Electrostatic Potential from High-Resolution X-Ray Diffraction. Application to a Pseudo-Peptide Molecule *

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The calculation of the electrostatic potential of a molecule removed from the crystal lattice is derived from the parameters obtained by a kappa refinement and by a Hansen-Coppens electron density model. These calculations in direct space are applied to N-acetyl-α,β-dehydrophenylalanine; deformation potentials calculated by Fourier transformation are compared to those obtained in direct space.

Key words: Electrostatic potential; Kappa refinement; Multipole refinement; Peptides; Net charges.

Introduction

The electrostatic potential is a scalar representation of the interaction between the charges inside and outside a distribution. The charge density alone does not provide complete information about the interaction between molecules, but it is linked to the electrostatic potential via Poisson's law $\nabla^2 V = -\frac{\varrho(\boldsymbol{r})}{\varepsilon_0}$. Several models [1] of the charge density derived from X-ray experiments are available. Starting with a multipolar model of the valence deformation density, Stewart was the first to give an analytical expression of the electrostatic potential in this case [2]; his first papers are based mainly on reciprocal-space calculations by Fourier transformation of $[H^2]^{-1}$-weighted structure factors. Direct calculations are described in X.M. He's Ph.D. thesis from the University of Pittsburgh (1984, USA). We have applied [3] this formalism to the Hansen-Coppens [1 d] multipolar model of an atomic electron density,

$$\varrho(\boldsymbol{r}) = \varrho_c(r) + P_v \varkappa'^3 \varrho_{fv}(\varkappa' r) + \sum_l \sum_m \varkappa''^3 P_{lm} \mathscr{R}_l(\varkappa'' r)\, Y_{lm}(\boldsymbol{r}/r)\,, \qquad (1)$$

where P_v, $\varkappa'$, $\varkappa''$, P_{lm} and $\mathscr{R}_l(r)$ have the usual meaning [1 d]. The main difference between Stewart's preliminary model [1 a] and the Hansen-Coppens fit is the kappa formalism [4]. Our paper is divided into three parts: In the first part we describe the formalism used; in the second part we present results concerning a pseudo-peptide molecule (N-acetyl-α-β-dehydrophenylalanine-methylamide [AcΔ] [5] (Figure 1); in the third part we compare the two different ways to obtain the electrostatic potential (i.e. direct calculations and reciprocal-space calculations).

Direct Calculations

The electrostatic potential at a given point $\boldsymbol{r}$ for an atom positioned at $\boldsymbol{R}$ (Scheme 1) is calculated in direct

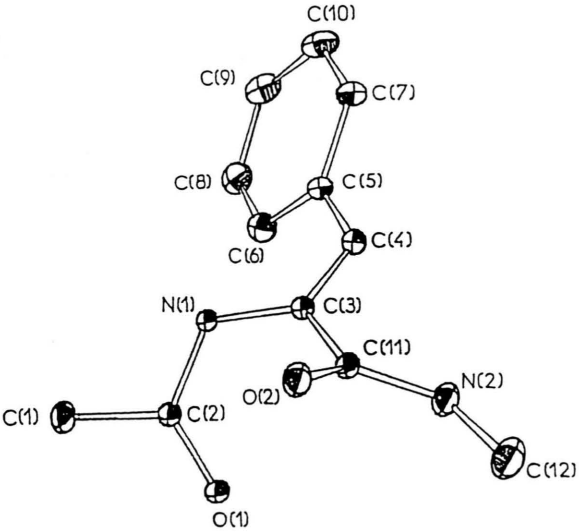

Fig. 1. Ortep view of N-acetyl-α,β-dehydrophenylalanine-methylamide.

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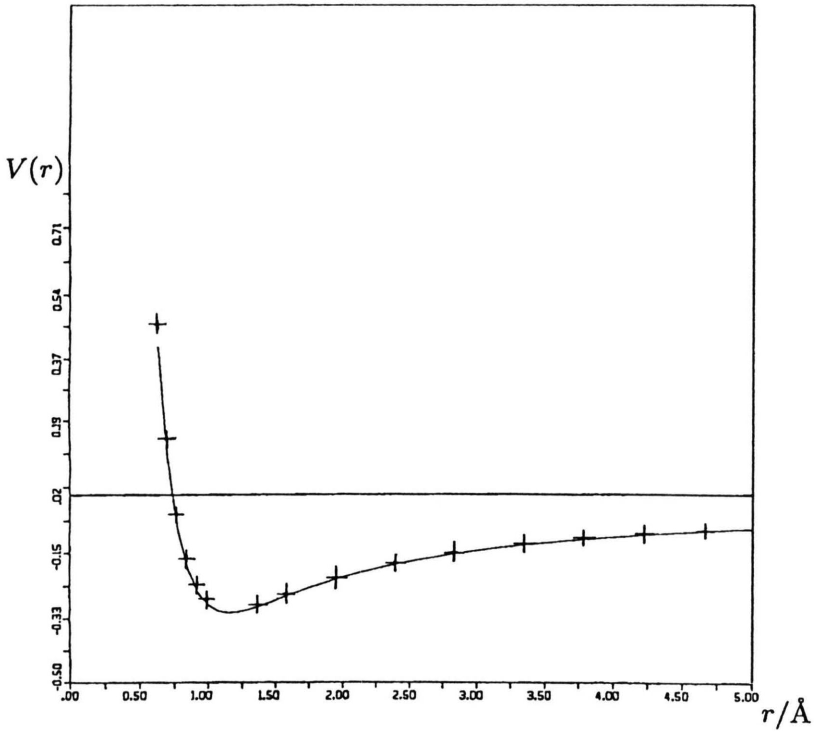


Fig. 2. Effect of the $\varkappa'$ parameter on the electrostatic potential $V(r)$ of a negatively charged oxygen atom: the continuous curve corresponds to $\varkappa' = 1.00$, the crosses to $\varkappa' = 0.97$.

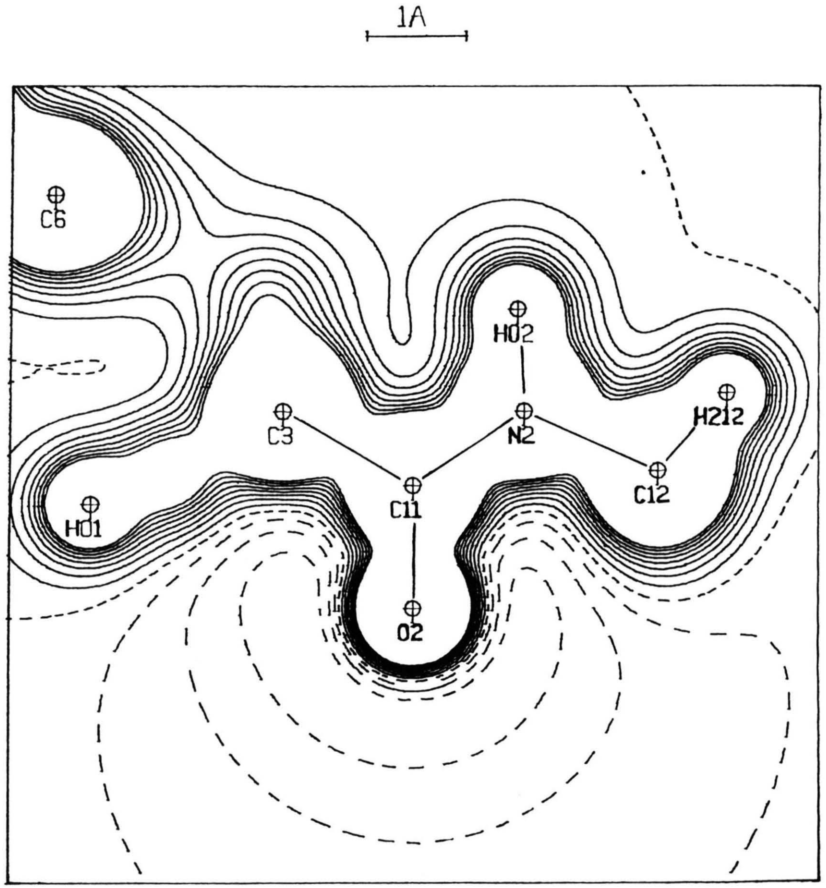


Fig. 3. Effect of the multipole part of the deformation density on the electrostatic potential of a peptide link: 3a) without the $\Delta V(\mathbf{r})$ part; 3b) total potential; 3c) $\Delta V(\mathbf{r})$. Contours ± 0.1 eÅ^{-1}, negative contours are dashed, zero contours are short dashed.

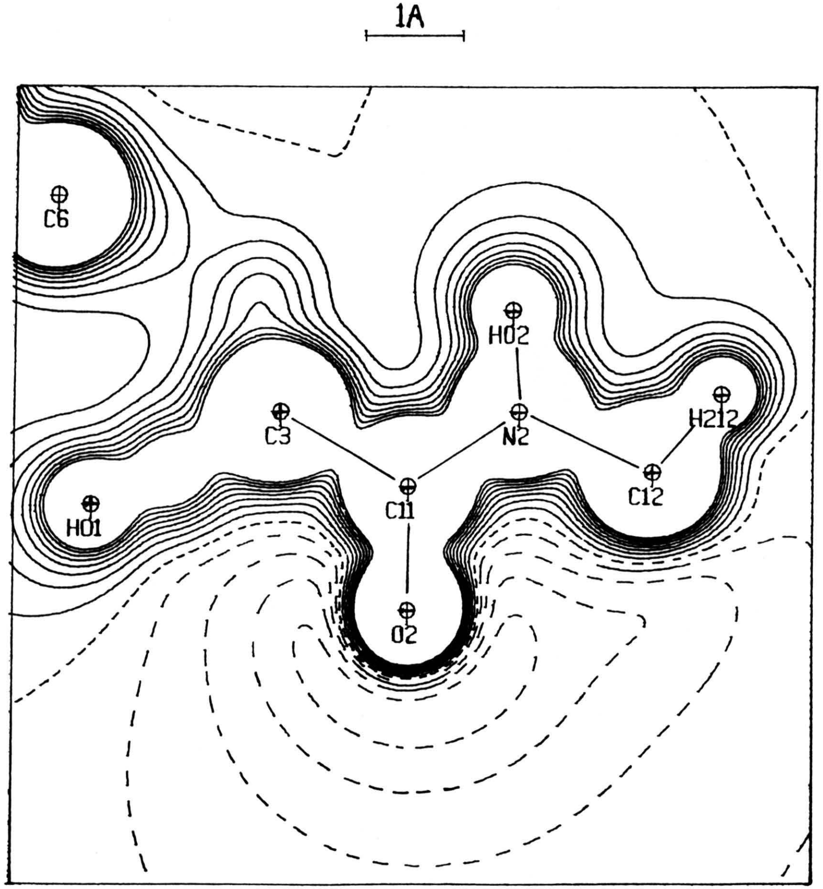


Fig. 3b. Total potential.

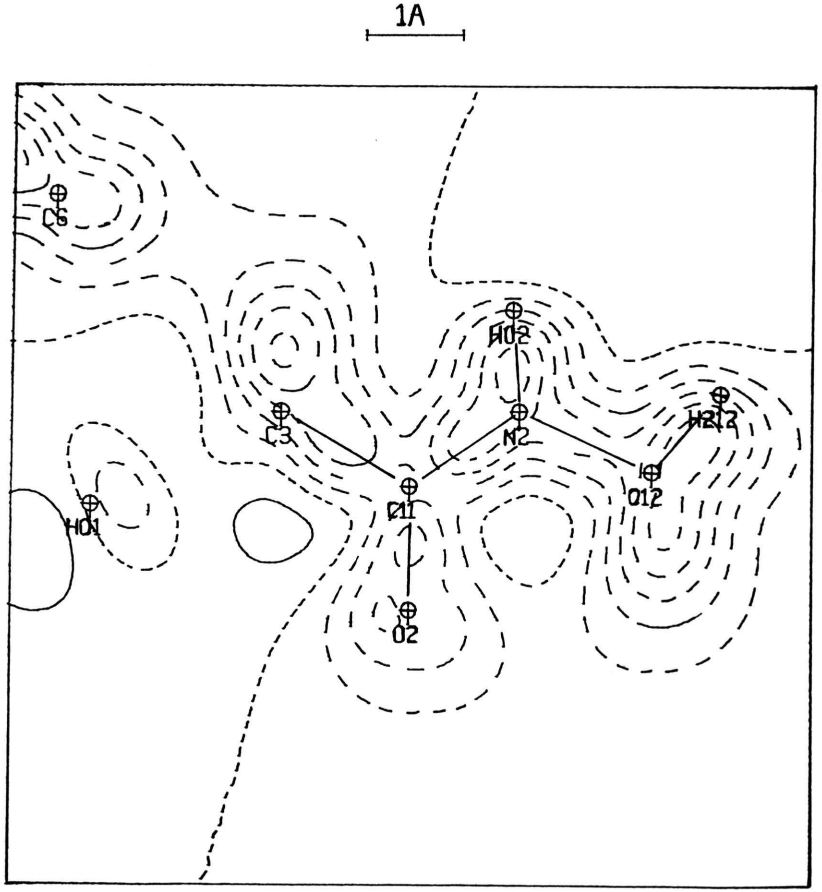
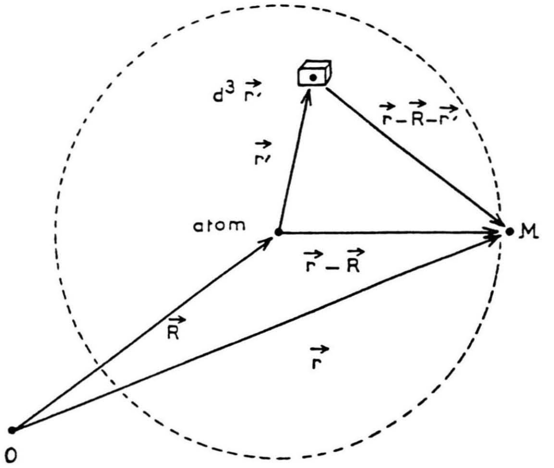


Fig. 3c. $\Delta V(r)$.



Scheme 1

space as follows:

$$V(\boldsymbol{r}) = V_{\text{core}}(\boldsymbol{r}) + V_{\text{val}}(\boldsymbol{r}) + \Delta V(\boldsymbol{r})$$

with

$$V_{\text{core}}(\boldsymbol{r}) = \frac{Z}{|\boldsymbol{r}-\boldsymbol{R}|} - \int_0^\infty \frac{\varrho_{\text{core}}(r')\,\mathrm{d}^3\boldsymbol{r}'}{|\boldsymbol{r}-\boldsymbol{R}-\boldsymbol{r}'|};$$

$$V_{\text{val}}(\boldsymbol{r}) = -\int_0^\infty \frac{\varrho_{\text{val}}(r')\,\mathrm{d}^3\boldsymbol{r}'}{|\boldsymbol{r}-\boldsymbol{R}-\boldsymbol{r}'|};$$

Z is the charge of the nucleus and $\varrho_{\text{val}}(r') = P_{\text{v}}\,\varkappa'^3\,\varrho_{\text{fv}}(\varkappa' r')$; ϱ_{core} and ϱ_{fv} are the core and valence electron densities of the free atom and are calculated from the Clementi wave functions [6]. Then

$$V_{\text{val}}(\boldsymbol{r}) = -\int_0^\infty \frac{P_{\text{v}}\,\varkappa'^3\,\varrho_{\text{fv}}(\varkappa' r')\,\mathrm{d}^3\boldsymbol{r}'}{|\boldsymbol{r}-\boldsymbol{R}-\boldsymbol{r}'|};$$

let $r'' = \varkappa' r'$, $\mathrm{d}^3\boldsymbol{r}'' = \varkappa'^3\,\mathrm{d}r'^3$; then

$$V_{\text{val}}(\boldsymbol{r}) = -P_{\text{v}}\,\varkappa' \int_0^\infty \frac{\varrho_{\text{fv}}(r'')\,\mathrm{d}^3\boldsymbol{r}''}{|\varkappa'(\boldsymbol{r}-\boldsymbol{R})-\boldsymbol{r}''|} = P_{\text{v}}\,\varkappa'\,V_{\text{fv}}(\varkappa'|\boldsymbol{r}-\boldsymbol{R}|).$$

Thus $V_{\text{val}}(r)$ can be calculated from the electrostatic potential V_{fv} of the free-atom valence contribution at the point $\varkappa'(|\boldsymbol{r}-\boldsymbol{R}|)$; because of the Gauss theorem, it is calculated as the sum of two integrals,

$$V_{\text{fv}}(\varkappa'|\boldsymbol{r}-\boldsymbol{R}|) = \frac{\int_0^{\varkappa'|\boldsymbol{r}-\boldsymbol{R}|} \varrho_{\text{fv}}(r'')\,\mathrm{d}^3\boldsymbol{r}''}{\varkappa'|\boldsymbol{r}-\boldsymbol{R}|} + \int_{\varkappa'|\boldsymbol{r}-\boldsymbol{R}|}^{\infty} \frac{\varrho_{\text{fv}}(r'')\,\mathrm{d}^3\boldsymbol{r}''}{|\varkappa'(\boldsymbol{r}-\boldsymbol{R})-\boldsymbol{r}''|},$$

where in the first term $\int_0^{\varkappa'|\boldsymbol{r}-\boldsymbol{R}|} \varrho_{\text{fv}}(r'')\,\mathrm{d}^3\boldsymbol{r}''$ is the electronic charge inside the sphere of radius $\varkappa'(|\boldsymbol{r}-\boldsymbol{R}|)$.

Figure 2 shows the effect of this $\varkappa'$ parameter on the radial electrostatic potential:

$$V(\boldsymbol{r}) = V_{\text{core}}(\boldsymbol{r}) + \varkappa'\,P_{\text{v}}\,V_{\text{fv}}(\varkappa'(|\boldsymbol{r}-\boldsymbol{R}|)).$$

$V(\boldsymbol{r})$ is calculated on the oxygen atom O2 of AcΔ ($\varkappa' = 0.977$, $P_{\text{v}} = 6.44$ e), and with $\varkappa' = 1$ for the same P_{v}. As expected, when $\varkappa'$ decreases, the radial electron density and the negative electrostatic potential expands around the atom; thus the kappa parameter reinforces the rôle of the net charge on the atom in relation to the Slater rules, as shown by Coppens [7].

$\Delta V(\boldsymbol{r})$ is calculated from the non-spherical part of the electron density: using the Green function and the orthogonality of the spherical harmonic functions, the contribution of the deformation density to the electrostatic potential is given by (see Appendix A)

$$\Delta V(\boldsymbol{r}) = -4\pi \sum_{lm} \frac{\varkappa'' P_{lm}}{2l+1} \left[\frac{1}{\varkappa''^{\,l+1}\,|\boldsymbol{r}-\boldsymbol{R}|^{l+1}} \cdot \int_0^{\varkappa''|\boldsymbol{r}-\boldsymbol{R}|} t^{l+2}\,\mathscr{R}_l(t)\,\mathrm{d}t \right. \tag{2}$$
$$\left. + \varkappa''^{\,l}\,|\boldsymbol{r}-\boldsymbol{R}|^{l} \int_{\varkappa''|\boldsymbol{r}-\boldsymbol{R}|}^{\infty} t^{-(1-l)}\,\mathscr{R}_l(t)\,\mathrm{d}t \right] Y_{lm}(\theta', \phi').$$

All these calculations are coded in a FORTRAN V program called Electros [8].

Application to N-acetyl-α,β-dehhydrophenylalanine methylamide (Ac$\varDelta$) [5]

AcΔ is a small pseudopeptide molecule (see Fig. 1) that in the solid state is linked to four other molecules via linear hydrogen bonds ($\langle \mathrm{N} \cdots \mathrm{O} \rangle = 2.90$ Å). Figure 3 gives the electrostatic potential of the O2C11N2 peptide link of an isolated molecule (i.e. removed from the crystal lattice) calculated as follows: a) with the

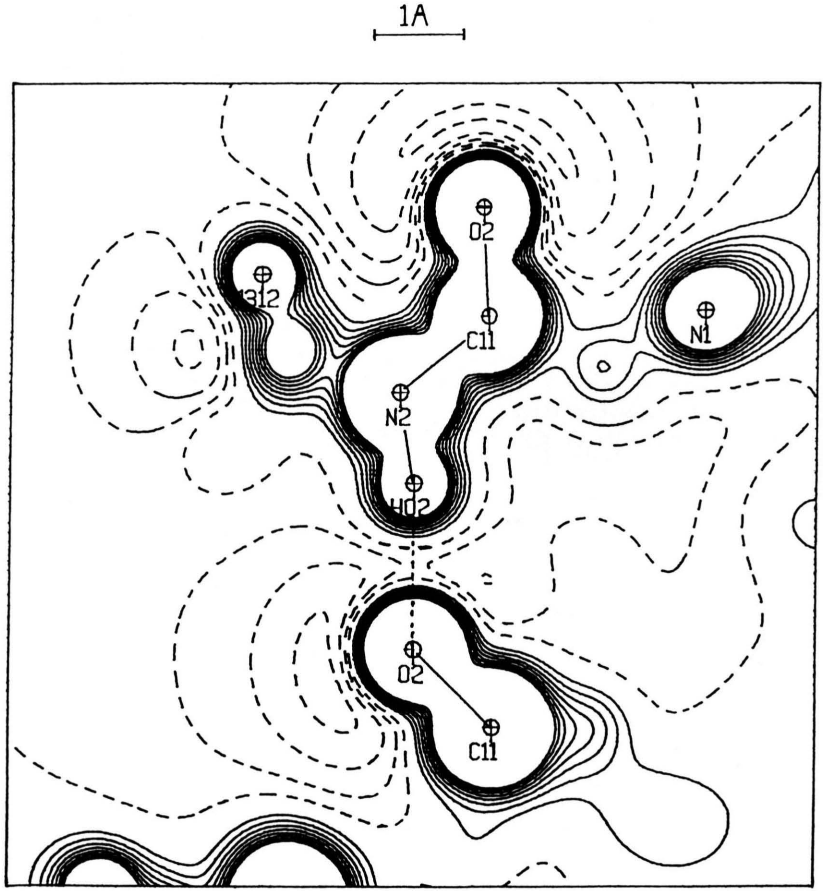


Fig. 4. Electrostatic potential of a hydrogen bond; contours as in Figure 3.

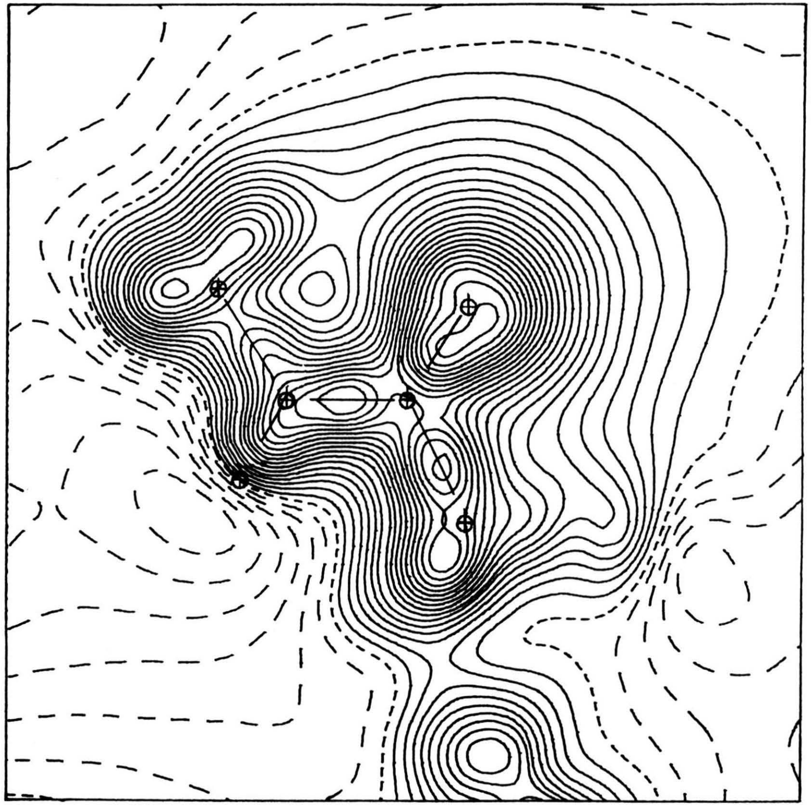


Fig. 6. Deformation potential of a single molecule in a box of 10 × 10 × 10 Å^3 calculated by Fourier transformation; contours as in Figure 5.

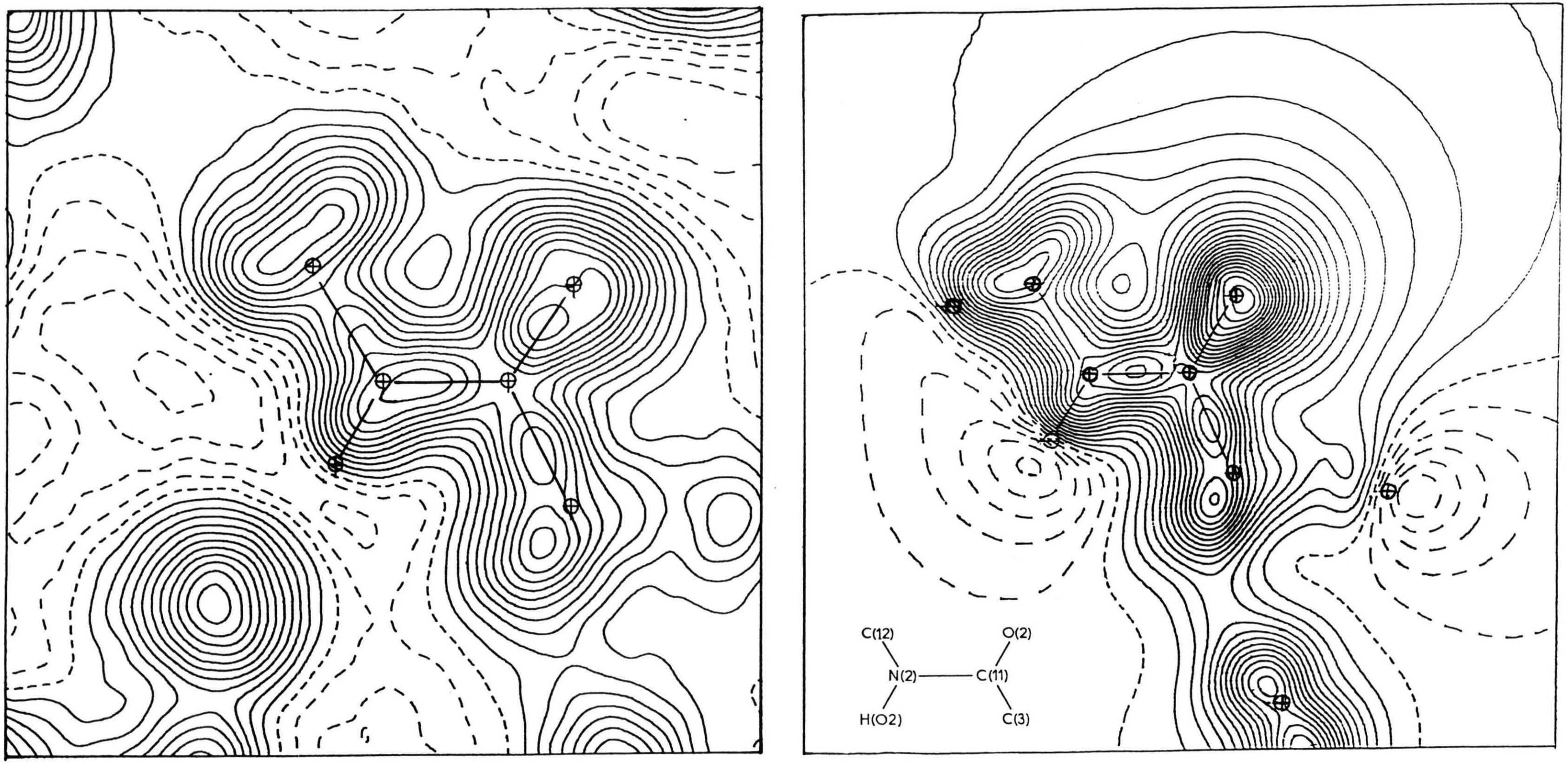


Fig. 5a.

Fig. 5b.

Fig. 5. Deformation potential of the crystal of AcΔ (5 a) compared to that of an isolated molecule (5 b). Contours ±0.05 eÅ^{-1}, zero contour is short dashed.

parameters resulting from the kappa refinement, and b) including the $\Delta V(\boldsymbol{r})$ term (see (2)). The difference between these two calculations is shown in Fig. 3c: the overall shape of the potential remains the same in the outer part of the molecule, whereas the contributions of the non-spherical part are important in the close surroundings of the atoms, in a region where the quantum effects are non-negligible. The non-spherical part adds ~ -0.08 eÅ^{-1} to the minimum potential. This observation, which is expected because the multipole expansion of the potential has a non-negligible value at short distances, shows that a kappa refinement of acceptable accuracy will lead to a realistic electrostatic potential. One other interesting feature of $V(\boldsymbol{r})$ is that, contrary to the deformation density, the electrostatic potential does not have a "rabbit ear" shape, but rather has an almost spherical "skull" shape; this means that the directionality observed in $\Delta\varrho(\boldsymbol{r})$ maps is in part lost when the electrostatic potential is calculated.

The electrostatic potential of two interacting molecules via hydrogen bonds is given in Fig. 4: the deep negative region around the oxygen atom divides into two parts on each side of the H···O hydrogen bond, leading to a flat valley of slightly negative potential (-0.05 eÅ^{-1}). These results are in very good agreement with those of Stewart [9] and of Craven [10] and with our calculations on other peptides [3].

Reciprocal-Space Calculations

The electron contribution to the potential can be calculated as

$$V_e(\boldsymbol{r}) = \int_{\boldsymbol{r}'} \frac{\varrho(\boldsymbol{r}')}{|\boldsymbol{r}-\boldsymbol{r}'|}\,\mathrm{d}^3\boldsymbol{r}',$$

and expanding $\dfrac{1}{|\boldsymbol{r}-\boldsymbol{r}'|}$ in reciprocal space,

$$\frac{1}{|\boldsymbol{r}-\boldsymbol{r}'|} = \frac{1}{\pi v}\int_{\boldsymbol{H}} \frac{\exp\{-2\pi i \boldsymbol{H}(\boldsymbol{r}-\boldsymbol{r}')\}}{H^2}\,\mathrm{d}^3\boldsymbol{H},$$

where v is the unit cell volume and $\boldsymbol{H}$ a reciprocal-space vector, the electrostatic potential becomes

$$V_e(\boldsymbol{r}) = \frac{1}{\pi v}\int_{\boldsymbol{H}} \frac{\exp\{-2\pi i \boldsymbol{H}\cdot\boldsymbol{r}\}}{H^2} \cdot \left[\int_{\boldsymbol{r}'} \varrho(\boldsymbol{r}')\exp\{+2\pi i \boldsymbol{H}\cdot\boldsymbol{r}'\}\,\mathrm{d}^3\boldsymbol{r}'\right]\mathrm{d}^3\boldsymbol{H}$$

$$= \frac{1}{\pi v}\int_{\boldsymbol{H}} \frac{F(\boldsymbol{H})}{H^2}\exp\{-2\pi i \boldsymbol{H}\cdot\boldsymbol{r}\}\,\mathrm{d}^3\boldsymbol{H}.$$

In other words, the electronic part of the electrostatic potential is the Fourier transform of $F(\boldsymbol{H})/H^2$. As pointed out by Stewart [2], there is a singularity for $\boldsymbol{H}=\boldsymbol{O}$ (when we approach the crystal surfaces in direct space).

In order to avoid this problem, we will briefly discuss the deformation electrostatic potential

$$\Delta V(\boldsymbol{r}) = \frac{1}{\pi V}\int \frac{1}{H^2}\left(|F_{\mathrm{M}}|\,e^{i\phi_{\mathrm{M}}} - |F_{\mathrm{S}}|\,e^{i\phi_{\mathrm{S}}}\right) \cdot \exp\{-2\pi i \boldsymbol{H}\cdot\boldsymbol{r}\}\,\mathrm{d}^3\boldsymbol{H}, \quad (3)$$

where F_{M}, ϕ_{M}, F_{S}, ϕ_{S} are the moduli and phases of the static structure factors ($U^{ij}=0$), respectively, calculated from the multipole model [1 d] and from the promolecule. This deformation potential of the peptide link (Fig. 5a) is compared to the deformation potential calculated in direct space for a molecule removed from the crystal lattice (Figure 5b). The crystal effect is clearly visible. Finally, Fig. 6 gives the deformation potential calculated from (3) for a static molecule in a "crystal" of 10 × 10 × 10 Å^3 unit cell: the shortest distances between the molecules are larger than 4 Å, and the interactions with the surrounding molecules are still visible.

Appendix A

The contribution of the multipolar part of the charge density (Scheme 2)

$$\Delta\varrho(\boldsymbol{r}') = -\sum_{l,m} \varkappa''^3 P_{lm}\,\mathscr{R}_l(\varkappa''|\boldsymbol{r}'-\boldsymbol{R}|)\,Y_{lm}(\theta,\phi)$$

to the electrostatic potential is

$$\Delta V(\boldsymbol{r}) = -\int \frac{\Delta\varrho(\boldsymbol{r}')\,\mathrm{d}^3\boldsymbol{r}'}{|\boldsymbol{r}-\boldsymbol{r}'|}$$

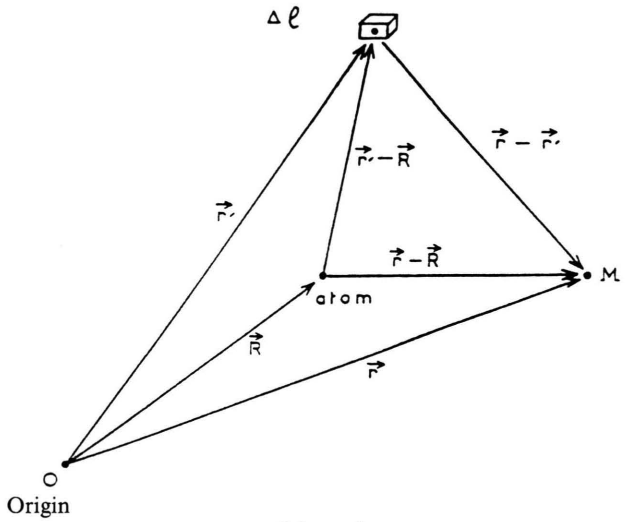
$$= \sum_{l,m} \varkappa''^3 P_{lm}\int \frac{1}{|\boldsymbol{y}|}\mathscr{R}_l(\varkappa''|\boldsymbol{r}-\boldsymbol{R}-\boldsymbol{y}|)\,Y_{lm}(\theta,\phi)\,\mathrm{d}^3\boldsymbol{y},$$

where

$$\boldsymbol{y} = \boldsymbol{r}-\boldsymbol{r}' \quad \text{and} \quad \mathrm{d}^3\boldsymbol{r}' = -\,\mathrm{d}^3\boldsymbol{y};$$

let

$$\boldsymbol{t} = \varkappa''(\boldsymbol{r}-\boldsymbol{R}-\boldsymbol{y}) \quad \Rightarrow \quad \mathrm{d}^3\boldsymbol{t} = -\,\varkappa''^3\,\mathrm{d}^3\boldsymbol{y}$$



Scheme 2

and

$$\frac{1}{|\boldsymbol{y}|} = \frac{\varkappa''}{|\boldsymbol{t}-\varkappa''(\boldsymbol{r}-\boldsymbol{R})|} .$$

The Green function

$$G(\boldsymbol{t}, \varkappa''(\boldsymbol{r}-\boldsymbol{R})) = \frac{1}{|\boldsymbol{t}-\varkappa''(\boldsymbol{r}-\boldsymbol{R})|}$$

can be expanded as

$$G(\boldsymbol{t}, \varkappa''(\boldsymbol{r}-\boldsymbol{R})) = \sum_{k=0}^{\infty} \sum_{p=-k}^{+k} \frac{4\pi}{2k+1} Y_{kp}^{*}(\theta, \phi)\, Y_{kp}(\theta', \phi')\, f(t, \varkappa''(\boldsymbol{r}-\boldsymbol{R}))$$

with

$$Y_{kp}^{*}(\theta, \phi) = (-1)^k\, Y_{k-p}(\theta, \phi)$$

and

$$f(t, \varkappa''(\boldsymbol{r}-\boldsymbol{R})) = \frac{t^k}{\varkappa''^{\,k+1}|\boldsymbol{r}-\boldsymbol{R}|^{k+1}} \quad \text{if} \quad t < \varkappa''|\boldsymbol{r}-\boldsymbol{R}| ,$$

$$f(t, \varkappa''(\boldsymbol{r}-\boldsymbol{R})) = \frac{\varkappa''^{\,k}|\boldsymbol{r}-\boldsymbol{R}|^k}{t^{k+1}} \quad \text{if} \quad t > \varkappa''|\boldsymbol{r}-\boldsymbol{R}| .$$

(θ, ϕ) and (θ', ϕ') are, respectively, the angular coordinates of $\boldsymbol{t}$, i.e. the direction of $\boldsymbol{r}'-\boldsymbol{R}$ and $(\boldsymbol{r}-\boldsymbol{R})$.

Using the orthogonality of the spherical harmonic functions

$$\int_{\phi=0}^{2\pi} \int_{\theta=0}^{\pi} Y_{kp}^{*}(\theta, \phi)\, Y_{lm}(\theta, \phi) \sin\theta \, d\theta \, d\phi = \delta_{k,l}\, \delta_{p,m} ,$$

only the terms with $k=l$ and $p=m$ are non-zero. We can also separate the space into two parts, from 0 to $\varkappa''|\boldsymbol{r}-\boldsymbol{R}|$ and from $\varkappa''|\boldsymbol{r}-\boldsymbol{R}|$ to ∞. The electrostastic potential then becomes

$$\Delta V(\boldsymbol{r}) = -4\pi \sum_{lm} \frac{\varkappa'' P_{lm}}{2l+1} \left[\frac{1}{\varkappa''^{\,l+1}|\boldsymbol{r}-\boldsymbol{R}|^{l+1}} \cdot \int_{0}^{\varkappa''|\boldsymbol{r}-\boldsymbol{R}|} t^{l+2} \mathscr{R}_l(t)\, dt + \varkappa''^{\,l}|\boldsymbol{r}-\boldsymbol{R}| \int_{\varkappa''|\boldsymbol{r}-\boldsymbol{R}|}^{\infty} t^{(1-l)} \mathscr{R}_l(t)\, dt \right] Y_{lm}(\theta', \phi') .$$

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