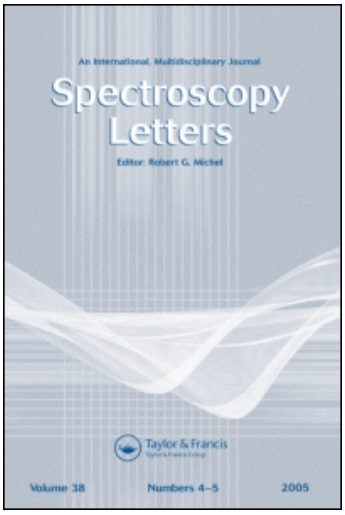

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Lanthanide Shift Reagents. Paper 20. Lanthanide Binding Constants for Amides and Quaternary Salts

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LANTHANIDE SHIFT REAGENTS PAPER 20[1]

LANTHANIDE BINDING CONSTANTS FOR AMIDES AND QUATERNARY SALTS

Key Words: Europium Shift Reagents, NMR,
Equilibrium Binding Constants.

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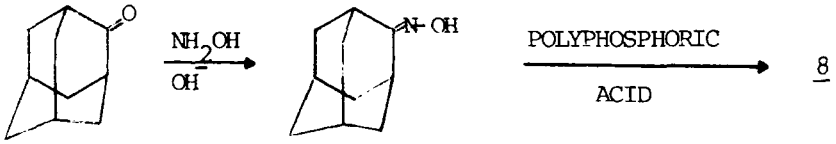
INTRODUCTION

In continuation of our work[1] on the interaction of organic materials with Europium shift reagents we report the first absolute binding constants (K) for amide substrates with $Eu(thd)_3$. We have also measured K for some quaternary ammonium and phosphonium salts with the fluorinated analogue, $Eu(fod)_3$-d_{27}.

EXPERIMENTAL

Equilibrium binding constants (K) were determined by 60MHz ^1H NMR spectroscopy at 27° using the method of Bouquant and

Chuche as described in previous publications[1,3]. They are considered to be accurate to ±5%. All amide and quaternary salt substrates were obtained from commercial sources with the exception of the azahomoadamantanone, 8, which was synthesised by the following route[4].



Deuterated chloroform (99.8% isotopic purity, Merck Sharp and Dohme Ltd.) was pre-dried thoroughly[2] before use with 4A molecular sieve.

RESULTS AND DISCUSSION

Values of the binding constants, K, are given in the Table.

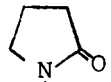
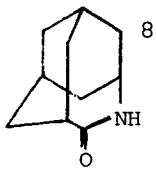
AMIDES

Large values of K were obtained for the amides, lactams and urea (1-8) with the non-fluorinated reagent, $Eu(thd)_3$. These can be contrasted with the low values derived for aliphatic and alicyclic ketones[1] (between 5 and 20) and the surprisingly high figures of greater than 100 for some nitrogen heterocycles[5] with the same lanthanide complex. The maximum

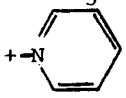
TABLE

Equilibrium Binding Constants (K) at 27° in $CDCl_3$ for amides with $Eu(thd)_3$ and quaternary salts with $Eu(fod)_3$-d_{27}.

A. Amides with $Eu(thd)_3$*.

	COMPOUND	K		COMPOUND	K
1.	$HCON(CH_3)_2$	190			
2.	$CH_3CON(CH_3)_2$	422	6.	R=H	211
3.	$(CH_3)_2CHCONH_2$	155	7.	R=CH_3	244
4.	$C_6H_5CONH_2$	575	8.		210
5.	$(CH_3)_2NCON(CH_3)_2$	302			

B. Quaternary halide salts $R_1R_2R_3R_4M^+X^-$ with $Eu(fod)_3$-d_{27}

COMPOUND	R_1	R_2	R_3=R_4	M	X	K
9.	$CH_3(CH_2)_{11}$	$CH_3(CH_2)_{11}$	CH_3	N	Br	954
10.	$CH_3(CH_2)_{15}$	CH_3	CH_3	N	Br	313
11.	$CH_3(CH_2)_{15}$				Br	600
12.	CH_3	C_6H_5	C_6H_5	P	Br	359
13.	C_2H_5	C_6H_5	C_6H_5	P	Br	145

* Infrared carbonyl stretching frequencies in chloroform solution were: 1, 1665; 2, 1630; 4, 1675; 5, 1625; 7, 1670cm^{-1}.

value was found for benzamide, 4, and this can be related to electron donation from the phenyl ring. A similar enhancement of K was noted for α-tetralone (when compared with cyclohexanone[1]) and acetophenone compared with dialkyl

ketones[6]. Changing the ring size from 5 to 6 in the lactams (compounds 6 and 8) had no noticable effect on the value of K (as was also found in the alicyclic ketones[1] cyclo-pentanone, -hexanone and -heptanone).

The increase in the binding constant from dimethylformamide to dimethylacetamide (1 to 2) can be attributed to the inductive electron release of the methyl group on the carbonyl function. (Lewin[7] has shown, by a relative method of measuring K, that 2 binds $Eu(thd)_3$ about three times as strongly as 1).

There was no apparent correlation between the values of K for five amides and the carbonyl infrared stretching frequencies in chloroform solution (see Table). Because the incremental dilution procedure needs equimolar amounts of a single substrate, we were unable to measure K for unsymmetrical amides like $CH_3NHCOCH_3$ and $PhNHCOCH_3$ which are known to exist as rotameric mixtures with the lanthanides[8].

QUATERNARY AMMONIUM AND PHOSPHONIUM SALTS

The proton NMR signals for quaternary ammonium salts in $CDCl_3$ are not shifted on addition of $Eu(thd)_3$. We have previously shown that simple ethers are similarly uncomplexed by this non-fluorinated reagent[1]. By contrast, the fluorinated $Eu(fod)_3$ and $Yb(fod)_3$ reagents cause large shifts with ethers and epoxides and several K values have been

determined[1]. The success of $Eu(fod)_3$ in simplifying the spectra of some quaternary ammonium and phosphonium salts[9-11] led us to measure K by the incremental dilution procedure for five of these compounds (see Table). The only comparative figures for K were determined[11] by Armitages method for tetraethylammonium and phosphonium halides. They are lower than the figures reported here (e.g. K for Et_4PCl with $Eu(fod)_3 > 100$) and this feature of the Armitage method has been noted previously for aliphatic alcohols[12].

There is now general agreement that the lanthanide reagent binds to the anion involved[11] and the Table shows that the greater steric hindrance to binding in the ethyl salt, 13, than in the methyl analogue, 12, results in a lower value for K. There is also obviously tigher binding in the less crowded pyridinium salt 11 than the tetra alkyl ammonium bromide, 10.

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