β-Diketone Interactions. Part 2.† Pentane-2,4-dione and Tertiary Amines; Infrared, Nuclear Magnetic Resonance, and *Ab Initio* Investigations

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The claim that pentane-2,4-dione (PD) is the 100% enol tautomer in triethylamine (TEA) has been shown to be based on a misinterpretation of ^{1}H n.m.r. spectra. I.r. analysis shows the presence of 8.2% of the keto tautomer at infinite dilution in TEA. An alternative mode of interaction, other than the accepted hydrogen bonding one, is proposed and supported by *ab initio* calculations on propanedial (malondialdehyde, MDA) and NH_3. This interaction involves amine addition to the carbonyl group of PD.

The hydrogen bonding of the enol tautomers of β-diketones, and in particular that of pentane-2,4-dione (PD), has fascinated chemists for many years.[1] The equilibrium between the keto (**k**) and enol (**e**) tautomers is conventionally expressed as the percentage of **e** and this is sensitive to a variety of influences, the chief of which is the polarity of the solvent. Low polarity favours (**Ie**).

Triethylamine (TEA) as solvent behaves anomalously; in it PD is reported to be 100% (**Ie**) even when PD is in excess.[2–5] Only at very low mole fractions of TEA (<0.1) can the signals of the keto tautomer be detected by 60 MHz ^{1}H n.m.r. spectroscopy.[4] The explanation for the complete enolization of PD in TEA has been in terms of stronger hydrogen bonding, with or without proton transfer as in (**II**) and (**III**). This supposedly displaces the equilibrium entirely in favour of (**Ie**).

Such bifurcated hydrogen bonding as (**III**) has been proved to be the mode of interaction between PD and diethylamine, the crystal structure of a 1:1 adduct being reported in Part 1.[6] This revealed (**IV**), a unique arrangement of NHO hydrogen bonds in a dimer array.

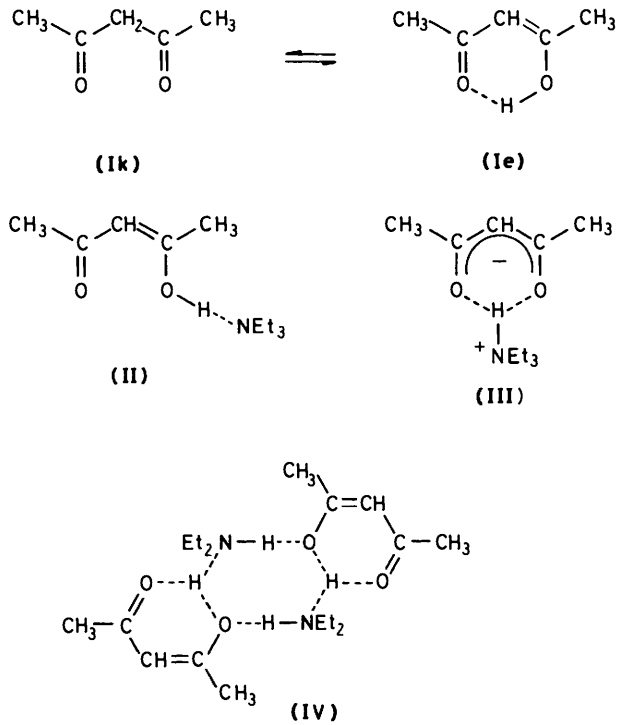
Although ^{1}H n.m.r. spectra of PD in TEA solutions do indeed show only signals due to (**Ie**), it was observed during our i.r. investigations of the same solutions that beside the dominant carbonyl absorption of the enol tautomer, there was the separate absorption of the keto tautomer albeit much weaker. This peak persisted even when the mole fraction of PD was very low.

Since the initial work of Reeves 30 years ago, ^{1}H n.m.r. analysis has been the method of choice for analysing the keto ⇌ enol equilibrium almost without exception. Curiously an i.r. method for enol determination was published many years ago.[7] We have returned to this approach for PD–TEA and other systems, and through the results obtained we have been led to the conclusion that PD and TEA do not primarily interact in the manner of (**II**) or (**III**) but *via* labile carbon–nitrogen bonding.

Experimental and Results

Materials.—PD was purified by the method of Fujinaja and Lee[8] and distilled from P_2O_5 before use. Amines except TEA were analytical grade reagents used as supplied. TEA, CCl_4, and dimethyldiethylene glycol (diglyme) were dried and distilled before use.

Instruments.—N.m.r.: 60 MHz ^{1}H n.m.r. on PE R12B and JEOL PMX60si spectrometers; 250 MHz on a Bruker WM250 instrument. I.r.: PE 983G spectrometer, BaF_2 0.1 mm cells, QUANT program for analysis of peak areas.



PD–TEA.—Under certain conditions the keto signal of PD can be observed in ^{1}H n.m.r. spectra of this system and below 0.1 mole fraction of TEA a broad CH_2 signal is seen even in the 60 MHz spectrum. Table 1 lists spectra details for PD–TEA and reveals certain features, in addition to the disappearance of the keto signals, which require explanation.

First, over the critical range of concentration below 0.3 mole fraction TEA there is no convergence of the labile proton signals, so that although bases catalyse the keto ⇌ enol exchange this is not sufficient to reduce half-lives below that of the n.m.r. timescale. Second, all signals broaden with increasing TEA but to a limiting width for (**Ie**) whereas for (**Ik**) this broadening is eventually so large as to make the signals unobservable. Third, the enol proton shifts only slightly upfield on dilution with TEA, not dramatically as previously reported.[2] These results are more in keeping with an interaction between TEA and (**Ik**) rather than the conventional hydrogen bonding explanation involving (**Ie**).

† Part 1, ref. 6.

Table 1. ^{1}H N.m.r. spectral details of CH, CH_2, and OH signals of PD in TEA

Mole fraction TEA	enol CH δ	enol CH $\omega_{\frac{1}{2}}$/Hz	enol OH δ	enol OH $\omega_{\frac{1}{2}}$/Hz	keto CH_2 δ	keto CH_2 $\omega_{\frac{1}{2}}$/Hz
0.005	5.54	2.7	15.58	2.0	3.6	2.7
0.010	5.53	2.0	15.59	2.0	3.59	5.3
0.015	5.51	2.7	15.55	2.7	3.60	8.7
0.020	5.54	3.3	15.58	3.3	3.60	10.7
0.048	5.53	6.0	15.56	6.7	3.59	21.3
0.074	5.55	7.3	15.55	9.3	3.59	33.3
0.083	5.50	8.0	15.53	10.7	3.58	40.0
0.163	5.47	14.7	15.54	12.0	~3.6	45
0.256	5.48	10.7	15.41	14.7	~3.6	60
0.329	5.49	9.3	15.39	13.2	*a*	

[a] Signal no longer observable.

Table 2. ^{1}H N.m.r. spectral details of CH, CH_2, and OH signals of PD in TBA

Mole fraction TBA	enol CH δ	enol CH $\omega_{\frac{1}{2}}$/Hz	enol OH δ	enol OH $\omega_{\frac{1}{2}}$/Hz	keto CH_2 δ	keto CH_2 $\omega_{\frac{1}{2}}$/Hz
0.026	5.57	2.0	15.30	4.0	3.63	4.0
0.049	5.53	4.7	15.23	6.0	3.59	18.0
0.078	5.52	8.0	15.03	10.7	~3.5	40
0.098	5.52	10.7	14.83	11.3	~3.5	43
0.133	5.51	13.3	14.57	14.7	~3.5	53
0.195	5.51	16.0	14.54	18.7	~3.6	60

Table 3. ^{1}H N.m.r. spectral details of CH, CH_2, and OH signals of a 1:1 mole ratio of PD–TEA in $CDCl_3$ solution (5% w/v)

Temperature (°C)	enol CH δ	enol CH $\omega_{\frac{1}{2}}$/Hz	enol OH δ	enol OH $\omega_{\frac{1}{2}}$/Hz	keto CH_2 δ	keto CH_2 $\omega_{\frac{1}{2}}$/Hz
+25	5.51	5.0	14.9	425	2.60	20
−10	5.55	2.5	14.7	400	3.65	10
−50	5.59	2.0	15.0	250	3.71	5

The CH_2 signals of the keto tautomer of PD in the presence of an equimolar amount of TEA can still be seen by diluting the system with $CDCl_3$ and using 250 MHz ^{1}H n.m.r. spectroscopy. At 25 °C the signals were clearly evident and sharper than in PD–TEA mixtures, and cooling to −50 °C resulted in further sharpening (Table 3). Dilution of PD–TEA by $CDCl_3$ also allowed the keto signals to be seen with the 60 MHz spectrometers, but not as clearly. Whatever process is responsible for the loss of keto signals under normal conditions would appear to have a half-life in the same range as n.m.r. processes.

Although it has proved possible to demonstrate the presence of (**Ik**) in PD–TEA mixtures by n.m.r. spectroscopy the method is unsuitable for estimating the composition of this system in terms of percentage enol. However, i.r. spectra clearly display keto and enol carbonyl stretching vibrations at 1 709 and 1 618 cm^{-1}, the former being the out-of-phase mode and part of a doublet.[9] The in-phase mode is at 1 727 cm^{-1}

The i.r. spectrum of a 0.5 mole fraction PD–TEA mixture is shown in Figure 1. The absence of a characteristic broad and

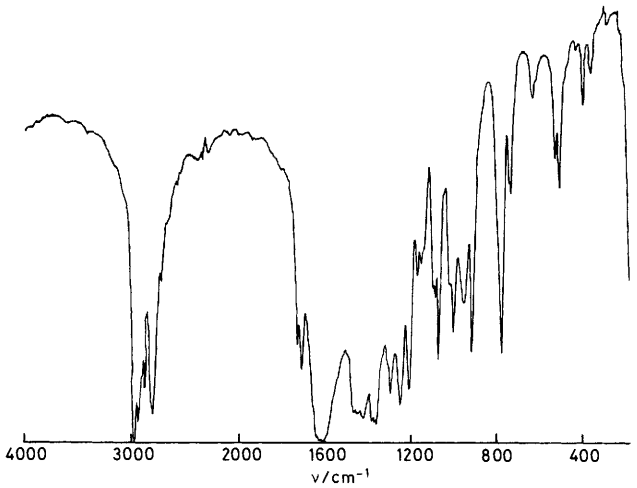


Figure 1. I.r. spectrum of 1:1 PD–DEA mixture

intense hydrogen bonding absorption mode in the region above 2 000 cm^{-1} that could be attributed to OHN is further evidence for the absence of such an interaction. The enol tautomer's intramolecular hydrogen bond OHO vibration is at 2 801 cm^{-1} showing a marked similarity to that of neat PD at 2 750 cm^{-1}.[9]

Accurate calibration is necessary if i.r. peak intensities are to be used for quantitative analysis. Diglyme was chosen as a suitable solvent for PD since n.mr. studies on this system showed there to be no change in tautomer composition over a wide range of concentration, unlike other solvents. Curiously this solvent has not been reported on previously, probably since its relative permittivity (ε) is not in the literature, and this is the parameter most used in discussion solvent polarity.

Solutions of PD in diglyme (1—5% w/w) were left to attain equilibrium for several days. Temperature equilibrium was assumed in the sample compartment of the i.r. spectrometer after 4 h. Absorbance spectra yielded linear plots of carbonyl absorbance *versus* mole fraction for both the enol and keto bands. The ratio of the slopes of these plots was 0.287 from which the percentage enol tautomer is calculated as 77.7 ± 1.2%. This value is in good agreement with that of 79.6 ± 0.5% obtained by ^{1}H n.m.r. signal integration of the CH_3 resonances at δ 1.99 (enol) and 2.16 (keto).

The i.r. method assumes that enol and keto carbonyl bands share the same extinction coefficient. Calculation of these, using the ^{1}H n.m.r. result, gave ε (keto) 800 ± 124 and ε (enol) 798 ± 14 dm^3 mol^{-1} cm^{-1}.

Once the PD–diglyme system had been used to calibrate the concentration of the respective species against absorbance peak areas, the QUANT software package of the PE983G spectrometer was used to determine the enolic composition of another solvent system with a polarity similar to TEA (ε 2.5) and which also had a window in its i.r. spectrum in the region above 1 500 cm^{-1}.

Carbon tetrachloride (ε 2.2) met these requirements and gave % enol values of 96.8 ± 0.3% by i.r. and 94.7 ± 0.2% by n.m.r. analysis. A value of 95% is reported in the literature.[10] In CCl_4 the i.r. result is quoted for extrapolation to infinite dilution whereas the value for the n.m.r. is for a mole fraction of 0.1 as conventionally reported.

The system PD–TEA gave 91.8 ± 0.1% enol by i.r. analysis, again at infinite dilution. This value is in keeping with the behaviour in a solvent of low polarity. The value of 100% enol reported in the literature [2–5] is wrong.

PD–Tributylamine (TBA).—PD in excess of TBA also shows no keto signals in the n.m.r. spectrum. From a serial dilution

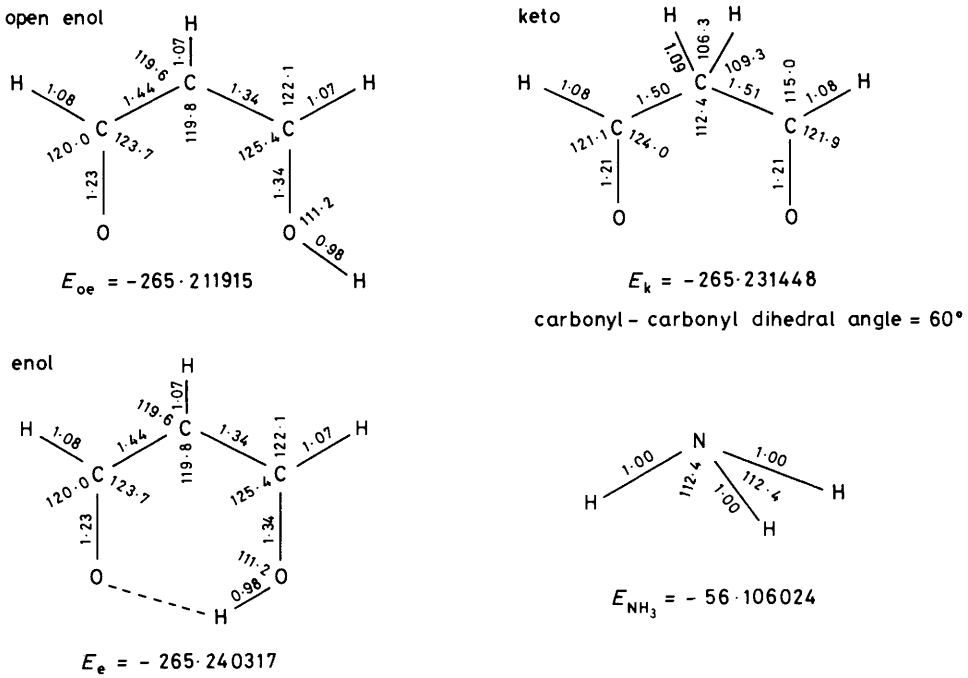


Figure 2. Propanedial (MDA) and NH_3 4-31G total energies (hartree)

study it was observed that the CH_2 signal broadened with increasing TBA concentration and disappeared above 0.20 mole fraction TBA. The i.r. spectrum clearly exhibited the keto carbonyl band at 1 711 cm^{-1} at higher TBA mole fractions, proving again that this tautomer was still present. The n.m.r. results are given in Table 2.

PD–Di-isopropylethylamine (DPEA).—The keto CH_2 signal in the n.m.r. spectrum is observed at higher mole fractions of DPEA than either for TEA or TBA. Serial dilution studies showed that even at 0.3 mole fraction of the amine the keto signals are clearly distinguishable. In this system the OH signal shifted upfield significantly and there was also considerable sharpening.

2,2,6,6-*Tetramethylheptane*-3,5-*diones–TEA.*—The t-butyl β-diketone, $(CH_3)_3CCOCH_2COC(CH_3)_3$ and TEA gave ^1H n.m.r. spectra in which the keto tautomer CH_2 signal was clearly observed at all concentrations even on a 60 MHz spectrometer. The OH chemical shift was insensitive to TEA, and the CH signal sharp. The percentage enol is 99%, determined by both n.m.r. and i.r. analysis. In $CDCl_3$ this β-diketone is reported to be 100% enol.[11] No other solvent has been studied.

Theory

Ab initio LCAO-MO-SCF calculations were performed on the ULCC CRAY-1S computer using the GAMESS program.[12] Single determinant SCF wave functions are generally adequate for calculations of the energies of hydrogen bonds between closed shell molecules since the molecular extracorrelation energy and the zero-point vibrational corrections are both small, *ca.* 5%.[13–15]

Theoretical Calculations.—The fully optimized geometries (bond lengths to within ±0.005 Å and angles to within ±0.1°) and total energies for propanedial (malondialdehyde MDA) and NH_3 are given in Figure 2. Total energies have been calculated using the split-valence 4-31G basis set.[16] Figure 3 gives the fully optimized geometries and total energies for MDA + NH_3 interactions along selected intermolecular vectors.

The energy E_{oe} (open enol tautomer) is reported here for the first time. The energies E_k (keto) and E_e (enol) have been computed previously by others but the values we report are significantly lower.[17,18]

The hydrogen-bond energy of MDA enol tautomer is defined as $E_e - E_{oe}$ and is computed to be −75 kJ mol^{-1}. Previous estimates of this energy have been as disparate as −18[19] and −97 kJ mol^{-1},[20] with a third value of −33 kJ mol^{-1}[21] also offered. A review of the hydrogen bonding of the enol tautomer concludes that it is strong, and estimates that the bond energy should be above 50 kJ mol^{-1} judging by molecular parameters such as $R(O \cdots O)$.[1] The value reported here is very much in keeping with this conclusion.

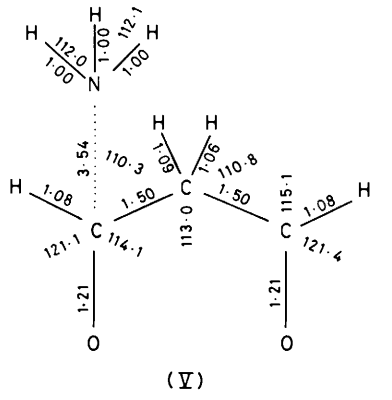
The energy of enolization of PD has been measured in the gas phase at −8.9 kJ mol^{-1}[22] and in the liquid phase at −11.9 kJ mol^{-1}.[22,23] For MDA we can define it as $E_e - E_k$ and the value obtained theoretically is −23 kJ mol^{-1}.

Discussion

In 1958 Reeves[2,3] studied PD and amine mixtures and interpreted his observation in terms of hydrogen-bonding adducts such as (**II**) and (**III**) which explained the 100% enolization he and later workers reported. Indeed this view would appear to be strengthened by the *X*-ray crystal structure of PD·DEA which does involve bifurcated hydrogen bonding between the two.[6]

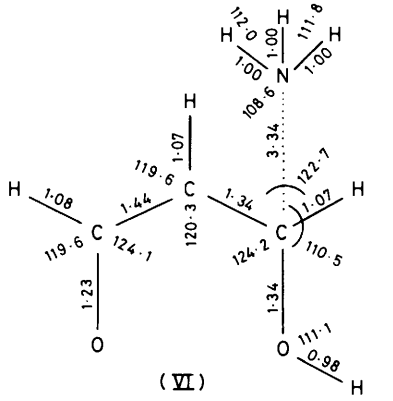
For PD and TEA we now offer an alternative explanation of their mode of interaction and one in which hydrogen bonding is not the primary attraction. Putting PD into TEA does have an effect on the keto $\rightleftharpoons$ enol equilibrium, shifting it towards the enol tautomer, but only to the same extent that any other low-polarity medium would. In other words our proving that there is 8.2% of the keto tautomer still present in an infinitely dilute solution of PD in TEA removes the need to postulate any

Non-hydrogen bonding structures



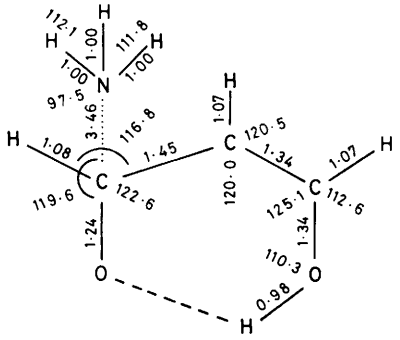
(V)

E_{V} = -321·343740



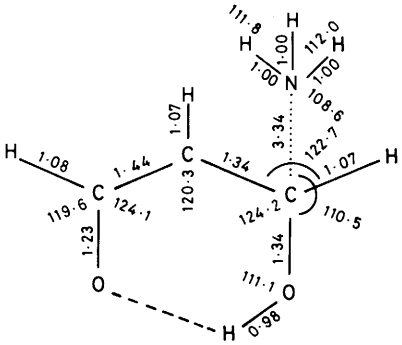
(VI)

E_{VI} = -321·325087



(VII)

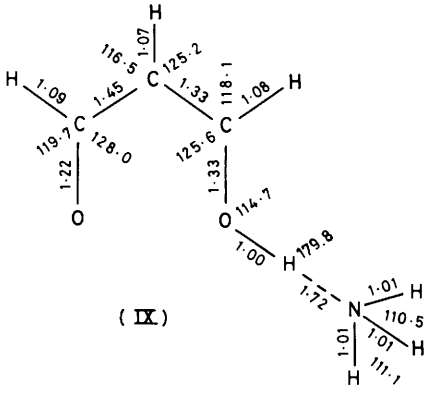
E_{VII} = -321·351984



(VIII)

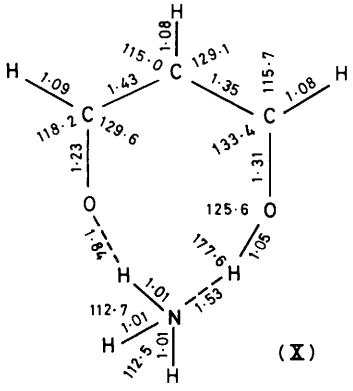
E_{VIII} = -321·353678

Hydrogen-bonded structures



(IX)

E_{IX} = -321·345711



(X)

E_{X} = -321·360867

Figure 3. Propanedial (MDA)–NH_3 4-31G total energies (hartree)

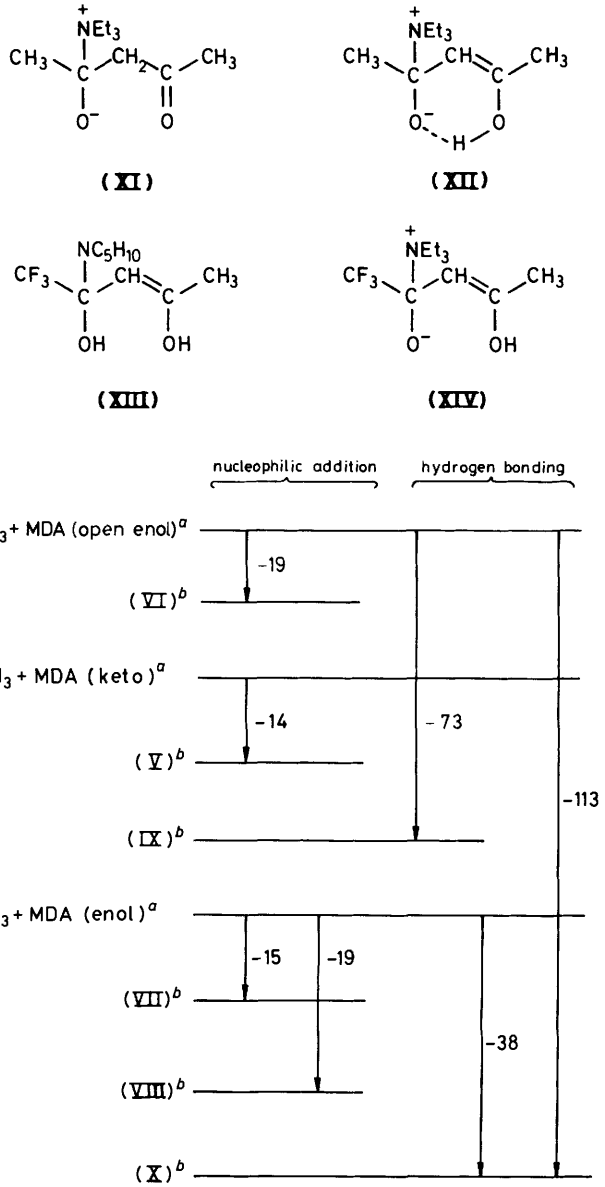


Figure 4. Energy differences (kJ mol^{-1}) of the molecular species (not to scale). [a]See Figure 2. [b]See Figure 3

special interaction between the two. Nevertheless it is still necessary to explain why the keto CH_2 signals are not observed in the ^1H spectra of such solutions.

We believe that PD and TEA interact through carbon–nitrogen bonding which produces a labile adduct with a sufficiently short half-life to make the keto form just unobservable by 60 MHz n.m.r. spectroscopy under normal operating conditions. Using an excess of PD, or diluting the system with $CDCl_3$, or employing 250 MHz, or reducing the temperature are all steps which should favour the observation of the keto signal and this has proved to be so.

Using bulkier amines should make the adduct less stable and the combination PD–TBA and PD–DPEA allow the keto signal to be seen at higher amine concentration than with TEA. Moreover these amines also produce a marked upfield shift of the enol OH signal, indicating that hydrogen bonding may be the preferred interaction for these combinations where carbon–nitrogen approach is restricted.

The adduct PD–TEA probably takes the form of a zwitterion with either the keto or enol tautomers (**XI**) and (**XII**). Support for this thesis also comes from the work of Gazit and Rappoport[24] who showed that the condensation of $CH_3COCH_2COCF_3$ and aryl aldehydes to give $ArCH{=}CHCOCH_2COCF_3$ occurs in the presence of piperidine but not TEA. They postulated that the reaction proceeded *via* a carbinolamine (**XIII**) which the secondary amine produces. This then reacts with the aldehyde to give a methyl condensation product.

The use of TEA in place of piperidine led to the formation of a zwitterion (**XIV**) from which loss of a proton prior to condensation is much less likely to occur.

Additional support for the zwitterion adduct has been obtained from *ab initio* calculations on MDA and NH_3, modelling the β-diketone and amine respectively. Figure 3 shows that, of the various interactions possible between these molecules; the lowest computed energy state for carbon–nitrogen interaction is (**VIII**), lower than for the classical hydrogen-bonding interaction (**IX**).

The minimum-energy geometry of the MDA–NH_3 complex is in fact computed to be a hydrogen-bonded arrangement (**X**) where the NH_3 acts in the capacity of both acceptor and donor. This latter role however is not available to TEA. Figure 4 shows the relative energies and energy differences of the key species. The two hydrogen bonds of (**X**) have a total energy of −113 kJ mol^{-1} relative to the open enol form, and −38 kJ mol^{-1} relative to the closed enol. In (**X**) the average NHO hydrogen bond is −57 kJ mol^{-1}, again relatively strong with respect to normal hydrogen bonds.

It is gratifying to discover that our *ab initio* calculations on MDA–NH_3 predict that for PD–TEA nucleophilic attack intermediates are favoured over hydrogen bonding. The MDA–NH_3 calculations show that interaction of NH_3 at keto and enol tautomers is not significantly different (*ca.* 15 kJ mol^{-1}). Thus the keto $\rightleftharpoons$ enol equilibrium is not disturbed by this interaction and the polarity of the medium remains the primary perturbing factor.

The life-times of the adducts varies but it cannot at this stage be said whether the enol–amine forms are longer or shorter lived than the keto–amine forms.

Acknowledgements

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