Observation of an Amide Enol of Bis(2,4,6-triisopropylphenyl)acetic Acid

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Enols of carboxylic acid derivatives are very rare species.[1] A few acid enols (1,1-enediols) were generated recently by Wirz's[2], Kresge's,[2c,d,3] and Hegarty's[4] groups but were not characterized by NMR spectroscopy. Amide enols are even more scarce than 1,1-enediols, and it was noted that they "do not appear to have been described in the literature"[5a] although $(NC)_2C{=}C(OH)NH_2$ is enolic in the solid state.[6] Amide enols were suggested as intermediates in electrophilic reactions of malonamide,[5] and the hydration of ketenimine[7] and preparation of the bulky amide enols **1** by acid-catalyzed hydration of bis(pentamethylphenyl) ketenimine were recently reported.[8] Ketonization of **1** to amides **2** competes with elimination of amine to form ketene **3**.

$$\underset{\mathbf{1}}{Ar_2C{=}C(OH)NHR} \quad \underset{\mathbf{2}}{Ar_2CHCONHR} \quad \underset{\mathbf{3}}{Ar_2C{=}C{=}O}$$

$$Ar{=}C_6Me_5$$

We have recently reported the generation of ≥98% solution of the 1,1-enediol **5** of ditipylacetic acid **6** (tipyl = Tip = 2,4,6-$iPr_3C_6H_2$)[9,10] by hydration of the bulky ketene **4**[11] (eq 1) and fully characterized it by NMR spectroscopy. We report now the use of a similar methodology for the generation and observation of the enol of *N*,*N*-dimethylditipylacetamide by addition of dimethylamine to ketene **4**.

$$\underset{\mathbf{4}}{Tip_2C{=}C{=}O} + H_2O \rightleftharpoons \underset{\mathbf{5}}{Tip_2C{=}C(OH)_2} \rightarrow \underset{\mathbf{6}}{Tip_2CHCOOH} \quad (1)$$

Several amines were found unsuitable for generating enols of ditipylacetamide. For example, the reaction of Ph_2NH consumed <10% of **4** in 3 days and was much slower than the following tautomerization of the intermediate. The amine should be secondary in order to avoid an enamine−imine tautomerization (eq 2).[12] Me_2NH was found suitable since its low boiling point enables an easy removal of its excess at the end of the reaction, and its low molecular weight enabled the use of high concentrations, making the formation of the intermediate faster than its tautomerization, thus enabling its observation.

$$Ar_2C{=}C(OH)NHR \rightleftharpoons Ar_2CHC(OH){=}NR \quad (2)$$

Due to the low solubility of **4** in many solvents,[10] we used THF-d_8 or CCl_4 as a cosolvent with CD_3CN and DMF-d_7. The reaction was conducted at 243 K since detection of the final product, *N*,*N*-dimethylditipylacetamide, **7**, is hampered because its ^{1}H NMR spectrum is broad at >243 K due to the occurrence of a stereodynamic process on the NMR time scale.

When liquid Me_2NH was added to **4** in a 5:1 DMF-d_7−CCl_4 mixture at 243 K in an NMR tube, the ^{1}H NMR spectrum which was recorded immediately (Figure 1) was consistent with that of the enaminol **8** (eq 3). Chemical shifts and signal assignments are given in Table 1. The presence of the high-field (δ 0.03 ppm) two Me-iPr signals is typical of $Tip_2C{=}CRR'$ systems (e.g, when R = R′ = OH, H, $OSiMe_3$ or R = H, R′ = OH). The four Ar-H signals and the individual signal for each iPr-Me group except for accidental overlap indicate diastereotopicity of these signals, reflecting a slow rotation around the Tip-C bonds.[10] This is consistent with the chiral propeller conformation (cf. **8a**) typical to gem-diarylvinyl systems.[13] The low-field OH signal in the DMF-rich mixture is reminiscent of the positions of the OH signals of enols[14] and of the enediol **5**.[10] **8** was also generated in 5:1 CD_3CN−THF-d_8, but its enolic OH signal (at a higher field than in DMF:CCl_4) was broad, and its assignment is only tentative.

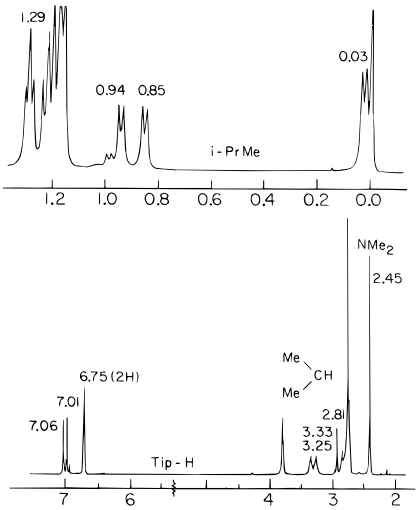
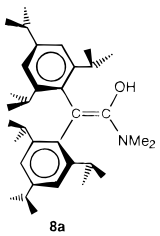


Figure 1. ^{1}H NMR spectrum of enolamine **8** in 5:1 DMF-d_7:CCl_4 at 243 K. (Upper) the iPr-Me region (expanded); (lower) from the NMe_2 to the OH region. The numbers are the chemical shifts in ppm.

$$\underset{\mathbf{4}}{Tip_2C{=}C{=}O} + Me_2NH \rightleftharpoons \underset{\mathbf{8}}{Tip_2C{=}C(OH)NMe_2} \rightarrow \mathbf{9} \rightarrow \underset{\mathbf{7}}{Tip_2CHCONMe_2} \quad (3)$$



8a

The ^{13}C NMR spectrum of **8** in 5:1 DMF−CCl_4 displays distinct signals for almost all its carbons, corroborating the

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Table 1. ^{13}C and ^{1}H NMR Chemical Shifts (in ppm) for Enol **8** at 243 K[a]

	DMF-d_7:CCl_4[b]		CD_3CN:THF-d_8[b]
assignment	^{13}C NMR	^{1}H NMR	^{1}H NMR
iPr-Me	22.53	0.03 (2 Me)	0.04 (2 Me)
	22.61	0.85	0.93
	23.99	0.94	0.97
	24.09	1.17 (4 Me)	1.15
	24.32 (2 Me)	1.21	1.16 (4 Me)
	24.33 (3 Me)	1.23	1.23
	24.52	1.29 (2 Me)	1.25
	25.68		1.28
	25.83		
o-iPr-CH	30.63	2.81 (3 CH)[c,d]	2.75 (4 CH)[c]
	30.74	2.86[c]	3.16[c]
	30.94	3.25[c]	3.29[c]
	d	3.33[c]	
p-iPr-CH	34.04		
	34.29		
NMe	37.62	2.45, 2.81	2.44, 2.72
	42.12		
C_β	82.98		
m-Tip-C	121.61	6.75 (2 H)	6.77
or Tip-H	121.76	7.01	6.79
	122.04	7.06	7.02
	122.12		7.04
ipso-Tip-C	138.88		
	138.99		
p-Tip-C	145.42		
	145.45		
o-Tip-C	147.26		
	147.98		
	148.40		
	149.29		
C_α	157.43		
OH		9.40	6.84[e]

[a] All chemical shifts versus internal TMS standard. Integration values are given only in the case of signal overlap or accidental isochrony. [b] Solvents ratio is 5:1. [c] Either *o*- or *p*-CH signal. [d] Signals overlap the solvent multiplet. [e] Tentative assignment; see text.

existence of a conformation **8a**. A gated decoupled ^{13}C NMR spectrum enabled the signal assignment given in Table 1. Comparison with the spectra of the related enediol **5** shows many similarities; i.e., $\delta^{13}C_\alpha$ and $\delta^{13}C_\beta$ of **5** in DMF-d_7 are at 157.02 and 80.4 ppm, respectively.[10]

The ^{1}H NMR spectrum of a sample of **8** in CD_3CN-THF-d_8 which stood for 1 day at 243 K was identical with that of an independently prepared amide **7**. From integration of the Tip-H signals, the half-life ($t_{1/2}$) for the disappearance of **8** in 5:1 CD_3CN:THF-d_8 at 273 K is ca. 20 min. When a catalytic amount of TFA was added to **8** at 243 K, **4** was formed and started to accumulate according to the ^{1}H spectrum. When Me_2NH was added to this solution, all the newly formed **4** reacted immediately to give **8**, suggesting that under these conditions the Me_2NH can be lost to regenerate **4**. This resembles the formation of **3** from **1** under acidic conditions.[8]

The ^{1}H NMR spectrum of the initially observed product **9** from the tautomerization of **8** at 273 K differs from that of amide **7** isolated at the end of the reaction.[15] After 2 h at 273 K, enol **8** had disappeared completely and both **9** and amide **7** were formed. With the progress of time, **9** was converted to **7**. Since identification of **7** at 273 K by its 400 MHz ^{1}H NMR spectrum is complicated by broadening, probably due to a rotation around the Tip-C bonds, **7** was identified by its spectrum at 243 K. At 243 K the number of iPr and Ar-H signals suggest a frozen propeller conformation[16] for **7**. The α-CH signal of **7** in solution remains sharp at all temperatures.

We were unable so far to identify unequivocally the primary product **9**. Fortunately, we once isolated it, admixed with ketene **4**, and immediately recorded its ^{1}H NMR spectrum at 243 K. Unfortunately, it decomposed before we had time to determine its ^{13}C NMR and IR spectra, and further isolation experiments had failed. In the C-*Me* region **9** displays seven one iPr-Me doublets and one four iPr-Me signals (another Me overlaps the residual ketene signals); 2 N-Me singlets at 2.78 and 2.90, a singlet at 5.90 (presumably α-CH), and four Tip-H singlets at 6.78, 6.84, 6.98, and 6.99 ppm are observed. **7** displays eight one iPr-Me doublets and one four iPr-Me signals, 2 N-Me signals at 3.06 and 3.08, a singlet at 5.73 (Tip_2CH), and four Tip-H signals at 6.80, 6.84, 6.91, and 6.97 ppm. The $t_{1/2}$ value for generation of **7** from **9** was estimated as 96 min at 273 K from the integration ratios of the α-CH singlets.

The similarity of the spectra of **7** and **9** tentatively suggests that they are different conformers of the amide. The slow conversion of **9** to the presumably more stable **7** at the low reaction temperature is not unreasonable in view of the crowding of the system which seems higher than that of related derivatives, such as acid **6**, for which a free rotation at 243 K is shown by its sharp NMR spectrum.

In conclusion, we have shown that enols of carboxylic acid derivatives like the 1,1-enediol[10] and an amide enol can be prepared in solution as relatively long-lived species whose NMR spectra can be recorded and analyzed, when bulky aryl groups confer on them kinetic stability. These and related species are under study.

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(16) The propeller conformation is suggested by analogy with that of other polyarylalkyl moieties.