CRYSTAL STRUCTURE OF A HYPOLIPIDAEMIC AGENT: *N*-METHYL-*N'*-METHYL(DIISOPROPYLPHOSPHONATE)AMINE-CYANOBORANE, $C_9H_{22}BN_2O_3P$

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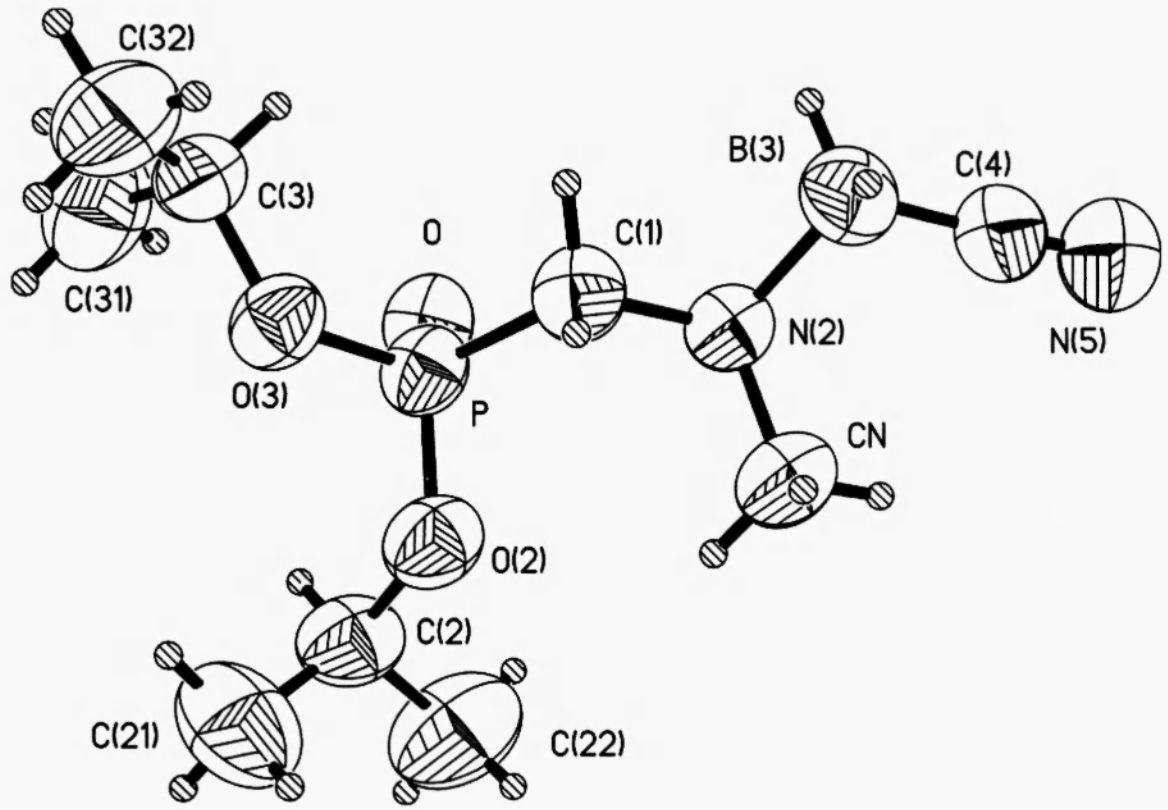

Figure 1. Molecular structure (50% displacement ellipsoids) of $C_9H_{22}BN_2O_3P$. The selected bond distances and angles: P-O 1.460(2), P-O(2) 1.556(2), P-O(3) 1.565(2), P-C(1) 1.800(3), O(2)-C(2) 1.470(4), O(3)-C(3) 1.468(3), C(1)-N(2) 1.493(3), N(2)-CN 1.483(4), N(2)-B(3) 1.597(4), B(3)-C(4) 1.571(6), C(4)-N(5) 1.140(4) Å; O-P-O(2) 116.70 (11), O-P-O(3) 114.67(11), O(2)-P-O(3) 103.15(11), O-P-C(1) 112.59(14), O(2)-P-C(1) 104.28(13), O(3)-P-C(1) 104.04(12), C(2)-O(2)-P 121.61(19), C(3)-O(3)-P 122.28(18), N(2)-C(1)-P 115.65(17), CN-N(2)-C(1) 111.2(2), CN-N(2)-B(3) 112.4(3), C(1)-N(2)-B(3) 109.5(2), C(4)-B(3)-N(2) 109.4(3), N(5)-C(4)-B(3) 177.7(4)°.

Comment

A report on boron analogues of phosphonoacetates, showed that these compounds demonstrated significant hypolipidaemic activity in rodents, specifically lowering serum cholesterol and triglyceride levels [1]. The most important compound among these is the title compound, *N*-methyl-*N'*-methyl-(diisopropylphosphonate)amine-cyanoborane (**1**) [2], trimethylaminecarbomethoxyborane [3], *N,N'*-dimethyl-*n*-octadecylamineborane [4], boron-containing tri- and dipeptides [5], aminecyanoboranes [6], and tetrakis-μ-(trimethylamineboranecarboxylato)-bis(trimethylaminecarboxyborane)-dicopper(II) [7]. Our recent results on these compounds show that they lower serum lipids by inhibiting the activities of key regulatory enzymes in the *de novo* synthesis of cholesterol, for

example, HMG-CoA reductase [2,8]. Although, the chemistry and biological activity of these compounds have been well established [2], the unambiguous molecular geometries of these derivatives have not been reported to date. Here we report the crystal structure of the title compound (**1**) that confirms our previous characterization by conventional spectroscopy and other analytical techniques [2]. The crystal structure of **1** is shown in **Figure 1**. The P=O, P-O, P-N, N-C and O-C distances in the phosphonoacetate moiety are within the expected region reported for those containing similar moiety [9]. The C-C bond distances in the alkyl moiety show bond anomaly [1.488(5)-1.512(5)Å]. The bond angles in the phosphonoacetate moiety are unexceptional and deserve no special comment. Further investigation on **1** for use in Boron Neutron Capture Therapy (BNCT) for treatment of glioblastoma multiforme (GBM) is currently in progress.

Experimental

Synthesis: The title compound (**1**) was synthesized from a reaction involving *N*-methyl-*N'*-methyl-(diisopropylphosphonate)amine and trimethylaminecyanoborane and characterized as described previously [2].

Table 1. Crystallographic Data[a] for *N*-methyl-*N'*-methyl-(diisopropylphosphonate)amine-cyanoborane (**1**)

Formula	$C_9H_{22}BN_2O_3P$	Diffractometer	Siemens SMART CCD
Formula weight	248.07	Temperature, K	293(2)
Crystal System	monoclinic	scan mode	ω
Space group	$P2_1/c$	θ_{max}, °	23.26
a, Å	8.4288(16)	No. reflns meas., unique	5868, 2029
b, Å	14.449(3)	No. parameters	168
c, Å	12.121(2)	GoF	1.195
β, deg	96.532(3)	$\Delta\rho_{(min, max)}$, $e/Å^3$	-0.23, 0.17
V, $Å^3$	1466.6(5)	*R*, $wR(F^2$, obs. data)	0.053, 0.144
Z	4	*R*, $wR(F^2$, all data)	0.061, 0.149
D_{calcd}, g cm^{-3}	1.124	Programs used	SADABS [10], SHELXTL [11], SMART and SAINT [12]
Abs coeff, mm^{-1}	0.183	Deposition no.	CCDC 168980
F(000)	536		
Crystal size, mm	0.08 x 0.08 x 0.14		

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References and Notes

[a] Contribution from Metallo-Biotech International, Inc.

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