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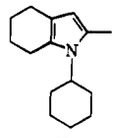

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Carbon-13 and Low-Temperature Proton Nuclear Magnetic Resonance Study of the Interaction of Acetylacetone with Diethylamine and Triethylamine[1a]

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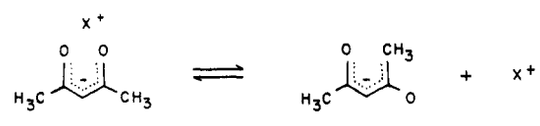
The ^1H NMR spectra of mixtures of acetylacetone with diethylamine and triethylamine have been examined at low temperature under conditions such that torsion about the partial double bonds in the acetylacetonate moiety is slow on the NMR time scale. Configurational assignments and distributions and NMR chemical shifts are used to define the nature of the interaction between the amine and acetylacetonate molecules in methanol and chloroform as solvents. The data suggest that, in methanol, mixtures of chelated ion pairs and solvent separated ions are found for both amines. Proton and carbon spectra indicate that in chloroform diethylamine gives rise to a chelated ion pair, while the diketone–triethylamine complex is best described as one in which the chelated enol form of acetylacetone is hydrogen bonded to triethylamine.

Reeves and Schneider have used proton nuclear magnetic resonance spectroscopy to study the interactions between acetylacetone (Hacac) with diethylamine and triethylamine.[2] Their study of spectra above room temperature was used to provide information about the rates of keto–enol tautomerism and proton exchange. We have shown that low-temperature ^1H NMR spectra of acetylacetonates[3-5] can be used to determine the configuration of the acetylacetonate moiety and draw conclusions about the degree and kind of association of the acac anion with alkali metal cations. For this reason, it seemed likely that examination of the low-temperature spectra of mixtures of Hacac and amines might provide further information about these interactions and could complement and extend the findings of Reeves and Schneider.

Results

The ^1H NMR spectrum of an equimolar mixture of acetylacetone (Hacac) and diethylamine in methanol-d_4 at −57 °C exhibits three singlets deriving from the acetyl methyl groups of the acac moiety. Two of these singlets at δ 1.89 and 2.27 are of equal intensity and must arise from species with the *E,Z* configuration, which have diastereotopic methyl groups. The signal at δ 1.85 arises from species with the *Z,Z* configuration in which the methyl groups are homotopic. Integration of the acetylmethyl signals indicated that the *Z,Z* configuration was present to the extent of 47% under these conditions. The use of triethylamine as base instead of diethylamine changed the situation only slightly. The proportion of acetylacetonate in the *Z,Z* form increased to ca. 60%.



When the solvent was changed to deuteriochloroform, both mixtures exhibited only single resonances for the acetyl methyl peaks at δ 1.92 at −57 °C. Unless the coalescence point for topomerization has been drastically lowered in this solvent, the observation of only a single resonance can be taken to mean that only the *Z,Z* form is present. The chemical shifts observed for the resonances both in the amine and acac moieties can provide further information about the states of association of these ammonium acetylacetonates. These data are given in Tables I and II. The ^{13}C NMR spectra of both mixtures in chloroform were also measured. The ^{13}C chemical shifts of the ethyl carbon atoms provide complementary information about protonation at nitrogen and are given together with the shifts in free amines and their benzoates in Table III.

Discussion

Reeves and Schneider concluded from their study that the keto–enol equilibrium of acetylacetone was markedly shifted

Table I. ^{1}H NMR Chemical Shifts (δ Units) in Methanol-d_4

	Hacac[d] Ambient	Et_2NH Ambient	Et_2NH·Hacac[a] −57 °C	$\Delta\delta$[b]	Et_3N Ambient	Et_3N·Hacac[a] −57 °C	$\Delta\delta$[b]
NCH_2CH_3		1.11	1.22	−0.11	1.05	1.18	−0.13
NCH_2CH_3		2.62	2.92	−0.30	2.56	2.95	−0.29
Acetyl	2.05		1.85 *Z,Z*			1.93 *Z,Z*	
Methyl			1.89 *E,Z*			1.93 *E,Z*	
			2.27 *E,Z*			2.21 *E,Z*	
Methine[c]	5.64						

[a] Amines were in slight excess (2–5%) over acetylacetone. [b] Shifts are defined as $\Delta\delta = \delta_{amine} - \delta_{complex}$. [c] Obtained in methanol. In methanol-d_4 this signal could not be observed due to facile H/D exchange. [d] Enolic.

Table II. ^{1}H NMR Chemical Shifts (δ Units) in Chloroform-*d*

	Hacac[c] Ambient	Et_2NH Ambient	Et_2NH·Hacac[a] −57 °C	$\Delta\delta$[b]	Et_3N Ambient	Et_3N·Hacac[a] −57 °C	$\Delta\delta$[b]
NCH_2CH_3		1.11	1.28	−0.17	1.03	1.07	−0.04
NCH_2CH_3		2.67	2.96	−0.30	2.53	2.61	−0.04
Acetyl	2.02		1.92	+0.10		2.10	−0.08
Methyl							
Methine	5.56		5.28	+0.28		5.57	−0.01

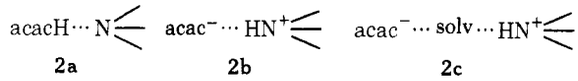
[a] Amines were in slight excess (2–5%) over acetylacetone. [b] Shifts are defined by $\Delta\delta = \delta_{amine} - \delta_{complex}$. [c] Enolic.

Table III. ^{13}C NMR Chemical Shifts (δ Units) in Chloroform-*d* at Ambient Temperature

	Et_2NH	Et_2NH·Hacac	$\Delta\delta$[a]	$Et_2NH_2^+C_6H_5CO_2^-$	$\Delta\delta$[a]
NCH_2CH_3	15.5	14.6	+0.9	11.4	+4.1
NCH_2CH_3	44.3	43.9	+0.6	41.9	+2.4
	Et_3N	Et_3N·Hacac	$\Delta\delta$	$Et_3NH^+C_6H_5CO_2^-$	$\Delta\delta$
NCH_2CH_3	11.9	12.1	−0.2	8.7	+3.2
NCH_2CH_3	46.6	46.6	0	44.9	+1.7

[a] Shifts are defined as $\Delta\delta = \delta_{amine} - \delta_{complex}$.

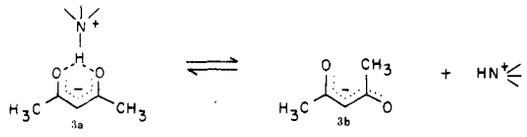
by amines to the point that such solutions are completely enolic. We, too, failed to observe resonances which could be attributed to the keto form. However, we can further differentiate between three limiting structures for "enolic" acetylacetone. Two of these structures, **2a** and **2b**, represent tightly associated complexes. Structure **2a** can be described



2a **2b** **2c**

as "enol-like" while **2b** is "enolate-like". The enolate-like form can also exist as solvent-separated ions **2c**, in addition to the intimate ion pair represented by **2b**.

Examination of the chemical shifts of the diethylamine–acac mixture indicates that the complex is completely ionized (or nearly so) in methanol. The acetyl methyl resonances are very similar to those observed for Na(acac), and the methyl and methylene resonances of the amine moiety experience downfield shifts from their positions in the free amine. We can thus represent the *Z,Z* configuration as **3a**. The similarity of

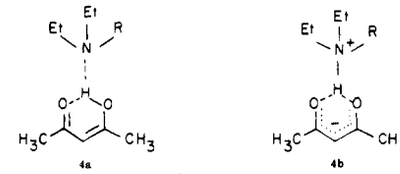


chemical shifts between this complex and those of Na(acac), which is known to be dissociated,[4,5] suggest that the *E,Z* form exists mostly as solvent-separated ions. Approximately the same interpretation can be given to the data for the triethylamine complex in methanol. The proportion of the *Z,Z* form is greater, suggesting that the conjugate acid of triethylamine is a stronger hydrogen-bond donor and thus better able to stabilize the *Z,Z* configuration in which the hydrogen is chelated by the two oxygen atoms.

This interpretation is in accord with the pK_a values for these three compounds (measured in aqueous solution at 30 °C): diethylamine (conjugate acid), 11.00;[6] triethylamine (conjugate acid), 10.74;[6] acetylacetone, 9.00.[7] Acetylacetone is substantially more acidic than the conjugate acids of either diethylamine or triethylamine, and essentially complete proton transfer is expected in aqueous solution or a comparable polar, ionizing solvent. The ions are not completely separated in methanol, and considerable association is observed, with a greater degree observed for the complex with the more acidic triethylammonium ion.

The situation is different in the less polar, poorly ionizing solvent chloroform. Here, relative acidities of Hacac and the amine conjugate acids must be changed. Acetylacetone is an uncharged acid and its acidity is reduced, while the conjugate acids of the amines are charged and dissociation does not increase the number of ions.

In this solvent the behavior of the two amines is different,



R = H, Et

reflecting their different relative acidities. The proton and carbon chemical shifts (Tables II and III) suggest that structure **4b** makes a major contribution to the structure of the diethylamine complex, which is best considered as an ion pair, while the triethylamine complex is essentially un-ionized and is best represented by structure **4a**.

The resonance of the protons in acetyl methyl groups of the diethylamine complex appears at δ 1.92, shifted upfield from that in the enol form of acetylacetone, as is the signal at δ 5.28 arising from the methine proton. The ethyl protons in the amine moiety exhibit downfield shifts comparable to those observed for both amines in methanol solution. These shifts are in accord with the behavior expected for ionic structure **4b**.

The shifts observed for triethylamine are quite different. The resonances from both the amine and acetylacetone moieties suffer very small downfield shifts. The small shifts observed suggest that the structures are not changed very much from the separate neutral compounds and that the complex is best represented by the un-ionized structure **4a**. Apparently, in this solvent the greater acidity of the conjugate acid of triethylamine (over that of diethylamine) is sufficient to suppress proton transfer, and the complex is one in which the triethylamine is only hydrogen bonded to the enolic proton of acetylacetone.

Carbon chemical shifts are also sensitive to amine protonation. Protonation is accompanied by characteristic upfield shifts of several ppm for the β carbons and smaller variable shifts for the α carbons.[8] Table III gives carbon chemical shifts for the two complexes and those in the free amines and the benzoate salts for comparison. Both amines exhibit upfield shifts for the β carbons (methyl carbons) upon conversion to the benzoates in accord with previous observations. The chemical shifts of both methyl and methylene carbon atoms in the triethylamine complex are essentially unchanged from those in the free amine, while those in the diethylamine complex experience upfield shifts which are about 25% of those in the benzoate. While these data may not quantitatively reflect the contributions of the two structures **4a** and **4b**, they do indicate that the contribution of **4b** is much greater for diethylamine.[9]

Experimental Section

Acetylacetone, diethylamine, triethylamine, and benzoic acid were obtained from commercial sources. The complexes were prepared in situ by mixing weighed amounts of the appropriate compounds.

^{1}H NMR spectra were measured on a Varian A60-A spectrometer (60 MHz). Chemical shifts are given in δ units relative to internal tetramethylsilane. Temperatures were controlled with a V-6040 variable-temperature controller and determined by measurement of methanol spectra as outlined in the Varian users manual. Carbon spectra were measured at ambient temperature on a JEOL FX-60 spectrometer (15.04 MHz) and are expressed in δ units relative to internal Me_4Si.

Registry No.—Et_2NH·Hacac, 62154-14-7; Et_3N·Hacac, 62154-15-8; $Et_2NH_2^+C_6H_5CO_2$, 940-90-9; $Et_3NH^+C_6H_5CO_2^-$, 941-02-6.

References and Notes

(1) (a) This work was supported by the National Science Foundation and the National Institute of General Medical Sciences. We also thank the National Science Foundation for an equipment grant used for the purchase of the FX-60 FT-NMR spectrometer used to obtained ^{13}C spectra for this study. (b) Alfred P. Sloan Foundation Fellow, 1972–1976. (c) On leave from the University of Tokyo.
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(9) The changes in the chemical shifts of the acetylacetone moiety are also greater when diethylamine is added. The chemical shifts for the carbonyl, methine, and methyl groups were: Hacac, 191.2, 100.3, 24.7; Hacac·$NHEt_2$, 190.5, 99.4, 26.0; Hacac·NEt_3, 191.2, 100.1, 25.0.

Alkylation and Ring Contraction Reactions of 1,3,4-Benzotriazepine-2,5-dione Systems

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Alkylation studies on 3,4-dihydro-3-methyl-1*H*-1,3,4-benzotrazepine-2,5-dione (**1**) and its 4-methyl isomer **2** have led to a method for the regiospecific introduction of one or two (similar or dissimilar) alkyl groups to these systems, which allows the preparation of a wide variety of 1,3,4-trialkyl-3,4-dihydro-3-methyl-1*H*-1,3,4-benzotriazepine-2,5-diones. When ethyl bromoacetate was employed as the alkylating agent, ring contraction reactions occurred to produce 3-methyl-2,4(1*H*,3*H*)-quinazolinedione (**15**) from both **1** and **2**. Treatment of **2** with aqueous base also resulted in ring contraction to produce 3-(methyl)amino-2,4(1*H*,3*H*)-quinazolinedione (**30**), whereas **1**, under the same conditions, yielded 2-(*o*-aminobenzoyl)-1-methylhydrazine (**25**). Further utility of 1-acetyl-1-methylhydrazine was demonstrated in the preparation of authentic samples of **25** and **30**. Mechanisms of the ring contraction reactions are discussed.

We have recently reported[1] syntheses of 3,4-dihydro-3-methyl-1*H*-1,3,4-benzotriazepine-2,5-dione (**1**) and its 4-methyl isomer **2**. It was found that both **1** and **2** undergo selective monomethylations with sodium hydride and methyl iodide in dimethylformamide, to yield the same benzotriazepinedione **3**.[2] In this report we describe additional alkylation studies on **1** and **2**, some of which have led to interesting ring contraction reactions.

Alkylation reactions which were performed with **1** and **2** are described in Scheme I. All of the depicted reactions generally produced a single product in good yield. The selectivity of the monoalkylation reactions which produced 4-alkyl derivatives of **1** and 3-alkyl derivatives of **2** allowed the systematic introduction of a variety of alkyl groups into the benzotriazepinediones. In all cases, sodium hydride was the base employed and the solvent was dimethylformamide. Thus,