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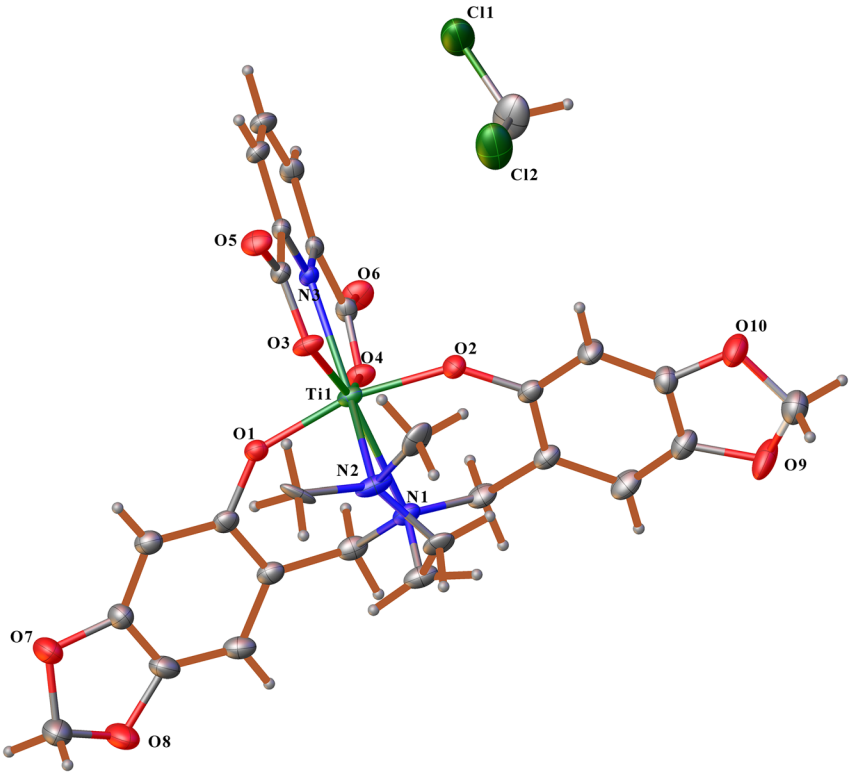
The crystal structure of 6,6′-(((2-(dimethylamino) ethyl)azanediyl)bis(methylene))bis(benzo[*d*][1,3] dioxol-5-ol ato-κ^4*N*,*N*′,*O*,*O*′)-(pyridine-2,6-dicarboxylato-*N*,*O*,*O*′)-titanium(IV)-dichloromethane(1/1), $C_{27}H_{25}N_3O_{10}Ti$



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Abstract

$C_{27}H_{25}N_3O_{10}Ti$, monoclinic, $P2_1/n$ (no. 14), a = 11.3366(11) Å, b = 11.0253(11) Å, c = 23.7160(2) Å, β = 100.839(2)°, V = 2911.4(5) Å^3, Z = 4, $R_{gt}(F)$ = 0.0615, $wR_{ref}(F^2)$ = 0.1411, T = 296(2) K.

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The asymmetric unit of the title crystal structure is shown in the figure. Table 1 contains crystallographic data and

Table 1: Data collection and handling.

Crystal:	Brown needle
Size:	0.10 × 0.08 × 0.05 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.54 mm^{-1}
Diffractometer, scan mode:	Bruker SMART CCD 6000, ω
θ_{max}, completeness:	25.0°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	15,865, 5125, 0.108
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs} > 2 σ(I_{obs}), 2257
$N(param)_{refined}$:	433
Programs:	Bruker [1], SHELX [2]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	−0.4489 (6)	0.7802 (6)	0.2015 (3)	0.081 (2)
H1A	−0.429279	0.788647	0.163611	0.098*
H1B	−0.535503	0.774862	0.197427	0.098*
C2	−0.2933 (5)	0.7167 (5)	0.2655 (2)	0.0558 (15)
C3	−0.1981 (5)	0.6518 (5)	0.2953 (2)	0.0527 (14)
H3	−0.194986	0.567773	0.292551	0.063*
C4	−0.1058 (5)	0.7172 (5)	0.3299 (2)	0.0439 (13)
C5	−0.1136 (5)	0.8426 (4)	0.3349 (2)	0.0463 (13)
C6	−0.2121 (6)	0.9042 (5)	0.3035 (2)	0.0590 (16)
H6	−0.217843	0.988100	0.305703	0.071*
C7	−0.2999 (6)	0.8383 (6)	0.2694 (3)	0.0643 (16)
C8	−0.0160 (5)	0.9117 (4)	0.3747 (2)	0.0488 (14)
H8A	−0.028769	0.997847	0.367904	0.059*
H8B	−0.023795	0.895600	0.414085	0.059*
C9	0.1879 (5)	0.9597 (4)	0.4098 (2)	0.0498 (14)
H9A	0.169009	0.945426	0.447518	0.060*
H9B	0.167964	1.043482	0.399791	0.060*
C10	0.3220 (5)	0.9432 (4)	0.4139 (2)	0.0457 (14)
C11	0.3745 (5)	0.8275 (5)	0.41923 (19)	0.0447 (13)
C12	0.4979 (5)	0.8121 (4)	0.4275 (2)	0.0538 (15)
H12	0.532396	0.735278	0.431800	0.065*
C13	0.5662 (5)	0.9132 (5)	0.4291 (2)	0.0510 (14)
C14	0.5184 (6)	1.0273 (5)	0.4232 (2)	0.0591 (16)
C15	0.3965 (6)	1.0456 (5)	0.4157 (2)	0.0607 (16)
H15	0.364303	1.123427	0.411826	0.073*
C16	0.7129 (6)	1.0462 (5)	0.4290 (3)	0.0745 (19)
H16A	0.775256	1.075645	0.459690	0.089*
H16B	0.740544	1.055731	0.392983	0.089*
C17	0.1242 (5)	0.9118 (4)	0.3086 (2)	0.0567 (16)
H17A[a]	0.048027	0.899867	0.282679	0.068*
H17B[a]	0.145389	0.996851	0.307210	0.068*
H17C[b]	0.064704	0.972860	0.293880	0.068*
H17D[b]	0.202625	0.948521	0.310633	0.068*
C18[a]	0.2133 (11)	0.8408 (7)	0.2897 (4)	0.055 (3)
H18A[a]	0.291428	0.860201	0.312439	0.066*
H18B[a]	0.215012	0.859918	0.249936	0.066*
C18A[b]	0.113 (2)	0.8161 (11)	0.2686 (5)	0.057 (6)
H18C[b]	0.141105	0.842609	0.234408	0.069*
H18D[b]	0.029491	0.792911	0.257673	0.069*
C19[a]	0.3086 (11)	0.6529 (13)	0.2931 (10)	0.068 (4)
H19A[a]	0.331197	0.673817	0.257277	0.101*
H19B[a]	0.305068	0.566204	0.296355	0.101*
H19C[a]	0.366915	0.684576	0.324231	0.101*
C19A[b]	0.3113 (19)	0.700 (2)	0.2837 (18)	0.068 (4)
H19D[b]	0.308421	0.695053	0.243092	0.101*
H19E[b]	0.350989	0.629200	0.301989	0.101*
H19F[b]	0.354719	0.771124	0.298696	0.101*
C20[a]	0.0959 (17)	0.6547 (14)	0.2497 (8)	0.072 (6)
H20A[a]	0.020248	0.693342	0.250341	0.108*
H20B[a]	0.088821	0.569168	0.255765	0.108*
H20C[a]	0.118098	0.668316	0.213054	0.108*
C20A[b]	0.119 (3)	0.613 (2)	0.2563 (13)	0.056 (8)
H20D[b]	0.036909	0.612454	0.261361	0.083*
H20E[b]	0.153606	0.534056	0.265569	0.083*
H20F[b]	0.122058	0.632000	0.217161	0.083*
C21	0.1431 (4)	0.5651 (4)	0.50894 (19)	0.0341 (12)
C22	0.1540 (4)	0.4811 (5)	0.5524 (2)	0.0436 (13)
H22	0.139530	0.502514	0.588431	0.052*
C23	0.1867 (4)	0.3652 (5)	0.5414 (2)	0.0519 (15)
H23	0.194805	0.306826	0.570211	0.062*
C24	0.2076 (4)	0.3349 (4)	0.4882 (2)	0.0441 (13)
H24	0.230167	0.256522	0.480406	0.053*
C25	0.1944 (4)	0.4230 (4)	0.4466 (2)	0.0352 (12)
C26	0.1069 (4)	0.6962 (4)	0.5112 (2)	0.0377 (13)
C27	0.2125 (4)	0.4104 (4)	0.3862 (2)	0.0393 (13)
C28[c]	0.4514 (13)	0.6270 (18)	0.6156 (6)	0.109 (6)
H28A[c]	0.387638	0.686930	0.609304	0.130*
H28B[c]	0.524684	0.668342	0.633042	0.130*
C28A[d]	0.482 (5)	0.630 (6)	0.632 (3)	0.109 (6)
H28C[d]	0.499894	0.707729	0.615931	0.130*
H28D[d]	0.548003	0.611352	0.662685	0.130*
Cl1[c]	0.4185 (3)	0.5227 (3)	0.66285 (11)	0.1324 (12)
Cl1A[d]	0.3577 (8)	0.6493 (10)	0.6609 (4)	0.1324 (12)
Cl2[c]	0.4692 (3)	0.5734 (4)	0.55111 (13)	0.1268 (12)
Cl2A[d]	0.4827 (11)	0.5253 (13)	0.5800 (4)	0.1268 (12)
N1	0.1101 (4)	0.8806 (3)	0.36802 (16)	0.0427 (11)
N2	0.1882 (5)	0.7057 (3)	0.29519 (19)	0.0578 (13)
N3	0.1622 (3)	0.5363 (3)	0.45716 (15)	0.0332 (10)
O1	−0.0092 (3)	0.6574 (3)	0.35818 (12)	0.0391 (8)
O2	0.3034 (3)	0.7284 (3)	0.41510 (13)	0.0451 (9)
O3	0.1941 (3)	0.5131 (3)	0.35855 (12)	0.0483 (9)
O4	0.1024 (3)	0.7497 (3)	0.46334 (14)	0.0482 (9)
O5	0.2403 (3)	0.3148 (3)	0.36641 (14)	0.0545 (10)
O6	0.0868 (3)	0.7420 (3)	0.55495 (15)	0.0620 (11)
O7	−0.3936 (4)	0.6743 (3)	0.22904 (17)	0.0795 (12)
O8	−0.4049 (4)	0.8802 (4)	0.23612 (19)	0.0918 (14)
O9	0.6077 (4)	1.1132 (3)	0.4277 (2)	0.0884 (14)
O10	0.6894 (4)	0.9221 (3)	0.43814 (17)	0.0746 (12)
Ti1	0.15050 (8)	0.67378 (7)	0.39021 (3)	0.0383 (3)

[a]Occupancy: 0.630(13), [b]Occupancy: 0.370(13), [c]Occupancy: 0.752(3), [d]Occupancy: 0.248(3).

Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

ONON ligand L_1: (6,6′-(((2-(dimethylamino)ethyl)azanediyl)bis (methylene))bis(benzo[*d*][1,3]dioxol-5-ol)) was prepared following the literature reported method by raising the reaction temperature (from r.t. to 50 °C) [3]. The corresponding Ti(IV) complex was synthesized according

to Lit [4]. Under a nitrogen atmosphere, L_1 (1 mmol, 400 mg) was dissolved in anhydrous THF (20 mL), $Ti(O^iPr)_4$ (0.98 mmol, 0.29 mL) was then added to the solution. The reaction mixture was heated to 50 °C and kept stirring for 2 h,Dipic (pyridine-2,6-dicarboxylic acid) (0.98 mmol, 163.0 mg) was added and the reaction was left stirring for another 12 h and monitored by TLC. When reaction was complete [$L_1Ti^{(IV)}$(Dipic)] was separated by flash column chromatography (CH_2Cl_2/CH_3OH = 40/1) to obtain a crimson solid (0.84 mmol, 506.2 mg, 86%). Suitable crystals for X-ray measurement were obtained by slow diffusion of *n*-Hexane to a dichloromethane solution of [$L_1Ti^{(IV)}$(Dipic)] at room temperature.

Experimental details

H atoms bonded to C atoms were positioned geometrically with C–H = 0.95 Å (aromatic), 0.99 Å (methylene) and 0.98 Å (methyl) and refined in a riding mode [U_{iso}(H) = 1.2U_{eq}C (aromatic and methylene)], 1.5U_{eq}C(methyl).

Comment

The two titanium complexes titanocene dichloride (TDC) and Budotitane (*cis*-diethoxy-bis(1-phenylbutane-1,3-dionato)titanium(IV)) were found having anti-tumor activities and eventually will enter the clinical trial. Numerous efforts have been made seeking novel titanium molecules with enhanced aqueous stability which led to the failure of TDC and Budotitane [5]. The ONNO Salan ligand stabilized titanium complexes which demonstrated satisfactory anti-tumor activity in both *in vitro* and *in vivo* experiments [6]. A new generation of heptacoordinated Salan titanium complexes was found by using pyridine-2,6-dicarboxylic acid as a second chelator [4, 7]. The much enhanced stability amplified the field of complex modification and PET tumor probes [8, 9]. However, ONON ligand coordinated titanium complexes are less explored despite that they exhibit more flexibility because of the difficult ligand synthesis approach [10]. We have previously demonstrated an unexpected Mannich synthetic approach for ONON ligands from naphthalen-2-ol, and its titanium bis-chelates have been be synthesized smoothly. To further expand the substrate scope for this synthetic approach to phenyl containing ONON ligands we used starting materials which can be easily obtained.

The title compound crystallizes in the monoclinic space group $P2_1/n$ with four formula units in one unit cell. The cental Ti cation is seven-coordinated by three nitrogen atoms and four carboxylate oxygen atoms, forming a distorted penta-dentated bipyramidal geometry. The bond lengths of four Ti–O and three Ti–N are ranging from 1.825(3) to 2.089(3) Å and from 2.181(3) to 2.365(4) Å, respectively. Surprisingly, as for the reaction in which producing the titled compound the Mannich reaction of benzo[*d*][1,3]dioxol-5-ol gave a rearranged ONON ligand L_1, thus giving a novel ONON–Ti(IV) complex.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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