The Isomeric Enol Acetates of Acetylacetone. Evidence for an Unusual Stabilizing Interaction between *cis* Acetyl and Acetoxy Groups

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The configuration and conformation of the isomeric enol acetates of acetylacetone have been elucidated. P.m.r. shift data obtained by the use of tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)-europium(III) ($Eu(fod)_3$) allow assignment of the (*S*)-*cis* conformation to both isomers. The remarkable stability of the isomer having acetyl *cis* to acetoxy is attributed to neighboring group interaction, a rationale consistent with p.m.r. spectroscopic data.

La configuration et la conformation des deux acétates énoliques de l'acétylacétone ont été élucidées. Les déplacements chimiques paramagnétiques de r.m.p. obtenus par l'emploi du tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium(III) ($Eu(fod)_3$) démontre une conformation (*S*)-*cis* pour les deux isomères. La stabilité remarquable de l'isomère ayant le groupement acétyl en position *cis* par rapport au groupement acétoxy est attribuée à l'interaction des groupements environnants et sa rationalisation est supportée par des données spectroscopiques obtenues par r.m.p.

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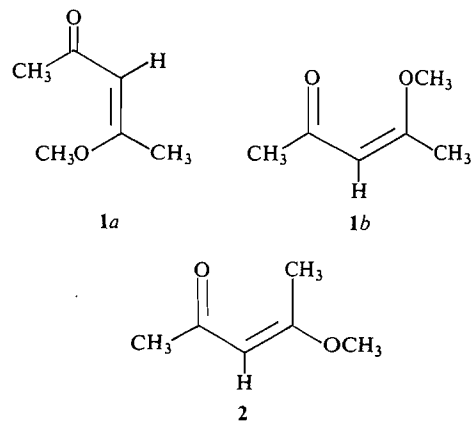
It has been reported (1) that acetylacetone is converted to an enol acetate in good yield when refluxed with isopropenyl acetate in the presence of an acid catalyst. We have repeated this preparation several times and it has been observed to give rise consistently to *two* isomeric monoacetates, hitherto unreported, in close to a 1:1 ratio.[1]

The physical properties of these enol acetates are too similar to permit separation by fractional distillation but the pure liquid isomers can readily be obtained by preparative t.l.c.

The configuration and conformation of the two isomeric methyl enol ethers of acetylacetone have recently been assessed by observation of nuclear Overhauser effects and p.m.r. solvent shift techniques (3); conclusions based on analysis of data collected in the latter study were supported by $Eu(thd)_3$-induced shift data (4).[2] The less stable isomer, having acetyl *cis* to methoxyl adopts the (*S*)-*trans* conformation (**1***a*) and suffers remarkably facile acid-catalyzed isomerization to the other isomer in which the acetyl group is *trans* to methoxyl in an (*S*)-*cis* conformation (**2**). Compound **1** also undergoes ready thermal isomerization to **2**.



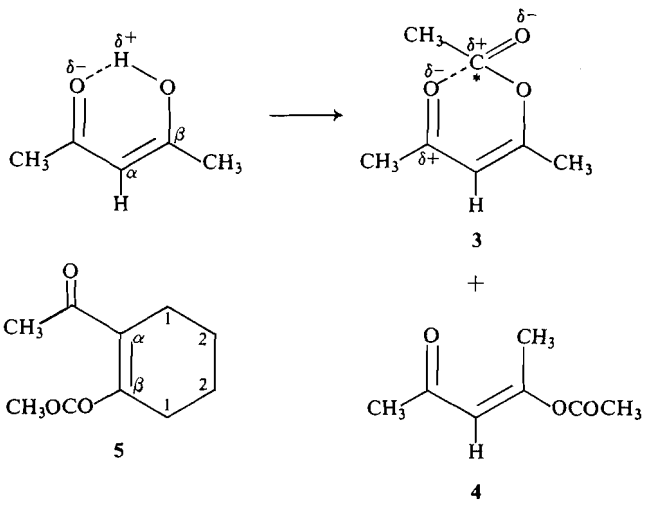
1*a* **1***b*

2

Adoption of the (*S*)-*trans* conformation, generally disfavored by β-disubstituted-α,β-unsaturated acyclic ketones, was attributed to a strong repulsive interaction between *cis* methoxyl and carbonyl in the (*S*)-*cis* conformation (**1***b*) of the less stable enol ether. An analogous situation was expected to exist in the case of the enol acetates of acetylacetone. However, no hope of isolating the acetate corresponding to **1** was seriously entertained, since no mild and relatively neutral method for preparation of enol acetates

[1]Taylor *et al.* (2) have reported a 90% yield of *O*-acetyl derivative from treatment of the thallium(I) salt of acetylacetone with acetylchloride at −78°. However, no spectral data were cited in support of structure.

[2]Tris(2,2,6,6-tetramethyl-3,5-heptanedionato)europium (III), also referred to as tris(dipivalomethanato)europium (III) ($Eu(DPM)_3$).



SCHEME 1

(comparable with the diazomethane method which yields **1**) is yet available.

The configuration and conformation of the isomeric enol acetates were revealed by examination of their p.m.r. spectra utilizing the superior paramagnetic shift reagent, tris(1,1,1,2,2,3,3-heptafluoro - 7,7 - dimethyl - 4,6 - octanedionato)-europium(III) ($Eu(fod)_3$) (5); $Eu(thd)_3$, which was successfully employed in the case of the analogous methyl enol ethers, was of no assistance, presumably because of the reduced Lewis basicity of the enol acetates, allied with a low inherent solubility of the reagent in organic solvents.

As illustrated in Scheme 1, the preferred conformation for both enol acetates of acetylacetone is the (*S*)-*cis*. The increased stability of acetate **3** compared with the analogous enol ether **1** is attributed to a stabilizing attractive interaction between acetyl oxygen and the carbonyl carbon atom of the *cis* acetate group. Table 1 lists Δ_{Eu} values (6), which represent the slopes of the straight lines obtained from plots of δ *vs.* $Eu(fod)_3$/substrate mol ratio; the larger the Δ_{Eu} value the greater the particular proton or set of protons is shifted downfield by the shift reagent.

The assignments made on the basis of $Eu(fod)_3$-induced shifts observed for enol acetate **4** are reinforced by observations of its benzene-induced shifts (3) (Table 2), complexation occurring predominantly at acetyl carbonyl.

The shifts induced by solvent benzene in the proton signals of **3**, however, are not so readily rationalized, being of the same sense and of almost identical value for all protons in the molecule. These enigmatic benzene-induced shifts, the identical Δ_{Eu} values for acetate and acetyl protons,[3] and the fact that the latter two groups of protons exhibit a smaller Δ_{Eu} value than does the vinylic proton, can be explained on the basis of competitive complexation. Involvement of a lone pair of electrons of acetyl oxygen in an electrostatic interaction[4] with the carbonyl carbon of the acetoxy group (as illustrated in Scheme 1) would be expected to reduce the ability of acetyl oxygen to complex with the shift reagent. It is not yet possible to separate electronic from purely steric components. Also the relative values for Δ_{Eu} indicate that when europium is coordinated with either doubly bonded oxygen atom, the methyl protons alpha to the other must be rather less influenced by the ligand than is the vinylic proton.

The fact that the enol acetate (**5**) of 2-acetylcyclohexanone, a cyclic analog of acetate **3**, exists predominantly in the (*S*)-*trans* conforma-

[3]The p.m.r. signal for these protons, under the influence of the shift reagent, is markedly broadened compared with all other signals.

[4]A ^{13}C spectroscopic study bearing upon the nature of this interaction and on conformational variation among some enol derivatives of labile 1,3-diketones will be the subject of a forthcoming publication.

TABLE 1. Δ_{Eu} values for protons of enol acetates of acetylacetone and 2-acetylcyclohexanone

Compound	=CH	$=CCH_3$	$OCOCH_3$	$CCOCH_3$
3	11.6	5.6	7.5	7.5
4	12.0	14.7	5.0	17.5
5[a]	—	—	4.8	12.9

[a]Under the influence of the shift reagent the ring proton pattern is resolved into three broad resonances of relative intensity 1:1:2, corresponding to Δ_{Eu} values of 11.1, 5.6, and 2.8, respectively. Since complexation occurs predominantly at the oxygen atom of the acetyl group, the former resonances are assigned to the methylene protons attached to α-C-1 and -2 carbon atoms; the latter resonance would then be due to the paired β-C-1 and -2 protons.

TABLE 2. Chemical shift displacement[a] of the p.m.r. signals of the enol acetates of acetylacetone and 2-acetylcyclohexanone, induced by benzene solvent

Compound	=CH	$=CCH_3$	$OCOCH_3$	$CCOCH_3$
3	+0.23	+0.25	+0.25	+0.25
4	+0.12	−0.02	+0.40	+0.10
5[b]	—	—	+0.42	+0.01

[a]$\delta_{CCl_4} - \delta_{benzene}$ in p.p.m.
[b]The α-C-1 and -2 protons undergo a positive shift of 0.01 p.p.m. while the β-C-1 and -2 protons are displaced by 0.42 p.p.m. in the same sense.

tion may be explained on the basis of ring constraint in the cyclic compound, preventing rotation about the olefinic bond; such rotation may be necessary for an attractive interaction sufficiently great to counteract the serious 1,3 O–O repulsion that would normally disfavor the (*S*)-*cis* conformation for such molecules.

Experimental

The p.m.r. spectra were recorded using a Varian A-60A spectrometer; spectral grade solvents containing tetramethylsilane (TMS) as internal reference were employed in all cases. The i.r. spectra were obtained with a Perkin-Elmer Model 621 spectrophotometer and u.v. spectra on a Beckman DB spectrophotometer.

Enol acetates **3**, **4**, and **5** were prepared by the method of Hagemeyer and Hull (1) employing commercially available isopropenyl acetate, acetylacetone, and 2-acetylcyclohexanone. The latter two compounds were distilled prior to use.

Enol Acetates 3 and 4

Fractional distillation of the product of reaction of acetylacetone with isopropenylacetate yielded a mixture of isomers **3** and **4**, b.p. 88–90°/6 mm, in a ratio of 9:11, as estimated by integration of the p.m.r. signals of their respective vinylic protons. (No evidence of *C*-acetylation was found.)

The isomers were isolated by preparative t.l.c. on 20 × 20 cm glass plates, precoated with silica gel GF of thickness 1 mm (Fisher), using benzene–ether (9:1). Isomer **4** gives a higher R_f value under these conditions.

Spectral characteristics for **3** are: p.m.r. (CCl_4) δ 5.72 (s, 1H), 2.13 (s, 3H, $=CCH_3$), and 2.00 p.p.m. (s, 6H, $CCOCH_3$; $OCOCH_3$); i.r. ($CHCl_3$) ν 1755 (C=O, ester), 1690 (C=O, ketone), 1655 (?), and 1625 cm^{-1} (C=C); u.v. (95% EtOH) λ_{max} 230 nm (ε 9350). Spectral characteristics for **4** are: p.m.r. (CCl_4) δ 5.98 (s, 1H),[5] 2.25 (d, 3H, $C=CH_3$, $J_{1,3}$ = 1.3 Hz), 2.11 (s, 3H, $OCOCH_3$), and 2.08 p.p.m. (s, 3H, $CCOCH_3$);[6] i.r. ($CHCl_3$) ν 1755 (C=O, ester), 1695 (C=O, ketone), and 1615 cm^{-1} (C=C); u.v. (95% EtOH) λ_{max} 229 nm (ε 6480).

Enol Acetate 5

Enol acetate **5** was obtained pure in 75% yield by fractional distillation of the neutralized reaction product. It had b.p. 95–96°/4.5 mm.

[5]This signal is considerably broadened compared with that of the vinylic proton signal for acetate **3**, whose allylic methyl protons are much less strongly coupled and give rise to a sharp singlet under all conditions of observation employed in this study. Its appearance 0.26 p.p.m. downfield from the vinylic proton signal for acetate **3** is probably not significantly due to any deshielding anisotropic effect of the *cis* acetoxy group, since the p.m.r. (60 MHz, CCl_4) signals for the vinylic protons of isopropenyl acetate are coincident. This latter observation prompted Jackman and Wiley (7) to conclude that the acetoxy substituent "prefers those conformations in which the carbonyl group is well removed from *cis*-β-olefinic proton".

[6]These assignments were arrived at by observation of the relative movement of the two signals when very small quantities of the shift reagent were added to the sample solution. No crossover of signals was noted.

Spectral characteristics for **5** are: p.m.r. (CCl_4) δ 2.17 (s, 3H, $CCOCH_3$)[6], 2.13 (s, 3H, $OCOCH_3$),[6] and 2.25 and 1.70 p.p.m. (centers of multiplets, corresponding to 4H each, of α-C-1 and -2, and β-C-1 and -2, respectively); i.r. ($CHCl_3$) ν 1755 (C=O, ester), 1710 (C=O, ketone), 1690 (?), and 1650 cm^{-1} (C=C); u.v. (95% EtOH) λ_{max} 239 nm (ε 7360).

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1. H. J. Hagemeyer, Jr. and D. C. Hull. Ind. and Eng. Chem. **41**, 2920 (1949).
2. E. C. Taylor, G. H. Hawks, III, and A. McKillop. J. Am. Chem. Soc. **90**, 2421 (1968).
3. D. V. C. Awang. Can. J. Chem. **49**, 2672 (1971).
4. D. V. C. Awang and A. Vincent. J. Org. Chem. **37**, 2625 (1972).
5. R. E. Rondeau and R. E. Sievers. J. Am. Chem. Soc. **93**, 1522 (1971).
6. P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert. J. Am. Chem. Soc. **92**, 5734, 5737 (1970).
7. L. M. Jackman and R. H. Wiley. J. Chem. Soc. 2881 (1960).