Inorg. Chem. **2008**, *47*, 11902−11909

Tetradentate Bis(hydroxamate) and Hydroxamate-Diketonate Ligands and Their Titanium(IV) Complexes

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Received August 28, 2008

A 2,2′-bis(methylene)biphenyl-bridged bis(hydroxamic acid) ($HoxH_2$) is prepared by reaction of 2,2′-biphenyldiacetyl chloride with 2 equiv of *N*-methylhydroxylamine. Use of 1 equiv of CH_3NHOH gives the cyclic diacylhydroxylamine, which is selectively ring-opened to give a mixed monohydroxamate-monodiketonate ligand $HobH_2$. Both ligands are metalated by $Ti(O^iPr)_4$ to give the corresponding $LTi(O^iPr)_2$ complexes as exclusively the *cis*-α, (*R*)-Λ/(*S*)-Δ isomers, similar to the previously prepared bis(diketonate) analogues $(Bob)TiX_2$. The carbonyl oxygens of the hydroxamates in the Hox ligand are constrained to be *cis* to each other, and the crystal structure of $(Hob)Ti(O^iPr)_2$ suggests that the carbonyl oxygen is a slightly weaker donor than the diketonate oxygen, based on a modest difference in their *trans* influences. A differential *trans* effect is also manifest in the observation of only a single geometric isomer of $(Hob)Ti(O^iPr)(O_3SCF_3)$ and in a 15.6:1 preference for the isomer of $(Hob)Ti(OCH_2CMe_2CO_2)$ in which the alkoxide is *trans* to the hydroxamate ligand.

Introduction

Anionic oxygen donor ligands, such as alkoxides, aryloxides, carboxylates, diketonates, and the like, form an important class of ligands. In particular, for hard or oxophilic metal ions, chelating ligands with multiple oxygen donors can satisfy the metal's thirst for oxygen and can therefore promote high thermodynamic stability in aqueous environments even for species such as titanium(IV) or iron(III) with a high propensity for hydrolysis.[1−3] While bidentate or tridentate examples are common, tetradentate ligands consisting of exclusively anionic oxygen donors are rare. Because of the geometric constraints imposed on anionic oxygen donor atoms, with their single substituent, most ligands with four or more anionic oxygen donors have, like ethylenediaminetetraacetate, additional neutral donor atoms with greater numbers of substituents that allow the ligand to wrap around the metal ion. Notable exceptions include naturally occurring tris(catecholate) or tris(hydroxamate) siderophores[3] or their synthetic analogues,[4] as well as the tetraanionic calixarenes.[5] In all of these cases, complex ligand scaffolds allow facile formation of the large chelate rings necessary for chelation to take place.

We recently reported that the dianions of substituted 2,2′-biphenylbis-2,4-butanediones ("R_2Bob^{2-}") form thermodynamically stable tetradentate chelates with titanium(IV).[6] Furthermore, the 2,2′-bis(methylene)biphenyl linker confers excellent geometric and stereoselectivity on the complexes, with only the *cis*-α geometric isomers and only the (*R*,Λ)/(*S*,Δ) diastereomers being formed. We wondered if the thermodynamic and structural biases of this readily prepared scaffold could be extended to other bidentate, monoanionic oxygen donors suitable for binding to titanium(IV). Here we report that 2,2′-bis(methylene)biphenyl-bridged bis(hydroxamates) also bind stereoselectively to titanium(IV). Furthermore, we describe the efficient preparation of a mixed hydroxamate-diketonate ligand using this linker, which has

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(1) Ugrinova, V.; Ellis, G. A.; Brown, S. N. *Chem. Commun.* **2004**, 468–469.
(2) (a) Collins, J. M.; Uppal, R.; Incarvito, C. D.; Valentine, A. M. *Inorg. Chem.* **2005**, *44*, 3431–3440. (b) Peri, D.; Alexander, J. S.; Tshuva, E. Y.; Melman, A. *Dalton Trans.* **2006**, 4169–4172.
(3) (a) Raymond, K. N.; Carrano, C. J. *Acc. Chem. Res.* **1979**, *12*, 183–190. (b) Boukhalfa, H.; Crumbliss, A. L. *BioMetals* **2002**, *15*, 325–339.
(4) Roosenberg, J. M.; Lin, Y.-M.; Lu, Y.; Miller, M. J. *Curr. Med. Chem.* **2000**, *7*, 159–197.
(5) (a) Floriani, C. *Chem.—Eur. J.* **1999**, *5*, 19–23. (b) Fantacci, S.; Sgamellotti, A.; Re, N.; Floriani, C. *Inorg. Chem.* **2001**, *40*, 1544–1549.
(6) Ugrinova, V.; Noll, B. C.; Brown, S. N. *Inorg. Chem.* **2006**, *45*, 10309–10320.

10.1021/ic8016479 CCC: $40.75
Published on Web 11/12/2008

allowed us to compare the donor properties of these two common chelating ligands.

Experimental Section

General Procedures. Chloroform and methylene chloride were dried over 4 Å molecular sieves, followed by CaH_2. Benzene and toluene were dried over sodium, and ether and tetrahydrofuran over sodium benzophenone ketyl. Deuterated solvents were obtained from Cambridge Isotope Laboratories, dried using the same procedure as their protio analogues, and stored in the drybox prior to use. 2,2′-Biphenyldiacetyl chloride was prepared as previously described.[6] All other reagents were commercially available and used without further purification. NMR spectra were measured on a Varian VXR-300 spectrometer. Chemical shifts for ^1H and $^{13}C\{^1H\}$ spectra are reported in ppm downfield of TMS, referenced to the chemical shifts of the solvent residuals; those for ^{19}F are reported in ppm downfield of internal $CFCl_3$. Infrared spectra were recorded on KBr plates on a Perkin-Elmer PARAGON 1000 FT-IR spectrometer. Mass spectra were obtained on a JEOL LMS-AX505HA mass spectrometer using the FAB ionization mode and 3-nitrobenzyl alcohol or nitrophenyl octyl ether as a matrix. Peaks reported are the mass number of the most intense peak of isotope envelopes. Elemental analyses were performed by M-H-W Laboratories (Phoenix, AZ) or Canadian Microanalytical Service, Ltd. (Vancouver, BC).

***N,N′*-Dimethyl-2,2′-biphenyldiacetohydroxamic acid, $(C_6H_4CH_2CON(CH_3)OH)_2$ ($HoxH_2$).** In the drybox, 2,2′-biphenyldiacetyl chloride (1.79 g, 5.83 mmol) and a magnetic stirbar were added into a 100 mL two-neck round-bottom flask. One neck was capped with a rubber septum and the other was attached to a Teflon needle valve. The flask was taken out of the drybox and affixed to a vacuum line. Methylene chloride (50 mL) was added by vacuum transfer. Into a 250 mL two-neck round-bottom flask with one neck sealed with a rubber septum were added *N*-methylhydroxylamine hydrochloride (0.9734 g, 11.65 mmol, Aldrich) and a magnetic stirbar. The flask was attached to a Teflon needle valve, which was then affixed to the vacuum line. Methylene chloride (20 mL) was added by vacuum transfer. After that, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 3.49 mL, 23.3 mmol, Aldrich) was added by syringe through the rubber septum to the resulting suspension at 0 °C. After stirring for 10 min, the solution of 2,2′-biphenyldiacetyl chloride was added dropwise to the CH_3NHOH solution over a period of 20 min via a syringe under N_2. A clear yellow solution was formed immediately. Upon completion of the addition, the reaction mixture was removed from the ice bath and stirred at room temperature for 1 h. The resulting solution was transferred into a 250 mL separatory funnel, washed with 1 M HCl (70 mL) and then with brine (70 mL). The organic layer was collected, dried over $MgSO_4$, filtered, and stripped down on a rotary evaporator, leaving a thick yellow oil. The oil was redissolved in 8 mL of chloroform, and the product crystallized on standing at 10 °C overnight. Isolation by filtration on a glass frit, followed by washing with 2 × 2 mL of ice-cold chloroform, yielded the compound as a white powder. The filtrate was collected and stripped down on a rotary evaporator. The yellow oily residue was redissolved in 1 mL of chloroform. After standing at 10 °C overnight, a second crop of the product was produced and isolated by the method mentioned above, giving a combined yield of 0.9016 g (47%). ^1H NMR (acetone-d_6): δ 3.08 (s, 6H, NCH_3), 3.52 (d, 15 Hz, 2H, CHH′), 3.72 (br d, 15 Hz, 2H, CHH′), 7.13 (dd, 7, 1.5 Hz, 2H, 3-H), 7.26 (td, 7, 1 Hz, 2H, 4- or 5-H), 7.31 (td, 7, 1 Hz, 2H, 4- or 5-H), 7.38 (d, 7 Hz, 2H, 6-H), 9.01 (s, 2H, OH). $^{13}C\{^1H\}$ NMR (acetone-d_6): δ 36.50 (CH_2), 36.57 (NCH_3), 127.15, 128.27, 130.92, 131.53, 135.31, 142.23, 160.89 (CO). IR (nujol mull, cm^{-1}): 3217 (m, br, ν_{OH}), 1638 (m, $\nu_{C=O}$), 1616 (s, $\nu_{C=O}$), 1480 (w), 1413 (w), 1393 (w), 1207 (w), 760 (m), 667 (w). FABMS (NBA matrix): m/z 329 $(M + H)^+$. Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.62; H, 6.30; N, 8.30.

2-Methyl-2-aza-3-oxadibenzo-6,8-cyclodecadien-1,4-dione, $(C_6H_4CH_2CO)_2N(CH_3)O$. In the drybox, 2,2′-biphenyldiacetyl chloride (1.5828 g, 5.15 mmol) and a magnetic stirbar were added into a 100 mL, two-neck round-bottom flask. One neck was sealed with a rubber septum and the other was attached to a Teflon needle valve. The flask was taken out of the drybox and affixed to a vacuum line. Methylene chloride (50 mL) was added by vacuum transfer, and the flask was cooled in an ice bath. Into a 50 mL, two-neck round-bottom flask with one neck capped with a rubber septum, *N*-methylhydroxylamine hydrochloride (0.4304 g, 5.15 mmol, 1.00 equiv) and a magnetic stirbar were added. A Teflon needle valve was attached to the flask, which was then affixed to a vacuum line. Methylene chloride (10 mL) was added by vacuum transfer. After allowing the flask to warm to room temperature, it was filled with nitrogen, and DBU (2.31 mL, 15.5 mmol, 3.0 equiv) was added by syringe through the rubber septum. After stirring for 10 min, the hydroxylamine solution was added to the solution of 2,2′-biphenyldiacetyl chloride dropwise over a period of 10 min via a syringe under N_2. Upon completion of the addition, the reaction flask was removed from the ice bath and the reaction mixture was stirred at room temperature for 1 h. The resulting solution was transferred into a 250 mL separatory funnel, washed with 1 M HCl (70 mL) and brine (70 mL). The organic layer was collected and dried over $MgSO_4$ and the solvent removed on a rotary evaporator, leaving a thick yellow oil. The oil was dissolved in 5 mL of a 25:1 mixture of methanol and benzene. The solid that precipitated upon standing at 10 °C overnight was isolated by filtration on a glass frit and washed with 2 × 1 mL of ice-cold methanol to yield the diacylhydroxamate as a white or light yellow solid. The filtrate was stripped down on a rotary evaporator, and the purification step was repeated as described above to give three further crops of the compound; the combined yield was 0.3576 g (25%). ^1H NMR ($CDCl_3$): δ 3.22 (s, 3H, NCH_3), 3.44 (AB quartet, $\Delta\delta_{AB} = 0.03$ ppm, $J_{AB} = 15$ Hz, 2H, CH_AH_BCON), 3.60 (d, 17 Hz, 1H, CHH′COO), 3.79 (d, 17 Hz, 1H, CHH′COO), 7.17 (m, 2H, ArH), 7.33 (m, 2H, ArH), 7.41 (m, 3H, ArH), 7.48 (m, 1H, ArH). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 35.84 (NCH_3), 39.71 (CH_2), 39.88 (CH_2), 127.77, 127.92, 128.46, 129.23, 129.67, 129.88, 130.11, 130.41, 132.33, 132.67, 139.60, 141.22, 168.35 (CON), 172.35 (COO). IR (evapd film, cm^{-1}): 3056 (w), 3015 (w), 2919 (w), 1788 (s, $\nu_{C=O}$), 1677 (s, $\nu_{C=O}$), 1477 (m), 1440 (w), 1412 (w), 1374 (w), 1213, (w), 1134 (m), 1116 (m), 1084 (w), 760 (m). FABMS (NBA matrix): m/z 282 $(M + H)^+$. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 73.14; H, 5.50; N, 4.97.

2′-(4-*p*-Tolyl-2,4-dioxobutyl)-*N*-methylbiphenyl-2-acetohydroxamic acid, $(C_6H_4CH_2COCH{=}C(OH)C_6H_4$-*p*-$CH_3)(C_6H_4CH_2CON(CH_3)OH)$, $HobH_2$. In the drybox, $LiN(Si(CH_3)_3)_2$ (1.4510 g, 8.67 mmol) and a magnetic stirbar were added into a 250 mL round-bottom flask, and then 40 mL of ether was added. 4′-Methylacetophenone (1.16 mL, 8.66 mmol) was added dropwise to the solution of $LiN(Si(CH_3)_3)_2$. The flask was capped with a rubber septum. A solution of the cyclic diacylhydroxylamine $(C_6H_4CH_2CO)_2N(CH_3)O$ (1.2181 g, 4.33 mmol) in 20 mL of THF was prepared in a 50 mL round-bottom flask capped with a rubber septum. The two solutions were taken out of the drybox. The enolate solution was cooled in an ice bath for 20 min. The solution of cyclic diacylhydroxylamine was added dropwise to the stirring enolate

solution via a syringe, causing immediate formation of a precipitate. The reaction mixture was stirred for 5 min in the ice bath and then opened to the air. Removal of the solvent on a rotary evaporator left a yellow residue, which was stirred in ether (40 mL) at 0 °C for 10 min and then filtered on a glass frit in the air. The solid was washed with 3 × 25 mL ice-cold ether and transferred into a 250 mL round-bottom flask. The filtrate was reduced in volume to about 20 mL on a rotary evaporator and then cooled in an ice bath for 10 min to give a second crop of precipitate which, after filtration and washing with 3 × 10 mL ice-cold ether, was combined with the first crop. The solid was digested by stirring with 70 mL of 2 M HCl and 70 mL of ether until it had completely dissolved. The mixture was transferred into a 250 mL separatory funnel, and the bottom aqueous layer was discarded. The clear light yellow organic layer was washed with 70 mL of saturated $NaHCO_3$, dried over $MgSO_4$, filtered, and stripped down on a rotary evaporator to yield a thick yellow oil (1.2837 g, 71%). ^{1}H NMR (acetone-d_6): δ 2.39 (s, 3H, tolyl CH_3), 3.09 (br s, 3H, NCH_3), 3.56 (d, 16 Hz, 1H, CHH′), 3.58 (AB quartet overlapped with the other CH_2, $J_{AB} = 16$ Hz, 2H, CHH'), 3.63 (d, 16 Hz, 1H, CHH'), 6.06 (s, 1H, C[OH]CHCO), 7.29 (m, 10H, ArH), 7.74 (d, 8 Hz, 2H, Tol 2,6-H), 8.79 (s, 1H, NOH), 16.22 (s, 1H, C[OH]CHCO). ^{13}C{^{1}H} NMR (acetone-d_6): δ 21.57 (tolyl CH$_3$), 36.36 (NCH$_3$), 37.28 (hydroxamate CH$_2$), 43.87 (diketonate CH$_2$), 97.04 (C[OH]CHCO), 127.07, 127.57, 127.89, 128.38, 128.52, 130.27, 130.76, 131.00, 131.26, 131.40, 132.81, 134.96, 135.38, 141.94, 142.26, 144.13, 172.71 (hydroxamate CO), 183.59 (diketonate CO), 196.13 (diketonate CO). IR (evapd film, cm^{-1}): 3189 (w, br), 3061 (w), 3022 (w), 2922 (w), 1725 (w), 1610 (s, ν_{CO}), 1571 (m), 1503 (w), 1478 (m), 1440 (m), 1269 (w), 1185 (m), 1118, (w), 1008 (w), 830 (w), 756 (s). HRMS (FAB, NBA matrix): Calcd. for $C_{26}H_{26}NO_4$ $(M + H)^+$: 416.1862. Found: 416.1874.

(Hox)Ti(O^{i}Pr)$_2$. Into a 130 mL glass bomb were placed the dihydroxamic acid $HoxH_2$ (1.025 g, 3.12 mmol) and a magnetic stirbar. Titanium(IV) isopropoxide (2.74 mL, 9.36 mmol) was added into the bomb in the drybox. The bomb was closed with a Teflon valve, taken out of the drybox, and then affixed to the vacuum line. Benzene (75 mL) was added into the bomb by vacuum transfer. The light yellow suspension was heated in a 75 °C oil bath overnight under N_2, with stirring, to give a cloudy solution. The volume of the mixture was reduced in vacuo to about 10 mL. The white solid deposited was filtered on a glass frit in the drybox, washed with 3 × 5 mL hexanes and dried in vacuo for 1 h. Yield 1.2722 g, 83%. ^{1}H NMR (C_6D_6): δ 1.47 (d, 6 Hz, 6H, CH(CH_3)(CH′$_3$)), 1.49 (d, 6 Hz, 6H, CH(CH$_3$)(CH'_3)), 2.37 (s, 6H, NCH_3), 2.52 (d, 15 Hz, 2H, CHH′), 3.37 (d, 15 Hz, 2H, CHH'), 5.18 (sept, 6 Hz, 2H, CH(CH$_3$)$_2$), 6.71 (dd, 7, 1 Hz, 2H, 3-H), 6.91 (td, 7, 1 Hz, 2H, 4- or 5-H), 7.04 (td, 7, 1 Hz, 2H, 4- or 5-H), 7.14 (d, 7 Hz, 2H, 6-H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 25.47 (CH(CH_3)(C′H$_3$)), 25.56 (CH(CH$_3$)(C'H$_3$)), 34.66 (NCH$_3$), 38.11 (CH$_2$), 77.44 (CH(CH$_3$)$_2$), 127.37, 128.09, 129.48, 133.91, 134.33, 139.57, 163.40 (CO). IR (nujol mull, cm^{-1}): 1590 (s), 1124 (m), 997 (m), 980 (m), 840 (w), 756 (m), 744 (m), 572 (s), 480 (s). FABMS (NPOE matrix): m/z 433 (M-O^{i}Pr)$^+$. Anal. Calcd for $C_{24}H_{32}N_2O_6Ti$: C, 58.54; H, 6.55; N, 5.69. Found: C, 58.29; H, 6.78; N, 5.44.

(Hox)Ti(O^{i}Pr)(OSO$_2$CF$_3$). In the drybox, (Hox)Ti(O^{i}Pr)$_2$ (0.5062 g, 1.03 mmol) was weighed into a 50 mL Erlenmeyer flask. A magnetic stirbar and 5 mL of CH_2Cl_2 were added. After the compound dissolved, 10 mL of benzene was added. To the vigorously stirred resulting suspension was added trimethylsilyl trifluoromethanesulfonate (0.19 mL, 1.05 mmol, Aldrich) dropwise via syringe. A yellow precipitate formed immediately. After stirring for 10 min at room temperature, the solid was filtered on a glass frit, washed with 3 × 1 mL of hexanes, and dried in vacuo 1 h to give 0.4245 g (Hox)Ti(O^{i}Pr)(O_3SCF_3) (71%). The compound was stored at −30 °C in the drybox to retard its decomposition. ^{1}H NMR ($CDCl_3$): δ 1.30 (d, 6 Hz, 3H, CH(CH_3)(CH′$_3$)), 1.31 (d, 6 Hz, 3H, CH(CH$_3$)(CH'_3)), 2.83 (s, 3H, NCH_3), 2.87 (s, 3H, NCH_3), 3.40 (d, 15 Hz, 1H, CHH′), 3.45 (d, 15 Hz, 1H, CHH′), 4.10 (d, 15 Hz, 1H, CHH'), 4.11 (d, 15 Hz, 1H, CHH'), 4.83 (sept, 6 Hz, 1H, CH(CH$_3$)$_2$), 7.24 (m, 2H, 3-H), 7.42 (m, 6H, Ar−H). ^{13}C{^{1}H} NMR (CD_2Cl_2): δ 24.69 (CH(CH$_3$)$_2$, the diastereotopic carbons are accidentally degenerate), 34.79 (NCH$_3$), 35.17 (NCH$_3$), 38.71 (CH$_2$), 38.77 (CH$_2$), 84.47 (CH(CH$_3$)$_2$), 128.52, 128.61, 128.98, 129.10, 130.16, 130.42, 132.75, 133.29, 134.37, 134.47, 139.37, 139.64, 164.59 (CO), 166.18 (CO); CF$_3$ not observed. ^{19}F NMR ($CDCl_3$): δ −77.64. IR (nujol mull, cm^{-1}): 1588 (m), 1346 (s, ν_{SO3}), 1238 (m), 1210 (s, ν_{CF3}), 1136 (w), 1112 (m), 1018 (m), 998 (m), 862 (w), 840 (w), 823 (w), 778 (w), 757 (m), 745 (m), 665 (w), 639 (w). Anal. Calcd for $C_{22}H_{25}F_3N_2O_8STi$: C, 45.37; H, 4.33; N, 4.81. Found: C, 45.03; H, 4.26; N, 4.73.

(Hob)Ti(O^{i}Pr)$_2$. The alkoxide complex was generated as described for (Hox)Ti(O^{i}Pr)$_2$ using $HobH_2$ (1.2239 g, 2.95 mmol), titanium(IV) isopropoxide (2.59 mL, 8.84 mmol, Aldrich) and 25 mL of benzene. After heating at 75 °C overnight, the volume of the mixture was reduced in vacuo to about 5 mL to produce a light yellow solid. The bomb was taken into the drybox. The solid was isolated by filtration on a glass frit, washed with 3 × 5 mL of hexanes, and dried in vacuo for 1 h to give 1.0870 g (Hob)Ti(O^{i}Pr)$_2$ (64%). ^{1}H NMR (C_6D_6): δ 1.40 (d, 6 Hz, 3H, CH(CH_3)(CH′$_3$)), 1.45 (d, 6 Hz, 3H, CH(CH$_3$)(CH'_3)), 1.52 (d, 6 Hz, 3H, CH(CH_3)(CH′$_3$)), 1.56 (d, 6 Hz, 3H, CH(CH$_3$)(CH'_3)), 2.02 (s, 3H, tolyl CH_3), 2.20 (s, 3H, NCH_3), 2.56 (d, 15 Hz, 1H, CH_aH$_b$CON(CH$_3$)O), 3.12 (d, 15 Hz, 1H, CH_cH$_d$COCHCOTol), 3.35 (d, 15 Hz, 1H, CH$_a$$H_b$CON(CH$_3$)O), 3.79 (d, 15 Hz, 1H, CH$_c$$H_d$COCHCOTol), 5.15 (sept, 6 Hz, 1H, CH(CH$_3$)$_2$), 5.31 (sept, 6 Hz, 1H, CH(CH$_3$)$_2$), 5.53 (s, 1H, COCHCO), 6.74 (dd, 7.5, 1.5 Hz, 1H, biphenyl 6-H), 6.88 (td, 7.5, 1.5 Hz, 1H, biphenyl 5-H), 6.96 (m, 6H, biphenyl Ar−H and Tol 3,5-H), 7.06 (m, 1H, biphenyl Ar−H), 7.15 (dd, 8, 1 Hz, 1H, biphenyl 3-H), 7.82 (d, 8 Hz, 2H, Tol 2,6-H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 21.72 (tolyl CH$_3$), 25.32 (CH(CH$_3$)(C′H$_3$)), 25.39 (CH(CH$_3$)(C'H$_3$)), 25.50 (CH(CH$_3$)$_2$, the diastereotopic carbons are accidentally degenerate), 34.63 (NCH$_3$), 38.07 (hydroxamate CH$_2$), 46.42 (diketonate CH$_2$), 77.35 (CH(CH$_3$)$_2$), 78.21 (CH(CH$_3$)$_2$), 99.16 (COCHCO), 127.26 (2C), 127.81 (2C), 127.91, 128.12, 128.99 (2C), 129.55, 129.59, 133.39, 133.93, 134.04, 134.72, 137.55, 139.92, 140.21, 141.78, 162.27 (hydroxamate CO), 179.79 (diketonate CO), 191.64 (diketonate CO). IR (nujol mull, cm^{-1}): 1590 (s), 1562 (w), 1521 (s), 1498 (s), 1159 (m), 1120 (s), 984 (s), 841 (m), 768 (m), 755 (m). FABMS (NPOE matrix): m/z 579 $(M)^+$, 520 $(M - O^iPr)^+$. Anal. Calcd for $C_{32}H_{37}NO_6Ti$: C, 66.32; H, 6.44; N, 2.42. Found: C, 66.52; H, 6.53; N, 2.42.

(Hob)Ti(O^{i}Pr)(OSO$_2$CF$_3$). (Hob)Ti(O^{i}Pr)$_2$ (0.8337 g, 1.44 mmol) was dissolved in benzene (25 mL) in a 100 mL round-bottom flask in the drybox. After addition of trimethylsilyl trifluoromethanesulfonate (0.26 mL, 1.44 mmol) and stirring for 5 min at room temperature, the flask was attached to a Teflon needle valve, taken out of the drybox, and affixed to a vacuum line. The volume of the solution was reduced in vacuo to about 5 mL to produce a yellow precipitate. The solid was filtered on a glass frit in the drybox, washed with 3 × 5 mL of hexanes, and dried in vacuo for 1 h. Yield 0.8972 g, 93%. ^{1}H NMR (C_6D_6): δ 1.34 (d, 6 Hz, 3H, CH(CH_3)(CH′$_3$)), 1.35 (d, 6 Hz, 3H, CH(CH$_3$)(CH'_3)), 1.90 (s, 3H, tolyl CH_3), 2.16 (s, 3H, NCH_3), 2.58 (d, 15 Hz, 1H, CH_aH$_b$CON(CH$_3$)O), 2.99 (d, 14 Hz, 1H, CH_cH$_d$COCHCOTol),

Table 1. Crystal Data for $(C_6H_4CH_2CO)_2N(CH_3)O$, (Hob)Ti($O^iPr)_2$, and (Hob)Ti($O_2CCMe_2CH_2O$)

	$(C_6H_4CH_2CO)_2N(CH_3)O$	(Hob)Ti($O^iPr)_2$	(Hob)Ti($O_2CCMe_2CH_2O$)
empirical formula	$C_{17}H_{15}NO_3$	$C_{32}H_{37}NO_6Ti$	$C_{31}H_{31}NO_7Ti$
temperature (K)	100(2)	100(2)	100(2)
λ	0.71073 Å (Mo Kα)	0.71073 Å (Mo Kα)	0.71073 Å (Mo Kα)
space group	$P2_1/c$	$P\bar{1}$	$P2_1/c$
total data collected	74156	53248	88006
no. of indep reflns.	5202	7216	9179
R_{int}	0.0258	0.0348	0.0271
obsd. refls. [$I > 2\sigma(I)$]	4683	5911	8043
a (Å)	11.2449(3)	11.0070(12)	14.5051(6)
b (Å)	15.8005(4)	11.816(3)	11.2042(4)
c (Å)	7.6152(2)	12.4624(12)	16.9288(6)
α (deg)	90	74.389(13)	90
β (deg)	93.2695(13)	67.345(8)	95.254(2)
γ (deg)	90	80.338(15)	90
V (Å^3)	1350.83(6)	1436.8(4)	2739.68(18)
Z	4	2	4
cryst size (mm)	0.43 × 0.22 × 0.20	0.32 × 0.15 × 0.10	0.39 × 0.21 × 0.19
no. refined params.	250	516	485
R indices [$I > 2\sigma(I)$][a]	$R1 = 0.0372$, $wR2 = 0.1094$	$R1 = 0.0338$, $wR2 = 0.0856$	$R1 = 0.0340$, $wR2 = 0.0965$
R indices (all data)[a]	$R1 = 0.0414$, $wR2 = 0.1047$	$R1 = 0.0476$, $wR2 = 0.0937$	$R1 = 0.0410$, $wR2 = 0.1065$
goodness of fit (S)[a]	1.017	1.032	1.045

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$; $wR2 = (\sum[w(F_o^2 - F_c^2)^2]/\sum w(F_o^2)^2)^{1/2}$.

3.25 (d, 15 Hz, 1H, $CH_aH_bCON(CH_3)O$), 3.68 (d, 14 Hz, 1H, $CH_cH_dCOCHCOTol$), 5.01 (sept, 6 Hz, 1H, $CH(CH_3)_2$), 5.58 (s, 1H, COC*H*CO), 6.57 (dd, 7.5, 1.5 Hz, 1H, biphenyl 6-H), 6.71 (dd, 7.5, 1.5 Hz, 1H, biphenyl 6′-H), 6.78 (d, 8 Hz, 2H, Tol 3,5-H), 6.82 (m, 3H, biphenyl Ar−H), 6.89 (td, 7.5, 1.5 Hz, 1H, biphenyl 4- or 5-H), 6.99 (td, 7.5, 1.5 Hz, 1H, biphenyl 4- or 5-H), 7.05 (dd, 7.5, 1.5 Hz, 1H, biphenyl 3-H), 7.84 (d, 8 Hz, 2H, Tol 2,6-H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 21.98 (tolyl *C*H_3), 24.54 ($CH(CH_3)_2$, the diastereotopic carbons are accidentally degenerate), 34.78 (NCH_3), 38.45 (hydroxamate *C*H_2), 45.04 (diketonate *C*H_2), 85.02 (*C*$H(CH_3)_2$), 103.47 (COC*H*CO), 119.77 (q, 318 Hz, *C*F_3), 127.69, 127.86, 128.34, 128.46, 129.05, 129.53, 129.59, 129.71, 131.74, 132.65, 134.04, 134.25, 136.18, 139.49, 139.74, 144.65, 164.18 (hydroxamate *C*O), 184.22 (diketonate *C*O), 190.75 (diketonate *C*O). ^{19}F NMR ($CDCl_3$): δ −77.27. IR (nujol mull, cm^{-1}): 1569 (w), 1523 (s), 1499 (m), 1336 (s, ν_{SO3}), 1308 (w), 1288 (w), 1236 (m), 1202 (s, ν_{CF3}), 1177 (m), 1118 (m), 1026 (m), 1007 (m), 982 (m), 866 (w), 813 (w), 799 (w), 775 (w), 756 (m), 742 (w), 666 (w), 632 (w). FABMS (NPOE matrix): *m*/*z* 669 (M)$^+$, 610 (M − O^{i}Pr)$^+$, 520 (M − OTf)$^+$. Anal. Calcd for $C_{30}H_{30}F_3NO_8STi$: C, 53.82; H, 4.52; N, 2.09. Found: C, 53.86; H, 4.55; N, 2.06.

(Hob)Ti($O_2CCMe_2CH_2O$). In the drybox, (Hob)Ti($O^iPr)_2$ (0.3007 g, 0.52 mmol), hydroxypivalic acid (0.0744 g, 0.63 mmol, TCI), 10 mL of $CHCl_3$, and a stirbar were charged into a 25 mL round-bottom flask. The reaction mixture was stirred at room temperature until all the compounds dissolved. The flask was taken out of the drybox, and the solvent removed on a rotary evaporator. The yellow residue was dissolved in 8 mL of CH_2Cl_2 in the air and layered with 16 mL of hexanes. Yellow crystals precipitated out on standing at 10 °C overnight. Isolation by decanting and washing with 2 × 2 mL hexanes yielded 0.1787 g of the compound (60%). ^1H NMR ($CDCl_3$, major isomer only): δ 1.26 (s, 3H, C(C*H*$_3$)(CH′$_3$)), 1.40 (s, 3H, C(CH_3)(C*H*′$_3$)), 2.39 (s, 3H, tolyl C*H*$_3$), 2.66 (s, 3H, NCH_3), 3.24 (d, 15 Hz, 1H, $CH_aH_bCON(CH_3)O$), 3.47 (d, 14 Hz, 1H, $CH_cH_dCOCHCOTol$), 3.93 (d, 11 Hz, 1H, TiOC*H*H′), 4.03 (d, 15 Hz, 1H, $CH_aH_bCON(CH_3)O$), 4.11 (d, 14 Hz, 1H, $CH_cH_dCOCHCOTol$), 4.93 (d, 11 Hz, 1H, TiOCHH′), 5.71 (s, 1H, COC*H*CO), 7.16 (d, 8 Hz, 2H, Tol 3,5-H), 7.17 (m, 2H, biphenyl Ar−H), 7.28−7.49 (m, 6H, biphenyl Ar−H), 7.58 (d, 8 Hz, 2H, Tol 2,6-H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 21.90 (tolyl *C*H_3), 22.16 (C(*C*H_3)(CH′$_3$)), 23.87 (C(CH_3)(*C*H′$_3$)), 34.62 (NCH_3), 38.37 (hydroxamate *C*H_2), 41.46 (*C*$(CH_3)_2$), 45.63 (diketonate *C*H_2), 85.04 (TiO*C*H_2), 103.42 (CO*C*HCO), 127.59, 127.93, 128.40, 128.43, 128.58, 129.49, 129.53, 129.75, 131.91, 132.70, 134.06, 134.48, 136.52, 139.43, 139.96, 144.34, 163.87 (hydroxamate *C*O), 180.33 (TiO_2C), 183.48 (diketonate *C*O), 191.28 (diketonate *C*O). IR (evapd film, cm^{-1}): 2924 (w), 2853 (w), 1666 (m, $\nu_{TiOC=O}$), 1582 (m), 1544 (m), 1521 (s), 1498 (s), 1475 (w), 1390 (w), 1357 (m), 1327 (m), 1296 (m), 1246 (m), 1167 (m), 1058 (m), 984 (w), 896 (w), 755 (w), 742 (w). FABMS (NPOE matrix): *m*/*z* 578 (M + H)$^+$. Anal. Calcd for $C_{31}H_{31}NO_7Ti$: C, 64.48; H, 5.41; N, 2.43. Found: C, 63.39; H, 5.07; N, 2.35.

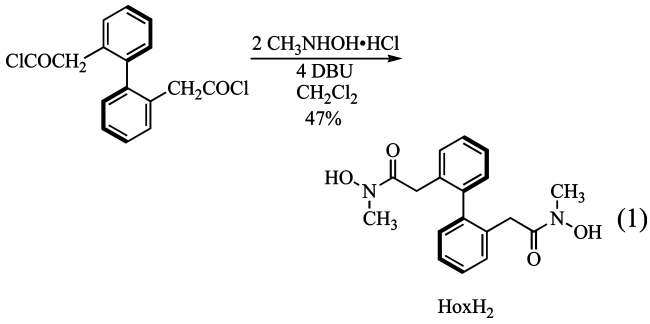
X-ray Crystallography of $(C_6H_4CH_2CO)_2N(CH_3)O$, (Hob)Ti($O^iPr)_2$, and (Hob)Ti($O_2CCMe_2CH_2O$). Crystals were grown by liquid diffusion (hexanes into chloroform for the cyclic diacylhydroxylamine, hexanes into benzene for (Hob)Ti($O^iPr)_2$), or in the case of (Hob)Ti($O_2CCMe_2CH_2O$), by cooling a solution of the compound in 1:2 dichloromethane/hexanes at 10 °C overnight. The crystals were placed in inert oil and transferred to the tip of a glass fiber in the cold N_2 stream of a Bruker Apex CCD diffractometer (T = 100 K). Data were reduced, correcting for absorption and decay, using the program SADABS. The structures were solved using direct methods. All nonhydrogen atoms were refined anisotropically. Hydrogen atoms were located on difference maps and refined isotropically, except for those bonded to the minor component of the disordered isopropyl group in (Hob)Ti($O^iPr)_2$, which were placed in calculated positions. One of the CH_3 groups and the CH group of one of the isopropyl groups in this structure (C61 and C62, respectively) were found in two orientations, with the occupancy of the major orientation refining to 75.2(3)%. Calculations used SHELXTL (Bruker AXS),[7] with scattering factors and anomalous dispersion terms taken from the literature.[8] Further details about the structures are in Table 1.

Results and Discussion

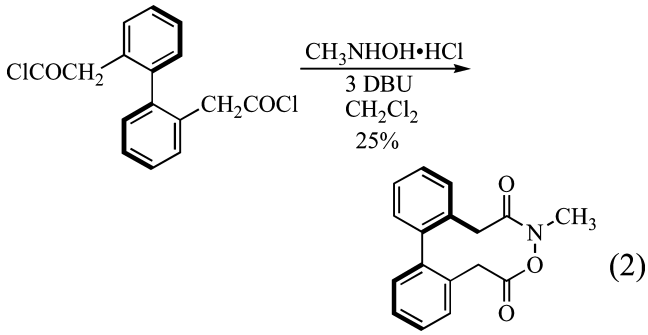
Preparation of Bis(hydroxamate) and Mixed Hydroxamate-Diketonate Ligands. *N*-acylation of hydroxylamines by acyl chorides is a common method for the preparation of

(7) Sheldrick, G. M. *Acta Cryst. A* **2008**, *A64*, 112–122.
(8) *International Tables for Crystallography*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1992; Vol. *C*.

hydroxamic acids.[9] 2,2′-Biphenyldiacetyl chloride reacts with *N*-methylhydroxylamine hydrochloride in the presence of DBU to give the expected 2,2′-biphenyldi-(*N*-methylaceto-hydroxamic acid), $HoxH_2$, in 47% yield (eq 1). Multiple species are observed in the ^1H NMR spectrum of $HoxH_2$ in $CDCl_3$, presumably because of the presence of slowly interconverting rotamers around the C(O)−N bond. This interconversion is faster in acetone-d_6, where only the slight broadening of the diastereotopic methylene protons attests to the presence of multiple rotamers. Rotation about the biphenyl C−C bond is slow on the NMR time scale.[10]



A minor product in this preparation of $HoxH_2$, isolable by chromatography of the reaction mixture, contains biphenyl and *N*-methyl groups in a 1:1 ratio by NMR. The NMR spectra show that the two aryl groups of the biphenyl (and all four methylene protons) are inequivalent, and mass spectrometry indicates that it contains only one biphenyl group, suggesting it is the cyclic *N*,*O*-diacylhydroxylamine $(C_6H_4CH_2CO)_2N(CH_3)O$. Particularly diagnostic is the IR spectrum of the material, which shows no N−H or O−H stretches, but two very different C═O stretches, a high-frequency band (1788 cm^{-1}) due to the *O*-acyl group and a low-frequency band (1677 cm^{-1}) due to the *N*-acyl group. Conducting the reaction with a 1:1 stoichiometry of biphenyldiacetyl chloride to hydroxylamine leads to the formation of the cyclic compound as the major product and allows its isolation by direct crystallization from the reaction mixture, albeit in modest yield (eq 2).



X-ray crystallography of the cyclic diacylhydroxylamine (Figure 1, Tables 1–2) confirms the presence of a 10-membered ring in which the 2,2′-disubstituted biphenyl

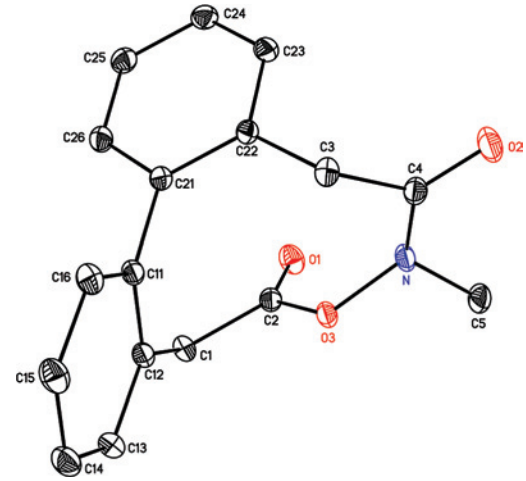


Figure 1. Thermal ellipsoid plot (50% ellipsoids) of $(C_6H_4CH_2CO)_2N(CH_3)O$.

Table 2. Selected Bond Distances (Å) and Angles (deg) in $(C_6H_4CH_2CO)_2N(CH_3)O$

N−O3	1.4170(8)
N−C4	1.3728(9)
N−C5	1.4501(10)
O1−C2	1.1965(9)
O2−C4	1.2207(9)
O3−C2	1.3862(8)
C11−C21	1.4954(9)
O3−N−C4	114.55(6)
O3−N−C5	114.46(6)
C4−N−C5	123.98(6)
N−O3−C2	112.34(5)
O1−C2−O3	123.27(6)
O1−C2−C1	126.98(6)
O3−C2−C1	109.68(6)
O2−C4−N	119.75(7)
O2−C4−C3	123.37(7)
N−C4−C3	116.79(6)

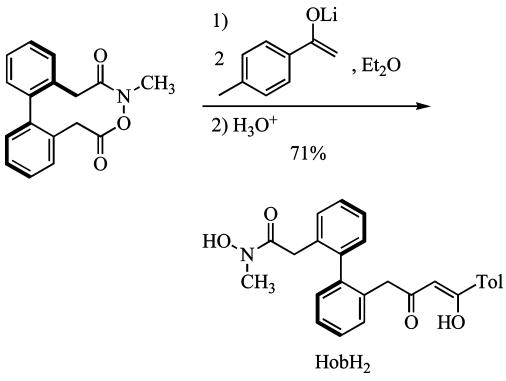
moiety is able to adopt its customary twisted conformation (angle between the phenyl planes of 101.3°). The nitrogen is very slightly pyramidalized (sum of angles = 353.0°) and the diacylhydroxylamine is markedly nonplanar (the C2−O3−N−C4 dihedral angle is 115.3°). Such nonplanarity is typical of known acyclic *N*,*O*-diacyl hydroxylamines (with dihedral angles of 82 ± 7° in 11 examples[11]), and the N−O distance of 1.4170(8) Å is also typical. The metrical data, in accord with the infrared data, suggest much stronger donation from the nitrogen than from oxygen to their respective carbonyl groups. Thus, the *O*-acyl C═O bond (O1−C2) is 0.0252(13) Å shorter than the *N*-acyl C═O bond (O2−C4), while the distance from N to the acyl carbon is 0.0134(13) Å shorter than the corresponding O−C distance, despite the larger size of nitrogen than oxygen.

(9) (a) Hoffman, R. V.; Nayyar, N. K.; Chen, W. *J. Org. Chem.* **1992**, *57*, 5700–5707. (b) Clark, A. J.; Al-Faiyz, Y. S. S.; Broadhurst, M. J.; Patel, D.; Peacock, J. L. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1117–1127.

(10) (a) Meyer, W. L.; Meyer, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2170–2171. (b) Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618–5626.

(11) (a) Göttlicher, S.; Ochsenreiter, P. *Chem. Ber.* **1974**, *107*, 398–413. (b) Masui, M.; Ueshima, T.; Ozaki, S.; Fujiwara, T.; Tomita, K.-I. *Chem. Pharm. Bull* **1983**, *31*, 784–786. (c) Baert, F.; Lamiot, J.; Couturier, D.; Roussel, D.; Ricart, G. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1984**, *40*, 1071–1072. (d) Grassi, G.; Cordaro, M.; Bruno, G.; Nicolò, F. *Helv. Chim. Acta* **2002**, *85*, 196–204. (e) Schraml, J.; Sýkora, J.; Fiedler, P.; Roithová, J.; Mindl, J.; Blechta, V.; Císaøová, I.; Exner, O. *Org. Biomol. Chem.* **2004**, *2*, 2311–2314. (f) Buscemi, S.; Pace, A.; Piccionello, A. P.; Pibiri, I.; Vivona, N. *J. Org. Chem.* **2006**, *71*, 8106–8113.

These results suggest that the cyclic diacylhydroxylamine could serve as to desymmetrize the 2,2′-biphenyldiacetyl moiety, with the C(O)−N bond fairly unreactive and the C(O)−O bond serving as a reactive acylating agent, reminiscent of the "active esters" of *N*-hydroxysuccinimide or *N*-hydroxybenzotriazole used in peptide synthesis.[12] Indeed, reaction of $(C_6H_4CH_2CO)_2N(CH_3)O$ with 2 molar equiv of the lithium enolate of 4′-methylacetophenone gives Claisen condensation selectively at the C(O)−O bond to give, after protonation, the mixed hydroxamate-β-diketonate ligand $HobH_2$ in good yield (eq 3). The second equivalent of enolate is required to deprotonate the newly formed β-diketone (use of other bases is successful with non-enolizable acyl chlorides,[13,14] but results in side reactions with enolizable acyl chlorides[6]).



(3)

Metalation of Ligands. Both $HoxH_2$ and $HobH_2$ react with $Ti(O^iPr)_4$ in benzene to give the corresponding $LTi(O^iPr)_2$ complexes (eq 4). As was observed with the analogous bis(diketonate) (R_2Bob) complexes,[6] metalation proceeds immediately at room temperature, but a small amount of polymeric material is formed initially (as judged by broad peaks in the ^1H NMR). Heating in the presence of excess $Ti(O^iPr)_4$ results in conversion of the oligomeric species to the monomeric complexes.

$$LH_2 + Ti(O^iPr)_4\ (3\ \text{equiv}) \xrightarrow[75\ ^\circ C]{C_6H_6} LTi(O^iPr)_2 \qquad L = \begin{matrix}\text{Hox, 83\%}\\ \text{Hob, 64\%}\end{matrix} \qquad (4)$$

The monomeric nature of both complexes is confirmed by mass spectrometry. The bis(hydroxamate) complex (Hox)-$Ti(O^iPr)_2$ shows C_2 symmetry by NMR, with the diastereotopic C*HH*′ protons from the Hox ligand appearing as well-separated doublets in the ^1H NMR (δ 2.52 and 3.37, J = 15 Hz in C_6D_6) and the isopropyl groups equivalent but showing diastereotopic methyl groups. Only a single geometric isomer and a single diastereomer (involving the relative configuration of the titanium center and the axially chiral biphenyl moiety) is observed. The intrinsically unsymmetrical hydroxamate-diketonate complex, not surprisingly, shows C_1 symmetry by NMR, but the large chemical shift separation of the diastereotopic C*HH*′ protons again suggests a similar chelated structure, and again only a single geometric and stereoisomer is observed. We presume that the structures involve a *cis*-α geometry (i.e., one in which the carbonyl groups adjacent to the CH_2 groups are trans to the isopropoxides) and the (*R*,Λ)/(*S*,Δ) relative configuration of the biphenyl and the titanium, as has been demonstrated by structural studies on the $(R_2Bob)TiX_2$ complexes.[6] The geometric stereocontrol exerted by the bis(hydroxamate) Hox^{2-} is somewhat reminiscent of that imposed by the C_2-symmetric bis(hydroxamate) siderophore alcaligin, which also forms an unusual isomer with the carbonyl groups of the hydroxamates *cis* and their NO donors trans in its crystallographically characterized L_3Fe_2 complex,[15] although the chirality at the metal is apparently different in the alcaligin complexes L_3Fe_2 and $LFe(OH_2)_2^+$.[16]

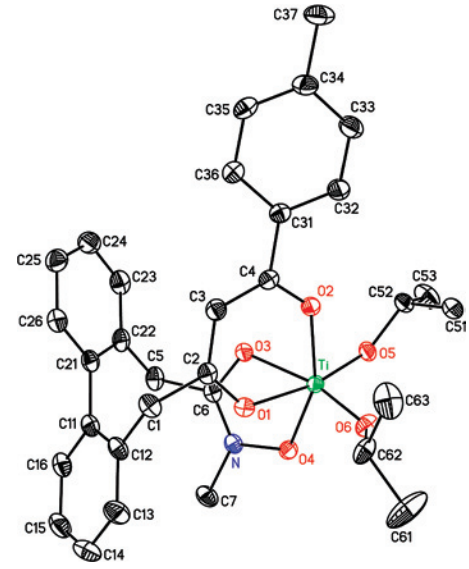


Figure 2. Thermal ellipsoid plot (50% ellipsoids) of $(Hob)Ti(O^iPr)_2$. Hydrogen atoms are omitted for clarity, and only the major orientation of the disordered isopropyl group (C61 and C62) is shown.

X-ray crystallography of the mixed diketonate-hydroxamate complex $(Hob)Ti(O^iPr)_2$ (Figure 2) confirms its close structural analogy to $(^tBu_2Bob)Ti(O\text{-}2,6\text{-}^iPr_2C_6H_3)_2$ (Table 3). The structure of the mixed-donor ligand allows a detailed comparison of the diketonate and hydroxamate groups. Since the hydroxamate oxygen bonded to nitrogen is formally negatively charged, while its carbonyl oxygen is formally neutral, one would anticipate that the hydroxamate N*O* would be a stronger donor, and the hydroxamate C*O* a weaker donor, than the diketonate oxygens (each of which bears a formal charge of −1/2). Indeed, the hydroxamate N*O* forms the shortest Ti−O bond of the Hob chelate, at 1.9465(10) Å, 0.0365 Å shorter than the trans diketonate and 0.0220 Å shorter than the corresponding diketonate in the bis(diketonate) compound $(^tBu_2Bob)Ti(O\text{-}2,6\text{-}^iPr_2C_6H_3)_2$. The distinc-

(12) Bodzansky, M.; Bednarek, M. A. *J. Protein Chem.* **1989**, *8*, 461–469.
(13) Fortner, K. C.; Bigi, J. P.; Brown, S. N. *Inorg. Chem.* **2005**, *44*, 2803–2814.
(14) Schroeder, T.; Ugrinova, V.; Noll, B. C.; Brown, S. N. *Dalton Trans.* **2006**, 1030–1040.
(15) Hou, Z.; Sunderland, C. J.; Nishio, T.; Raymond, K. N. *J. Am. Chem. Soc.* **1996**, *118*, 5148–5149.
(16) Hou, Z.; Raymond, K. N.; O'Sullivan, B.; Esker, T. W.; Nishio, T. *Inorg. Chem.* **1998**, *37*, 6630–6637.

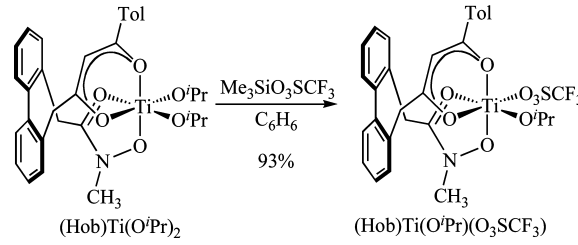
Table 3. Selected Bond Distances (Å) and Angles (deg) in (Hob)Ti(O^iPr)$_2$, (Hob)Ti($O_2CCMe_2CH_2O$), and (^{t}Bu$_2$Bob)Ti(O-2,6-^{i}Pr$_2$C$_6$H$_3$)$_2$[a]

	(Hob)Ti(O^iPr)$_2$	(^{t}Bu$_2$Bob)Ti (O-2,6-^{i}Pr$_2$C$_6$H$_3$)$_2$[a]	(Hob)Ti(O_2 CCMe$_2$CH$_2$O)
Ti−O1	2.0819(11)	2.0808(11)	2.0201(8)
Ti−O2	1.9830(10)	1.9685(10)	1.9698(8)
Ti−O3	2.0849(11)	2.0808(11)	2.0568(8)
Ti−O4	1.9465(10)	1.9685(10)	1.9352(8)
Ti−O5	1.8161(11)	1.8173(11)	1.9292(8)
Ti−O6	1.7983(11)	1.8173(11)	1.7896(8)
N−O4	1.3740(15)		1.3711(12)
N−C6	1.3066(19)		1.3170(14)
C6−O3	1.2672(17)		1.2724(12)
C2−O1	1.2564(17)	1.2685(18)	1.2750(13)
C4−O2	1.2820(17)	1.2922(18)	1.2860(13)
C41−O5			1.3094(13)
C41−O7			1.2183(14)
O1−Ti−O2	82.15(4)	82.62(4)	82.83(3)
O1−Ti−O3	78.74(4)	79.99(6)	82.61(3)
O1−Ti−O4	84.07(4)	82.60(4)	88.43(3)
O1−Ti−O5	169.04(4)	171.18(5)	168.21(3)
O1−Ti−O6	87.94(5)	91.39(5)	100.71(4)
O2−Ti−O3	84.21(4)	82.60(4)	90.62(3)
O2−Ti−O4	157.88(4)	160.67(6)	165.53(3)
O2−Ti−O5	88.76(4)	94.46(5)	89.39(3)
O2−Ti−O6	99.84(5)	98.28(4)	103.32(4)
O3−Ti−O4	76.16(4)	82.62(4)	76.78(3)
O3−Ti−O5	94.31(5)	91.39(5)	88.66(3)
O3−Ti−O6	165.47(5)	171.18(5)	165.94(4)
O4−Ti−O5	102.64(5)	98.28(4)	97.30(3)
O4−Ti−O6	96.87(5)	94.46(5)	89.59(4)
O5−Ti−O6	99.70(5)	97.28(7)	89.66(4)
Ti−O5−C52	135.31(9)	170.25(10)	
Ti−O5−C41			134.06(7)
Ti−O6−C62	134.16(12)	170.25(10)	
Ti−O6−C43			126.57(7)

[a] Ref. 6. Values given are for the atoms analogous to the ones in (Hob)Ti(O^iPr)$_2$.

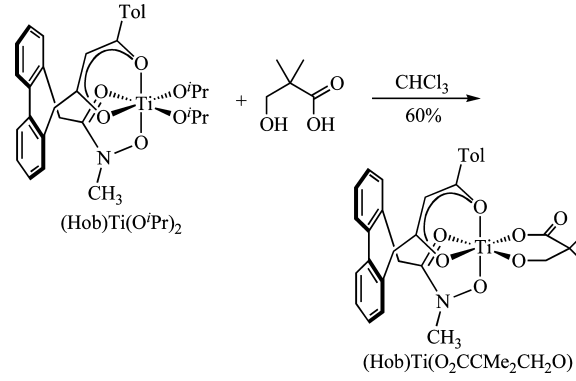
tion between the hydroxamate C*O* and diketonate is more subtle. The Ti−O distances of the two groups (both trans to isopropoxide) are identical within experimental error, but the slight difference between Ti−O^{i}Pr distances, with the bond trans to the hydroxamate CO 0.0178 Å shorter than the bond trans to the diketonate, suggests that the diketonate exerts a stronger trans influence than the hydroxamate carbonyl, consistent with a stronger bond to titanium. As expected, the five-membered hydroxamate chelate has a somewhat smaller bite angle than the six-membered diketonate chelate (76.16(4)° vs 82.15(4)°).

Reactivity of Titanium Complexes; Further Comparison of Hydroxamate and Diketonate Ligands. The diisopropoxide complex (Hob)Ti(O^iPr)$_2$ reacts with trimethylsilyl trifluoromethanesulfonate with loss of one isopropoxide group and formation of the monotriflate complex (Hob)Ti(O^iPr)(O_3SCF_3) (eq 5). The dihydroxamate complex (Hox)Ti(O^iPr)$_2$ reacts analogously to form (Hox)Ti(O^iPr)(O_3SCF_3). Because of the inequivalence of the two chelate arms, (Hob)Ti(O^iPr)(O_3SCF_3) could potentially exist as two geometric isomers, depending on whether the triflate is trans to the hydroxamate or to the diketonate. In fact, only a single species is observed by NMR (>30:1 selectivity). In principle, this could be due to rapid equilibration between the two geometric isomers, but this seems very unlikely, as both analogues with symmetrical ligands, (Hox)Ti(O^iPr)(O_3SCF_3) and (Tol$_2$Bob)Ti(O^iPr)(O_3SCF_3),[6] are C_1-symmetric by NMR, indicating that rapid interchange of the isopropoxide and triflate groups does not take place. Observation of a single isomer of (Hob)Ti(O^iPr)(O_3SCF_3) is most plausibly attributed to selective formation of one geometric isomer. Since the selectivity is unlikely to be steric in origin in these unhindered compounds, this result indicates that the difference in trans influence between diketonate and hydroxamate is great enough to differentiate between the two trans binding sites. On the basis of the crystallographic data, we assign the observed isomer as having the more strongly donating isopropoxide trans to the more weakly donating hydroxamate. Control of geometry on the basis of relative trans influence is widely observed in titanium(IV) complexes;[17] the unusual feature of (Hob)Ti(O^iPr)(O_3SCF_3) is that the magnitude of the effect is essentially quantitative despite the apparent similarity of the two donors.



(5)

To confirm the direction of regioselectivity, we sought to prepare other unsymmetrically substituted (Hob)Ti complexes. Hydroxypivalic acid, $HOCH_2CMe_2CO_2H$, reacts smoothly with (Hob)Ti(O^iPr)$_2$ to form the bright yellow, air- and moisture-stable hydroxypivalate complex (Hob)Ti($O_2CCMe_2CH_2O$) (eq 6), in which a strongly donating alkoxide and a less strongly donating carboxylate compete for the two inequivalent binding sites on titanium. This reaction is also quite regioselective, but in this case traces of a minor isomer are observed by ^{1}H NMR (selectivity = 15.6:1 in $CDCl_3$ at 20 °C).



(6)

The structure of (Hob)Ti($O_2CCMe_2CH_2O$) was elucidated by X-ray crystallography (Figure 3). The isomer observed in the solid state is indeed that in which the more strongly bonded alkoxide (Ti−O distance of 1.7896(8) Å) is trans to the hydroxamate and the more weakly bonded carboxylate

(17) Gau, H.-M.; Lee, C.-S.; Lin, C.-C.; Jiang, M.-K.; Ho, Y.-C.; Kuo, C.-N. *J. Am. Chem. Soc.* **1996**, *118*, 2936–2941.

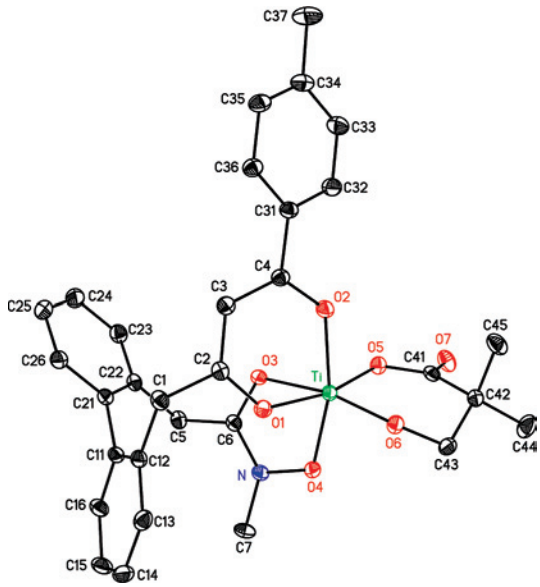


Figure 3. Thermal ellipsoid plot (50% ellipsoids) of (Hob)Ti($O_2CCMe_2CH_2O$). Hydrogen atoms are omitted for clarity.

(Ti−O distance of 1.9292(8) Å) is trans to the diketonate. The lower donor strength of the carboxylate (compared to isopropoxide) results in a marked shortening of the Ti−O1 distance (by 0.062 Å) on going from the diisopropoxide to the hydroxypivalate complex, with the other three Ti−O distances in the Hob ligand also shortening, but by much less (0.01−0.03 Å). The overall conformation of the Hob ligand, including the relative configuration of the biphenyl and the titanium centers, are the same as in the diisopropoxide complex.

The isomer observed in the solid state was confirmed to be the major isomer in solution by redissolving the crystals in CD_2Cl_2 at −78 °C. NMR spectra taken at −70 °C showed only the major isomer, while warming the solution allowed equilibration within a few minutes at 0 °C. These results confirm that the hydroxamate carbonyl oxygen is indeed a noticeably weaker donor than a diketonate oxygen. However, the fact that even groups as disparate as alkoxide and carboxylate are only modestly aligned with the two groups in the Hob ligand suggests that the difference in trans influence between these groups is also only modest, consistent with the subtle structural asymmetry observed in (Hob)Ti(O^iPr)$_2$. Studies aimed at further quantitating this difference in trans influence, as well as exploring the consequences of this electronic asymmetry in chemical reactions, are currently in progress.

Conclusions

A series of dianionic, tetradentate, oxygen donor ligands based on a 2,2′-bis(methylene)biphenyl linker, containing two hydroxamates (Hox), two diketonates (Bob), or one hydroxamate and one diketonate (Hob), has been prepared. All of the ligands bind to titanium(IV) in a structurally well-defined manner, forming (*R*,Λ)/(*S*,Δ)-*cis*-α complexes with the carbonyl groups adjacent to the CH_2 groups cis to each other. The availability of this structurally analogous series allows a systematic comparison of the properties of the diketonate and hydroxamate groups. Crystallographic studies suggest that the hydroxamate N*O* group is an appreciably stronger donor than the diketonate ligand, which is in turn a stronger donor to titanium than the hydroxamate carbonyl. The difference between the latter is modest, a conclusion supported by studies of the equilibrium of unsymmetrical complexes such as (Hob)Ti(O^iPr)(O_3SCF_3) or (Hob)Ti($O_2CCMe_2CH_2O$).

Acknowledgment. This work was supported by the National Science Foundation (CHE-0518243). Partial support for the X-ray diffraction facility was provided by the NSF (CHE-0443233).

Supporting Information Available: Crystallographic information on ($C_6H_4CH_2CO)_2N(CH_3)O$, (Hob)Ti(O^iPr)$_2$, and (Hob)Ti($O_2CCMe_2CH_2O$) in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

IC8016479