Observable Enols of Anhydrides: Claimed Literature Systems, Calculations, and Predictions

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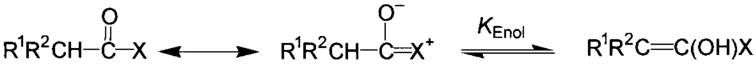
Dedicated to Prof. *Edgar Heilbronner* on the occasion of his 80th birthday

The literature describing the observation of enols of carboxylic anhydrides and mixed carboxylic-sulfuric anhydrides was examined. In the phenylbutyric anhydride system, the alleged enol was shown to be ethylphenylketene, and the monoenol EtC(Ph)=C(OH)OC(=O)CH(Ph)Et (**5**) and the dienol (**6**) should not be observed according to calculations. Calculations also show that the claimed enols $H_2C{=}C(OH)OSO_2Y$, Y = SO_3^-, Ac (**15**) and the enol of 2*H*-pyran-2,6(3*H*)-dione (**7**) are too unstable to be observed. The bulky enols of *β*,*β*-ditipylacetic formic (**35a**) or trifluoroacetic (**35b**) anhydride were calculated to be unstable with $pK_{Enol} = 7.7$ (6.2). The suggestion that compounds with the 3-acyl or 3-aroyl-2*H*-pyran-2,6(3*H*)-dione skeleton are enolic was examined. In the solid state, all the known structures show that enolization takes place on C(5)=O. However, B3LYP/6-31G** calculations show that, for 3-acetyl-4-methyl-2*H*-pyran-2,6(3*H*)-dione (**10**, R^1 = Me, R^2 = H), which is completely enolic, the enol on the acetyl group (*cf.* **12**) is only 0.9 kcal/mol more stable than the enol on the anhydride (*cf.* **11**). Calculations also revealed that 3-(trifluoroacetyl)-2*H*-pyran-2,6(3*H*)-dione (**28**) should exist in nearly equal amounts of the enol of anhydride (*cf.* **30**) and the enol of the acyl group (*cf.* **29**), whereas the enol of anhydride (*cf.* **32**) is the only stable species for 3-(methoxycarbonyl)-2*H*-pyran-2,6(3*H*)-dione (**31**). Furan-2,5-diol (**27**) and 5-hydroxyfuran-2-one (**26**) are calculated not to give observable isomers of succinic anhydride (**25**) ($pK_{Enol} = 30$ and 18, resp.) in spite of the expected aromatic stabilization of **27**. Surprisingly, the calculations reveal that the enol $(NC)_2C{=}C(OH)OCHO$ (**38**) is less stable than its tautomeric anhydride (**37**) ($pK_{Enol} = 1.6$). Comparison of calculated pK_{Enol} values for $(NC)_2CHC({=}O)X$ (**41**) and $MeC({=}O)X$ indicates that the assumption that substitution by two *β*-CN groups affects similarly all the systems regardless of X is incorrect. A $pK_{Enol}((NC)_2CHC({=}O)X)$ *vs.* $pK_{Enol}(MeC({=}O)X)$ plot is linear for most substituents with severe and mild negative deviations, respectively, for $X = NH_2$ and MeO. Appropriate isodesmic reactions have shown that the *β*,*β*-$(CN)_2$ substitution increases the stabilization of the enol of amide ($X = NH_2$) by 14.6 kcal/mol over that for the anhydride (X = OCHO), whereas the amide form is 7.1 kcal/mol less destabilized than for the anhydride. The pK_{Enol} value for $(MeOCO)_2CHCOOCHO$ (**43**) is 3.6, *i.e.*, stabilization by these *β*-electron-withdrawing groups is insufficient to make the enols observable.

1. Introduction. – Enols of carboxylic acid derivatives are rare species [1]. The calculated energy differences between the favored tautomer, *i.e.*, the parent (*β*,*β*-di-H) carboxylic acid or its derivatives (**2**) and its enols (**1**) are 24–33 kcal/mol, depending on the derivative and the method of calculation [2]. Nevertheless, enols of carboxylic acids, esters, and amides were observed in recent years, based on three approaches. Their generation by a fast reaction technique such as flash photolysis as short lived species was developed by *Kresge* and *Wirz* (for a review, see [1b]), their formation from bulky *β*,*β*-diaryl-substituted ketenes as observable species, although of short or moderate life-time was developed by *Hegerty* and co-workers [3] and by us [4], and their generation as stable species was developed by us, using systems carrying strongly *β*-electron-withdrawing groups (EWGs) [5]. Such enols, *e.g.*, of esters were also suggested as unobservable intermediates on the basis of kinetic and stereochemical evidence (see, *e.g.*, [6]).

The calculations of the parent system give a rough order of the relative stability, measured as pK_{Enol} ($= -\log K_{Enol}$) of *Scheme 1*, as a function of the α-substituent X [2]. The order of pK_{Enol} values for X in $CH_2{=}C(OH)X$ is: H (9.9) < Me(11.5) < OCHO (17.6) < Br (18.7) ~ Cl (18.6) < F (19.8) < NMe_2 (21.2) ~ NH_2 (21.3) < OH (22.0), OMe (22.3) at B3LYP/6-31G**. In practice, when a competition between an amide and an ester group is possible, formation of enols of amides is more facile than formation of enols of esters [5a,b] as expected from the calculations.

Scheme 1



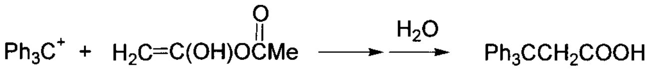
$$R^1R^2CH-\overset{O}{\overset{\|}{C}}-X \longleftrightarrow R^1R^2CH-\overset{O^-}{\overset{|}{C}}{=}X^+ \xrightleftharpoons{K_{Enol}} R^1R^2C{=}C(OH)X$$

2 **1**

According to these calculations, enols of anhydrides should be relatively more stable than the other enols of carboxylic acid derivatives **1** [2]. Hence, their preparation is potentially more favored than that of enols of systems with, *e.g.*, X = NHR or MeO, which were already observed.

Several suggestions for observation, detection, or intermediacy of enols of anhydrides appear in the literature. As early as 1911 and 1912, *Thorpe* and co-workers [7] had written 3-substituted glutaconic anhydrides in the enol form, although with no evidence. *Deno et al.* suggested in 1970 [8] that alkylation of Ac_2O with Ph_3C^+ cation proceeds by electrophilic reaction on traces of the enol of the anhydride **3** (*Scheme 2*). Except for the product, there is no evidence for this suggestion, and the fact that acetone is not alkylated by Ph_3C^+ under more drastic conditions does not support this assumption. Note that the percentage of **3** in Ac_2O is extremely low according to our calculations [2].

Scheme 2



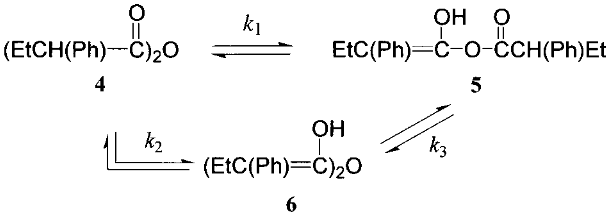
$$Ph_3C^+ + H_2C{=}C(OH)O\overset{O}{\overset{\|}{C}}Me \longrightarrow \xrightarrow{H_2O} Ph_3CCH_2COOH$$

3

In two works, the isolation and observation of an enol of carboxylic acid anhydride was reported. *Gordon* and co-workers [9] distilled optically active 2-phenylbutyric acid anhydride and found that it undergoes racemization, that the distillate is bright yellow, and that the color disappears after a few hours. They interpreted the NMR and IR spectra of the freshly distilled anhydride as indicative of the presence of three species, the diketone (*i.e.*, anhydride, **4**), keto-enol (*i.e.*, monoenol, **5**) and the yellow dienol (**6**; *Scheme 3*), and that an equilibrium between the species is established in CCl_4.

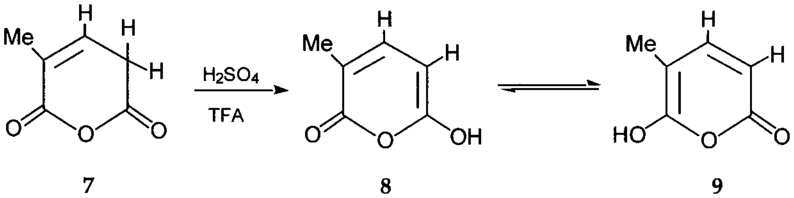
Kagan et al. [10], in a re-analysis of tautomerism and isomerism in the α- and γ-methylglutaconic acid and derivatives, prepared γ-methylglutaconic anhydride (5-methyl-2*H*-pyran-2,6(3*H*)-dione) **7** and identified it by its ^1H-NMR spectrum (δ 2.30 (Me), 3.58 (CH_2), and 6.47 (=CH)). The compound did not isomerize on distillation, in spite of an earlier claim [11], neither when HCl was bubbled into its $CDCl_3$ solution

Scheme 3

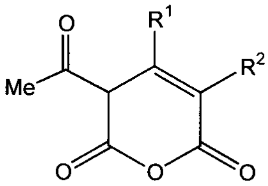


nor when heated in TFA at 100° for 60 h. However, when a drop of conc. H_2SO_4 was added to the TFA solution, the ^{1}H-NMR changed (δ 2.28 (Me), 6.72, 8.38 (2*d*, *J* = 8 Hz)). It was deduced from the spectrum that enolization to rapidly exchanging isomeric enols of the anhydride **8** and **9** took place (*Scheme 4*). Analogs such as the parent compound (*i.e.*, with 5-H) or the 4-Me derivative were also written as existing in an equilibrium analogous to that of **8** and **9**, although with little evidence [12].

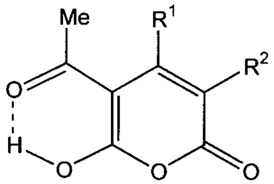
Scheme 4



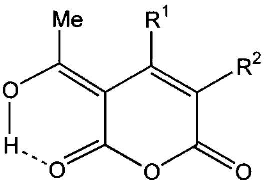
From our calculations and experience, it is unlikely that species **9** was indeed observed. However, a family of 3-acetyl-2*H*-pyran-2,6(3*H*)-diones **10** was suggested to exist in the H-bonded enol forms **11**/**12** [13], on the basis of rather convincing NMR, IR, and UV-spectral evidence. Enols **11** belong to the general case of systems carrying β-electron-withdrawing groups, of which we previously observed enols of amides and esters [5], and hence enols **11** are predicted to be relatively stable. The enolic structure was suggested also in some related structures [14].



10



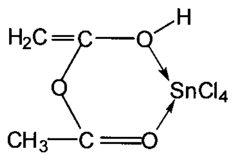
11



12

A complexed enol of an anhydride **13** was suggested by *Hunt* and *Satchell* [15] on the basis of IR spectra.

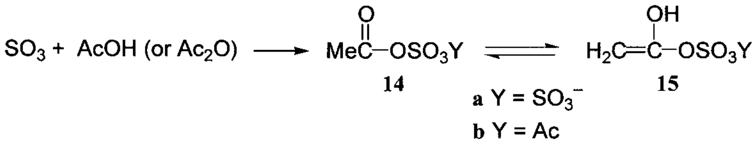
The observation of mixed acetic sulfuric anhydrides was also reported. *Truce* and *Olsen* [16] suggested an intermediate in the side-chain sulfonation of phenylalkanoic acids with SO_3 in dioxane, which has one resonance hybrid of the structure



13

$PhCH_2CH=C(OH)OSO_3H$. *Montoneri* and co-workers [17] have suggested that, in equimolar SO_3/Ac_2O or $SO_3/AcOH$ mixtures the keto form **14** exists in equilibrium with the enol **15** of the mixed anhydrides at ≤ 253 K (*Scheme 5*), and that **15** is observable by NMR and IR spectroscopy. The enol was suggested to be involved in elimination to ketene [14] and in chlorination of AcOH [17b]. From NMR band areas, the **15b**/**14b** ratio is 2 in Ac_2O and the **15a**/**14a** ratio is 0.67 in AcOH. The δ values for the vinylic protons of **15** are assigned as 2.57 and 2.75, and a rapid exchange between **14a** and **15a** was suggested. The assignment of structure **15b** in SO_3/Ac_2O is based also on assignment of IR absorptions at 1600 and 1555 cm^{-1}, but with no unequivocal evidence. A low field OH signal is observed at δ 15.13 and, since its position is concentration-independent, an intramolecular H-bond (*cf.* **16b**) is suggested. The enol is not observed at room temperature. Additional species are formed in some of these reactions.

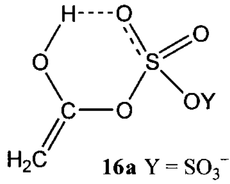
Scheme 5



$$SO_3 + AcOH\ (or\ Ac_2O) \longrightarrow MeC(=O){-}OSO_3Y \rightleftharpoons H_2C{=}C(OH){-}OSO_3Y$$

14 **15**

a Y = SO_3^-
b Y = Ac



16a Y = SO_3^-, $S_2O_6^-$
b Y = Ac

In $AcOH/SO_3$ 1:1 in SO_2, the changes in the IR spectrum after several hours at ≥ 253 K suggest the establishment of an equilibrium **14a** $\rightleftharpoons$ **15a**, although this was not established unambiguously.

Ogata and *Adachi* [18] have suggested on the basis of some kinetic evidence that α-halogenation of aliphatic acids proceeds *via* the analog of **16** with Y=H and $H_2C=$ replaced by $RR'C=$. According to them, enols of carboxylic anhydrides are not the intermediates in halogenation of carboxylic acids.

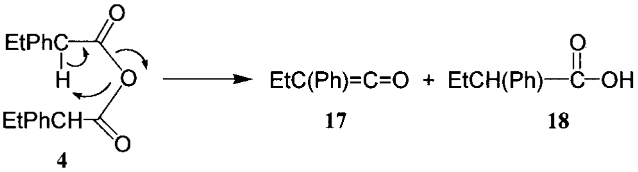
Consequently, we conclude that the present experimental evidence for the observation of enols of anhydrides is meager and mostly questionable. We, therefore, analyze below the literature data with the aid of former and new calculations as well as with a few experiments to exclude unequivocally the formation of these species in some cases and to search for evidence for them in other cases, and as a guide for attempts to identify such species unequivocally in the future.

2. Results and Discussion. – *The 2-Phenylbutanoic Anhydride System.* Our experience and the results of the calculations mentioned above indicate that it is extremely unlikely that **4** will enolize to an observable mono-enol **5** and certainly not to a bis-enol **6**. Mandelic acid and 2-cyano-2-phenylacetic acid, whose skeletons contain the EWGs OH or CN, respectively, instead of the Et group of **18** (*cf. Scheme 6*), have pK_{Enol} values in H_2O of 15.6 [19a] and 7.2 [19b], and even if the anhydride pK_{Enol} is 4.4 units lower than that for the acid (disregarding the less-polar solvent) no enol is supposed to be detected by IR or NMR.

The spectral evidence brought in support of the enol structure in the freshly distilled sample includes disappearance of a strong sharp IR peak at 2100 cm^{-1} that disappears at the same rate as one at 1700 cm^{-1}. No specific assignment could be made for this peak [9]. A broad disappearing peak at 3000 cm^{-1} was ascribed to an intermolecular H-bond between **4** and **6**. The enol OH signal was assumed to be at δ 11.5.

We suggest that the process occurring on distillation is an elimination of the carboxylic acid (**18**) with formation of the ketene **17** (*Scheme 6*). This is the reversal of the general method of addition of a carboxylic acid to a ketene to form the anhydride. The 'most interesting' but unassigned sharp peak at 2100 cm^{-1} is most likely due to the characteristic ketene absorption, which appears in this region. The absorptions at 1700 cm^{-1} and the broad peak at 3000 cm^{-1} will then be those of the carboxylic acid. The two elimination products react relatively rapidly with one another with a temperature-dependent rate to regenerate the anhydride, and hence the disappearance of the peaks at 1700 and 2100 cm^{-1} occurs at the same rate.

Scheme 6



Likewise, the lowest field signal at δ 11.5 is not due to enol signals. The H enol signals in the ditipylacetic acid enol [4] or in various enols of amides or esters carrying EWGs [5] appear < 15 ppm. In contrast, the OH signal of carboxylic acids appears in the observed region of δ 11.5. Moreover, each of the Me, CH_2, and OH signals of alleged **5** and **6** are given at the same δ values, and it is clear that they belong to one compound rather than two.

Although we believe that this interpretation accounts for all the observations, we conducted several experiments and calculations in order to completely exclude the presence of the anhydride enols **5** and **6**. When the reaction was repeated and the ^{13}C-NMR spectrum determined at 298 K in $CDCl_3$, the main signals were those of the anhydride, but also ten new signals were observed. The most revealing ones were at 42.10 and 205.5 ppm, which almost coincide with those reported for ethylphenylketene at 42.1 (C(α)) and 205.6 (C(β)) [20], which is characteristic for Ph-substituted ketenes [21].

The ^{13}C-NMR spectra of the mixture were also compared with that of 2-phenylbutanoic acid. Authentic 2-phenylbutanoic acid at 240 K in $CDCl_3$ displays Et signals at δ 12.15 (Me), 26.00 (CH_2), 53.05 (CH), 127.45 – 128.58 (*o*-, *m*-, *p*-C), 137.96 (C_{ipso}), 181.12 (CO) (with the expected coupling in the ^{1}H-coupled spectrum). The signals in the distilled mixture that are not identified with those of the ketene or the anhydride appear at the same positions as those of the acid, except for the C=O signal, which appears at 180.60 ppm, and the 0.5 ppm difference can be ascribed to different type of H-bonding. Regardless of the explanation, neither the anhydride nor the ketene has a C=O signal at *ca.* 180 ppm.

The ratio ketene **17**/acid **18** was 1:1 as expected. The **4**/**17**/**18** ratios changed from 1.0:0.3:0.3 at 240 K to 1.0:0.2:0.2 at 298 K. The higher percentage of the anhydride **4**, and the temperature effect are ascribed to a rapid reaction of **17** and **18** to form **4** before the NMR experiment was conducted. In the crude distillate, a very broad signal at δ 12 is observed, and from its position we ascribe it to the OH group of the acid **18**.

Three attempts to capture the pyrolysis products of the reaction in *Scheme 6* were made. Addition of cyclopentadiene to the distillate at 253 K did not give an expected cycloadduct of cyclopentadiene and ketene **17**. Apparently, the reaction was too slow compared with other reactions in the system. Following the work of *Tidwell* and co-workers [22] on reactions of ketenes with radical reagents, we attempted the reaction with TEMPO (2,2,6,6-tetramethylpiperidine *N*-oxide). The NMR of the crude product shows an aromatic *AB quadruplet*, suggesting that a reaction occurred at the *para*-position, with elimination of the Et group rather than reaction on the C=C bond. This reaction, which cannot be an indicator for the nature of the ketene, was, therefore, abundant without identifying the product. A reaction with CH_2N_2 gave methyl 2-phenylbutanoate, thus capturing the acid **18**, which was formed in the thermal reaction of **4**. No reaction product with the ketene was observed. However, the capture of the acid, the observation of an acidic OH, and the coincidence of the signals of the distillate with those of the ketene **17** indicate that reaction according to *Scheme 6* takes place.

The experimental results are supported by calculations on all three species **4**, **5** and **6** (*Table 1*). Several conformations are at local minima for each species both at HF/3-21G and B3LYP/6-31G** level of theories. The anhydride has two stereogenic centers, and the (*S*,*S*)-conformer (*Fig. 1*,*a*) was found to be the most stable one, but only by 0.1 kcal/mol over the (*RS*) conformer (*Fig. 2*,*a*) at B3LYP. Another conformer (*Fig. 2*,*b*) is 1.4 kcal/mol less stable¹).

The mono-enol displays four local minima, all with energies higher than for the neutral anhydride by 13.6, 15.1, 15.6, and 18.1 kcal/mol. The most stable one has (*Z*)-conformation at the enol C=C bond (*Fig. 1*,*b*). The derived pK_{Enol} value is 10.0, which is in the range roughly estimated from the values for the parent anhydride superimposed on the stabilization by a β-Ph group.

The bis-enol **6** has four different stable conformations, and, as could have been guessed, it has a much higher energy than the monoenol. The conformers are 39.3, 39.6,

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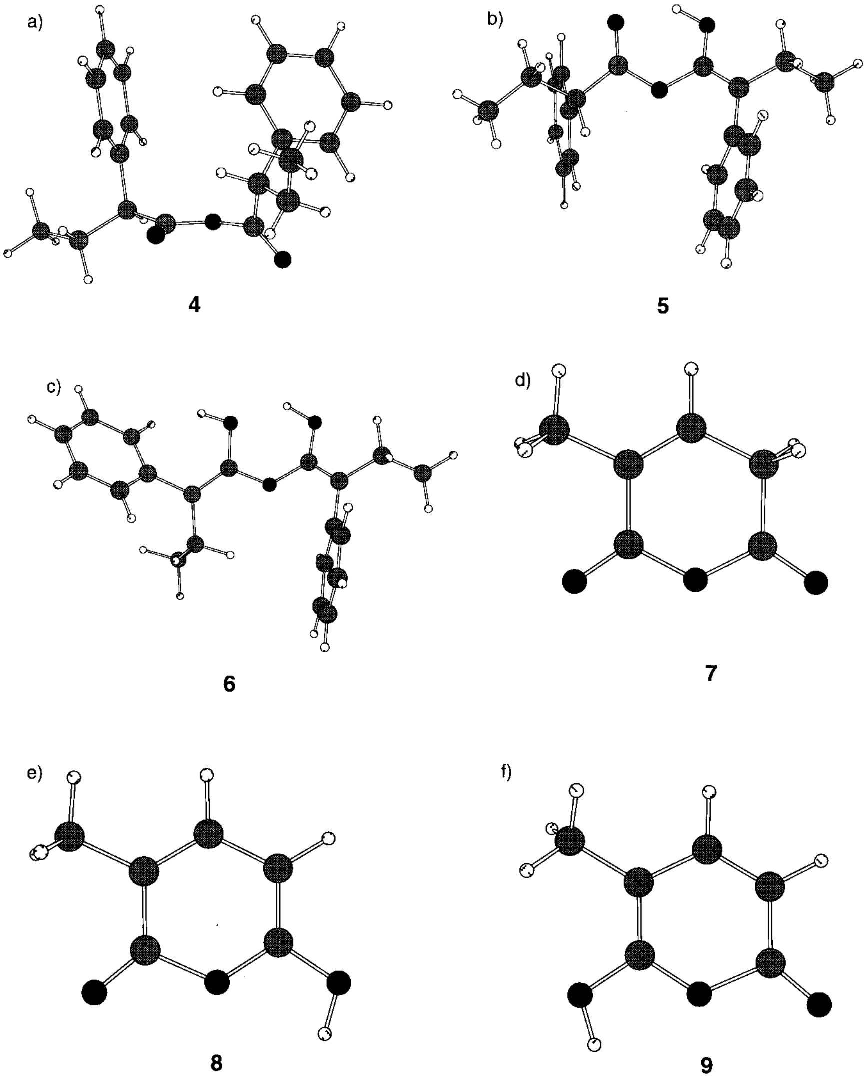
¹) *Fig. 1* contains all the most stable conformers of the species calculated. Structures of higher-energy isomers are shown in *Fig. 2*.

Table 1. *Calculated Electronic Energy*, Gibbs *Energy* (in Hartree), *and* pK_{Enol} *Values in Keto-Enol Isomerization of Acid Anhydrides at B3LYP/6-31G***[a])

Compound	Electronic energy	ΔE [kcal/mol]	*Gibbs* energy	ΔG [kcal/mol]	pK_{Enol}
4	– 1001.113189	0.0	– 1000.792497	0.0	
5	– 1001.090718	14.1	– 1000.770754	13.6	10.0
6	– 1001.04839	40.0	– 1000.729875	39.3	28.8
7	– 457.935248	0.0	– 457.856922	0.0	
8	– 457.927299	5.0	– 457.847271	6.1	4.4
9	– 457.924989	6.4	– 457.845836	7.0	5.1
10[b])	– 610.576297	0.0	– 610.465336	0.0	
11[b])	– 610.589077	– 8.0	– 610.476195	– 6.8	– 5.0
12[b])	– 610.591355	– 9.5	– 610.477673	– 7.7	– 5.7
14a	– 1476.164359	0.0	– 1476.127610	0.0	
15a	– 1476.128416	22.6	– 1476.092275	22.2	16.3
14b	– 1005.516951	0.0	– 1005.444761	0.0	0.0
15b	– 1005.483403	21.1	– 1005.408971	22.5	16.5
22	– 646.484100	0.0	– 646.396741	0.0	
23	– 646.507575	– 14.7	– 646.417574	– 13.1	– 9.6
24	– 646.509512	– 16.0	– 646.419902	– 14.5	– 10.7
25	– 380.528779	0.0	– 380.480526	0.0	
26	– 380.490623	23.9	– 380.442149	24.1	17.7
27	– 380.462622	41.5	– 380.415101	41.1	30.1
28	– 908.272549	0.0	– 908.188470	0.0	
29	– 908.287612	– 9.5	– 908.200922	– 7.8	– 5.7
30	– 908.287732	– 9.5	– 908.201137	– 8.0	– 5.8
31	– 685.805644	0.0	– 685.690833	0.0	
32	– 685.820859	– 9.6	– 685.703055	– 7.7	– 5.6
35a	– 1512.195161	0.0		0.00[c])	
36a	– 1512.180267	9.4		10.5[c])	7.7
35b	– 1849.217237	0.0		0.0[c])	
36b	– 1849.205205	7.6		8.5[c])	6.2
37	– 526.851463	0.0	– 526.820157	0.0	
38	– 526.850750	0.5	– 526.816714	2.2	1.6
43	– 798.147897	0.0	– 798.035909	0.0	
44	– 798.141859	3.8	– 798.028025	5.0	3.6

[a]) ΔH and ΔG are relative energies (in kcal/mol) with respect to the most stable anhydride form. [b]) $R^1 = Me$, $R^2 = H$. [c]) Relative *Gibbs* energy with respect to the most stable anhydride form at B3LYP/6-31G** calculated from the relative electronic energy at B3LYP/6-31G** and the relative thermochemical contribution obtained at HF/6-31G** frequency analysis.

42.5, and 43.2 kcal/mol above the stable anhydride conformer, and their C=C–O–H conformations are (*E*(*syn*),*Z*) (*E*(*syn*),*E*), (*Z*,*Z*), and (*E*(*anti*),*Z*), respectively. Here, (*E*/*Z*) refers to the configuration at the enolic C=C bonds, and *syn*/*anti* represents the direction of OH with respect to the Ph group. The most stable (*E*(*syn*),*Z*)-conformer is shown in *Fig. 1,c*, and others in *Fig. 2*. Solvent effects will not change this value much, and, in H_2O, when the anhydride can take a more stable conformation with a single H_2O molecule bridging the two C=O groups, the pK_{Enol} value will be higher. We conclude, on both experimental and theoretical grounds, that neither **5** nor **6** is formed in observable concentrations in solution, and that the report of their observation [9] is erroneous.

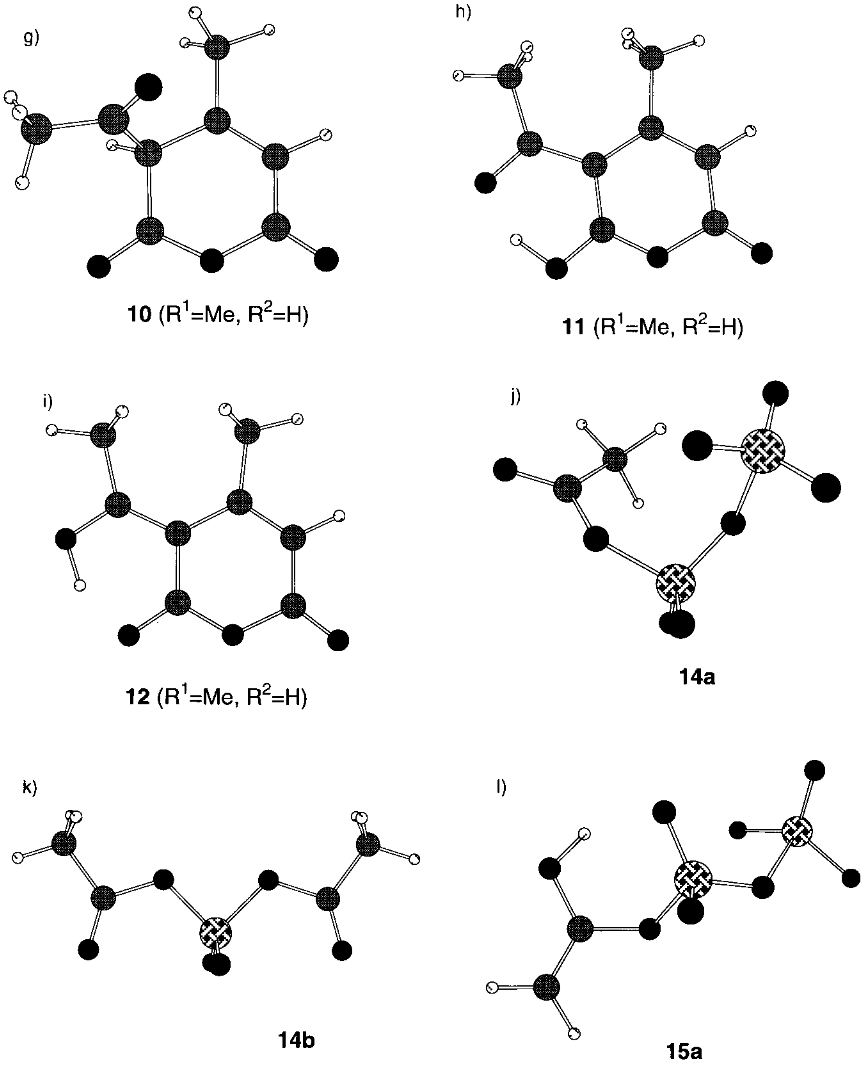


4 **5** **6** **7** **8** **9**

Fig. 1. *Structures of the most stable conformers for each species optimized at B3LYP/6-31G***

*The 5-Methyl-2*H*-pyran-2,6(3*H*)-dione ((*Z*)-γ-Methylglutaconic Anhydride) System*. There are some difficulties with the interpretation of the data for **7**–**9**. The role of the acid according to *Scheme 4* is of a keto → enol catalyst, and it is unclear why the presence of HCl or TFA at 100° for a long time does not lead to any enolization, especially since it is implied that the enols **8**/**9** are thermodynamically more stable than **7**. A possible protonation on the C=C bond is not mentioned at all, in spite of the known protonation of enones [23].

On the other hand, compounds **8** and **9** are conjugated and, judging from data on simple enols, conjugation increases the stability of the enols by a few kcal/mol [24].



10 (R^1=Me, R^2=H)

11 (R^1=Me, R^2=H)

12 (R^1=Me, R^2=H)

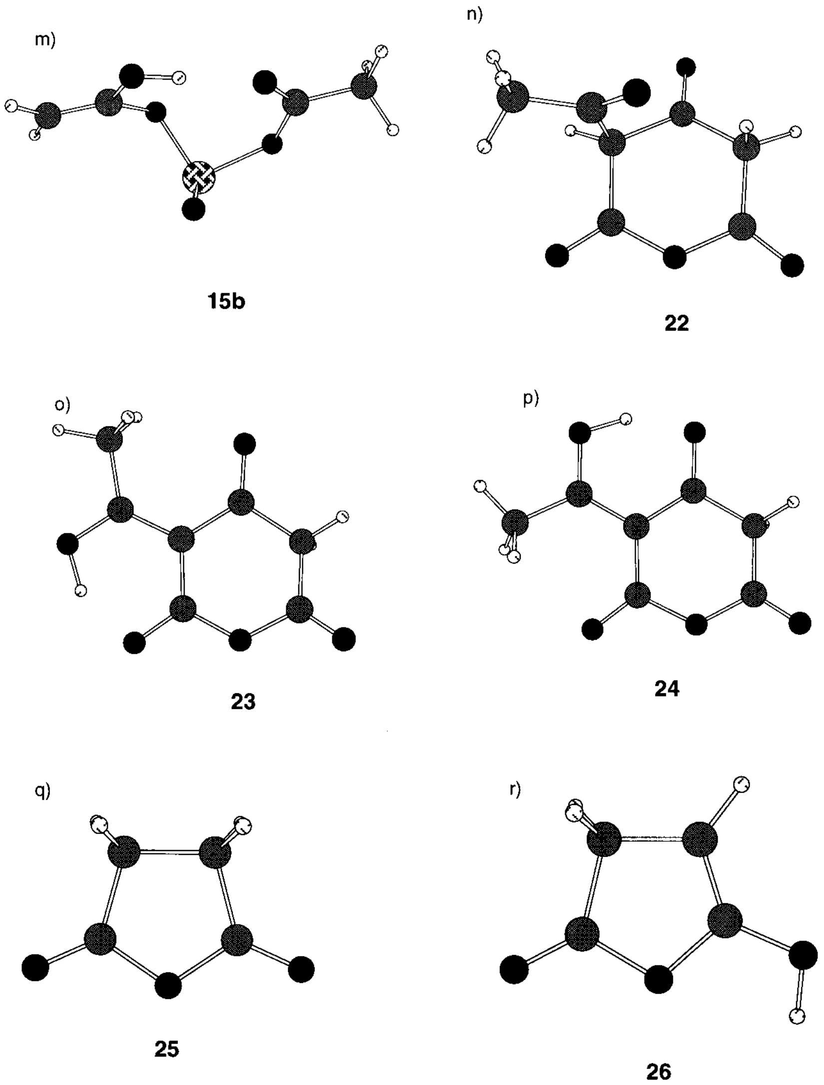
14a

14b

15a

Fig. 1 (cont.)

Moreover, the electron-withdrawing carbonyl group at the end of the conjugated system should make it more enolic [5], with a consequent decrease of pK_{Enol}. Since the probability that **8**/**9** will be observable is larger than for other systems, calculations to check this possibility were conducted. Several possible conformations for **7**–**9** were examined. In the most stable conformers (*Fig. 1,d–f*), the Me H-atom that lies on the molecular plane points away from the anhydride moiety; the other conformation in which the H-atom is directed to the C=O is the transition state for Me rotation. For **8** and **9**, the enolic OH can be placed either toward or away from the other C=O group, and the former conformation is more stable by 2.9 (for **8**) and 3.5 (for **9**) kcal/mol. The



15b **22** **23** **24** **25** **26**

Fig. 1 (cont.)

most stable conformers of **8** and **9** are less stable than **7** by 6.1 and 7.0 kcal/mol, respectively (*Table 1*), indicating that the anhydride form is significantly more stable than its enols.

*The 3-Acyl-2*H*-pyran-2,4(3*H*)-dione System.* In contrast with the 5- (or 3-) unsubstituted pyran-2,4-dione system, the substituted 3-acyl system is capable of forming the anhydride enol for two reasons: *a*) The acyl group is *β* to the potentially enolizable dione of the anhydride while the other *β*-substituent is an enone moiety attached *via* its vinylic C-atom. Consequently, the system is a *β*,*β*-EWG-substituted anhydride system, that can enolize according to our generalization [2]. *b*) The enolic

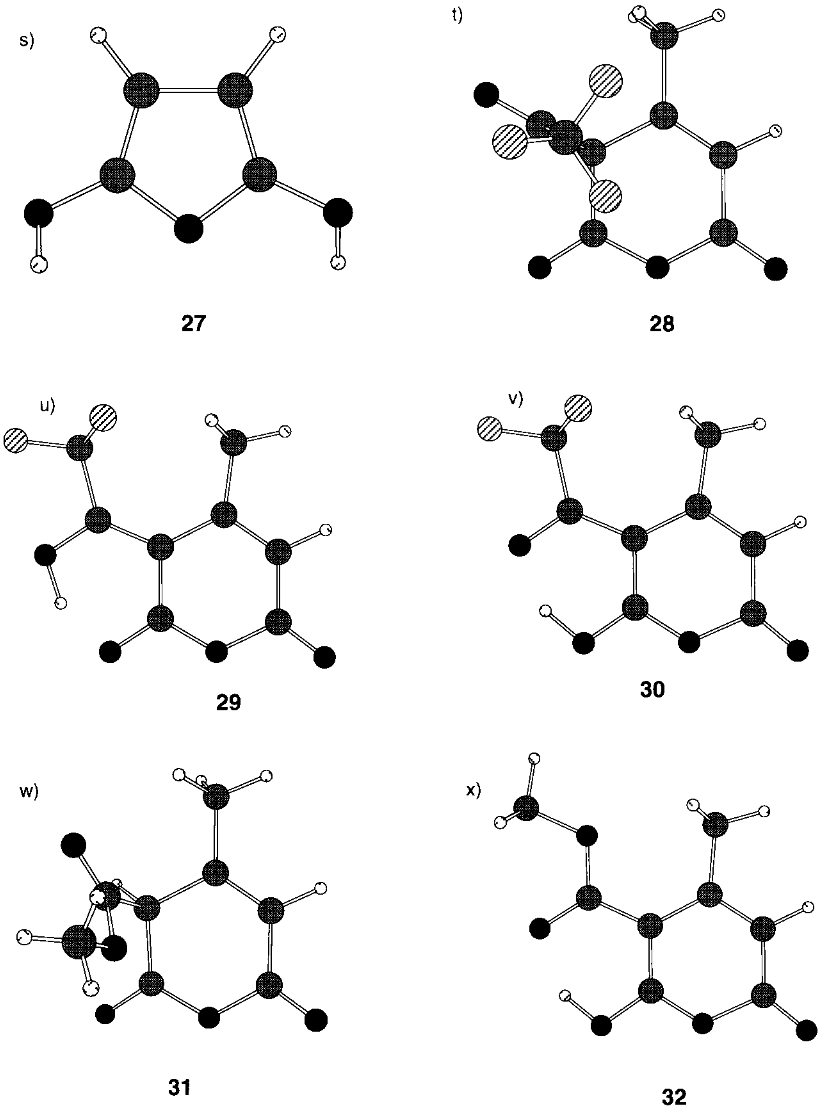


Fig. 1 (cont.)

OH group derived from the anhydride can form a stable six-membered ring *via* H-bond to the acyl C=O group. However, there are features that operate against or compete with such enolization. *i*) The enolizable H-atom at C(5) can enolize not only on the anhydride C(6)=O but also on the acyl C=O substituting C(5), and, *a priori*, enolization on the latter is favored. *ii*) Stabilization of the latter enol is sometimes possible by H-bonding to another site, *i.e.*, to a C(4)=O, and, in this case, the anhydride C=O will have a relatively lower probability of being involved in the enolization.

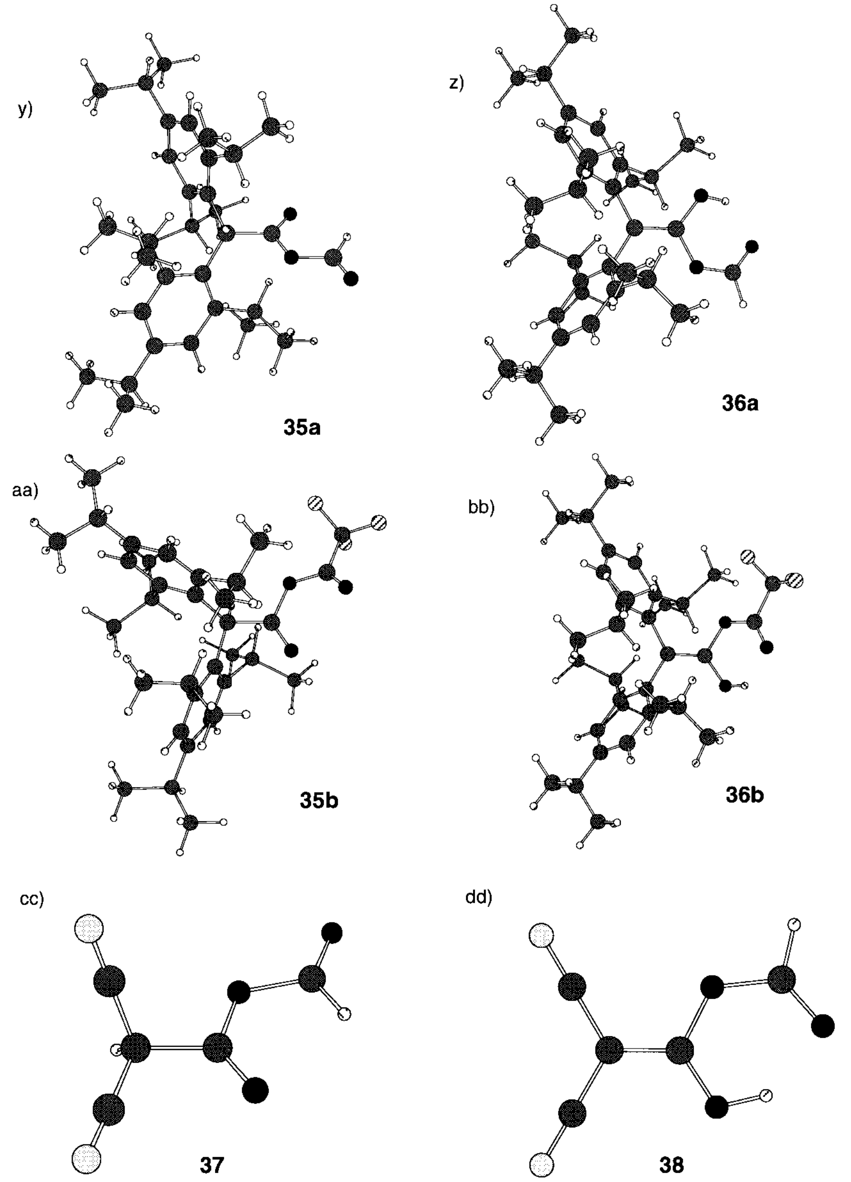


Fig. 1 (cont.)

Inspection of all the anhydride structures in the *Cambridge Structural Database* (*CSDB*) shows no solid-state structure with an enol of anhydride moiety, including compounds with a H-atom at C(3) or C(5). There are six structures with a formal acyl or aroyl group on the C-atom neighboring the anhydride C=O, and all have an enol structure, but *significantly* in all of them the acyl or aroyl group is enolized (*cf.*

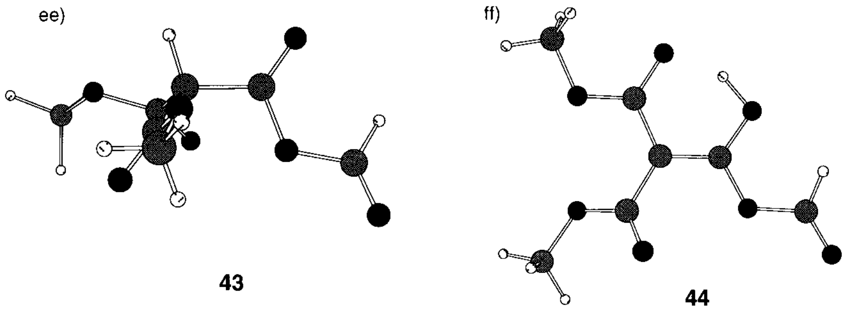
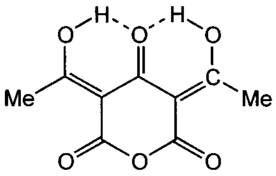


Fig. 1 (cont.)

structures **19** [25], **20** [26] and **21** [27]). Moreover, in structure **19**, which was previously regarded as a mixture of isomers in the solid (based on IR spectra) [13c] and in solution (based on NMR spectra) [13c] the two (former Ac) enol groups are H-bonded to the C(4)=O according to recent X-ray study [25]. In the other five structures there are O–H ··· O=C (anhydride) H-bonds, but definitely the H-atom is bonded to the former Ac group: the O ··· O, acetyl O–H, and anhydride C=O ··· H distances in Å are 2.496, 0.965, and 1.607 in **20a**, 2.496, 0.955, and 1.588 in **20b**, 2.514, 0.963, and 1.623 in **20c**, and 2.537, 0.850, and 1.780 in **21**. Consequently, there is no evidence for an enol of anhydride structure in the solid in these systems, either.



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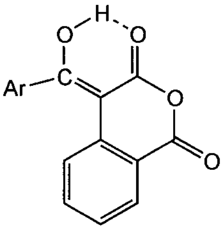
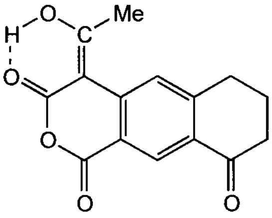


20a Ar = Ph
b Ar = 4-F–C_6H_4
c Ar = 4-NO_2–C_6H_4



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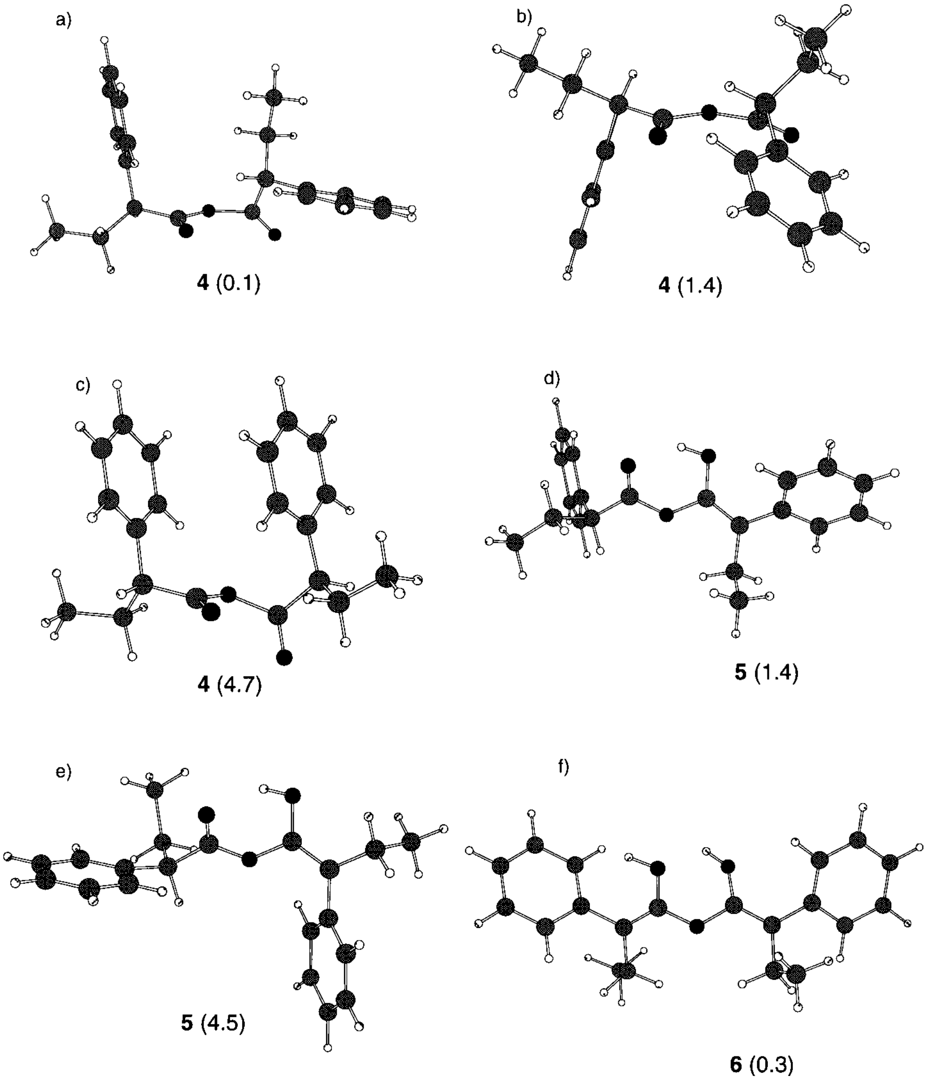
The situation is more complex in solution. The various authors who dealt with the structure, write it frequently [14] as the enol of anhydride, with or without a H-bond, or sometimes with an enolized acyl, usually in a H-bonded form. The NMR data seem to favor the anhydride enol data, or at least an important contribution from it as discussed by *Tan* and co-workers [13], and *Hansen et al.* [14d]. Note, however, that the latter [14d] had calculated the relative contributions of the enol of anhydride *vs.* enol of C=O structure and found that the former is 3.3 kcal/mol less stable, in contrast to experiment, but in line with our assumption.

The energy difference between **11** and **12**, R^1 = Me, R^2 = H was, therefore, calculated by B3LYP/6-31G**. The most stable conformers for **10**, **11**, and **12** are shown in *Fig. 1, g–i*. The enol **12** on the acyl group was found to be only 0.9 kcal/mol more stable than the enol in the anhydride **11**, *i.e.*, in the gas phase at 298 K, **11** will consist

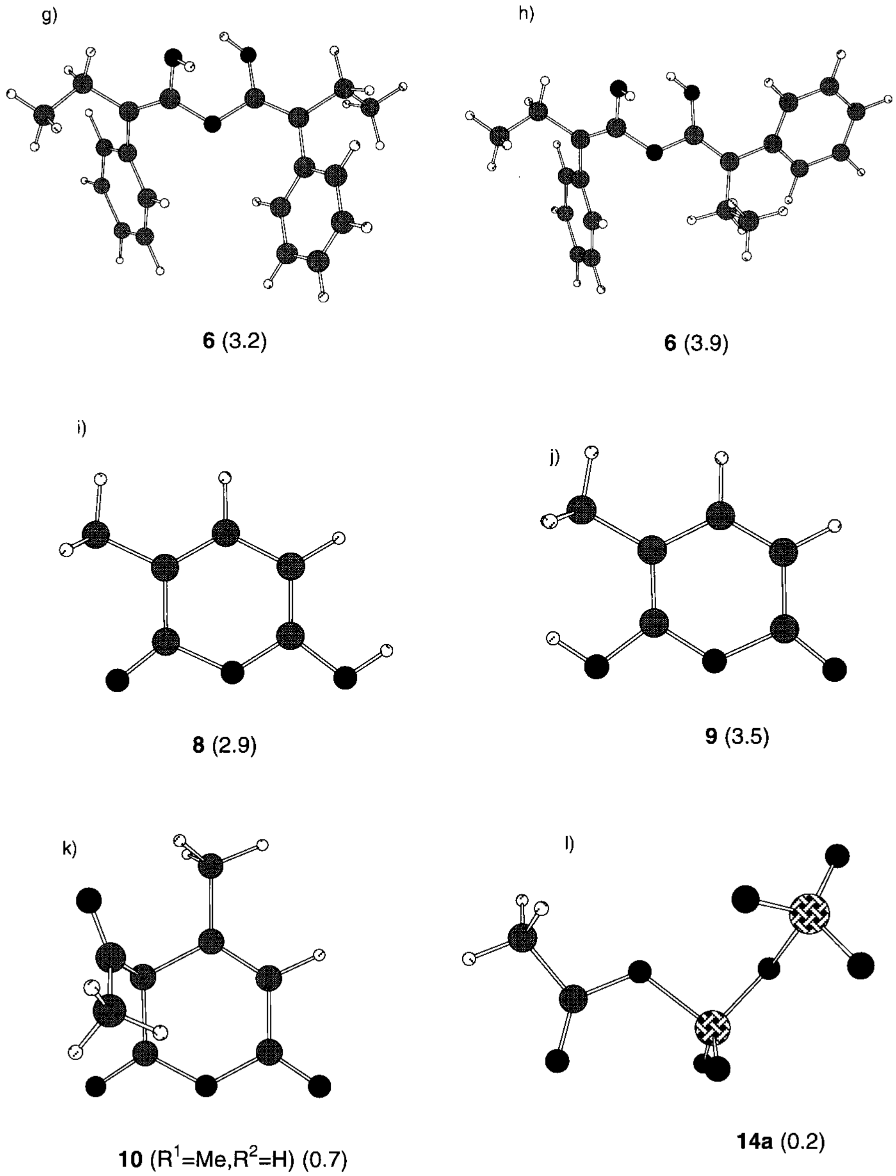


4 (0.1) **4** (1.4) **4** (4.7) **5** (1.4) **5** (4.5) **6** (0.3)

Fig. 2. *Structures and relative energies of unstable isomers of all species calculated at B3LYP/6-31G***. Numbers in parentheses are relative *Gibbs* energies with respect to the most stable conformers.

22% of the **11**/**12** equilibrium mixture. It is, therefore, clear that a minor structural variation can make the enol of anhydride more stable.

The 3-acetyl tetrahydropyran-2,4,6-trione system (**22**, *Fig. 1,n*) was also examined by B3LYP calculations, which revealed that two enol forms of former Ac, one H-bonded to anhydride (**23**, *Fig. 1,o*) and the other H-bonded to the C=O group (**24**, *Fig. 1,p*) were at a local minimum. Both are more stable than the keto form **22** by 14.5 and 13.1 kcal/mol, respectively. In contrast, the attempted optimization of the enol of anhydride led to **23**. Thus, introduction of additional C=O increases the stability of the



6 (3.2)

6 (3.9)

8 (2.9)

9 (3.5)

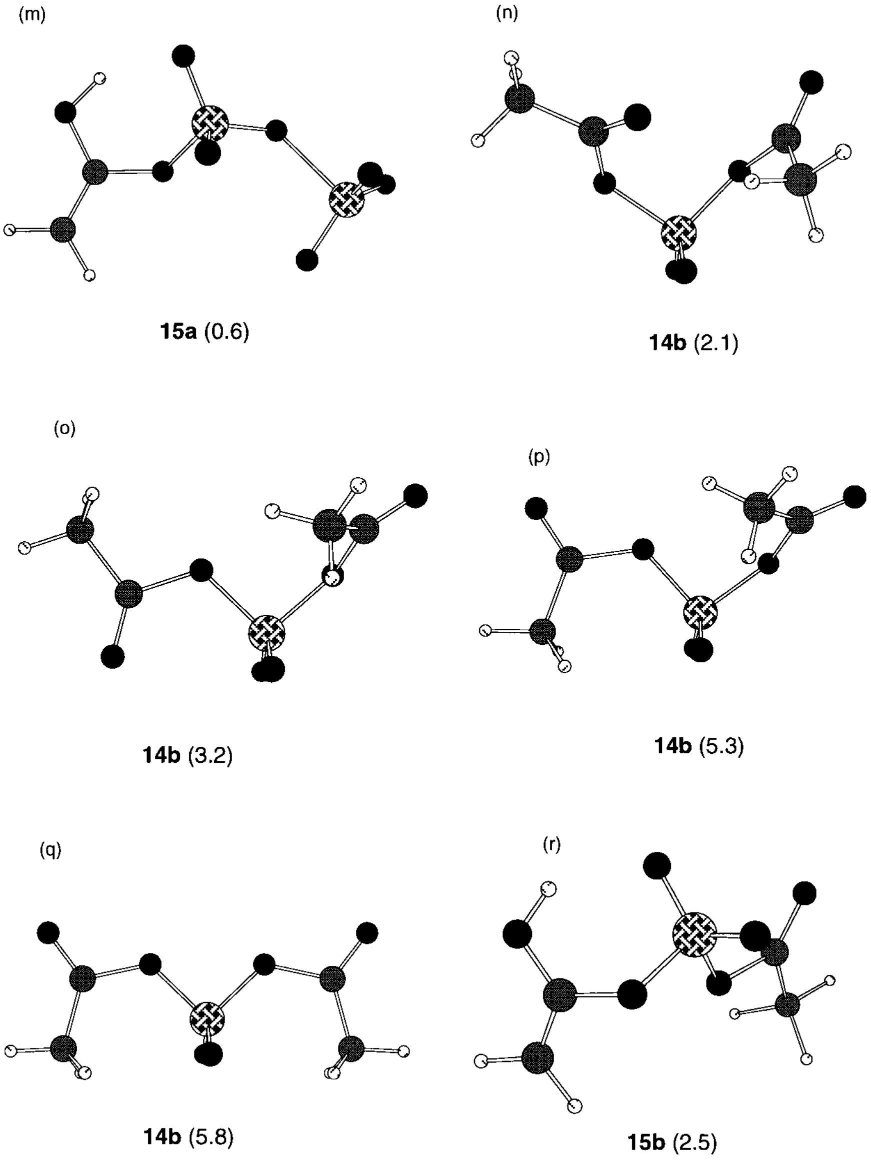
10 (R^1=Me,R^2=H) (0.7)

14a (0.2)

Fig. 2 (cont.)

enols on the acyl group, resulting in an overall reduced possibility for the formation of the enol of anhydride.

The Mixed Acetic Sulfuric Anhydride System. In view of the very high pK_{Enol} values for the β,β-unsubstituted systems [2], the assignment of structures **15** seems questionable. It is true that pK_{Enol} seems to decrease with the electron withdrawal of the substituent at C(α), that the Ac and OSO_3^- substituents are electron-withdrawing,



15a (0.6) **14b** (2.1)

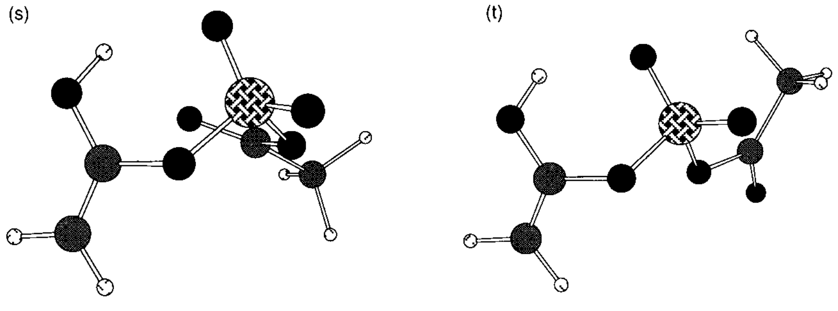
14b (3.2) **14b** (5.3)

14b (5.8) **15b** (2.5)

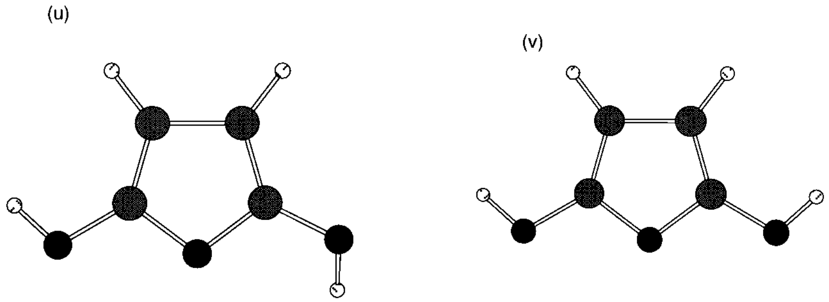
Fig. 2 (cont.)

and that H-bonding stabilizes the enols. Hence, these features will increase the enol stability, but they do not seem to be sufficient to stabilize the enol to such an extent that it will be observable.

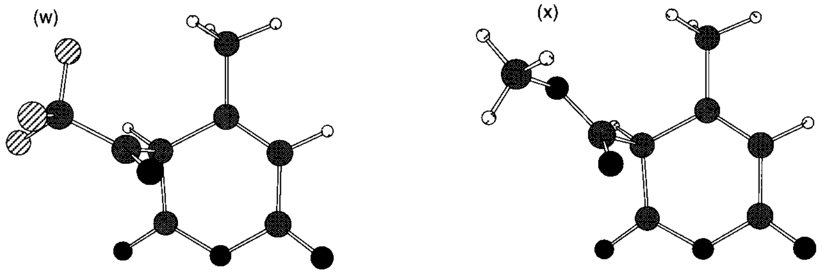
We again used calculations of the pair **14**/**15** to probe this problem. The results are listed in *Table 1*. B3LYP/6-31G** Calculations reveal five stable conformations for diacetyl sulfate **14b** with relative energies of 0.0, 2.2, 3.2, 5.3, and 5.8 kcal/mol. Four stable conformations were calculated for the enol **15b** with energies of 22.5, 24.9, 25.5,



15b (3.0) **15b** (5.3)



27 (0.8) **27** (2.0)



28 (0.1) **31** (0.6)

Fig. 2 (cont.)

and 27.8 kcal/mol above that of the most stable enol. The most stable conformations of **14b** and **15b** are shown in *Fig. 1,k* and *m*, and other conformations are given in *Fig. 2*. When the ΔG value is converted, it gives $pK_{\mathrm{Enol}} = 16.5$, which is the lowest value calculated so far for a β,β-unsubstituted system, but is still very far from making the enol observable. From past experience on solvent effect on equilibria of enols [2a] [28], we do not believe that this value, as well as other values calculated below, will be

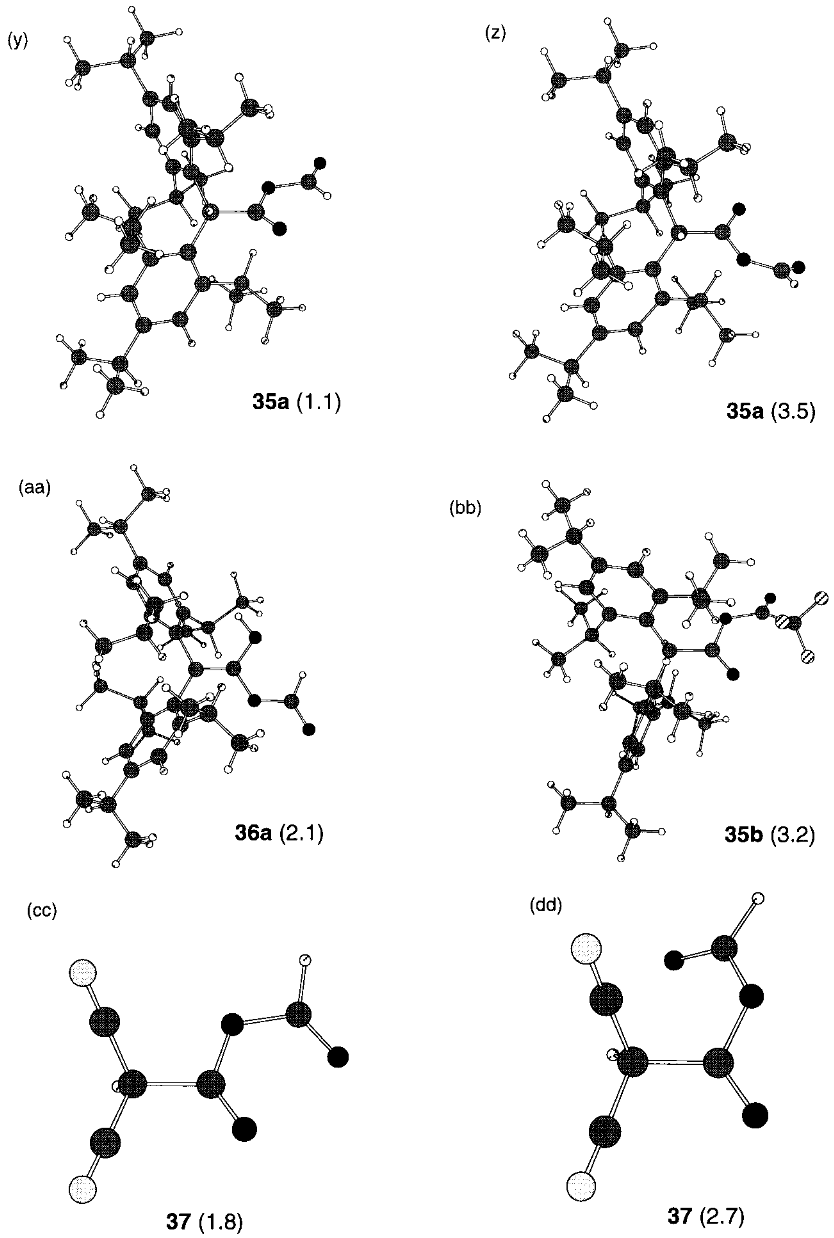
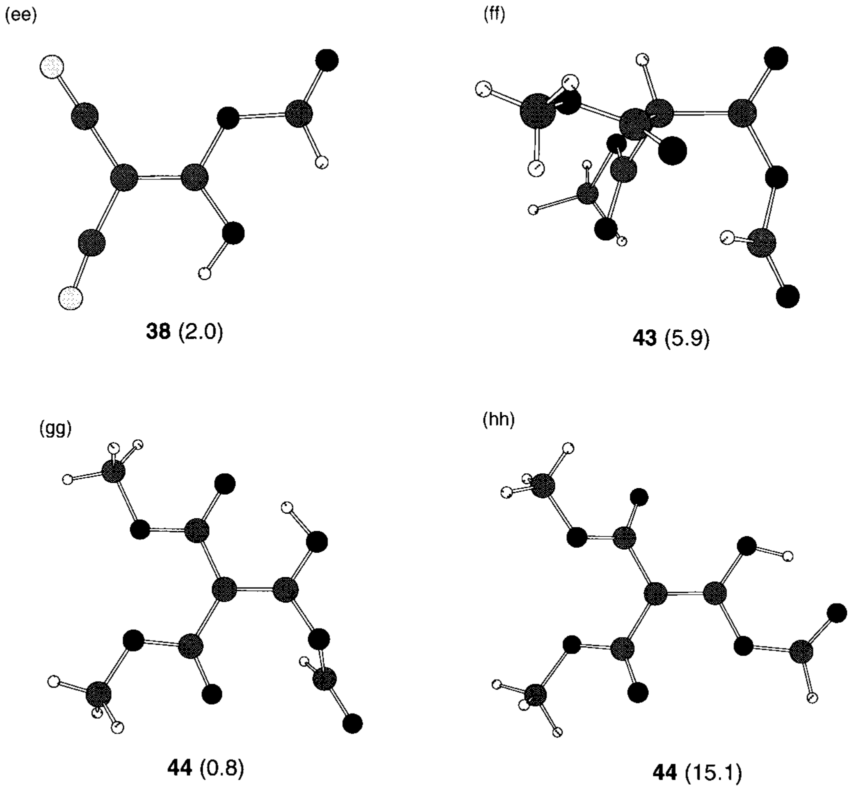

(y) **35a** (1.1)
(z) **35a** (3.5)
(aa) **36a** (2.1)
(bb) **35b** (3.2)
(cc) **37** (1.8)
(dd) **37** (2.7)

Fig. 2 (cont.)

changed by more than 1–2 units in a polar solution compared with the gas-phase calculated value. The same conclusions apply for **14a**/**15a** (*Fig. 1, j* and *l*) for which a pK_{Enol} value of 16.3 was calculated. Consequently, we are in doubt that these enols are the species observed.



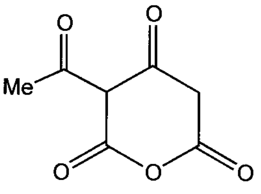
38 (2.0) **43** (5.9)

44 (0.8) **44** (15.1)

Fig. 2 (cont.)

Predictions for Observable Enols of Anhydrides. The results presented above indicate a high probability that none (but one) of the few systems reported to display observable enols, indeed form them in observable concentrations. Hence, the question arises of what type of systems will be able to generate observable enols. Consequently, pK_{Enol} values for three systems were calculated: *i*) for a system analogous to the cyclic **7**–**9** system *ii*) for a *β*,*β*-diaryl-substituted anhydride, and *iii*) for anhydrides carrying two *β*,*β*-strongly EWGs.

i) *Succinic Anhydride (Tetrahydrofuran-2,5-dione)/5-Hydroxyfuran-2(3*H*)-one/ Furan-2,5-diol.* This system is analogous to **7**–**9**, except that the bis-enol **27** should



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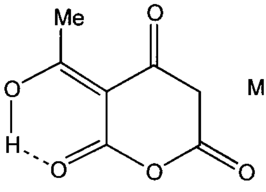

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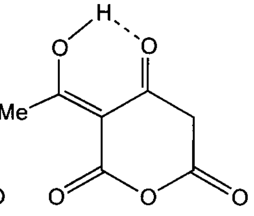

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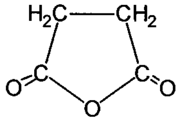
gain aromatic stabilization of the furan ring. B3LYP Calculations showed that the energy differences between succinic anhydride (**25**; *Fig. 1,q*) and the most stable conformations of 5-hydroxyfuran-2(3*H*)-one (**26**; *Fig. 1,r*), and furan-2,5-diol (**27**; *Fig. 1,s*) are 24.1 and 41.1 kcal/mol, which amounts to pK_{Enol} values of *ca.* 18 and 30, respectively. Hence, the situation resembles that for systems **4**–**6** and certainly the dienol and highly probably the monoenol will not be observable.



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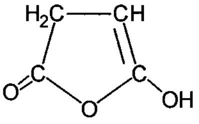

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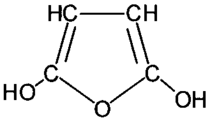

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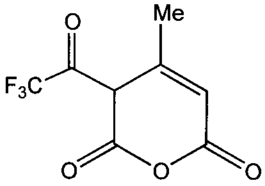
*3-Acetyl-2*H*-pyran-2,6(3*H*)-dione.* B3LYP/6-31G** Calculations show that 3-acetyl-4-methyl-2*H*-pyran-2,6(3*H*)-dione (**10**; $R^1 = Me$, $R^2 = H$) is much less stable than its enolic counterparts, the enol on the anhydride (**11**, $R^1 = Me$, $R^2 = H$) and the enol on the Ac group (**12**, $R^1 = Me$, $R^2 = H$), by 6.8 and 7.7 kcal/mol, respectively, giving pK_{Enol} values of – 5.0 for **11** and – 5.7 for **12**. However, the most stable species in this system is the enol on the Ac group.

*3-(Trifluoroacetyl)-2*H*-pyran-2,6(3*H*)-dione.* Replacement of the CH_3CO group of **10** by a CF_3CO group makes the enol on the acyl group less stable, and then the enol of anhydride may exist as the most stable tautomer, even though the H-bond to a CF_3CO group will be weaker than that to a CH_3CO group. B3LYP Calculations revealed that both the enol of the acyl group (**29**; *Fig. 1,u*) and the enol of anhydride (**30**; *Fig. 1,v*) are more stable than the anhydride form (**28**; *Fig. 1,t*) by 7.8 and 8.0 kcal/mol, respectively, as expected. The difference between the two enols is not large, the enol of anhydride being more stable than the enol of the acyl group by only 0.2 kcal/mol. The pK_{Enol} values for **29** and **30** are – 5.7 and – 5.8, respectively. Hence, **30** should be one of the observable species in the isomers mixture.



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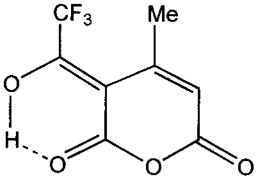

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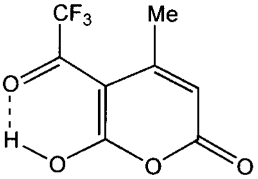

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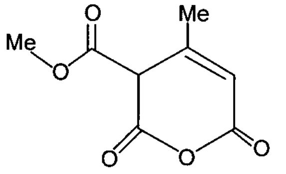
*3-(Methoxycarbonyl)-2*H*-pyran-2,6(3*H*)-dione.* Since an ester has the least propensity to become an enol among carboxylic acid derivatives, 3-(methoxycarbonyl)-2*H*-pyran-2,4(3*H*)-dione (**31**; *Fig. 1,w*) should have a higher probability than **28** to exist as the enol of anhydride (**32**; *Fig. 1,x*). B3LYP Calculations, indeed, indicated that, among the systems calculated, **32** is the only enol optimized and is 7.7 kcal/mol more stable than **31**, corresponding to pK_{Enol} of – 5.6.

ii) *β,β-Ditipylacetic Anhydride and its Enol.* β,β-Ditipylacetic acid **33** is 12.7 kcal/mol more stable than its enol **34** according to B3LYP/6-31G** calculations [29].



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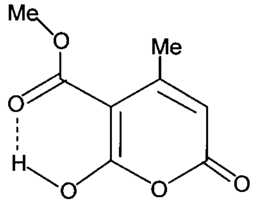

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However, **34** was observed by NMR and can be retained for a long time at 255 K, when generated from ditipyl ketene and H_2O under kinetically controlled conditions [4c]. Since the pK_{Enol} value of the parent enol of anhydride is 4.4 units lower than that of the parent acid [2a], it is expected that the enol **36** of the mixed anhydride of *β,β*-ditipylacetic acid with another acid, *e.g.*, AcOH, *i.e.*, **35** (R = Me) will have $pK_{Enol} \leq 9.9$ and may hopefully be observed at least as a kinetically stable species.

$Tip_2CHCOOH$	$Tip_2C{=}C(OH)_2$	$Tip_2CHCOOCOR$	$Tip_2C{=}C(OH)OCOR$
33	**34**	**35**	**36**

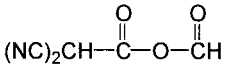
a R = H

Tip = Tipyl = 2,4,6-$(i\text{-}Pr)_3C_6H_2$ **b** R = CF_3

Calculation on the model system **35a** and **36a**, *i.e.*, the formate derivatives, by B3LYP/6-31G** showed two conformations each for **35a** and **36a**. For **35a**, a conformation in which two carbonyl O-atoms are oriented in the same direction (*Fig. 2*) is 3.5 kcal/mol less stable than the most stable conformer with the C=O group directed in opposite ways (*Fig. 1,y*). For **36a**, a conformation with the C=O/C–O bonds in the same direction is the species of lower energy (by 2.1 kcal/mol) since C=O ···H–O H-bonding is possible for this conformer (*Fig. 1,z*). The difference in B3LYP electronic energy of the two more-stable conformations is 9.4 kcal/mol in favor of **35a**. Addition of thermochemical contributions obtained from the frequency calculations at HF/3-21G to the B3LYP electronic energy gives a *Gibbs* energy difference of 10.5 kcal/mol, corresponding to a pK_{Enol} value of 7.7. This value resembles that for *α*-cyanoacetic acid, whose enol had been observed by *Kresge* and co-workers by flash photolysis [19b], and the value is lower than any value calculated so far for a *β,β*-di(bulky)aryl substituted enol [29]. In this respect, the effect of the *β,β*-ditipyl substitution is qualitatively in the expected direction. In view of the observation of **34**, it is likely that, if **36a** could be prepared under kinetically controlled conditions, it will be observable.

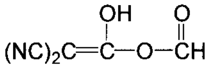
The situation was found to be even more favorable for **35b**/**36b** (*Fig. 1,aa* and *bb*). The calculated energy difference is 8.5 kcal/mol, giving a pK_{Enol} value of 6.2. This prediction could not yet be confirmed experimentally since attempts to prepare **35b** have failed so far.

iii) *β,β-Dicyano- and β,β-(Dimethoxycarbonyl)acetic Anhydrides and Their Enols.* The B3LYP calculations indicate that *β,β*-dicyano substituents strongly stabilize the enol of anhydride. Thus, enol **38** (*Fig. 1,dd*) is only 2.2 kcal/mol less stable than the anhydride isomer **37** (*Fig. 1,cc*), giving pK_{Enol} of 1.6. The pK_{Enol} for **37** is 16.0 units smaller than for the parent $CH_3COOCHO$ system. Nevertheless, since the amide **39** was found by calculations to be nearly of the same energy as **40** [5b], it is surprising that the β,β-$(CN)_2$ substitution does not make **38** the exclusive species in view of the significantly lower pK_{Enol} value of the parent acetic anhydride compared with the acetamide.



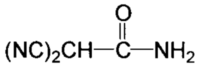
$(NC)_2CH-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}H$

37



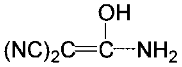
$(NC)_2C=\overset{\overset{OH}{|}}{C}-O-\overset{\overset{O}{\|}}{C}H$

38



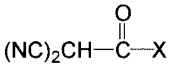
$(NC)_2CH-\overset{\overset{O}{\|}}{C}-NH_2$

39



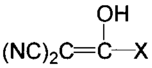
$(NC)_2C=\overset{\overset{OH}{|}}{C}-NH_2$

40



$(NC)_2CH-\overset{\overset{O}{\|}}{C}-X$

41



$(NC)_2C=\overset{\overset{OH}{|}}{C}-X$

42

The pK_{Enol} values for the series **41/42** were calculated by B3LYP/6-31G** (*Scheme 7*). The derived pK_{Enol} values for X are: H (−5.2) < NH_2 (−0.3) < OCHO (1.6) < Br (2.7) < Cl (3.0) < F (3.4) < OMe (4.4). The difference between the most- and the least-stabilized enols is 9.6 units. Consequently, the enol of the aldehyde (X = H) is practically the only species that will be observed in the mixture of **41** and **42**, whereas the corresponding methyl ester will be nearly exclusively in the ester form. An interesting result is the 4.6 pK_{Enol} units difference between $X{=}NH_2$ and X=OMe, which indicates that enolization on an amide C=O is significantly preferred over that of an ester C=O. This is consistent with the observation that, in amido esters $(EWG)CH(CO_2R')CONHR$, the enolization is exclusively on the amide group [5a,b]. The much smaller ΔpK_{Enol} of 1.0 for the parent compounds **1/2** let us to expect that, in a competitive intramolecular enolization, the ester may give a small percentage of observable enol.

Scheme 7

$(NC)_2CH-\overset{\overset{O}{\|}}{C}X \rightleftharpoons (NC)_2C=\overset{\overset{OH}{|}}{C}X$

41 **42**

Fig. 3 is a plot of pK_{Enol}(**41**) *vs.* pK_{Enol}(**2**) with a slope of 0.81. The plot is linear for six substituents including MeO, which shows a small deviation, but NH_2 shows a significant deviation (of *ca.* 4 pK_{Enol} units) from the line. Clearly the effect of the β,β-$(CN)_2$ substitution does not reduce pK_{Enol} to the same extent for different X groups, but there is a rather significant effect of X on pK_{Enol}.

To understand this behavior, appropriate isodesmic reactions *1*–*4*, based on either CH_4 or $H_2C{=}CH_2$ as the reference system, were used to calculate the separate effect of the β-substituents on the enol and the anhydride (or amide) species, and the results are listed in *Table 2*.

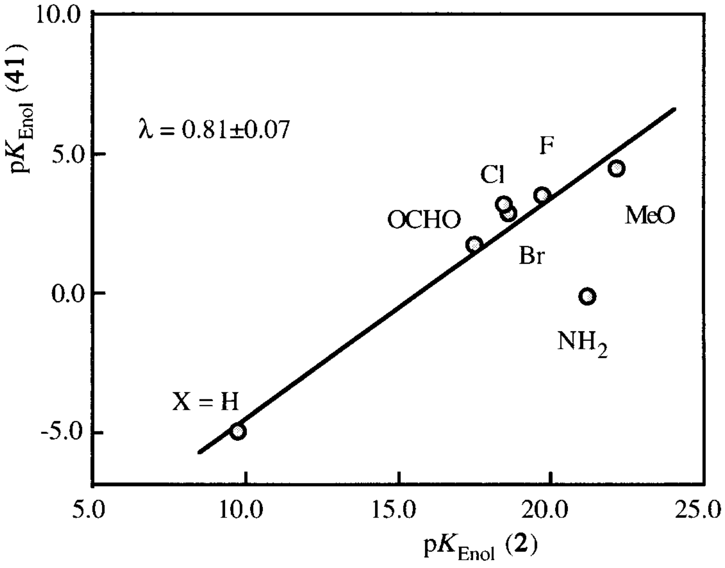


Fig. 3. *A plot of* pK_{Enol} *for* **41** vs. pK_{Enol} *for* **2**

Table 2. Gibbs *Energies* (in kcal/mol) *for the Isodesmic Reactions 1–4*

Reactions:

1 $(EWG)_2C{=}C(OH)X + CH_4 \rightleftharpoons H_2C{=}C(OH)X + CH_2(EWG)_2$

2 $(EWG)_2CHC({=}O)X + CH_4 \rightleftharpoons MeC({=}O)X + CH_2(EWG)_2$

3 $(EWG)_2C{=}C(OH)X + H_2C{=}CH_2 \rightleftharpoons H_2C{=}C(OH)X + (EWG)_2C{=}CH_2$

4 $(EWG)_2CHC({=}O)X + H_2C{=}CH_2 \rightleftharpoons MeC({=}O)X + (EWG)_2C{=}CH_2$

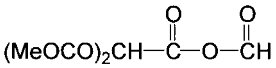
Reaction	EWG	X	ΔG
1a	CN	NH$_2$	26.3
b	CN	OCHO	11.7
c	AcO	OCHO	13.9
2a	CN	NH$_2$	– 2.6
b	CN	OCHO	– 9.9
c	AcO	OCHO	– 5.0
3a	CN	NH$_2$	16.3
b	CN	OCHO	1.7
c	AcO	OCHO	7.3
4a	CN	NH$_2$	– 12.9
b	CN	OCHO	– 20.0
c	AcO	OCHO	– 11.6

Since the quantitative differences between the CH_4 and $H_2C{=}CH_2$ references are the same for each EWG/X pair, we will use the values for the latter (*Table 2*, *Reactions 3* and *4*) in our discussion.

The effect of the *β*,*β*-$(EWG)_2$ substitution on the enols and the parent acid derivatives, is, as shown previously [2], composed of significant but opposite effects on both species. For EWG = CN, the enol of the amide (X = NH$_2$) is stabilized by 16.3 kcal/mol (*Table 2*, *Reaction 3a*), but the anhydride (X = OCHO) enol is stabilized by only 1.7 kcal/mol (*Reaction 3b*). For *Reaction 3c* (EWG = MeOOC, X = OCHO), the stabilization is higher, 7.3 kcal/mol. However, the acid derivative tautomer is destabilized by 12.9, 20.0, and 11.6 kcal/mol for *Reactions 4a* (EWG = CN, X = NH_2), *4b* (EWG = CN, X = OCHO), and *4c* (EWG = MeOCO, X = OCHO), respectively. The large enol stabilization, coupled with acid derivative destabilization for the dicyanoamide makes the pK_{Enol} value lower for **39**/**40** ($pK_{\mathrm{Enol}} = -0.3$) compared with the **1**/**2** system ($pK_{\mathrm{Enol}} = 21.3$).

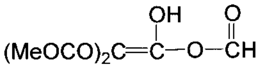
For EWG = CN, X = OCHO, the dissection of the effects shows that they behave in an opposite manner. The enol stabilization is minor (1.7 kcal/mol), which is insufficient to make the enol the dominating species at equilibrium.

Bis(methoxycarbonyl) substitution (**43**/**44**; *Fig. 1,ee* and *ff*) on the anhydride is more balanced: 7.3 kcal/mol enol stabilization, coupled with 11.6 kcal/mol anhydride isomer destabilization. The overall of 18.9 kcal/mol is the lowest of the three values and the β,β-$(MeO_2C)_2$ substituted anhydride is the thermodynamically less stabilized enol of an anhydride ($pK_{\mathrm{Enol}} = 3.6$). Consequently, the expectation of enol of anhydride stabilization by two β-EWGs based on our general considerations seems (computationally) fulfilled for the anhydrides, but in contrast with the amides, so far such stabilization is insufficient to make the enols observable.



$(\mathrm{MeOCO})_2\mathrm{CH}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{O}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{CH}}}$

43



$(\mathrm{MeOCO})_2\mathrm{C}=\overset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}-\mathrm{O}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{CH}}}$

44

It is interesting that similar doubts concerning the ability to observe enols of carboxylic acid halides by introducing β,β-$(EWG)_2$ substituents could be raised on the basis of the calculations of *Scheme 7* for the **41**/**42** pairs with X = Cl, Br, I.

3. Summary. – Analysis of the literature claims for the observation of enols of carboxylic acid anhydrides, mostly by calculations but also by experiment, suggests that such enols are mostly unlikely to be observed, except perhaps in the 3-acyl-2*H*-pyran-2,6(3*H*)-dione system. B3LYP/6-31G** Calculations suggest that 3-(trifluoroacetyl)-2*H*-pyran-2,6(3*H*)-dione will exist partially and the 3-(methoxycarbonyl) analog will exist completely in the enol of anhydride form. β,β-Dicyano or β,β-dimethoxycarbonyl substitution of the parent system showed that the species stable by calculation is still the anhydride rather than its enol.

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Experimental Part

General. M.p., and IR and NMR spectra were recorded as described in [4a].

The Reaction of 2-Phenylbutanoic Anhydride (**4**). 2-Phenylbutanoic anhydride was prepared according to the literature [30] by converting commercial 2-phenylbutanoic acid (**18**) to both its sodium salt and the corresponding acyl chloride and allowing the two reagents to react. The yellow anhydride was distilled at reduced pressure according to the literature; it formed a yellow mixture whose color faded rapidly. The IR spectra of the distillate in the absence of a solvent (3082*w*, 3058*w*–*m*, 3027*m*, 2966*s*, 2934*s*, 2873*s*, 2092*s*, 1815*s*, 1741*s*, 1700*m*), which were taken at intervals of a few min after the distillation, showed a decrease in intensity of the signals at 2093 cm^{-1} (ketene) and 2500–2900 and 1700 (acid), *e.g.*, from transmittance of 0.3 to 0.65 after 12 min. The ^1H- and ^{13}C-NMR spectra of pure **4** and acid **18** were recorded and compared with those of the distillate.

Acid **18**: ^1H-NMR ($CDCl_3$, 240 K): 0.91 (2 overlapping *t*, Me); 1.78, 2.10 (2 *oct.*, CH_2); 3.46 (2 overlapping *t*, CH); 7.25–7.36 (*m*, 5 arom. H); 12.68 (br., 0.75 H, OH). ^1H-NMR (CCl_4, 298 K): 0.11 (*t*, Me); 0.98, 1.29 (*sept.*, CH_2); 2.57 (*t*, CH); 6.36–6.45 (*s*, 5 arom. H); 11.54 (*s*, OH). ^{13}C-NMR ($CDCl_3$, 240 K): 12.16 (Me); 26.02 (CH_2); 53.05 (CH); 127.45, 127.94, 128.58, 137.96 (arom. C); 181.13 ($C{=}O$).

Anhydride **4**: ^1H-NMR ($CDCl_3$, 240 K): 0.82 (t, $J = 5.7$, 2 Me), 1.73, 2.03 (*m*, 2 CH_2); 3.42 (2 overlapping *t*, 2 CH); 7.12 (*s*, 4 arom. H); 7.30 (*s*, 6 arom. H). ^{13}C-NMR ($CDCl_3$): 11.74, 11.79 (Me); 25.35, 25.50 (CH_2); 53.66, 53.77 (CH); 127.45, 127.51, 127.88, 127.92, 128.62, 128.68, 136.66, 136.72 (arom. C); 168.96, 169.10 ($C{=}O$). We note that most signals are doubled, and this can be due to different conformations of the two anhydride moieties.

The identification of the ketene signals is based on the NMR spectra of the reaction mixture after subtracting the signals for the anhydride and the acid. Ketene **17**: ^1H-NMR ($CDCl_3$, 240 K): 1.24 (t, $J = 6.9$, Me); 2.44 (q, $J = 7.0$, CH_2); 7.05 (*d*, 2 arom. H). ^{13}C-NMR ($CDCl_3$, 240 K): 12.14 (Me); 16.54 (CH_2); 42.10 ($C{=}$); 123.52, 123.88, 128.82, 132.58 (arom. C); 205.50 ($C{=}O$).

Attempts to Capture the Ketene **17**. a) *Reaction of the Distillate with Cyclopentadiene.* Anhydride **4** (5 g, 16 mmol) was distilled *in vacuo*, and to the fresh distillate in Et_2O (20 ml) at 253 K was added freshly distilled cyclopentadiene (1.0 g, 15.2 mmol) at 253 K. The mixture was stirred for 2 h and left overnight at r.t. After evaporation of the solvent at reduced pressure, the ^1H-NMR spectrum of the residue showed that no reaction had taken place.

b) *Reaction with TEMPO.* A soln. containing **4** (0.5 g, 16 mmol) and TEMPO (0.6 g, 3.9 mmol) in *p*-xylene (10 ml) was refluxed for 48 h. TLC showed no signals of **4** and only one spot corresponding to product. This was separated by chromatography (silica gel; AcOEt/petroleum ether 1:9). The solvent was removed, and ^1H-NMR spectrum of the residue showed an aromatic *AB quadruplet* and no Et group. Since the ketene structure had not remained intact, the reaction was not investigated further.

c) *Reaction with* CH_2N_2. Anhydride **4** (3 g, 9.7 mmol) was distilled *in vacuo* into a dry-ice cooled beaker. CH_2N_2 Soln. in Et_2O (*ca.* 12 mg/ml, 22 ml) was added to this soln. at 273 K, and the mixture was kept at 273 K for 1 day. The solvent was evaporated, and the ^1H-NMR spectrum of the crude product showed the presence of at least three products: **4**, methyl 2-phenylbutanoate and a very broad signal at *ca.* 12 ppm, indicating the presence of **18**. Chromatography (silica gel; Et_2O/petroleum ether 1:9) gave the ester (0.55 g, 32%). ^1H-NMR ($CDCl_3$, 298 K): 0.89 (t, $J = 7.4$, Me); 1.79, 2.10 ($2m$, $J = 7.5$, CH_2); 3.45 (t, $J = 7.7$, CH); 3.65 (*s*, MeO); 7.22–7.35 (5 arom. H). ^{13}C-NMR ($CDCl_3$, 298 K): 12.11 (qq, $J = 126$, 3.6, Me); 26.70 (*t quint.*, $J_t = 129$, $J_q = 4.2$, CH_2); 51.82 (q, $J = 147$, MeO); 53.33 (br. d, $J = 126$, CH); 127.14 (dt, $J_d = 160$, $J_t = 4.5$, arom. C); 127.90 (dt, $J_d = 158$, $J_t = 5.2$, arom. C); 128.52 (dd, $J = 160$, 5.9, C_p of Ph); 139.07 (*s*, C_{ipso}); 174.48 ($C{=}O$).

Calculations. The compounds studied in the present paper were optimized by the Gaussian 98 program [31] both at the *ab initio* HF/3-21G and the hybrid-density-functional B3LYP/6-31G** method [32]. The latter method was extensively used in recent calculations of enols of carboxylic acid derivatives and was shown to give pK_{Enol} values reliable to within 2 units [2a][28][33]. All optimized structures, including higher-energy conformers, were verified by means of their *Hessian* matrices to be local minima on the potential-energy surfaces at both levels of theories, except for the ditipyl derivatives, for which frequency calculations at the higher level are too demanding. Structures determined at the B3LYP level showed the same geometric characteristics as in the HF level. The calculated energies of the compounds are given in *Table 1*. Structures of the most stable conformer for each species are illustrated in *Fig. 1*, and structures of higher energy isomers are in *Fig. 2*.

REFERENCES

[1] a) A. F. Hegarty, P. O'Neill, in 'The Chemistry of Enols', Ed. Z. Rappoport, Wiley, Chichester, 1990, Chapt. 10, p. 639; b) A. J. Kresge, *Chem. Soc. Rev.* **1996**, *25*, 275.

[2] a) S. Sklenak, Y. Apeloig, Z. Rappoport, *J. Am. Chem. Soc.* **1998**, *120*, 10359; b) P. Perez, A. Toro-Labbé, *J. Phys. Chem. A* **2000**, *104*, 1557.

[3] P. J. O'Neill, A. F. Hegarty, *J. Chem. Soc., Chem. Commun.* **1987**, 744; B. M. Allen, A. F. Hegarty, P. O'Neill, M. T. Nguyen, *J. Chem. Soc., Perkin Trans. 2* **1992**, 927; B. M. Allen, A. F. Hegarty, P. O'Neill, *J. Chem. Soc., Perkin Trans. 2* **1997**, 2733.

[4] a) J. Frey, Z. Rappoport, *J. Am. Chem. Soc.* **1995**, *117*, 116; b) J. Frey, Z. Rappoport, *J. Am. Chem. Soc.* **1996**, *118*, 3994; c) J. Frey, Z. Rappoport, *J. Am. Chem. Soc.* **1996**, *118*, 5169, 5182; d) Z. Rappoport, J. Frey, M. Sigalov, E. Rochlin, *Pure Appl. Chem.* **1997**, *69*, 1933.

[5] a) J. K. Mukhopadhyaya, S. Sklenak, Z. Rappoport, *J. Am. Chem. Soc.* **2000**, *122*, 1325; b) J. K. Mukhopadhyaya, S. Sklenak, Z. Rappoport, *J. Org. Chem.* **2000**, *65*, 6856; c) Y. X. Lei, G. Cerioni, Z. Rappoport, *J. Org. Chem.* **2000**, *65*, 4028.

[6] H. E. Zimmerman, T. W. Cutshall, *J. Am. Chem. Soc.* **1958**, *80*, 2893; H. E. Zimmerman, T. W. Cutshall, *J. Am. Chem. Soc.* **1959**, *81*, 4305; L. Graham, D. L. H. Williams, *J. Chem. Soc., Chem. Commun.* **1991**, 407; D. L. H. Williams, L. Xia, *J. Chem. Soc., Perkin Trans. 2* **1992**, 747; D. L. H. Williams, L. Xia, *J. Chem. Soc., Perkin Trans. 2* **1993**, 1429.

[7] F. B. Thole, J. F. Thorpe, *J. Chem. Soc.* **1911**, *99*, 2208; N. Bland, J. F. Thorpe, *J. Chem. Soc.* **1912**, *101*, 856.

[8] W. C. Deno, W. E. Billups, R. E. DiStefano, K. M. McDonald, S. Schneider, *J. Org. Chem.* **1970**, *35*, 278.

[9] J. E. Hendon, A. W. Gordon, M. Gordon, *J. Org. Chem.* **1972**, *37*, 3184.

[10] J. Kagan, L. Tolentino, M. G. Ettlinger, *J. Org. Chem.* **1970**, *45*, 3085.

[11] J. S. Fitzgerald, G. A. R. Kon, *J. Chem. Soc.* **1937**, 725.

[12] M. E. Jung, R. W. Brown, *Tetrahedron Lett.* **1981**, *22*, 3355; S. F. Tan, *Aust. J. Chem.* **1972**, *25*, 1367; P. F. Vlad, M. Z. Krimer, *Org. Prep. Proced. Inter.* **1998**, *30*, 657.

[13] a) S. F. Tan, K.-P. Ang, H. Jayachandran, *J. Chem. Soc., Perkin Trans. 2* **1986**, 973; b) S. F. Tan, K. P. Ang, H. Jayachandran, *J. Chem. Soc., Perkin Trans. 2* **1983**, 473; c) S. F. Tan, K. P. Ang, H. L. Jayachandran, A. J. Jones, W. R. Begg, *J. Chem. Soc., Perkin Trans. 2* **1982**, 513; d) A. K. Kiang, S. F. Tan, W. S. Wong, *J. Chem. Soc. C* **1971**, 2721.

[14] a) L. Crombie, D. E. Games, M. H. Knight, *J. Chem. Soc. C* **1967**, 763; b) L. Crombie, R. V. Dove, *J. Chem. Soc., Chem. Commun.* **1987**, 438; c) L. Crombie, R. V. Dove, *J. Chem. Soc., Perkin Trans. 1* **1996**, 1695; d) P. E. Hansen, S. Bolvig, T. Kappe, *J. Chem. Soc., Perkin Trans. 2* **1995**, 1901.

[15] P. Hunt, D. N. P. Satchell, *J. Chem. Soc.* **1964**, 5437.

[16] W. E. Truce, C. E. Olsen, *J. Am. Chem. Soc.* **1953**, *75*, 1651.

[17] a) E. Montoneri, E. Tempesti, L. Giuffre, A. Castoldi, *J. Chem. Soc., Perkin Trans. 2* **1980**, 662; b) L. Guiffre, E. Montoneri, E. Tempesti, V. Pozzi, F. Rossi, *Chim. Indus., Milano* **1981**, *63*, 85.

[18] Y. Ogata, K. Adachi, *J. Org. Chem.* **1982**, *47*, 1182.

[19] a) Y. Chiang, A. J. Kresge, P. Pruszynski, N. P. Schepp, J. Wirz, *Angew. Chem., Int. Ed.* **1990**, *29*, 792; Y. Chiang, A. J. Kresge, V. V. Popik, N. P. Schepp, *J. Am. Chem. Soc.* **1997**, *119*, 10203; b) J. Andraos, Y. Chiang, A. J. Kresge, I. G. Pojarlieff, N. P. Schepp, J. Wirz, *J. Am. Chem. Soc.* **1994**, *116*, 73.

[20] J. Firl, W. Runge, *Z. Naturforsch.* **1974**, *29B*, 393; J. Firl, W. Runge, *Angew. Chem., Int. Ed.* **1973**, *12*, 618.

[21] G. Cerioni, A. Plumitallo, J. Frey, Z. Rappoport, *Magn. Reson. Chem.* **1995**, *33*, 669.

[22] A. D. Allen, B. Cheng, M. H. Fenwick, W.-W. Huang, S. Misshia, D. Tahmassebi, T. T. Tidwell, *Org. Lett.* **1999**, *1*, 693.

[23] K. Müllen, P. Wolf, in 'The Chemistry of Enones', Eds. S. Patai, Z. Rappoport, Wiley, Chichester, 1989, Chap. 12, pp. 513–558.

[24] B. Capon, in 'The Chemistry of Enones', Eds. S. Patai, Z. Rappoport, Wiley, Chichester, 1989, p. 1063.

[25] V. Bertolasi, P. Gilli, V. Ferretti, G. Gilli, *J. Chem. Soc., Perkin Trans. 2* **1997**, 945.

[26] a) R. Kakou-Yao, A. Saba, N. Ebby, M. Pierrot, J. P. Aycard, *Acta Crystallogr., Sect. C* **1999**, *55*, 1591; b) R. Kakou-Yao, E. Degny, N. Ebby, J. P. Aycard, *Z. Kristallogr. – New Cryst. Struct.* **1999**, *214*, 483; c) R. Kakou-Yao, A. Saba, N. Ebby, J. P. Aycard, *Z. Kristallogr. – New Cryst. Struct.* **1999**, *214*, 481.

[27] K. A. Parker, G. A. Breault, *Tetrahedron Lett.* **1986**, *27*, 3835.

[28] J. Gao, *J. Mol. Struct.* **1996**, *370*, 203; Y. Apeloig, D. Arad, Z. Rappoport, *J. Am. Chem. Soc.* **1990**, *12*, 9131; S. Sklenak, Y. Apeloig, Z. Rappoport, *J. Chem. Soc., Perkin Trans. 2* **2000**, 2269.

[29] H. Yamataka, Z. Rappoport, *J. Am. Chem. Soc.* **2000**, *122*, 9818.

[30] H. Falk, K. Schlögl, *Monatsh. Chem.* **1965**, *96*, 276; A. Horeau, *Tetrahedron Lett.* **1962**, 965.

[31] Gaussian 98, Revision A.6, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B.

Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh PA, 1998.
[32] a) A. D. Becke, *Phys. Rev.* **1988**, *A38*, 3098; b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev.* **1988**, *B37*, 785.
[33] P. G. Conrad, R. S. Givens, B. Hellrung, C. S. Rajesh, M. Ramseier, J. Wirz, *J. Am. Chem. Soc.* **2000**, *122*, 9346.

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