Effect of Alkali Metal Ions on the Torsional Barrier in Amides

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Summary The observed barrier height to torsion about the N–C(O) bond in *NN*-dimethylacetamide is found to be dependent on the presence of lithium ions, these ions serving to increase the barrier.

MANY papers concerning the torsional barrier about the N–C(O) bond in amides have appeared.[1] These investigations have mainly been concerned with establishing the nature of substituent and, to a lesser extent, solvent effects on the barrier height. So far, no information concerning the influence of alkali metal ions on the barrier height of amides is available; this is surprising, considering the known strength of amide–alkali metal interaction,[2] and the importance of these ions in the dynamics of protein denaturation.[3] We now report our initial findings with the system *NN*-dimethylacetamide (DMA)–lithium perchlorate.†

We find that the observed barrier height (expressed as $\Delta G^{\ddagger}$) to internal rotation in DMA (as a *ca.* 1M-solution in dioxan) is strongly dependent on the presence of lithium perchlorate, with increasing salt concentration serving to raise the barrier increasingly.‡ Thus, over the investigated $LiClO_4$ concentration range (0—1M), the torsional barrier height of DMA is observed to increase from *ca.* 17·7 to *ca.* 20·0 kcal mol^{-1} (Table). This dependence of the barrier height on lithium perchlorate concentration is not linear over the entire range of salt concentration; rather, the barrier tends to level off at the highest concentrations used (corresponding to 1·5:1 and 1:1 mole ratios of DMA to $LiClO_4$).

Spectral parameters[a] *and free energy of activation for torsion about the* N–C(O) *bond in DMA*;[b] *lithium ion dependence*

Lithium perchlorate concentration (M)	$\Delta\nu_{ab}$(Hz)[c]	T_c (°C)[d]	$\Delta G^{\ddagger}(T_c)$ (kcal mol^{-1})[e]
0	7·4	60·0	17·7
0·065	7·5	61·9	17·8
0·125	7·5	65·8	18·0
0·250	7·7	73·0	18·4
0·500	7·8	85·8	19·1
0·750	7·8	96·4	19·7
1·000	8·0	101·4	20·0

[a] All n.m.r. measurements were performed on a Varian A-60A spectrometer equipped with a V-6040 variable temperature accessory. The side-band modulation technique was used in the chemical shift measurements. [b] The DMA concentration was held constant at 1M. [c] Refer to the chemical shift difference between the *NN*-dimethyl proton resonances at the slow-exchange limit. [d] The coalescence temperature (T_c) measurements were based on the chemical shift difference of the protons of an ethylene glycol sample, and utilized the temperature-shift correlation of van Geet (*Analyt. Chem.*, 1970, **42**, 279). [e] Calculated from the Eyring equation at T_c.

These results, which we attribute to the influence of lithium ions,§ may be accounted for as follows. The hindered internal rotation in amides is usually ascribed, in the valence bond formalism, to the partial double bond character in the N–C(O) bond resulting from the contribution of the resonance form (**1B**) [(**1A**) is usually taken to be the only remaining principal contributing structure]. Complexation by lithium at the oxygen should, *via* an

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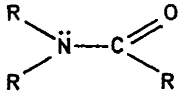
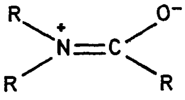
† All materials used in this study were purified by standard procedures.[4]

‡ Barrier heights were determined by substitution of rate constants derived from the n.m.r. coalescence method (use of a Gutowsky–Holm equation[5]) into the Eyring equation, assuming a transmission coefficient of unity.

§ We cannot as yet comment on the extent of ion pairing present in the investigated solutions.

inductive effect, serve to increase the relative importance of **(1B)** as a contributing structure, and thus raise the barrier. Complexation at nitrogen, on the other hand, should prevent the lone pair on nitrogen from delocalizing into the carbonyl bond, and thus decrease the barrier. Ample evidence exists that the preferred site of metal ion complexation is at oxygen;[6] a slight amount of complexation at nitrogen cannot be ruled out. Under conditions of rapid lithium ion exchange, the observed rate constant for rotation about the amide linkage will be given by the expression, $k_i = \sum_i p_i k_i$. where k_i is the rotational rate constant associated with the ith species existing in solution, with p_i being its fractional population. The dominant observed effect thus appears to be due to complexation at oxygen.


(1 A)


(1 B)

Our findings contrast with the only previously reported study of the influence of a metal ion on the rotational barrier of an amide, wherein Ag^+ was found to decrease markedly the observed $\Delta G^\ddagger$ to rotation in DMA(aq.).[7]

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[1] For a recent review, see W. E. Stewart and T. H. Siddall, tert., *Chem. Rev.*, 1970, **70**, 517.

[2] For example, see J. N. Butler and J. C. Synnot, *J. Amer. Chem. Soc.*, 1970, **92**, 2602.

[3] For a recent review, see P. H. von Hippel and T. Schleich in "Structure and Stability in Biological Macromolecules," eds. S. N. Timasheff and G. D. Fasman, Marcel Dekker, Inc., New York, 1966.

[4] D. D. Perrin, W. L. Armarego, and D. R. Perrin, "Purification of Laboratory Chemicals," Pergamon Press, New York, 1966.

[5] H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, 1956, **25**, 1228.

[6] For examples, see W. E. Bull, S. K. Madan, and J. E. Willis, *Inorg. Chem.*, 1963, **2**, 303; J. Bello, D. J. Haas, and H. R. Bello, *Biochem.*, 1966, **5**, 2539; C. Lassigne and P. Baine, *J. Phys. Chem.*, 1971, **75**, 3188.

[7] P. A. Temussi, T. Tancredi, and F. Quadrifoglio, *J. Phys. Chem.*, 1969, **73**, 4227.