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RESTRICTED ROTATION IN AMIDES IV. RESONANCE ASSIGNMENTS IN TERTIARY AMIDES AND THIOAMIDES UTILIZING NMR SHIFT REAGENTS[1]

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The use of lanthanide metal chelates to induce large chemical shifts in the NMR spectra of lone pair-bearing compounds has been recently reported.[3,4] It has been shown that the induced shift in a roughly planar molecule is related to the cube of the reciprocal distance between the metal and the proton in question.[3] We have now successfully employed europium (III)-2,2,6,6-tetramethyl-3,5-heptadione Eu(DPM)$_3$[5] for making resonance assignments in amides.

It is well known that NMR spectra of tertiary amides frequently exhibit separate signals for the groups syn and anti to the carbonyl oxygen.[6] We expected that the addition of Eu(DPM)$_3$ to a carbontetrachloride solution of an amide would lead to complexation of the metal by the lone pairs of the carbonyl oxygen[7], and thus the resonance associated with the syn group would suffer a larger induced shift than the resonance of the anti group. Examination of a number of simple tertiary amides, whose resonances we had previously assigned by means of the NOE[8] has shown that our expectations were borne out. (Table I, 1-5).

As usual, the gradual addition of Eu(DPM)$_3$ was necessary to avoid ambiguities resulting from signal crossover.[9] In each case the signal exhibiting the greatest shift sensitivity also broadened most presumably due to

TABLE I

Shift of N-CH Protons in CCl_4 at 60 MHz

No	Compound	Chemical Shift[a] (Hz)					
		syn to C=0			anti to C=0		
		no Eu	with Eu[b]	Δ[c]	no Eu	with Eu[b]	Δ[c]
1.	Dimethylformamide	167	216	49	175	199	24
2.	Dibenzylformamide	258	315	57	249	277	28
3.	Benzylmethylformamide CH_3	164	214	50	169	197	28
	CH_2	266	320	54	262	288	26
4.	Dimethylacetamide	171	225	54	181	213	32
5.	Dibenzylthioformamide	267	293	26	294	307	13
6.	Benzyl(o-tolyl)formamide	285	324	39	280	300	20
7.	Benzyl(o-tolyl)acetamide[d]	282[e]	326[e]	44			
8.	o-Chloro-Dibenzylbenzamide	275[e]	312[e]	37	245	271	26

a. Downfield from TMS.
b. $Eu(DPM)_3$/Amide = 0.1
c. Δ = induced shift
d. Single isomer
e. Center of AB quartet

electron-nucleus dipolar relaxation.[10] Thioamides apparently behave analogously to amides (5).

The preponderant isomers in N-benzyl-N-(o-tolyl)formamide and acetamide had been assigned[11] the structures with the benzyl group syn to the carbonyl oxygen and, indeed, these assignments are confirmed by the induced shift method (6,7). Similarly, our previous assignment[8] of the low field signals in the methylene region of the NMR spectra of o-substituted-N,N-dibenzyl-benzamides to the methylene group syn to the carbonyl oxygen (by extrapolation of the NOE results from the 3,5-dinitro-analog) has been shown to be correct (8).

Examination of the low temperature NMR behavior of o-chloro-N,N-dibenzylbenzamide with $Eu(DPM)_3$ is particularly revealing. It should be recalled that at low temperatures the methylene portion of the NMR spectrum consists of two, partly overlapping, AB quartets.[12] Thus, the effect of the shift reagent on each proton of the two pairs of geminal protons could be observed. A similar situation obtains in the case of N-benzyl-N-(o-tolyl)acetamide[11] and N-(o-tolyl)-4,4-dideutero-1,4-dihydro-3(2H)isoquinolinone[11] both of which exhibit AB quartets in the N-benzyl methylene portion of their NMR spectra. From the induced shifts observed (Table II) it is obvious that one benzyl proton in

TABLE II

Chemical Shift of Non-Equivalent $N-CH_2$-Protons in CCl_4 at 60 MHz

No.	Amide		Chemical Shift of Benzyl Methylene[a] syn to C=O		anti to C=O	
			A^b	B^b	A^b	B^b
9.	o-chloro-N,N-dibenzylbenzamide[c]	no Eu	322	234	255	243
		with Eu[d]	400	269	303	282
		Δ[e]	78	35	48	39
10.	N-Benzyl-N-(o-tolyl) acetamide[f]	no Eu	307	257		
		with Eu[d]	356	296		
		Δ[e]	49	39		
11.	N-(o-tolyl)-4,4-dideutero-1,4-dihydro-3(2H)-isoquinolinone[f]	no Eu			290	268
		with Eu[d]			313	292
		Δ[e]			23	24

a. Hz downfield from TMS
b. Calculated
c. -30°C
d. $Eu(DPM)_3$/amide = 0.1
e. Δ = induced shift
f. Single isomer

o-chloro-N,N-dibenzylbenzamide (9) is particularly deshielded (A) and suffers the largest induced shift as well. Thus, it would appear that there exists an energetically favored conformation in which a proton of the methylene group syn to the carbonyl is closest to the oxygen. Such a conformation, in which the C-H bond is essentially coplanar with and parallel to the C=O bond, would

also account for the significantly larger chemical shift non-equivalence observed for N-methylene groups syn to the carbonyl oxygen than that observed for the anti methylene groups.[12] In support of this interpretation, the two geminal N-benzyl methylene protons of N-(o-tolyl)-4,4-dideutero-1,4-dihydro-3(2H)-isoquinolinone, which are equidistant from the carbonyl moiety, are equally shifted upon $Eu(DPM)_3$ addition.

Complexation of tertirary amides with $Eu(DPM)_3$ is thus the most convenient and versatile experimental route currently available for resonance assignment. The method is completely unambiguous when signals for both amide isomers can be seen, because the induced shift of the group syn to the carbonyl oxygen is invariably larger than the induced shift of the anti group. Application to tertiray amides with single isomers and to secondary amides will be reported separately.

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