# Intermolecular Interactions in the Crystal Structure of Calcium Barbital Trihydrate

By B. BERKING

(*Department of Crystallography, University of Pittsburgh, Pittsburgh, Pennsylvania* 15213)

*Summary* The deprotonated nitrogen atoms in the barbital anions in calcium barbital trihydrate are involved either in co-ordination to the calcium cations or as acceptors in hydrogen bonds, whereas the non-deprotonated ones are involved as donors to form isolated hydrogen-bonded barbital dimers.

THERE has been controversy about whether the free acids[1] or the anionic forms[2] of barbiturates are more potent and whether barbiturates interfere with the binding of calcium to phospholipids.[3] This communication reports the intramolecular effects of deprotonation of the barbital molecules and the intermolecular interactions between barbital anions, calcium cations, and water molecules in the crystalline state.

*Crystal data:* space group $P\bar{1}$, $a = 16{\cdot}999$, $b = 9{\cdot}122$, $c = 16{\cdot}780$ Å, $\alpha = 77{\cdot}29$, $\beta = 89{\cdot}36$, $\gamma = 74{\cdot}86°$, $Z = 4$, $D_m = 1{\cdot}250$ g cm$^{-3}$. The asymmetric unit contains two calcium ions, four barbital ions and six water molecules. Using Cu-$K_\alpha$ radiation, 8237 $X$-ray diffraction data were measured on an automatic diffractometer. The structure was solved by a combination of Patterson and direct methods and refined to $R = 0{\cdot}046$. All hydrogen atoms

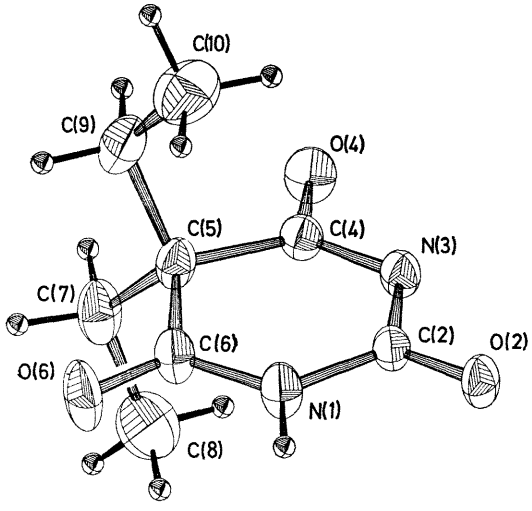


FIGURE 1

were located. Figure 1 shows the geometry of one barbital anion and the nomenclature.

Deprotonation of the four crystallographically independent pyrimidine rings at the imine nitrogen atoms N(3) causes a redistribution of electronic charge which is indicated by changes in the bond lengths and the internal bond angles. The values reported here are average values of the four barbital anions. The angles C(2)–N(3)–C(4) (126·4° in the barbital molecule, 120·1° in the barbital ion) decrease by 6° and those at the neighbouring atoms C(2) and C(4) increase by 5°. In all anions the C–N bonds at N(3) are 0·02—0·03 Å shorter (1·336 *vs.* 1·364 Å) and the C=O bonds at C(2) and C(4) are 0·02—0·03 Å longer (1·243 *vs.* 1·211 Å) than the corresponding bonds in the barbital molecule. The greater part of the formal negative charge seems to be equally distributed between the two oxygen atoms adjacent to the deprotonated nitrogen atom.

There are conformational differences in the barbiturate rings, one being flat and three flap-shaped with respect to puckering (0·09 Å) at the tetrahedrally surrounded atom C(5). These differences can only be explained by intermolecular factors because all substituents at C(5) are identical. The arrangement of the barbital anions with respect to themselves, the calcium ions, and the water molecules is shown in Figure 2.

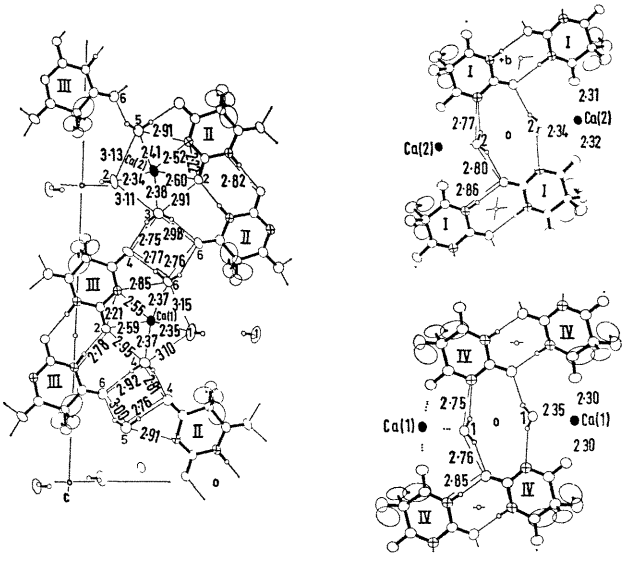


FIGURE 2

Whereas in the crystal structure of sodium barbital[4] the deprotonated nitrogen atom is not involved in intermolecular interactions, in calcium barbital trihydrate, all four independent atoms N(3) are: (1) those of barbital anions 1 and 4 as acceptors in hydrogen bonding, (2) those of anions 2 and 3 in co-ordinating the calcium cations. Each calcium ion is seven-co-ordinated by three oxygen atoms belonging to different barbital anions, three oxygen atoms belonging to water molecules, and one deprotonated barbital nitrogen atoms. The co-ordination may be pictured as pentagonal bipyramidal, the faces and apices of which are illustrated on the left and right side, respectively, of Figure 2. The Ca–N(3) distances and adjacent Ca–O(2) distances[O(2) belonging to the same barbital anion as N(3)] are significantly longer than all other Ca–O distances (2·52—2·60 *vs.* 2·30—2·41 Å).

Calcium ions usually prefer co-ordination by oxygen atoms to co-ordination by nitrogen atoms. In the few reported cases of co-ordination by nitrogen atoms, the Ca–N distance is either very long[5] (2·79 Å) or the nitrogen atom and other co-ordinating oxygen atoms are near neighbours within the same molecule;[6] both features occur in calcium barbital trihydrate.

Each of the four independent barbital anions and the corresponding anion related to it by a centre of symmetry form dimers using the non-deprotonated nitrogen atoms as donors in the two N(1)–H · · · O(2)=C(2) hydrogen bonds. These dimers are isolated in that they have no hydrogen bonds to other barbital ions. Usually barbiturate molecules or ions have extended hydrogen-bond interactions among each other. The dimers of anions **1** and **4** are linked to ribbons, and the dimers of anions **2** and **3** to sheets *via* water molecules and calcium ions. The only interaction between the ribbons and the nearly perpendicular sheets are by calcium ions.

All diethyl groups are located in infinite channels. Their atoms have few close intermolecular interactions; only ten H–H distances are smaller than 2·75 Å. This lack of van der Waals contacts indicates that efficient alkyl group packing is not important for the crystal packing which is dominated by one- and two-dimensional hydrogen-bonding and three-dimensional interactions of the calcium ions.

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[1] M. P. Blaustein, *J. Gen. Physiol.*, 1968, **51**, 293.
[2] S. K. Sharpless, in 'Pharmacological Basis of Therapeutics,' 3rd edn., eds. L. S. Goodman and A. Gilman, Macmillan, New York, 1968, p. 109.
[3] P. Kripp, C. P. Biauchi, and G. Saurez-Kurtz, *J. Pharm. Pharmacol*, 1969, **21**, 763.
[4] B. Berking and B. M. Craven, *Acta Cryst.*, in the press.
[5] D. A. Bekoe, P. K. Gantzel, and K. N. Trueblood, *Acta Cryst.*, 1967, **22**, 657.
[6] G. Strahs and R. E. Dickerson, *Acta Cryst.*, 1968, B**24**, 571.