# Structure and Bonding in N-Methylacetamide Complexes of Alkali and Alkaline Earth Metals

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# Structure and bonding in *N*-methylacetamide complexes of alkali and alkaline earth metals

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A detailed crystallographic investigation of *N*-methylacetamide complexes of Li, Na, K, Mg and Ca has been made in view of its importance in the coordination chemistry and biochemistry of alkali and alkaline earth metals. The metal ions bind to the amide oxygen causing an increase in the carbonyl distance and a proportionate decrease in the central C—N bond distance. The decrease in the central C—N distance is accompanied by an increase in the distance of the adjacent C—C bond and a decrease in the adjacent C—N bond distance. The metal ion generally deviates from the direction of the lone pair of the carbonyl oxygen and also from the plane of the peptide, the out-of-plane deviation varying with the ionic potential of the cation. The metal–oxygen distance in alkali and alkaline earth metal complexes of a given co-ordination number also varies with the ionic potential of the cation, as does the strength of binding of the cations to the amide. The amide molecules are essentially planar in these complexes, as expected from the increased bond order of the central C—N bond. The NH bonds of the amide are generally hydrogen bonded to anions. The structures of the amide complexes are compared with those of other oxygen donor complexes of alkali and alkaline earth metals. The structural study described here also provides a basis for the interpretation of results from spectroscopic and theoretical investigations of the interaction of alkali and alkaline earth metal cations with amides.

## 1. Introduction

Williams (1971) and Freeman (1973) reviewed the importance of ion–amide interactions in inorganic biochemistry. In particular, the binding of alkali and alkaline earth metal salts to the peptide bond is of significance in understanding a variety of phenomena of biological importance such as conformational transitions of polypeptides and proteins, ion-complexation by macrocyclic antibiotic ionophores and so on (von Hippel & Schleich 1969; Ovchinnikov *et al.* 1974; Balasubramanian & Misra 1977; Rao 1977). Several workers have

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made quantum-mechanical calculations on the interactions of model amides with alkali and alkaline earth metal cations while others have investigated these interactions through vibrational and n.m.r. spectroscopy. Yet, we do not have detailed information on the structure and bonding in alkali and alkaline earth metal complexes of amides, recent X-ray crystallographic investigations (Haas 1964; Bello *et al.* 1966) being limited to a preliminary examination of Li and Na complexes of *N*-methylacetamide. We, therefore, considered it extremely important to investigate crystal and molecular structures of a series of alkali and alkaline earth metal complexes of the reference secondary amide, *N*-methylacetamide (NMA). Such a study would also be of value to the coordination chemistry of the alkali and alkaline earth cations (Truter 1973; Poonia & Bajaj 1979). In this paper, we discuss the detailed structures of Li, Na, K, Mg and Ca complexes of NMA, paying particular attention to the nature of the metal coordination and the effect of cation binding on peptide geometry. Other aspects of interest are the dependence of metal–donor (oxygen) distances on the metal ion and the size of the polyhedron, the deviation of the metal ion from the oxygen lone-pair direction and from the peptide plane, the non-planarity of the peptide group, and the nature of the binding of anions to peptides. We also discuss the results from spectroscopic and theoretical studies of cation–amide interactions in the light of the structures of the amide complexes obtained by us. Further, the stereochemistry, metal–oxygen distances and other structural features of the amide complexes are compared with those of other alkali and alkaline earth metal complexes including those with antibiotics such as antamanide, nonactin and valinomycin.

## 2. EXPERIMENTAL

Attempts were made to grow single crystals of complexes of NMA with different salts of Li, Na, K, Mg and Ca. The complexes used in the study described here were made of the following salts: LiCl, $NaClO_4$, KSCN, $MgCl_2$ and $CaCl_2$. In general, the complexes were prepared by heating appropriate amounts of the salt and of NMA (Balasubramanian & Shaikh 1973; Gentile & Shankoff 1965) or by heating the two under reflux in a solvent. Anhydrous salts were used in all cases except that of the Ca complex where $CaCl_2 2H_2O$ was used. Crystals were grown by using different solvents; an acetone–methanol solvent system for the Li complex, and methanol for the Na complex. Crystals of K and Mg complexes were obtained after refluxing the salt with NMA in an acetone medium. Crystals of the Ca complex were obtained by refluxing a solution in methanol of $CaCl_2 2H_2O$ and four times its molar proportion of NMA. Identities of the complexes were established by elemental analysis.

## 3. CRYSTALLOGRAPHY

All the crystals used for data collection were sealed in Lindemann capillaries because of their hygroscopic nature. X-ray diffraction data were measured by means of a CAD-4 diffractometer equipped with a graphite monochromator. The unit-cell parameters were determined by a least-squares procedure based on twenty-five high-order reflexions. Crystal data on all the amide complexes studied by us are presented in table 1. The X-ray reflexions were measured by using an $\omega'/2\theta$ scan mode with a scan rate of $1°$ min$^{-1}$ to the limit of $\theta$ given in table 2. During the data collection for each crystal, the intensities of two standard reflexions were monitored after every 100 reflexions. Their intensities showed only statistical variation. The reflexion intensities were scaled by use of the reference reflexions, and corrections were made for Lorentz and polarization factors but not for absorption. The distribution of normalized structure factors was clearly centrosymmetric in all cases studied (Karle *et al.* 1965).

All the structures were solved by means of the heavy-atom technique. In the Li complex, four Li$^+$ and four Cl$^-$ ions per unit cell are constrained at two sets of special positions with $\bar{4}$-symmetry and there is only one NMA molecule in the asymmetric unit. In the Mg complex, an Mg$^{2+}$ ion occupies the centre of inversion. For the Ca complex, reflexions for which $k+l$ was odd were systematically weak, implying pseudo-A-centering; positions 000 and $0\frac{1}{2}\frac{1}{2}$ were assigned to two Ca$^{2+}$ ions. The locations of the anions in Mg and Ca complexes and the heavier atoms in Na and K complexes were calculated by Patterson synthesis. Subsequent difference Fourier maps revealed the rest of the structure in each case. NMA molecules were disordered in all except the Mg complex.

The structures were refined by a full-matrix least-squares method. The initial occupancy factors of the disordered atoms were fixed at 0.5 and all the atoms were refined isotropically. After a few cycles, the occupancy factors were modified on the basis of the isotropic temperature factors of the pair of disordered atoms. All atoms, except the disordered atoms having very low occupancy factors (values less than 0.30), were made anisotropic, and refinement was continued until convergence was achieved. Because of the disorder, all hydrogens could not be seen in difference Fourier maps. Their positions were fixed on stereochemical considerations (Radom *et al.* 1972; Perricaudet & Pullman 1973*a*). With hydrogens included and treated isotropically, refinement was continued. The hydrogen atoms for the Ca complex were not refined. The quantity minimized was $\sum w(|F_o| - |F_c|)^2$; the weighting scheme used for the various structures is given in table 2. The shifts in the parameters at the end of the last cycle were less than $0.1\sigma$. A final difference Fourier map was found to be featureless in each case. The atomic scattering factors were those of Cromer & Mann (1968) for non-hydrogen atoms and Stewart *et al.* (1965) for hydrogen atoms. Details of refinement are given in table 2.

To minimize the effects on the model of aspherical electron density in bonds

## TABLE 1. CRYSTAL DATA

| | Li | Na | K | Mg | Ca |
|---|---|---|---|---|---|
| mol. formula | LiCl4NMA | NaClO$_4$2NMA | KSCNNMA | MgCl$_2$6NMA | CaCl$_2$4NMA2H$_2$O |
| rel. mol. mass | 334.77 | 268.64 | 170.28 | 533.80 | 439.40 |
| m.p./°C | 133 | 52 | 110 | 186 | 130 |
| crystal system | tetragonal | monoclinic | orthorhombic | triclinic | triclinic |
| $a$/Å | 12.824 (5) | 6.831 (4) | 13.810 (6) | 8.162 (2) | 8.154 (2) |
| $b$/Å | — | 9.923 (4) | 7.030 (6) | 9.813 (2) | 10.398 (2) |
| $c$/Å | 12.313 (6) | 18.387 (4) | 16.750 (7) | 9.952 (2) | 16.878 (6) |
| $\alpha$/deg. | — | — | — | 107.85 (2) | 89.35 (2) |
| $\beta$/deg. | — | 94.19 (3) | — | 98.60 (2) | 104.90 (3) |
| $\gamma$/deg. | — | — | — | 81.28 (2) | 96.09 (2) |
| space group | I4$_1$/a | P2$_1$/c | Pbca | P$\bar{1}$ | P$\bar{1}$ |
| Z, molecule/unit cell | 4 | 4 | 8 | 1 | 2 |
| $D_{obs}$/(g cm$^{-3}$)† | 1.072 | 1.441 | 1.410 | 1.203 | 1.103 |
| $D_{calc}$/(g cm$^{-3}$) | 1.098 | 1.435 | 1.391 | 1.189 | 1.061 |
| V /Å$^3$ | 2025.0 | 1243.0 | 1626.1 | 745.4 | 1374.9 |
| $\mu$/cm$^{-1}$ | 18.36 | 3.63 | 8.19 | 2.81 | 4.39 |
| F(000) | 716 | 560 | 704 | 286 | 468 |

† By flotation method, from bromoform and benzene.

TABLE 2. DETAILS OF INTENSITY DATA MEASUREMENT AND REFINEMENT

| | Li | Na | K | Mg | Ca |
|---|---|---|---|---|---|
| *data* | | | | | |
| crystal dimensions/ $(10^{-4}\ \text{mm})$ | $5\times5\times6$ | $3\times3\times6$ | $3\times4\times5$ | $3\times7\times7$ | $5\times5\times7$ |
| radiation, $\lambda(\text{Mo K}\alpha) = 0.7107\ \text{Å}$, $\lambda(\text{Cu K}\alpha) = 1.5418\ \text{Å}$ | Cu K$\alpha$ | Mo K$\alpha$ | Mo K$\alpha$ | Mo K$\alpha$ | Mo K$\alpha$ |
| maximum angle $\theta$/deg. | 60 | 22.5 | 25 | 26 | 23 |
| no. of unique reflexions measured | 739 | 1879 | 1523 | 2586 | 4229 |
| no. of significant reflexions $(\lvert F_{\text{o}}\rvert > 2\sigma(F_{\text{o}}))$ | 537 | 1233 | 1064 | 2101 | 2553 |
| *refinement* | | | | | |
| no. of reflexions given zero weight† | 22 | 37 | 29 | 35 | 75 |
| weighting, $w$ | $3.6[\sigma^2(F_{\text{o}})+0.0004\lvert F_{\text{o}}\rvert^2]^{-1}$ | $[12+\lvert F_{\text{o}}\rvert+0.02\lvert F_{\text{o}}\rvert^2]^{-1}$ | $[15+\lvert F_{\text{o}}\rvert+0.001\lvert F_{\text{o}}\rvert^2]^{-1}$ | $[12+\lvert F_{\text{o}}\rvert+0.06\lvert F_{\text{o}}\rvert^2]^{-1}$ | $[10+\lvert F_{\text{o}}\rvert+0.01\lvert F_{\text{o}}\rvert^2]^{-1}$ |
| reliability factor, $R$‡ (excluding unobserved reflexions) | 0.056 | 0.067 | 0.068 | 0.060 | 0.110 |
| proportion of the two disordered forms of NMA molecules | | | | | |
| A | 0.5:0.5 | 0.57:0.43 | 0.725:0.275 | — | 0.7:0.3 |
| B | — | 0.8:0.2 | — | — | 0.5:0.5 |
| C | — | — | — | — | 0.75:0.25 |
| D | — | — | — | — | 0.55:0.45 |

† Reflexions believed to suffer extinction effects, as well as a few [with $\lvert F_{\text{o}}\rvert < 3\sigma(F_{\text{o}})$] which show large discrepancy between $\lvert F_{\text{o}}\rvert$ and $\lvert F_{\text{c}}\rvert$.

‡ $R = \Sigma\lvert\lvert F_{\text{o}}\rvert-\lvert F_{\text{c}}\rvert\rvert/\Sigma\lvert F_{\text{o}}\rvert$.

TABLE 3. FINAL POSITIONAL PARAMETERS FOR NON-HYDROGEN ATOMS;
E.S.D. IS GIVEN IN PARENTHESES

| atom | $10^4 x$ | $10^4 y$ | $10^4 z$ |
|---|---|---|---|
| Li | 0 (0) | 2500 (0) | 1250 (0) |
| Cl | 0 (0) | 2500 (0) | 6250 (0) |
| AC1 | 943 (9) | 438 (8) | 3799 (11) |
| AC' | 274 (14) | 530 (14) | 2712 (19) |
| AC2 | −811 (8) | −328 (7) | 1482 (9) |
| AN | −228 (7) | −315 (12) | 2401 (11) |
| AO | 213 (4) | 1321 (3) | 2154 (4) |
| AC'(D) | −80 (16) | 365 (24) | 2254 (16) |
| AN(D) | 275 (9) | −77 (12) | 3081 (10) |
| Na | 7530 (3) | 417 (2) | 5167 (1) |
| Cl | 7662 (2) | 3197 (1) | 6387 (1) |
| O1 | 7434 (11) | 2635 (13) | 5736 (5) |
| O2 | 6110 (10) | 4070 (9) | 6474 (3) |
| O3 | 9452 (10) | 3825 (7) | 6512 (6) |
| O4 | 7649 (16) | 2201 (11) | 6910 (8) |
| AC1 | 3101 (20) | 1335 (15) | 3083 (6) |
| AC' | 4961 (38) | 441 (27) | 3438 (16) |
| AC2 | 7744 (15) | −721 (12) | 3345 (6) |
| AN | 6216 (19) | 13 (12) | 3053 (9) |
| AO | 5173 (6) | 256 (4) | 4160 (2) |
| AC'(D) | 5748 (40) | 124 (29) | 3584 (17) |
| AN(D) | 4682 (23) | 633 (14) | 2970 (11) |
| BC1 | 12828 (12) | 3206 (10) | 5022 (5) |
| BC' | 10844 (16) | 2619 (9) | 4611 (5) |
| BC2 | 8160 (16) | 3153 (12) | 3811 (6) |
| BN | 9895 (11) | 3509 (9) | 4218 (4) |
| BO | 10282 (6) | 1468 (4) | 4677 (2) |
| BC'(D) | 9900 (58) | 2618 (45) | 4406 (20) |
| BN(D) | 11342 (34) | 3595 (25) | 4529 (12) |
| K | 8338 (1) | 1511 (2) | 7320 (1) |
| S | 10440 (1) | 3198 (3) | 6575 (1) |
| C | 11138 (5) | 1360 (9) | 6791 (4) |
| N | 11638 (5) | 103 (9) | 6921 (4) |
| AC1 | 5573 (8) | 2874 (19) | 5866 (8) |
| AC' | 6688 (16) | 3065 (18) | 5766 (9) |
| AC2 | 8038 (8) | 2806 (14) | 4914 (7) |
| AN | 7024 (10) | 2664 (14) | 5057 (8) |
| AO | 7244 (4) | 3647 (7) | 6309 (3) |
| AC'(D) | 7161 (28) | 3216 (38) | 5579 (23) |
| AN(D) | 6322 (17) | 2867 (30) | 5320 (23) |
| Mg | 0 (0) | 0 (0) | 0 (0) |
| Cl | 4719 (1) | 3441 (1) | 6628 (1) |
| AC1 | −2430 (10) | 3847 (7) | 87 (7) |
| AC' | −2539 (4) | 2723 (6) | 966 (5) |
| AC2 | −3108 (10) | 2357 (8) | 3011 (7) |
| AN | −3069 (5) | 3273 (5) | 2173 (5) |
| AO | −2114 (3) | 1422 (3) | 403 (3) |
| BC1 | 3057 (7) | 242 (6) | 3246 (7) |
| BC' | 2158 (4) | 1558 (4) | 2804 (4) |
| BC2 | 1741 (8) | 4132 (6) | 3334 (7) |

TABLE 3 (*cont.*)

| atom | $10^4x$ | $10^4y$ | $10^4z$ |
|------|---------|---------|---------|
| BN | 2495 (5) | 2830 (4) | 3640 (4) |
| BO | 1176 (3) | 1411 (3) | 1715 (2) |
| CC1 | 3414 (5) | 1704 (6) | − 602 (6) |
| CC′ | 1786 (4) | 1621 (4) | − 1542 (4) |
| CC2 | 181 (7) | 2162 (7) | − 3592 (6) |
| CN | 1684 (4) | 2164 (4) | − 2624 (3) |
| CO | 593 (3) | 1085 (3) | − 1335 (2) |
| Ca1 | 0 (0) | 0 (0) | 0 (0) |
| Ca2 | 0 (0) | 5000 (0) | 5000 (0) |
| Cl1 | 5885 (3) | 4523 (2) | 2113 (1) |
| Cl2 | 3611 (4) | 1787 (2) | 6283 (1) |
| AC1 | − 3457 (19) | − 572 (17) | − 2593 (9) |
| AC′ | − 3025 (16) | 296 (20) | − 1830 (8) |
| AC2 | − 3479 (17) | 2260 (14) | − 1400 (8) |
| AN | − 3739 (16) | 1400 (15) | − 1982 (7) |
| AO | − 2055 (9) | 103 (9) | − 1209 (5) |
| AC′(D) | − 2983 (60) | 1136 (46) | − 1674 (27) |
| AN(D) | − 3912 (62) | 745 (50) | − 2224 (31) |
| BC1 | 60 (20) | 3184 (18) | 1546 (12) |
| BC′ | − 1466 (47) | 2093 (26) | 1088 (15) |
| BC2 | − 4413 (29) | 1390 (18) | 776 (13) |
| BN | − 3056 (25) | 2302 (15) | 1168 (10) |
| BO | − 1537 (16) | 1086 (9) | 670 (6) |
| BC′(D) | − 2513 (47) | 1854 (25) | 973 (12) |
| BN(D) | − 1720 (25) | 2762 (21) | 1395 (11) |
| CC1 | 2253 (29) | 5919 (17) | 3116 (12) |
| CC′ | 2620 (16) | 4822 (13) | 3716 (7) |
| CC2 | 4358 (15) | 3239 (15) | 4248 (9) |
| CN | 3867 (15) | 4147 (12) | 3656 (8) |
| CO | 1853 (9) | 4555 (8) | 4242 (5) |
| CC′(D) | 3024 (48) | 4357 (38) | 3969 (24) |
| CN(D) | 3169 (53) | 5062 (37) | 3315 (26) |
| DC1 | − 2188 (23) | 914 (14) | 5494 (8) |
| DC′ | − 1859 (25) | 1629 (19) | 4688 (26) |
| DC2 | − 1231 (28) | 1788 (14) | 3458 (10) |
| DN | − 1856 (37) | 1140 (30) | 4122 (12) |
| DO | − 1204 (9) | 2912 (6) | 4826 (5) |
| DC′(D) | − 1526 (23) | 1893 (19) | 4510 (21) |
| DN(D) | − 2101 (26) | 812 (11) | 4708 (9) |
| O1(W) | 1275 (9) | 1959 (6) | − 372 (4) |
| O2(W) | 1972 (19) | 4342 (9) | 6162 (7) |

and lone-pairs (Jeffrey & Cruickshank 1953; Hanson *et al.* 1972) a refinement of the non-hydrogen atomic parameters was obtained for the Mg complex with high angle data ($\sin \theta/\lambda \geqslant 0.40$, 1350 reflexions). The coordinates obtained from this refinement were not significantly different from those obtained from full data set refinement. Final atomic parameters are listed in table 3; the nomenclature followed is that given in figure 1, except that the crystallographically independent NMA molecules in the asymmetric unit are distinguished by

putting A, B, C and D before the atom name. The coordinates for hydrogen atoms, thermal parameters for all atoms and lists of observed and calculated structure factors are available from the authors.
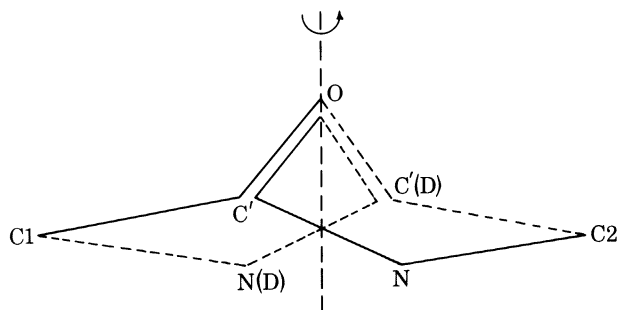


FIGURE 1. Disorder in NMA complexes.

As noted earlier, NMA molecules are disordered in all but the Mg complex. Such disorder has been reported in the crystal structures of NMA (Katz & Post 1960), an amide (P. Chakrabarti, K. Venkatesan, T. S. Cameron, T. Demir & R. A. Shaw, 1980, unpublished work) and a peptide (Harada & Iitaka 1974). The two disordered positions of NMA, as shown in figure 1, are related by a rotation of 180° through the oxygen atom such that the positions of the terminal carbon atoms remain unchanged. The position of the metal atom with respect to the C'—N bond differs in the two forms. If it is *trans* to the C'—N bond in one, it is *cis* in the other. Also, depending on the position of the metal ion, the M—O—C' angle can be different in the two cases. The fact that the two forms occur in different proportions in the different complexes may be taken to indicate a difference in the energy of the two forms. In reporting the structural parameters of the complexes, we have given the values associated with the predominant form because of the greater accuracy associated with it. It may be mentioned that the accuracy of the structure determination of the calcium complex is poor, as all the four crystallographically independent NMA molecules are disordered. Hence in the discussion of the results pertaining to the geometry of NMA molecules, the Ca complex is not taken into consideration.

## 3. RESULTS AND DISCUSSION

### LiCl4NMA *complex*

The unit cell and the coordination sphere of this complex are shown in figures 2 and 3 respectively. It is observed that Li$^+$ is bound to the carbonyl oxygen of the amide. The complex has tetrahedral geometry as shown by the O—Li—O angles listed in table 4. The Li—O distance is 1.897 (4) Å† (table 5), characteristic

† Å = $10^{-10}$ m = $10^{-1}$ nm.

of tetrahedral complexes of Li bound to oxygen donors (1.88–1.97 Å), octahedral complexes generally showing an Li—O distance of the order of 2.12 Å (Poonia & Bajaj 1979). This complex exhibits two forms in equal proportions, each with a unique geometry, and the consequent differences in cation–amide bonding.
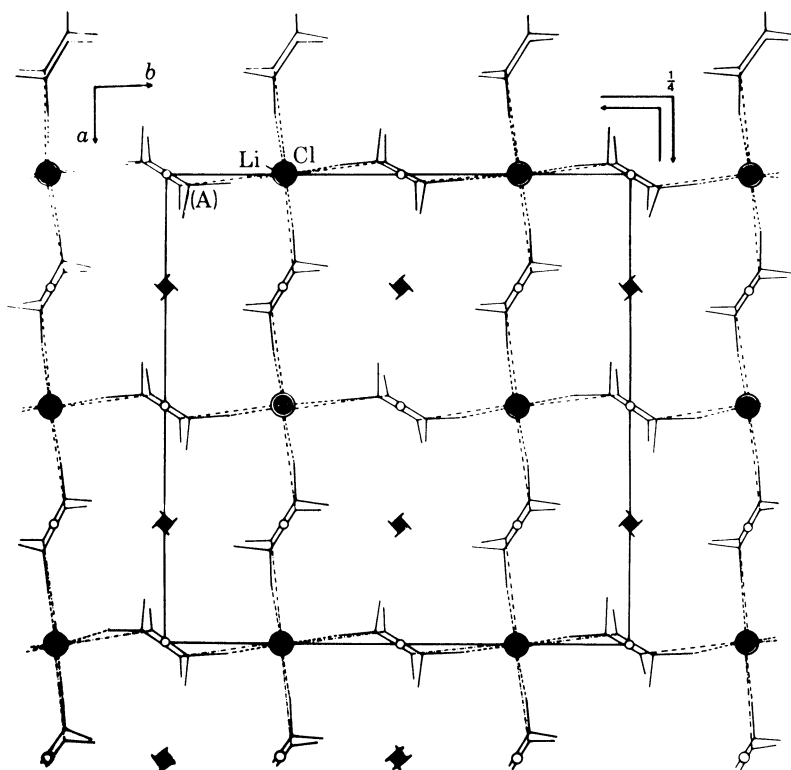


FIGURE 2. Unit cell of LiCl4NMA as seen by looking down the *c*-axis.

Thus, the central C—N (denoted as C′—N) and the carbonyl (C′=O) bond distances (table 6) are 1.32 (2) Å and 1.23 (2) Å respectively, while in the other the corresponding distances are 1.25 (3) Å and 1.29 (3) Å. Obviously, Li⁺ is bound more strongly in the latter form than in the former. The metal ion is in the plane of the peptide group but deviates from the lone-pair direction of the carbonyl oxygen in both forms (table 5); it is *trans* with respect to the C′—N bond in one and *cis* in the other.

The increase in the C′=O distance and the decrease in the C′—N distance in the Li–amide complex clearly implies an increase in the barrier to rotation about the C′—N bond. Such an increase in the barrier to rotation in amides in the presence of lithium salts has indeed been reported in n.m.r. studies (Rao *et al.* 1977*b*). Theoretical calculations (Balasubramanian *et al.* 1972; Armbruster & Pullman 1974) also support an increase in barrier height in complexes of amides

with lithium cations. A longer $C'{=}O$ distance in the complex is consistent with the lower $C{=}O$ stretching frequency in the complex, compared with that of the the parent amide (Rao *et al.* 1975). The tetrahedral stereochemistry of the $LiO_4$ polyhedron found in our study also justifies the assignment of low frequency bands found in i.r. spectra at *ca.* 400 cm$^{-1}$ in crystalline amide complexes of Li$^+$ and in solutions of Li salts in amides (Rao *et al.* 1973; Rao 1973*a*) as due to an asymmetric stretching mode of the $LiO_4$ tetrahedron (Rao *et al.* 1975). It would
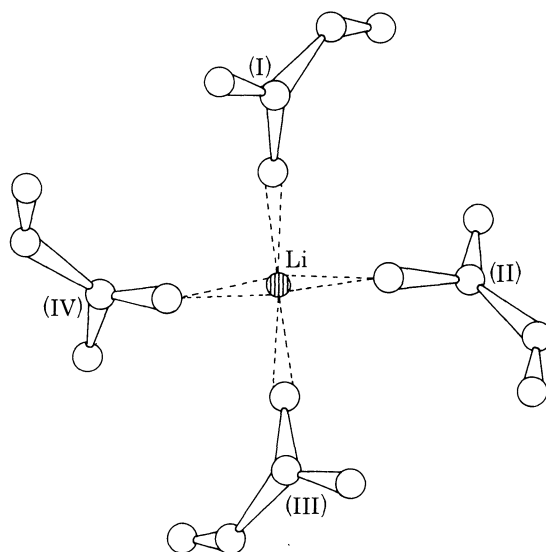


FIGURE 3. Coordination sphere in LiCl4NMA (for symmetry code see table 4).

be of interest to compare the results of the structure of the Li$^+$–NMA complex with that of the Li$^+$–antamanide complex (Karle 1974*a*). Unlike the LiCl4NMA complex, the Li–antamanide complex is not tetrahedral, but square-pyramidal, owing to the presence of $CH_3CN$ as one of the ligands. The average $C'{-}N$ and $C'{=}O$ distances in the antamanide complex are 1.344 and 1.226 Å respectively; the Li—O distances (2.04–2.24 Å) are between those found in tetrahedral and octahedral complexes of Li. The Li—O—C$'$ angles are in the range 132.1–155.5°, Li$^+$ being *trans* to the $C'{-}N$ bond in two peptide moieties and *cis* in the other two. In the LiBr complex of *L*-alanylglycine (Declercq *et al.* 1971), Li$^+$ is tetrahedrally coordinated with an Li—O (amide) distance of 1.943 Å and a Li—O—C$'$ angle of 146.6°, Li$^+$ being *cis* with respect to the $C'{-}N$ bond and deviating by 0.71 Å from the peptide plane. The $C'{-}N$ and $C'{=}O$ distances are 1.302 Å and 1.238 Å respectively in this complex. In the 2:1 complex of cyclodisarcosyl with $LiClO_4$ (Takahashi *et al.* 1977), the $C'{-}N$ distance shows a decrease (by 0.014–0.057 Å) and the $C'{=}O$ distance an increase (by 0.0–0.024 Å) compared with the parent molecule, the magnitude of the changes being greater in the peptide group

## TABLE 4. ANGLES/DEG. SUBTENDED AT THE METAL ION IN THE COORDINATION SPHERE

symmetry code for Roman numerals

| | | | |
|---|---|---|---|
| O(I)—Li—O(II) | 110.13(20) | (I) | molecule A at $x, y, z$ |
| O(I)—Li—O(III) | 108.15(20) | (II) | molecule A at $-\frac{1}{4}+y, \frac{1}{4}-x, \frac{1}{4}-z$ |
| | | (III) | molecule A at $-x, \frac{1}{2}-y, z$ |
| | | (IV) | molecule A at $\frac{1}{4}-y, \frac{1}{4}+x, \frac{1}{4}-z$ |
| O(I)—Na—O(II) | 79.29(26) | (I) | $ClO_4^-$ anion at $x, y, z$ |
| O(I)—Na—O(III) | 110.98(27) | | (O1 coordinates to Na$^+$) |
| O(I)—Na—O(IV) | 133.52(27) | (II) | molecule B at $x, y, z$ |
| O(I)—Na—O(V) | 89.11(27) | (III) | molecule A at $x, y, z$ |
| O(II)—Na—O(III) | 104.10(16) | (IV) | molecule B at $2-x, -y, 1-z$ |
| O(II)—Na—O(IV) | 83.38(14) | (V) | molecule A at $1-x, -y, 1-z$ |
| O(II)—Na—O(V) | 167.94(16) | | |
| O(III)—Na—O(IV) | 115.00(16) | | |
| O(III)—Na—O(V) | 83.03(16) | | |
| O(IV)—Na—O(V) | 102.62(15) | | |
| O(I)—K—O(II) | 81.90(16) | (I) | molecule A at $x, y, z$ |
| O(I)—K—S(III) | 93.08(12) | (II) | molecule A at $\frac{3}{2}-x, -\frac{1}{2}+y, z$ |
| O(I)—K—S(IV) | 170.58(12) | (III) | SCN$^-$ at $x, y, z$ |
| O(I)—K—N(V) | 78.09(18) | (IV) | SCN$^-$ at $2-x, -\frac{1}{2}+y, \frac{3}{2}-z$ |
| O(I)—K—N(VI) | 90.70(18) | (V) | SCN$^-$ at $2-x, \frac{1}{2}+y, \frac{3}{2}-z$ |
| O(II)—K—S(III) | 106.32(12) | (VI) | SCN$^-$ at $-\frac{1}{2}+x, y, \frac{3}{2}-z$ |
| O(II)—K—S(IV) | 88.79(12) | | |
| O(II)—K—N(V) | 159.09(18) | | |
| O(II)—K—N(VI) | 77.27(18) | | |
| S(III)—K—S(IV) | 90.84(6) | | |
| S(III)—K—N(V) | 80.92(14) | | |
| S(III)—K—N(VI) | 175.11(15) | | |
| S(IV)—K—N(V) | 111.01(15) | | |
| S(IV)—K—N(VI) | 85.89(14) | | |
| N(V)—K—N(VI) | 96.86(20) | | |
| O(I)—Mg—O(II) | 86.13(10) | (I), (II), (III) represent molecules | |
| O(I)—Mg—O(III) | 89.98(10) | B, A and C, respectively, at $x, y, z$, | |
| O(I)—Mg—O(V) | 93.87(10) | whereas (IV), (V), (VI) are for the | |
| O(I)—Mg—O(VI) | 90.02(10) | molecules at $\bar{x}, \bar{y}, \bar{z}$. | |
| O(II)—Mg—O(III) | 89.90(10) | | |
| O(II)—Mg—O(VI) | 90.10(10) | | |
| O(I)—Ca1—O(II) | 90.56(31) | (I), (II), (III) represent molecules | |
| O(I)—Ca1—O(III) | 90.73(34) | B, O1W and A, respectively, at | |
| O(I)—Ca1—O(V) | 89.44(31) | $x, y, z$, whereas (IV), (V), (VI) are | |
| O(I)—Ca1—O(VI) | 89.27(34) | for the molecules at $\bar{x}, \bar{y}, \bar{z}$. | |
| O(II)—Ca1—O(III) | 86.43(27) | | |
| O(II)—Ca1—O(VI) | 93.58(27) | | |
| O(I)—Ca2—O(II) | 87.86(36) | (I), (II), (III) represent molecules | |
| O(I)—Ca2—O(III) | 89.79(27) | D, O2W and C, respectively, at | |
| O(I)—Ca2—O(V) | 92.14(36) | $x, y, z$, whereas (IV), (V), (VI) are | |
| O(I)—Ca2—O(VI) | 90.21(27) | for the molecules at $\bar{x}, 1-y, 1-z$. | |
| O(II)—Ca2—O(III) | 87.95(36) | | |
| O(II)—Ca2—O(VI) | 92.05(36) | | |

with the shorter Li—O distance (1.899 Å) than in the one with the longer distance (1.945 Å). $Li^+$ is surrounded tetrahedrally by the peptide carbonyl groups, the $Li^+$ lying almost in the plane of the peptide close to the lone-pair direction (the Li—O—C′ angle is *ca.* 127°).

TABLE 5. METAL–OXYGEN DISTANCES, POSITION OF THE METAL WITH RESPECT TO THE OXYGEN LONE-PAIR, AND ITS DEVIATION FROM THE NMA PLANE

| complex | M—O distance/Å | M—O—C′ angle/deg. | deviation/Å of M from amide plane |
|---|---|---|---|
| Li: molecule A | 1.897 (4) | 174.9 (10) | 0.07 |
| | | 140.6 (11)† | |
| Na: molecule A | 2.369 (5) | 141.7 (12) | 1.12 |
| molecule B | 2.383 (4) | 135.52 (53) | 1.47 |
| molecule $A^I$ | 2.391 (5) | 121.3 (12) | 1.44 |
| molecule $B^{II}$ | 2.398 (4) | 123.16 (52) | 1.17 |
| K: molecule A | 2.720 (5) | 127.53 (84) | 2.10 |
| molecule $A^{III}$ | 2.750 (5) | 120.28 (83) | 1.51 |
| Mg: molecule A | 2.054 (2) | 140.28 (39) | 1.28 |
| molecule B | 2.053 (2) | 146.63 (25) | 0.04 |
| molecule C | 2.085 (2) | 140.07 (23) | 0.11 |
| Ca: molecule A | 2.294 (8) | 172.5 (10) | 0.19 |
| molecule B | 2.276 (11) | 142.6 (15) | 0.29 |
| | | 171.5 (14)† | |
| molecule C | 2.301 (8) | 152.16 (81) | 0.23 |
| molecule D | 2.275 (6) | 176.0 (13) | 0.24 |

Symmetry related atoms: I, at $1-x$, $-y$, $1-z$; II, at $2-x$, $-y$, $1-z$; III, at $\frac{3}{2}-x$, $-\frac{1}{2}+y$, $z$.

† Value for the corresponding disordered form, which occurs in equal proportion.

### $NaClO_4 2NMA$ *complex*

The unit cell of the complex is shown in figure 4 and the coordination sphere in figure 5. The geometry of this penta-coordinated $Na^+$ complex (with four amide and one perchlorate oxygens acting as donor sites) deviates considerably from that of a regular square-pyramid as can be seen from the angles listed in table 4; also, we cannot consider the four amide oxygens or any four of the oxygens to form a tetrahedron around the $Na^+$. The Na—O (amide) distances (table 5) lie between 2.369 (5) Å and 2.398 (4) Å, values within the range (2.25–2.40 Å) characteristic of penta-coordinated oxygen-donor complexes (Poonia & Bajaj 1979). The Na—O ($ClO_4$) distance of 2.440 (12) Å is also close to this range. The C′—N distances (table 6) indicate an increase in the double-bond character. The $Na^+$ ion does not deviate as much from the carbonyl lone-pair direction as $Li^+$, as shown by the M—O—C′ angles (table 5). The $Na^+$ ion, however, deviates by 1.12–1.47 Å from the various peptide planes, while the $Li^+$ ion is essentially in the peptide plane. With respect to the C′—N bond, $Na^+$ is in the *cis* position in the

TABLE 6. BOND LENGTHS/Å AND ANGLES/DEG. FOR NMA MOLECULES
(THOSE FOR THE STANDARD PEPTIDE GROUP ARE ALSO GIVEN)

| complex | C'—N | C'=O | C1—C' | N—C2 | C1—C'—N | C1—C'—O | O—C'—N | C'—N—C2 |
|---|---|---|---|---|---|---|---|---|
| **(1) Li:** | | | | | | | | |
| (i) molecule A† | 1.317 (23) | 1.228 (20) | 1.594 (25) | 1.356 (16) | 116.5 (15) | 124.4 (15) | 119.1 (17) | 121.5 (14) |
|  | 1.251 (26) | 1.288 (30) | 1.604 (26) | 1.397 (18) | 116.4 (18) | 129.9 (18) | 113.8 (19) | 121.6 (16) |
| **(2) Na:** | | | | | | | | |
| (i) molecule A | 1.227 (31) | 1.338 (30) | 1.645 (30) | 1.352 (17) | 120.6 (21) | 119.5 (19) | 119.7 (22) | 120.6 (17) |
| (ii) molecule B | 1.285 (12) | 1.214 (10) | 1.612 (13) | 1.400 (13) | 112.82 (81) | 123.63 (81) | 123.53 (89) | 120.00 (87) |
| **(3) K:** | | | | | | | | |
| (i) molecule A | 1.306 (21) | 1.259 (19) | 1.554 (24) | 1.425 (18) | 115.6 (14) | 123.7 (14) | 120.7 (14) | 119.2 (13) |
| **(4) Mg:** | | | | | | | | |
| (i) molecule A | 1.269 (6) | 1.245 (6) | 1.623 (9) | 1.407 (9) | 115.74 (46) | 117.92 (43) | 126.33 (45) | 118.05 (51) |
| (ii) molecule B | 1.313 (6) | 1.232 (4) | 1.538 (7) | 1.431 (7) | 116.68 (39) | 121.03 (38) | 122.29 (36) | 121.75 (42) |
| (iii) molecule C | 1.327 (5) | 1.245 (4) | 1.503 (6) | 1.442 (6) | 115.81 (35) | 123.08 (35) | 121.11 (33) | 121.09 (37) |
| **(5) Ca:** | | | | | | | | |
| (i) molecule A | 1.334 (24) | 1.169 (16) | 1.524 (22) | 1.297 (19) | 111.5 (14) | 125.4 (14) | 122.7 (15) | 119.5 (14) |
| (ii) molecule B | 1.377 (44) | 1.258 (28) | 1.630 (36) | 1.406 (28) | 114.1 (22) | 134.6 (24) | 111.2 (24) | 116.0 (20) |
| (iii) molecule C | 1.320 (19) | 1.224 (15) | 1.519 (23) | 1.379 (20) | 116.1 (13) | 124.7 (13) | 119.8 (12) | 117.6 (12) |
| (iv) molecule D | 1.088 (44) | 1.383 (22) | 1.612 (39) | 1.474 (31) | 125.0 (28) | 113.5 (20) | 120.2 (29) | 123.4 (28) |
| **(6) *trans*-peptide unit:** | | | | | | | | |
| (i) Marsh & Donohue (1967) | 1.325 | 1.24 | 1.51 | 1.455 | 116 | 120.5 | 123.5 | 122 |
| (ii) Benedetti (1977) | 1.335 | 1.229 | 1.522 | 1.449 | 116.6 | 120.4 | 122.9 | 121.9 |

† The values for the disordered form are also given.
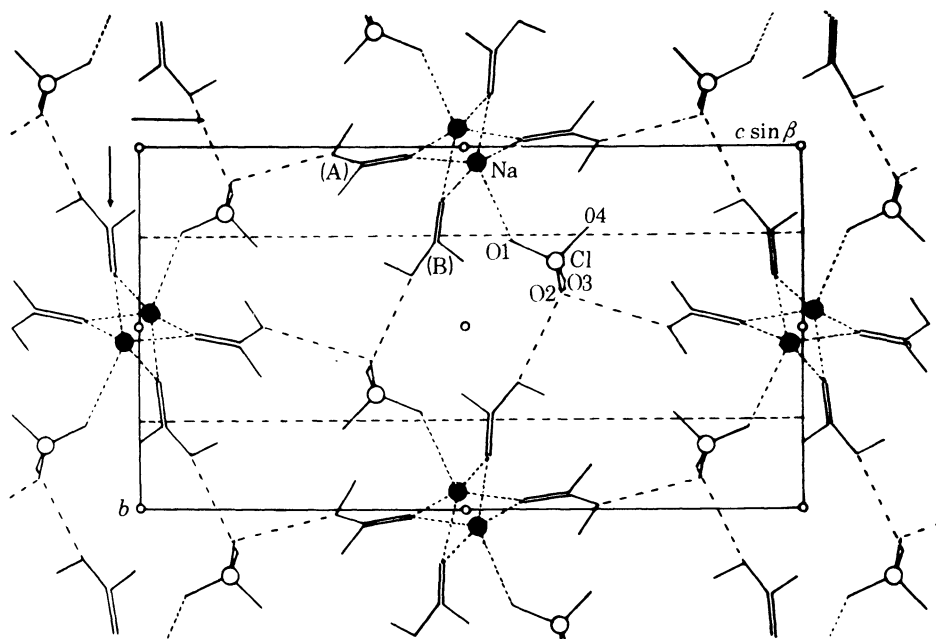
FIGURE 4. Unit cell of $NaClO_4 2NMA$ as seen by looking down the $a$-axis.
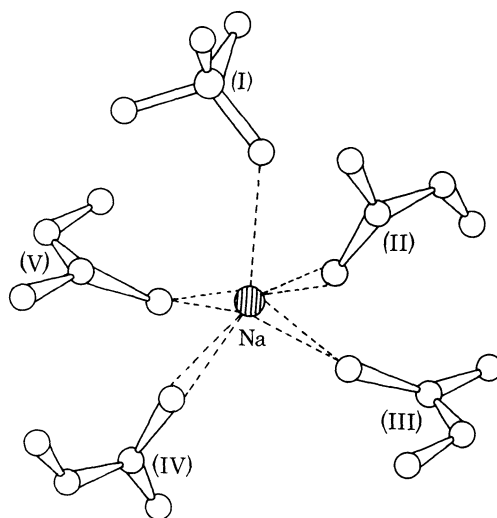
FIGURE 5. Coordination sphere in $NaClO_4 2NMA$ (for symmetry code see table 4).

two NMA molecules (A and B) whereas in the symmetry-related molecules in the unit cell, it is in the *trans* position.

The C'—N and C'=O distances found by us in the $Na^+$–NMA complex are consistent with the vibrational spectra, which shows a decrease in the C=O

stretching frequency in the complex (Rao *et al.* 1975). The i.r. spectrum also shows the $C_{3v}$ splitting of the degenerate perchlorate bands in accordance with the geometry found in our study. The geometry of the $ClO_4^-$ ion in the complex is the same as that reported in the literature (Hughes *et al.* 1978). In the $Na^+$–antamanide complex (Karle 1974*b*) also, the $Na^+$ ion is penta-coordinated with Na—O distances in the range 2.25–2.36 Å and Na—O—C′ angles in the range
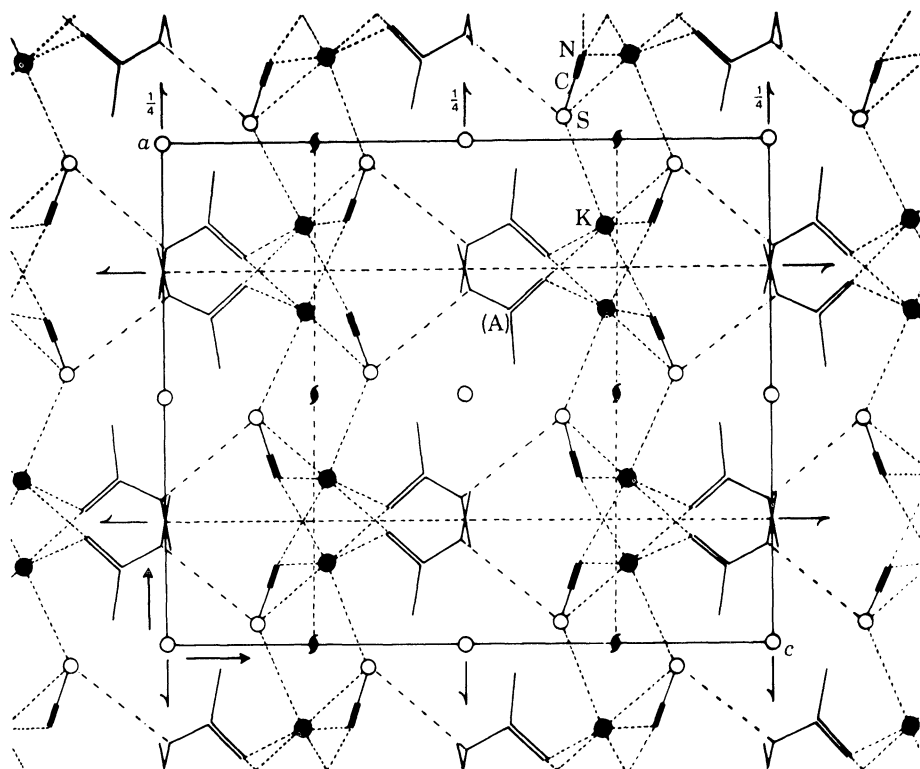


FIGURE 6. Unit cell of KSCN NMA as seen by looking down the *b*-axis.

138.4–156.0°, $Na^+$ being *trans* with respect to the C′—N bond in three peptide moieties and *cis* in another. The average C′—N and C′=O distances are 1.338 Å and 1.230 Å respectively. In the NaI3-dimethylformamide complex (Gobillon *et al.* 1962), $Na^+$ is octahedrally coordinated with an Na—O distance of 2.40 Å and an Na—O—C′ angle of 133.8°. The $Na^+$ ion is *cis* with respect to the C′—N bond and deviates from the amide plane by 1.64 Å.

### KSCN NMA *complex*

The unit cell of the complex is shown in figure 6 and the coordination sphere in figure 7. In the coordination octahedron of this complex, we have only two amide oxygens, the rest of the sites being provided by the SCN⁻ anions. The

coordination of SCN$^-$ is unusual in that two anions coordinate through sulphur while two others coordinate through nitrogen. Coordination of SCN$^-$ through sulphur is indeed unusual in the case of K$^+$. In this complex, as in the NaClO$_4$2NMA complex, the same carbonyl group binds to two K$^+$ ions with a K—O—K$'$ angle of 100.56° (K$'$ being related to K by a transformation $\frac{1}{2} - x$, $\frac{1}{2} + y$, $z$). We find that the K—O—C$'$ angles are close to 120° (table 5) and the K$^+$ ion deviates from the
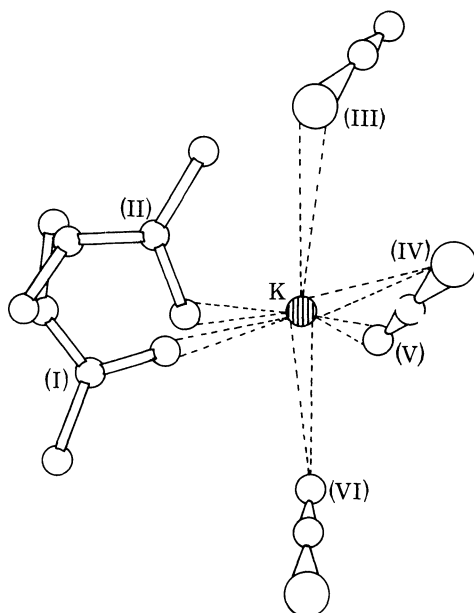


FIGURE 7. Coordination sphere in KSCN NMA (for symmetry code see table 4).

amide plane more than the Li$^+$ or Na$^+$ ions. The K—O distances in this complex are 2.720 (5) and 2.750 (5) Å and are in the range (2.7–2.9 Å) generally observed in octahedral oxygen–donor complexes of K$^+$. The K$^+$ ion is *cis* to the C$'$—N bond in one molecule and *trans* to it in the other. The C$'$—N and C$'$=O distances in the complex are 1.31 (2) Å and 1.26 (2) Å respectively (table 6). It appears that the K$^+$ ion does not affect these distances as markedly as Li$^+$ or Na$^+$ ions. It is indeed known from spectroscopic and other studies that the binding strength of alkali metal ions to peptides and other donors vary in the order Li$^+ >$ Na$^+ >$ K$^+$ (Perricaudet & Pullman 1973*b*; Rao *et al.* 1977*a*).

The geometry of the SCN$^-$ anion found by us (S—C, 1.652 (7) Å; C≡N, 1.143 (9) Å; S—C—N, 177.96 (64)° is close to that in the literature (Bats *et al.* 1977; Owen 1978). The K—N distances of 2.827 (7) Å and 2.847 (7) Å with the corresponding K—N—C angles of 141.6 (6)° and 108.3 (5)° also agree with the values given in the literature (Mercer & Truter 1973). The K—S distances and K—S—C

angles for the sulphur-coordinated $SCN^-$ ions are 3.375 (2) Å, 3.421 (2) Å and 98.4 (2)°, 97.2 (2)° respectively.

In the $K^+$–valinomycin complex (Neupert-Laves & Dobler 1975), the $K^+$ ion is coordinated to six carbonyl oxygens of ester groups in a nearly regular octahedron, the K—O distances varying in the range 2.69–2.83 Å, K—O—C′ angles in the range 154.5–160.7° and $K^+$ deviating by *ca.* 1.0 Å from the carbonyl plane. The $K^+$–nonactin complex (Dobler *et al.* 1969) with an approximate cubic coordination has K—O (carbonyl) distances (average 2.77 Å) shorter than the K—O (ether) distances (average 2.84 Å). Even in the $Na^+$–nonactin complex (Dobler & Phizackerley 1974) with cubic coordination around $Na^+$, the average Na—O (carbonyl) distance (2.42 Å) is shorter than the average Na—O (ether) distance (2.77 Å). An examination of the literature (Poonia & Bajaj 1979) has revealed that the distance between a carbonyl oxygen and a metal is generally shorter than that between an ether oxygen and a metal when both the ligand sides are available for coordination. The K—O—C′ angles in the $K^+$–nonactin complex are 110.3° and 115.4° and the deviation of $K^+$ from the carbonyl plane is *ca.* 2.5 Å.

### $MgCl_2 6NMA$ *complex*

The packing arrangement in the unit cell and the coordination sphere of this complex are shown in figures 8 and 9 respectively. This complex, which like the Li one has only NMA as the ligand, shows typical octahedral coordination, as can be seen from the O—M—O angles in table 4. The Mg—O distances (table 5) are between 2.053(2) and 2.085 (2) Å, characteristic of octahedral oxygen donor complexes of $Mg^{2+}$ (2.03–2.16 Å). The Mg—O—C′ angles deviate by about 20° from the lone-pair direction (table 5). The C′—N and C′=O distances in this complex are in the ranges 1.269 (6) to 1.327 (5) Å and 1.232 (4) to 1.245 (6) Å respectively (table 6). The out-of-plane deviation of $Mg^{2+}$ from the amide plane varies in the three independent NMA molecules, two of them showing little deviation, as in the Li complex. The amide molecule with the shortest C′—N distance also shows the largest deviation of the metal ion from the amide plane (table 5). Since the C′—N and C′=O distances depend on the strength of interaction of the metal ion with the peptide, the observed differences in these distances in the three unique NMA molecules clearly illustrate how metal–amide bonding depends on the position of the metal ion with respect to the amide molecule. The metal ion is *trans* with respect to the C′—N bond in all the molecules in the unit cell.

The $MgO_6$ polyhedron found in this complex is consistent with the assignment of i.r. and Raman spectra, which in addition to the shifted amide bands show the characteristic band at 390 $cm^{-1}$ due to the asymmetric stretching vibration of $MgO_6$ octahedron, the corresponding symmetric vibration frequency being found to be around 200 $cm^{-1}$ in the Raman spectrum (Rao *et al.* 1975). In the $Mg^{2+}$–antipyrine perchlorate complex (Vijayan & Viswamitra 1967), the six amide

carbonyl groups around $Mg^{2+}$ show the same Mg—O distance (2.059 Å) and Mg—O—C' angle (142.3°), the deviation of $Mg^{2+}$ from amide plane being 0.85 Å. Dimethyl formamide is also known to coordinate to $Mg^{2+}$ (Hollander *et al.* 1973) with an Mg—O distance of 2.095 Å, the Mg—O—C' angle being 128.19° and $Mg^{2+}$ deviating from the amide plane by 0.29 Å.



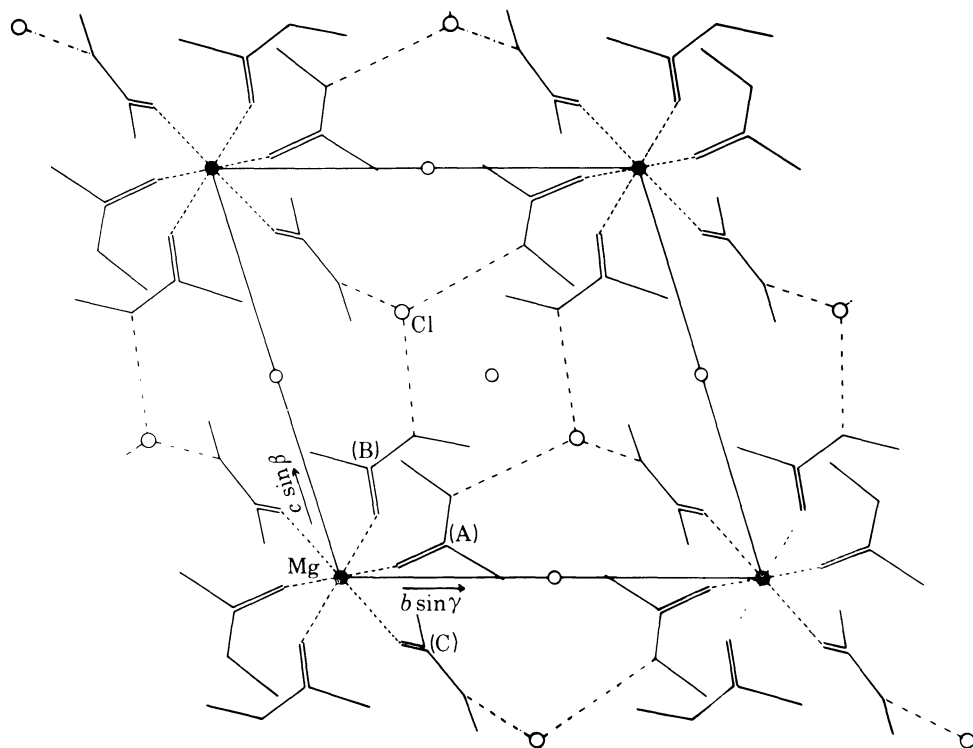FIGURE 8. Unit cell of $MgCl_2 6NMA$ as seen by looking down the *a*-axis.

### $CaCl_2 4NMA 2H_2O$ *complex*

The packing mode and the coordination sphere around two $Ca^{2+}$ ions are shown in figures 10 and 11. In addition to the four NMA molecules, each of the two $Ca^{2+}$ ions in the asymmetric unit has two water molecules bound to it, providing a regular octahedral coordination around the metal ion (table 4). The Ca—O (amide) distances (2.276 (11)–2.301 (8) Å) in the complex (table 5) are in the lower range of distances generally found in octahedral oxygen donor complexes of $Ca^{2+}$ (2.25–2.47 Å). The Ca—O (water) distances (2.342 (7) and 2.341 (12) Å) are slightly longer than the Ca—O (amide) distances, which indicates a greater strength of binding of the amide to $Ca^{2+}$ in comparison with water. Theoretical studies (Balasubramanian *et al.* 1972; Perricaudet & Pullman 1973*b*; Gupta & Rao 1973) have indeed shown that alkali and alkaline earth metal cations
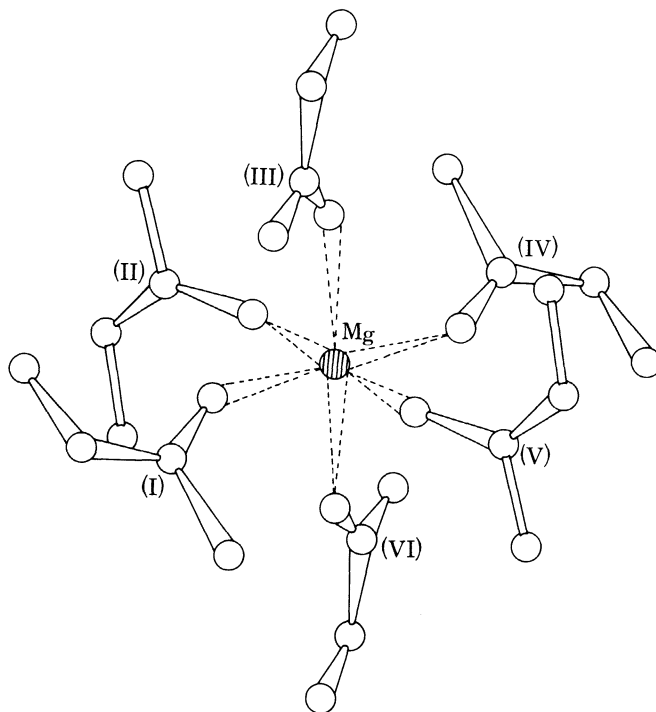
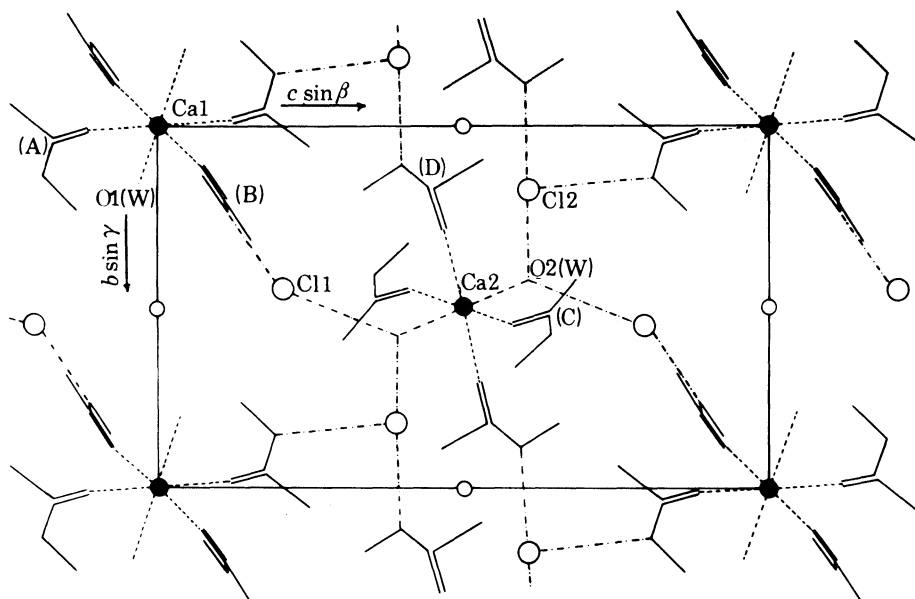FIGURE 9. Coordination sphere in $MgCl_2 6NMA$ (for symmetry code see table 4).



FIGURE 10. Unit cell of $CaCl_2 4NMA2H_2O$ as seen by looking down the *a*-axis.

bind more strongly to amides than to water. The values of the Ca—O—C′ angle (143 (2)° to 176 (1)°) in the NMA complex (table 5) show significant deviations from the lone-pair direction of the carbonyl bond. The $Ca^{2+}$ ion is slightly out of the amide plane in all the independent NMA molecules; the deviation from the amide plane is, however, not as large as in $Na^+$ or $K^+$ ions.
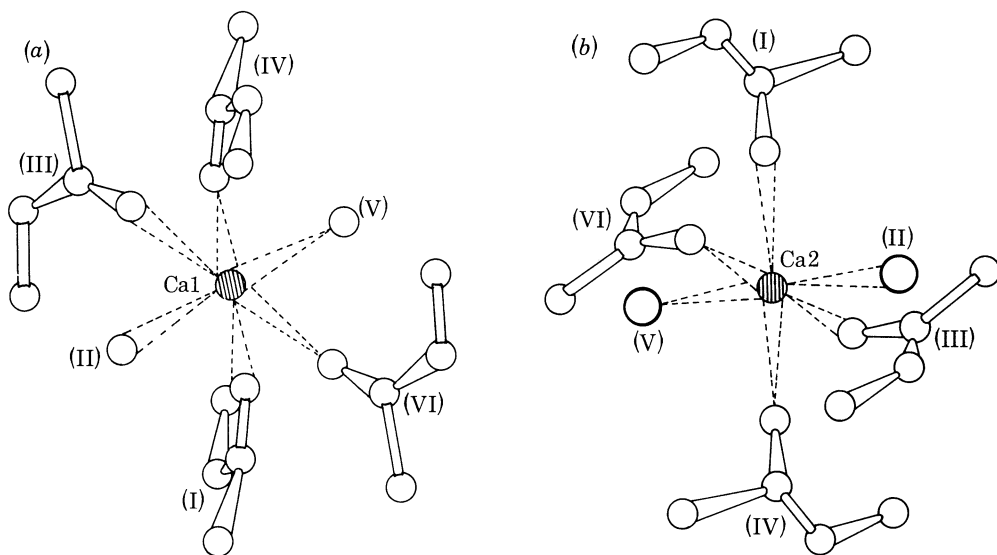


FIGURE 11. Coordination sphere in $CaCl_24NMA2H_2O$: (a) around Ca1, (b) around Ca2 (for symmetry code see table 4).

In the $CaCl_2$ glycylglycylglycine $3H_2O$ complex (Van der Helm & Willoughby 1969), with hepta-coordinated $Ca^{2+}$, Ca—O distances (2.296 and 2.398 Å) and Ca—O—C′ angles (148.9° and 144.1°) are similar to those found by us, but the deviations of $Ca^{2+}$ from the peptide plane (1.17 and 1.29 Å) are greater. The $Ca^{2+}$ ion is *cis* with respect to the C′—N bond in both the peptide groups. In the $CaBr_2$ salt of *D*-pantothenic acid (DeLucas *et al.* 1979), the hepta-coordinated $Ca^{2+}$ is *cis* with respect to the C′—N bond, and the Ca—O distance is 2.291 Å. The $Ca^{2+}$ ion deviates from the amide plane by 1.69 Å, and the Ca—O—C′ angle is 131.3°; the C′—N and C′=O distances are 1.320 and 1.243 Å respectively.

*Systematics in structural parameters in* NMA *complexes*
*and related systems*

In all the amide complexes investigated by us, the metal ions bind to the carbonyl oxygen which causes an increase in C′=O distance and a decrease in C′—N distance, the magnitude of the changes depending on the strength of

interaction. As mentioned earlier, such variations in bond distances are consistent with the vibrational spectra of the complexes (Rao *et al.* 1975) and also with the increase in the barrier to rotation found in solutions of alkali and alkaline earth metal salts in amides (Rao *et al.* 1977*b*; Rode 1977). Two carbonyl stretching frequencies found in the vibrational spectra of the complexes (Rao *et al.* 1975) could arise owing to the presence of crystallographically independent molecules of NMA having different strengths of interaction with the metal ion. The metal–oxygen distances found here are consistent with the vibrational frequencies of the metal–oxygen polyhedra; thus, the metal–oxygen stretching-force constants found in NMA complexes of Li, Na, K, Mg and Ca (0.6, 0.5, 0.4, 0.6 and 0.5 mdyn/Å†respectively) vary in the order of the ionic potentials of these cations, as do the metal–oxygen distances. It is interesting that we also find the $^{13}C$ chemical shifts of the $C'{=}O$ bond of amides to vary systematically with the ionic potential of the cations (Pulla Roa *et al.* 1980). Both semi-empirical and *ab initio* molecular orbital calculations on the interaction of amides with alkali and alkaline earth metal cations show that the interaction strengths vary in the order $Mg^{2+} > Li^+ > Na^+ > K^+$ (Perricaudet & Pullman 1973*b*; Rao 1977), which is exactly the trend of ionic potentials of these cations. Interestingly, the binding of these cations to amides as deduced from their effect on the barrier to rotation around the $C'{-}N$ bond, varies as $Li^+ \gtrsim Mg^{2+} > Na^+ \gtrsim Ca^{2+} > K^+ > Rb^+ > Cs^+$ (Fussenegger & Rode 1976), which is not very different from the trend in ionic potentials.

The bond lengths and angles of the NMA molecule in the complexes (table 6) illustrate some interesting features of bonding. We generally find that the $C'{-}N$ distance decreases as the $C'{=}O$ distance increases (see figure 12*a*). This is exactly what we would expect from the well known resonance structures of amides, according to which an increase in the double-bond order of the central $C{-}N$ bond is accompanied by a decrease in the $C{=}O$ bond order. Protonation is also known to change these bond lengths similarly (Rao *et al.* 1971*a*; Dunitz & Winkler 1975). More interesting is our observation that as the $C'{-}N$ distance decreases, the adjacent $N{-}C$ bond ($N{-}C2$) distance involving the amide N and the methyl group decreases (figure 12*b*), while the $C1{-}C'$ distance increases (figure 12*c*). These variations in $N{-}C2$ and $C1{-}C'$ distances have not been noticed hitherto. On examining the structures of $Li^+$ and $Na^+$ complexes of antamanide (Karle 1974*a,b*), we find that the $C^\alpha{-}C'$ bonds are slightly longer than average. The $N{-}C$ (methyl, *cis* to $C'{=}O$) bond in cyclodisarcosyl shows a shortening (*ca.* 0.04 Å) in the presence of $Li^+$ (Takahashi *et al.* 1977).

It is generally assumed that in the interaction of amides and other oxygen donors with metal ions or protons, bonding occurs along the lone-pair direction of the oxygen. We find that in all the complexes studied by us there is some deviation from the lone-pair direction (table 5). The deviation appears to depend on the strength of bonding and also on the packing of the molecules in the crystal,

† dyn = $10^{-5}$ N.

the range of the M—O—C′ angles in amide complexes being *ca.* $140 \pm 15°$. Deviation from the lone-pair direction is generally found in other oxygen donor complexes of alkali and alkaline earth metal cations (Poonia & Bajaj 1979), whose structures have been examined by making use of the published crystallographic data. The
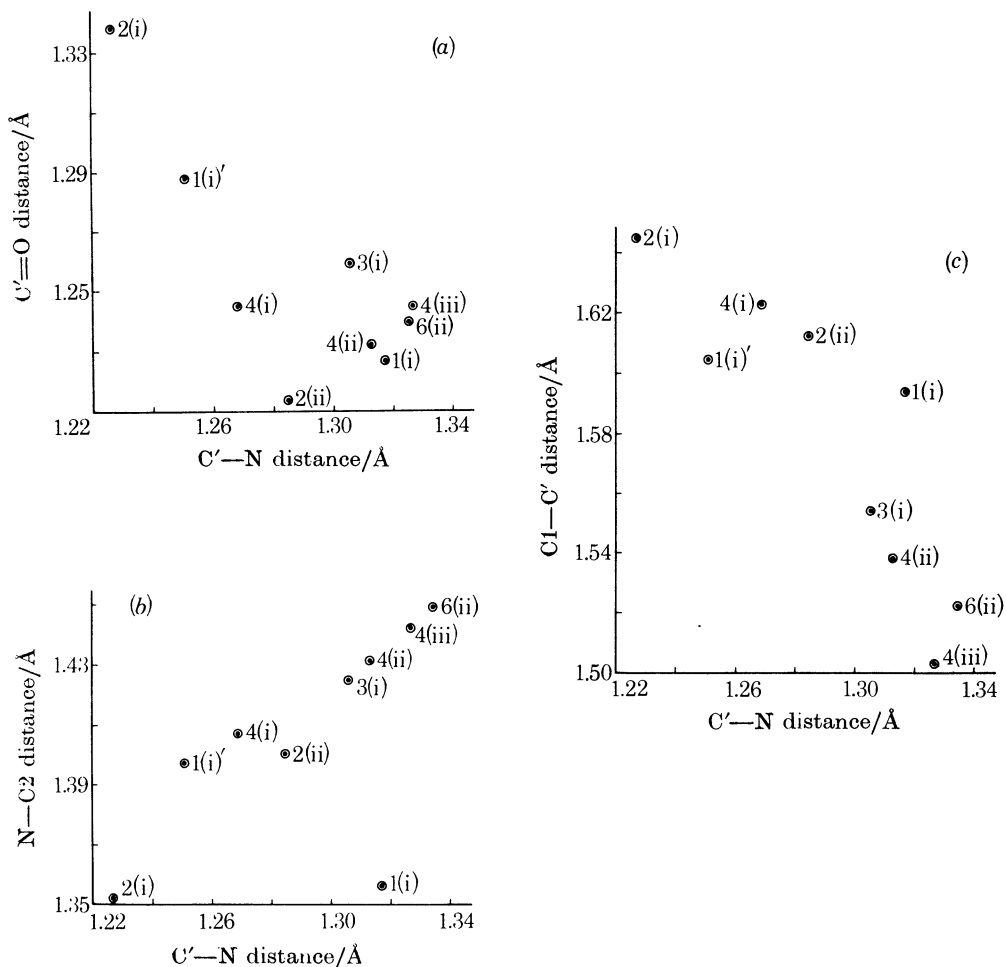


FIGURE 12. Plots showing systematics in the bond lengths of NMA: (*a*) C′=O length against C′—N length; (*b*) N—C2 length against C′—N length; (*c*) C1—C′ length against C′—N length. Values are from table 6; 1(i)′ corresponds to the disordered form of 1(i).

deviations from the M—O—C′ angle of 120° in the $Li^+$, $Na^+$, $K^+$, $Mg^{2+}$ and $Ca^{2+}$ complexes of oxygen donors are 10–30°, 20–35°, 4–40°, 10–22° and 10–30° respectively, the deviation generally being larger for amide donors than for other carbonyl donors. Deviations from the lone-pair direction are negligible in proton adducts (Winkler & Dunitz 1975*a*,*b*; Benedetti & DiBlasio 1980). Theoretical
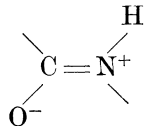
calculations (Gupta & Rao 1973; Perricaudet & Pullman 1973 *b*; Renugopala-krishnan & Urry 1978) on amide complexes also show that in the most stable configuration the metal ions deviate from the lone-pair direction. It should be noted that in hydrogen bonding in salt hydrates as well as in hydrogen-bonded

TABLE 7. SELECTED TORSIONAL ANGLES/DEG. AND DEVIATION/Å
OF NITROGEN FROM THE AMIDE PLANE

| complex | C1–C′–N–C2 | O–C′–N–C2 | deviation of N from the least-squares plane defined by C1, C′, O, N, C2 |
|---|---|---|---|
| Li: molecule A | −179.2 (12) | −0.2 (25) | 0.003 |
| Na: molecule A | 180.0 (19) | 4.5 (19) | 0.015 |
| molecule B | 178.5 (19) | −3.0 (19) | 0.017 |
| K: molecule A | 179.9 (12) | 2.9 (22) | 0.009 |
| Mg: molecule A | −176.81 (54) | 3.69 (82) | 0.028 |
| molecule B | 179.71 (47) | −0.19 (66) | 0.002 |
| molecule C | −179.34 (42) | −0.52 (59) | 0.005 |

complexes of amides and other carbonyl compounds (Rao 1971; Rao *et al.* 1971 *b*), deviation from the lone-pair direction of oxygen appears to be the general rule rather than the exception. In the discussion of individual complexes the deviation of the metal ion from the peptide plane (see table 5) was discussed. We have also examined such deviations in several oxygen-donor complexes of alkali and alkaline earth metals from the crystallographic data in the literature (Poonia & Bajaj 1979) and find the deviation to be least with $Li^+$ and $Mg^{2+}$ which form the strongest complexes. The trend in the out-of-plane deviation of the metal ions varies as $Li^+ < Mg^{2+} < Ca^{2+} \approx Na^+ < K^+$, which is the reverse of the trend in ionic potentials (which in turn seem to determine the strength of the metal–oxygen bond as discussed later in this section). The proton is always found to lie essentially in the amide plane (Winkler & Dunitz 1975 *a,b*; Benedetti & DiBlasio 1980).

The non-planarity of the peptide group is an important aspect of peptide conformation (Ramachandran *et al.* 1973; Dunitz & Winkler 1975). In all the complexes studied, the NMA molecules are essentially planar, the nitrogen atom showing negligible pyramidal character (as can be seen from the torsional angles and the deviation of the nitrogen atom from the least-squares plane passing through the C1, C′, O, N and C2 atoms which are given in table 7). This is to

be expected since the contribution of the resonance form $\begin{matrix} & & H \\ & & / \\ C = N^+ \\ / & & \backslash \\ O^- & & \end{matrix}$ to the

amide structure would be larger when cations are bound to the carbonyl oxygen. A similar effect on the planarity of the peptide geometry on protonation has been

observed by Dunitz *et al.* (1975). Vibrational spectroscopy studies (Rao *et al.* 1975) show that the $\tau(C'—N)$ frequency (amide VII band) is generally higher in complexes than in the parent amide.
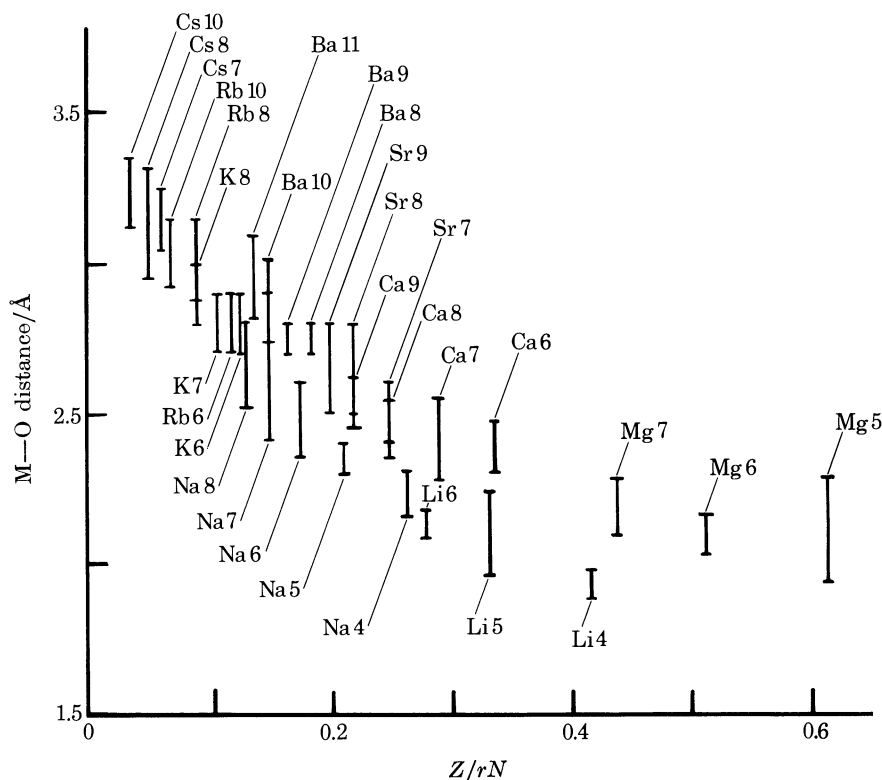


FIGURE 13. Variation of metal–oxygen distances in alkali and alkaline earth metal complexes and related systems with the ionic potential per ligand ($Z/rN$). The metal and the coordination number, $N$, are indicated in the plot.

While discussing the individual complexes, it was mentioned that the observed metal–oxygen distances fall in the ranges generally found in oxygen–donor co-ordination compounds of alkali and alkaline earth metals of the appropriate coordination number. We find that the ranges of metal–oxygen distances in the coordination compounds vary in the same direction as the ionic potential of the cation ($Z/r$, charge/radius) for a given coordination number. For a given metal–oxygen bond, the distance increases with the increase in coordination number for a given cation. To rationalize all the known M—O distances in alkali and alkaline earth metal salts and complexes, we have plotted them against the ionic potential per ligand ($Z/rN$, where $N$ is the coordination number). Such a plot is shown in figure 13, which illustrates an interesting relation. This plot is not unlike the relation between bond valence and bond distance (Brown 1978). The observed constancy of M—O distances for a given coordination number

explains why molecular orbital calculations gave the same M—O distance independent of the oxygen donor (Balasubramanian *et al.* 1972; Rao 1977) and showed an increase in this distance with increase in the number of amide molecules, or other ligands, around the cation (Rao 1973*b*; Gupta & Rao 1973).

TABLE 8. VARIOUS PARAMETERS FOR HYDROGEN BONDING,
NH $\cdots$ X INVOLVING AMIDE NH

| complex | N $\cdots$ X/Å | C'—N—X/deg. | C2—N—X/deg. | deviation/Å of X from amide plane |
|---|---|---|---|---|
| Li, molecule A† | 3.271 (10) | 120.9 (11) | 117.5 (8) | 0.180 |
| (N$^{I}$ $\cdots$ Cl) | 3.234 (12) | 127.1 (13) | 111.1 (8) | |
| Na, molecule A | 3.038 (18) | 118.6 (15) | 120.3 (9) | 0.537 |
| (N$^{II}$ $\cdots$ O2) | | | | |
| Na, molecule B | 3.014 (11) | 140.2 (7) | 94.5 (6) | 0.557 |
| (N$^{III}$ $\cdots$ O3) | | | | |
| K, molecule A | 3.553 (14) | 121.2 (10) | 119.2 (8) | 0.400 |
| (N$^{IV}$ $\cdots$ S) | | | | |
| Mg, molecule A | 3.231 (5) | 125.30 (34) | 116.32 (40) | 0.513 |
| (N$^{V}$ $\cdots$ Cl) | | | | |
| Mg, molecule B | 3.181 (4) | 125.94 (28) | 112.09 (32) | 0.277 |
| (N $\cdots$ Cl) | | | | |
| Mg, molecule C | 3.214 (4) | 123.77 (24) | 115.09 (29) | 0.152 |
| (N$^{VI}$ $\cdots$ Cl) | | | | |
| Ca, molecule A | 3.212 (12) | 119.9 (10) | 120.3 (10) | 0.010 |
| (N$^{VII}$ $\cdots$ C12) | | | | |
| Ca, molecule B | 3.136 (17) | 129.4 (16) | 114.6 (13) | 0.009 |
| (N$^{VII}$ $\cdots$ Cl1) | | | | |
| Ca, molecule D | 3.225 (31) | 120.9 (24) | 115.4 (16) | 0.477 |
| (N$^{VIII}$ $\cdots$ C12) | | | | |

Symmetry related atoms: I, $-\frac{1}{4}-y$, $\frac{1}{4}+x$, $\frac{1}{4}+z$; II, $x$, $\frac{1}{2}-y$, $\frac{1}{2}+z$; III, $2-x$, $1-y$, $1-z$; IV, $\frac{1}{2}+x$, $\frac{1}{2}-y$, $1-z$; V, $-x$, $1-y$, $1-z$; VI, $x$, $y$, $1+z$; VII, $1+x$, $y$, $1+z$; VIII, $-x$, $-y$, $1-z$.
† The values for the disordered form are also given.

In all the complexes studied by us, the anions form hydrogen bonds with the N—H bond of NMA (see table 8 for structural parameters of hydrogen bonds). In the Li complex, Cl$^-$ forms hydrogen bonds with four NH bonds, the nitrogen atoms forming a tetrahedron around the anion. The N $\cdots$ Cl distance of 3.27 (1) Å agrees with the value reported in the literature (Ashida *et al.* 1972; Dunitz & Winkler 1975). Because of its size and low formal charge, the perchlorate ion in the Na complex forms relatively weak hydrogen bonds, as evidenced by the N $\cdots$ O distance of *ca.* 3.02 Å (Haddad & Gentile 1975; Brown 1976) and the deviation of the angles (given in table 8) from 120°. Another perchlorate oxygen (O4) has an N $\cdots$ O distance of 3.44 Å, with the nitrogen of molecule A transformed by $1-x$, $-y$, $1-z$. In the K complex, the sulphur end of the SCN$^-$ ion is hydrogen bonded to an NH group, besides coordinating to the K$^+$ ion. The N $\cdots$ S distance of 3.55 (1) Å compares well with the value given in the literature

(Kamenar *et al.* 1973) for the N—H $\cdots$ S type of hydrogen bond. In the Mg complex, the $Cl^-$ ion is hydrogen bonded to three NH bonds (of three different NMA molecules) with N $\cdots$ Cl distances varying from 3.18 to 3.23 Å. In the Ca complex, the NH bonds of all the amide molecules, except that of molecule C, are involved in hydrogen bonding; N $\cdots$ Cl distances vary from 3.14 (2) to 3.23 (3) Å. Of the two water molecules, only O2(W) is hydrogen bonded (the $Cl^-$ ions being at distances 3.16 (1) and 3.08 (1) Å).

In all the complexes, C'—N—X and C2—N—X (X being the anion or the donor atom of the anion) angles are not far from 120°, but the latter is generally smaller than the former. The anion (X) is also found to deviate from the amide plane (table 8), the magnitude of the deviation being related to the deviation of the metal atom from the same peptide plane.

One may be concerned that the variation in peptide geometry due to cation binding may also be affected by the nature of anion. This may not be serious because the metal–oxygen distance, as well as some of the important amide distances, show expected systematics with the metal ion even though the anions vary in the complexes studied by us.

REFERENCES

Armbruster, A. M. & Pullman, A. 1974 *FEBS Lett.* **49**, 18.
Ashida, T., Bando, S. & Kakudo, M. 1972 *Acta crystallogr.* B **28**, 1560.
Balasubramanian, D., Goal, A. & Rao, C. N. R. 1972 *Chem. Phys. Lett.* **17**, 482.
Balasubramanian, D. & Shaikh, R. 1973 *Biopolymers* **12**, 1639.
Balasubramanian, D. & Misra, B. C. 1977 In *Metal–ligand interactions in organic chemistry and biochemistry* (ed. B. Pullman & N. Goldblum). Dordrecht: Reidel.
Bats, J. W., Coppens, P. & Kvick, Å. 1977 *Acta crystallogr.* B **33**, 1534.
Bello, J., Haas, D. & Bello, H. R. 1966 *Biochemistry, Philad.* **5**, 2539.
Benedetti, E. 1977 In *Peptides–Proceedings of the Fifth American Peptide Symposium* (ed. M. Goodman & J. Meienhofer), p. 257. New York: John Wiley.
Benedetti, E. & Di Blasio, B. 1980 *J. Chem. Soc. Perkin Trans.* II, 500.
Brown, I. D. 1976 *Acta crystallogr.* A **32**, 786.
Brown, I. D. 1978 *Chem. Soc. Rev.* **7**, 359.
Cromer, D. T. & Mann, J. B. 1968 *Acta crystallogr.* A **24**, 321.
Declercq, P. J. P., Meulemans, R., Piret, P. & Van Meerssche, M. 1971 *Acta crystallogr.* B **27**, 539.
DeLucas, L., Einspahr, H. & Bragg, C. E. 1979 *Acta crystallogr.* B **35**, 2724.
Dobler, M., Dunitz, J. D. & Kilbourn, B. T. 1969 *Helv. chim. Acta.* **52**, 2573.
Dobler, M. & Phizackerley, R. P. 1974 *Helv. chim. Acta.* **57**, 664.
Dunitz, J. D. & Winkler, F. K. 1975 *Acta crystallogr.* B **31**, 251.
Freeman, H. C. 1973 *Inorganic biochemistry* (ed. G. L. Eichhorn), vol. 1, p. 121. Amsterdam: Elsevier.
Fussenegger, R. & Rode, B. M. 1976 *Chem. Phys. Lett.* **44**, 95.
Gentile, P. S. & Shankoff, T. A. 1965 *J. inorg. nucl. Chem.* **27**, 2301.
Gobillon, P. Y., Piret, P. & Van Meerssche, M. 1962 *Bull. Soc. chim. Fr.* 551.

Gupta, A. & Rao, C. N. R. 1973 *J. Phys. Chem.* **77**, 2888.

Haas, D. J. 1964 *Nature, Lond.* **201**, 64.

Haddad, S. & Gentile, P. S. 1975 *Inorg. chim. Acta.* **12**, 131.

Hanson, J. C., Sieker, L. C. & Jensen, L. H. 1972 *Trans. Am crystallogr. Ass.* **8**, 133.

Harada, Y. & Iitaka, Y. 1974 *Acta crystallogr.* B **30**, 1452.

Hollander, F. J., Templeton, D. H. & Zalkin, A. 1973 *Acta crystallogr.* B **29**, 1289

Hughes, D. L., Mortimer, C. L. & Truter, M. R. 1978 *Inorg. chim. Acta.* **29**, 43.

Jeffrey, G. A. & Cruickshank, D. W. J. 1953 *Quart. Rev.* **7**, 335.

Kamenar, B., Prout, K. & Ganellin, C. R. 1973 *J. chem. Soc. Perkin Trans.* II, 1734.

Karle, I. L., Dragonette, K. S. & Brenner, S. A. 1965 *Acta crystallogr.* **19**, 713.

Karle, I. L. 1974a *J. Am. chem. Soc.* **96**, 4000.

Karle, I. L. 1974b *Biochemistry, Philad.* **13**, 2155.

Katz, J. L. & Post, B. 1960 *Acta crystallogr.* **13**, 624.

Marsh, R. E. & Donohue, J. 1967 *Adv. Protein Chem.* **22**, 235.

Mercer, M. & Truter, M. R. 1973 *J. chem. Soc. Dalton Trans.* 2469.

Neupert-Laves, K. & Dobler, M. 1975 *Helv. chim. Acta.* **58**, 432.

Ovchinnikov, Yu. A., Ivanov, V. T. & Shkrob, A. M. 1974 In *Membrane active complexones.* Amsterdam: Elsevier.

Owen, J. D. 1978 *J. chem. Soc. Dalton Trans.* 1418.

Perricaudet, M. & Pullman, A. 1973a *Int. J. Peptide Protein Res.* **5**, 99.

Perricaudet, M. & Pullman, A. 1973b *FEBS Lett.* **34**, 222.

Poonia, N. S. & Bajaj, A. V. 1979 *Chem. Rev.* **79**, 389.

Pulla Rao, Ch. Balaram, P. & Rao, C. N. R. 1980 *J. chem. Soc. Faraday Trans.* I **76**, 1008.

Radom, L., Lathan, W. A., Hehre, W. J. & Pople, J. A. 1972 *Aust. J. Chem.* **25**, 1601.

Ramachandran, G. N., Lakshminaryanan, A. V. & Kolaskar, A. S. 1973 *Biochim. biophys. Acta.* **303**, 8.

Rao, C. N. R. 1971 In *Water* (ed. F. Franks), vol. 1. New York: Plenum Press.

Rao, C. N. R., Rao, K. G., Goal, A. & Balasubramanian, D. 1971a *J. chem. Soc.* A 3077.

Rao, C. N. R., Goel, A., Rao, K. G. & Murthy, A. S. N. 1971b *J. phys. Chem.* **75**, 1744.

Rao, C. N. R. 1973a *J. Molec. Struct.* **19**, 493.

Rao, C. N. R. 1973b In *Conformation of biological molecules and polymers* (5th Jerusalem Symposium on Quantum Chemistry and Biochemistry). New York: Academic Press.

Rao, C. N. R., Bhujle, V. V., Goel, A., Bhat, U. R. & Paul, A. 1973 *J. Chem. Soc. chem. Commun.* 161.

Rao, C. N. R., Randhawa, H. S., Reddy, N. V. R. & Chakravorty, D. 1975 *Spectrochim. Acta.* A **31**, 1283.

Rao, C. N. R. 1977 In *Metal–ligand interactions in organic chemistry and biochemistry* (ed. B. Pullman & N. Goldblum), p. 147. Dordrecht: Reidel.

Rao, C. N. R., Agarwal, U. P. & Rao, K. G. 1977a *Discuss. Faraday Soc.* **64**, 160.

Rao, K. G., Becker, E. D. & Rao, C. N. R. 1977b *J. Chem. Soc. chem. Commun.* 350.

Renugopalakrishnan, V. & Urry, D. W. 1978 *Biophys. J.* **24**, 729.

Rode, B. M. 1977 In *Metal–ligand interactions in organic chemistry and biochemistry* (ed. B. Pullman & N. Toldblum), p. 127. Dordrecht: Reidel.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. 1965 *J. chem. Phys.* **42**, 3175.

Takahashi, N., Tanaka, I., Yamane, T., Ashida, T., Sugihara, T., Imanishi, Y. & Higashimura, T. 1977 *Acta crystallogr.* B **33**, 2132.

Truter, M. R. 1973 In *Structure and bonding*, vol. 16, p. 71. New York: Springer-Verlag.

Van der Helm, D. & Willoughby, T. V. 1969 *Acta crystallogr.* B **25**, 2317.

Vijayan, M. & Viswamitra, M. A. 1967 *Acta crystallogr.* **23**, 1000.

von Hippel, P. H. & Schleich, T. 1969 In *structure and stability of biological macromolecules* (ed. S. N. Timasheff & G. D. Fasman), vol. 2, p. 417. New York: Marcel Dekker.

Williams, R. J. P. 1971 *Adv. Chem. Ser.* 100, ch. 8.

Winkler, F. K. & Dunitz, J. D. 1975a *Acta. crystallogr.* B **31**, 273.

Winkler, F. K. & Dunitz, J. D. 1975b *Acta crystallogr.* B **31**, 278.