manner,[5,10] and is found to be (20/80) at 30°C, which corresponds to the free energy difference ($-\Delta G°$) of -0.83 kcal/mol. The chair conformers (ac, ec) are not obtained for 1, because the chair contains unfavorable eclipsing strains along the C_7-C_8 and C_{10}-C_{11} bonds, which make this conformation much less stable than the boat for the peri-8-membered ring system.[1,5] The interconversion between ab and eb in 1 can be explained most reasonably by a process with pseudorotations of the peri bonds *via* the twist-boat as described before.[1,5]

Table 1. IR Data of **1** and **2** in the Solid State (Nujol)[a] and in $CHCl_3$

	Mp(°C)	Ester νC=O	Ketone νC=O	Chelated conjugated νC=O	Conjugated νC=C
1[b]	128-129	1732 (1744)	1709 (1705)		
2[b,c]	103-104			1644 (1638)	1614 (1614)

[a] Values in parentheses. [b] Colorless needles. [c] νOH is strongly purterbed beyond recognition.

Table 2. ^1H- and ^{13}C-NMR Data of **1** and **2** in $CDCl_3$[a]

	H_{7in}	H_{7ex}	H_{8eq}	H_{10ax}	H_{10eq}	H_{11in}	H_{11ex}	$OC\underline{H}_2$	$C\underline{H}_3$	$O\underline{H}$
1-ab[b]	4.83 *J*=14.3 12.9	3.33 *J*=14.3 6.2	3.75 *J*=12.9 6.2 1.0	3.15 *J*=13.0 2.0	2.59 *J*=13.0 13.0 6.0 1.0	4.30 *J*=14.2 13.0	3.08 *J*=14.2 6.0 2.0	4.28*q* *J*=7.0	1.32*t* *J*=7.0 1.26*t*[f] *J*=7.0	
2[c]	4.71 *J*=15.7	3.79 *J*=15.7		...e	...e	4.01 *J*=15.8 12.7 6.0	...e	4.14*q* *J*=7.1	1.33*t* *J*=7.1	12.72*s*

	C-7	C-8	C-9	C-10	C-11	$\underline{C}OO$	$O\underline{C}H_2$	$\underline{C}H_3$
1-ab[d]	37.0	61.8	207.7	44.1	33.8	169.5	62.2	14.0
1-eb[d]	35.1	55.2	208.6	47.5	33.8	171.6	62.2	14.0
2[c]	31.6	101.0	174.2	37.4	34.4	173.2	60.6	14.2

[a] δ from internal TMS; *J* in Hz. [b] At -56.0°C. [c] At 30.0°C. [d] At -65.9°C. [e] An unassignable multiplet at δ2.5-3.4. [f] A signal due to the minor conformer (**1-eb**).

On the other hand, the NMR spectra of the enol (**2**) are invariant of temperature, suggesting that, in contrast to the ketonic isomer (**1**), none of the ring inversions occur in **2** at ambient temperature. The molecular model provides only one conformation for the enol form shown in the figure, which can be explained satisfactorily by both the IR and the NMR data given in the tables.

The molecule of **2** is much less mobile than **1**, because the cyclooctadiene ring of the former is more rigid than the cyclooctenone ring of the latter, and additionally because molecules of **2** may be highly stabilized by the H-bonded chelated structure, whereas **1** involves unfavorable dipolar interactions of the carbonyl groups as well as 1,3-diaxial repulsions within molecules.

IR studies reveal that a chloroform solution of **1** gives a small amount of **2** on standing overnight at room temperature, while **2** shows almost no change under the similar experimental condition. This indicates that tautomers of **1** and **2** are, even in solution, stable enough not to undergo a ready isomerization at ambient temperature. This is in striking contrast to hitherto-known β-ketoesters including the cyclohexane system, which are obtained only as an equilibrium mixture of the keto and the enol form,[11] or assume only either form of the two isomers.[12]

References

(1) T. Kamada and O. Yamamoto, *Tetrahedron Lett.*,1341 (1977).

(2) Elemental analyses and high-resolution mass spectra were satisfactory for these new compounds.

(3) ^{13}C-NMR spectra were measured on a Varian NV-14 FT NMR spectrometer operating at 15.087 MHz, using *ca.* 10%(w/v) solution of samples in $CDCl_3$ in 8-mm spinning tubes; chemical shifts are expressed in ppm (δ) downfield from internal TMS with an accuracy of ±0.1 ppm. The sample temperature was controlled by passing a stream of precooled nitrogen through the sample cavity and measured by a calibrated copper-constantan thermocouple.

(4) ^{1}H-NMR spectra were recorded on a Varian HA 100D spectrometer at 100 MHz, using $CDCl_3$ as a solvent and TMS as an internal standard (accuracy; ±0.1Hz).

(5) T. Kamada and O. Yamamoto, *Chem. Lett.*, 843 (1976).

(6) IR spectra were measured on a JASCO IR-G spectrophotometer, using a solution ($CHCl_3$) and a nujol mull. The positions of absorption maxima are quoted in wave numbers (cm^{-1}), calibrated with polystyrene ($\Delta\nu = \pm 0.4 cm^{-1}$).

(7) Frequency shifts from the parent ketone (**5**) (νC=O; 1703 cm^{-1}) and the enol (**4**) (νC=O; 1734 cm^{-1}), respectively.

(8) J. B. Stothers, "*Carbon-13 NMR Spectroscopy*", Academic Press, New York (1972).

(9) S. H. Grover, J. P. Guthrie, J. B. Stothers, and C. T. Tan, *J. Mag. Resonance*, **10**, 227 (1973).

(10) The populations of conformers, **eb** and **ab** (P_e, P_a), are obtained from the relationships: $P_e \cdot J_{10ax,11ex} + P_a \cdot J_{7in,8eq} = J_{av}$ and $P_e + P_a = 1$, where J_{av} is the averaged coupling constant.

(11) S. J. Rhoads, J. C. Gilbert, A. W. Decora, T. R. Garland, R. J. Spangler, and M. J. Ubrigkit, *Tetrahedron*, **19**, 1625 (1963), and references therein.

(12) S. Baldwin, *J. Org. Chem.*, **26**, 3280 (1961), E. Wenkert and T. E. Stevens, *J. Am. Chem. Soc.*, **78**, 5627 (1956), E. Wenkert and B. G. Jackson, *ibid.*, **81**, 5601 (1959), G. B. Kline, *ibid.*, **81**, 2251 (1959).

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