

Novel structural determination of a bilayer network formed by a tripodal lipophilic amide in the presence of anions

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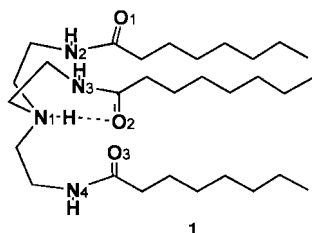
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The crystal structure of a protonated tripodal lipophilic amide, *N*-{2-[bis(2-octanoylaminoethyl)amino]ethyl}octanamide, identified an elegantly architected bilayer hydrogen bonded structure consisting of ladder-like cascades of the amide, with the rungs comprised of the lipophilic tails pointing inward and the poles made up of polar quaternary ammonium heads lining channels filled with nitrate ions.

In our investigation of the anion binding capabilities of a series of lipophilic amide receptors of varying chain length, we recently isolated the nitrate salt of a protonated triamide **1** with



three seven-carbon alkyl chains. The unanticipated structure shows a novel and elegant bilayer structure comprised of ladder-like cascades of the amide, with the rungs consisting of the lipophilic tails pointing inward and the polar heads lining channels filled with nitrate ions. Because of the high thermal motion usually exhibited by such chains, crystallographic determinations are limited. This most unusual structure thus provides solid state insights into the forces holding such frameworks together.

Anion complexation is a swiftly emerging field of chemistry with relevance to biology, the environment, and industry.¹ Of the oxo-anions, nitrate is important because of its prevalence in soil and groundwater as well as at nuclear waste facilities. Our interest in nitrate binding began several years ago with the isolation and structural characterization of the nitrate salt of an inclusion complex of nitrate with a polyammonium macrocycle,² and more recently with a dinitrate inclusion complex within a tripodal bicyclic aza cryptand.³ Drawbacks associated with polyammonium receptors, however, are their binding dependency on pH as well as high water solubilities, which limit their effectiveness in many applications. In this regard, receptors soluble in organic phases and capable of binding over a range of pH are desirable. Hence we, along with a number of other researchers, have begun to explore hosts containing amide functionalities, a logical choice considering that Nature employs such moieties in the biological binding and transport of anions.⁴

In our study of lipophilic receptors we have synthesized and characterized a series of tripodal amides with hydrocarbon tails based on the triamine building block, tren. In earlier work, Reinhoudt and coworkers examined related tren-based systems, and were successful in identifying several excellent neutral receptors for phosphate.⁵ Only one hydrocarbon chain (with six carbons) was included in that study, which focussed on aromatic

'tails'. Potvin and Jairam also have employed similar types of ligands, but primarily for binding metal ions and especially as models for zinc enzymes.⁶ Crystallographic characterization of such receptors with lipophilic tails tends to be very limited because of the floppy nature of the hydrocarbon chains, which generally results in poor crystallinity and in large thermal motion and very high *R* factors.⁷ By contrast, the structure reported herein was 'well behaved', and, as such, provides a significant addition to the structural database of bilayers.

Synthesis of the tripodal amide receptor from tren and octanoic acid was found to proceed in high yield using triphenyl phosphite as a coupling agent.^{8†} To purify the resulting triamide, the crude product was dissolved in DMSO and acidified with nitric acid to pH 1. The crystalline product, when recrystallized from a DMSO–water mixture, gave crystals suitable for X-ray diffraction.

The crystal structure shows the crystals to be the mononitrate salt of the amide, singly protonated at the apical nitrogen.‡ While it was initially disappointing to us that the nitrate was not encapsulated within the tren unit, the reason is apparent: one of the amide carbonyl oxygen atoms points into the cavity to hydrogen bond with the *endo*-oriented proton of the apical amine [O(2)⋯N(1) 2.74(1) Å], effectively 'closing' the cavity. The receptor packs in beautifully patterned three-dimensional arrays reminiscent of bilayer structures, with the hydrophilic tren 'heads' lining open channels for the nitrates [Fig. 1(a) and (b)]. The bilayer is held together by hydrogen bonding between pairs of cations, O(1)⋯N(3') 2.816(9) and O(3)⋯N(2'') 2.800(9) Å, in adjacent unit cells. The distance between apical nitrogens through the bilayer is 25.3 Å, while the distance between apical nitrogens across the bilayer is 6.2 Å. The torsion angles in **1** indicate that the carbon chains are highly ordered. Within the polar head of the tripod, the $N_{\text{apical}}\text{CC}N_{\text{amide}}$ angles approximate the *gauche* conformation, while the hydrocarbon portion of the tail exhibits a consistent array of *trans* angles. One exception to this pattern occurs on the chain in which the amide oxygen points inward, to hydrogen bond with the apical nitrogen of the tren unit. In the latter case both the $\text{CCN}(3)\text{C}(\text{O})$ [−73.1(6)°] and $\text{N}(3)\text{CC}(\text{O})\text{C}$ angles [132.3(5)°] differ significantly from their $\text{CN}_{\text{amide}}\text{C}(\text{O})\text{C}$ [−124.3(5)° and −139.1(5)°] and $\text{N}_{\text{amide}}\text{C}(\text{O})\text{CC}$ [176.6(5)° and 177.1(6)°] counterparts on adjacent tails.

The closest nitrate–nitrate approach along the channels is 5.75 Å between nitrogen centers. Only the two disordered oxygen atoms on the nitrate are within strong hydrogen bonding range of one of the amide nitrogens, O(6)⋯N(4) 2.98(2) and O(7)⋯N(4) 2.96(3) Å. One of the two ordered oxygens, O(5) of the nitrate, lies within a 3.5 Å distance of both N(3) and N(4).

In conclusion, while **1** is not a selective receptor for nitrate, having rather similar K_{as} values for a series of ions,⁹ this is one of the few crystallographically confirmed bilayer structures. A structure of 1,2-dilauroyl-DL-phosphatidylethanolamine with two chains forming the bilayer, in which the unweighted *R* factor was extremely high (0.28), would appear to be the only crystal structure closely related to **1**.⁷ Thus the structure of the

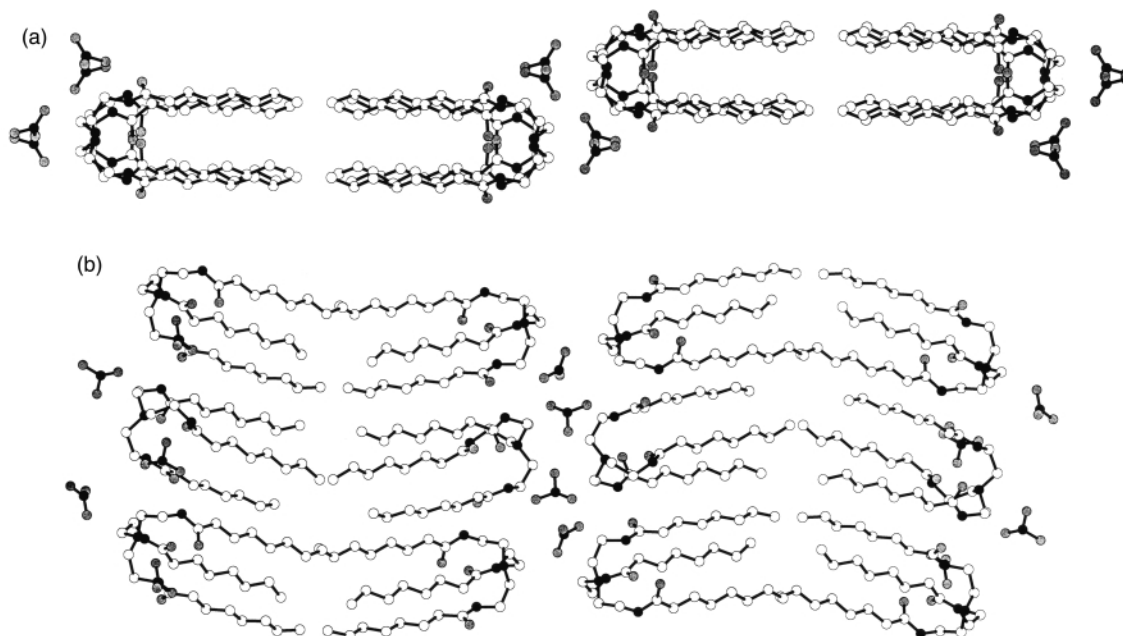


Fig. 1 (a) View of the *ab* plane (*b* along the horizontal axis) looking down *c*. (b) View of the *ac* plane (*b* along the horizontal axis) looking down *a*.

nitrate complex of **1** with its three-chain bilayer formation provides rare evidence of the elegant architectural pattern that is undoubtedly inherent in these systems in their biological habitats.

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Notes and references

† *Spectroscopic data*: ^1H NMR (300 MHz, CDCl_3 , TMS) δ 7.65 (t, 3H, NH), 3.63 (m, 6H, NCH_2), 3.47 (t, 6H, CH_2NH), 2.25 (t, 6H, COCH_2CH_2), 1.59 (t, 6H, COCH_2CH_2), 1.28 [m, 12H, $(\text{CH}_2)_2\text{CH}_3$], 0.88 (t, 9H, CH_3); Anal. Calc. for $\text{C}_{30}\text{H}_{61}\text{N}_5\text{O}_6$: C, 61.30; H, 10.46; N, 11.91. Found: C, 61.67; H, 10.16; N, 11.91%.

‡ *Crystal data*: $\text{C}_{30}\text{H}_{61}\text{N}_5\text{O}_6$, $M_w = 587.84$, orthorhombic, space group *Pccn* (no. 56), $a = 8.383(3)$, $b = 58.887(5)$, $c = 14.673(3)$ Å, $V = 7244(2)$ Å³, $D_c = 1.08$ g cm⁻³, $Z = 8$. Single crystal X-ray structure analysis was carried out on a crystal of dimensions $0.40 \times 0.40 \times 0.50$ mm using a Rigaku AFC5R diffractometer with graphite-monochromated Cu-K α ($\lambda = 1.54178$ Å) radiation at 23 °C. Data collection to $2\theta_{\text{max}}$ of 120.2° gave 6558 unique reflections. The structure was solved according to previously reported methods.² All of the hydrogen atoms were placed in calculated positions and were included in subsequent calculations but not refined. Refinement included 379 parameters on 2646 reflections for which $I > 3.00\sigma(I)$, to give $R = 0.063$, $R_w = 0.063$ and GOF = 3.17. As is common in nitrate structures, the nitrate exhibited disorder (four oxygen peaks, two given 50% occupancy). CCDC 182/1570. See <http://www.rsc.org/suppdata/cc/a9/a909341i/> for crystallographic files in .cif format.

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