Organometallics **1991**, *10*, 2015–2025

parameters for all of the non-hydrogen atoms are given in Table II.

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Supplementary Material Available: Tables of atomic coordinates of the hydrogen atoms and anisotropic thermal parameters of the non-hydrogen atoms (5 pages); a table of observed and calculated structure factor amplitudes (35 pages). Ordering information is given on any current masthead page.

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(12) Hamilton, W. C. *Acta Crystallogr.* **1965**, *18*, 502.

Multidentate Lewis Acids. Adducts of Monodentate and Bidentate Titanium Trichloroalkoxides with Ketones

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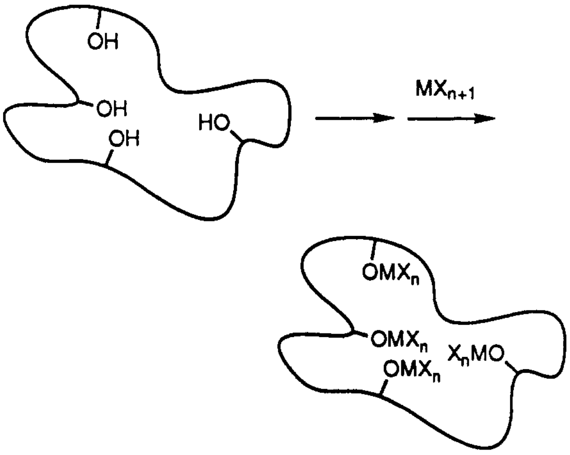
Like $TiCl_4$, titanium trichloroisopropoxide (4) is a strong Lewis acid able to form 1:2 adducts with ketones. Low-temperature ^1H and ^{13}C NMR spectra indicate that these adducts adopt a *mer* octahedral geometry. Exchange of free and bound pinacolone occurs by a dissociative mechanism with $\Delta G^{*}{}_{219}$ = 9.2 kcal/mol. Potentially bidentate titanium trichloroalkoxides **19–21** can be prepared by treating the bis(trimethylsilyl) ethers of *trans*-1,2-cyclohexanediols with 2 equiv of $TiCl_4$. Compounds **19–21** form crystalline 1:2 ketone adducts even in the presence of excess ketone. An X-ray crystallographic study has shown that the close proximity of the $OTiCl_3$ groups favors symmetric adducts **30** (X = Cl) with bridging chlorides, not adducts **31** with bridging, doubly activated carbonyl groups. Similar chloride-bridged structures are adopted in solution. Low-temperature ^1H and ^{13}C NMR spectra establish that unsymmetric 1:3 adducts **36** (X = Cl) are formed in solution in the presence of additional ketone. Symmetrization of the 1:3 pinacolone complex derived from bidentate titanium trichloroalkoxide **21** occurs by a normal dissociative mechanism with $\Delta G^{*}{}_{223}$ = 10.4 kcal/mol. Since this process is slower than exchange in 1:2 adducts of monodentate analogue **4**, symmetric intermediates or transition states **38** (X = Cl) with a single bridging carbonyl oxygen do not offer a low-energy intramolecular pathway for exchange. Slow exchange in the 1:3 adduct provides evidence that the two $OTiCl_3$ groups in compounds **19–21** cooperate by forming a single chloride bridge that enhances the Lewis acidity of one site at the expense of the other.

The unique ability of well-designed multidentate Lewis acids to recognize, bind, transport, and activate basic guests is attracting the attention of a growing number of chemists.[2,3] We have contributed to the study of multidentate Lewis acids by showing that they can be made conveniently by adding metal salts MX_{n+1} to compounds containing hydroxyl groups or similar sites suitably oriented by an organic framework (eq 1).[3] An important practical goal of this work is to devise bidentate Lewis acids **1** that can activate carbonyl compounds by forming complexes **2** in which the substrate is cooperatively bound (eq 2). These complexes promise to be unusually susceptible to nucleophilic additions,[4] and their rigid orientation should help



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(1) Fellow of the Natural Sciences and Engineering Research Council of Canada, 1986–1990. Fellow of the Ministère de l'Éducation du Québec, 1990–1991.

(2) For recent work on multidentate Lewis acids, see: Nadeau, F.; Simard, M.; Wuest, J. D. *Organometallics* **1990**, *9*, 1311–1314. Narasaka, K.; Sakurai, H.; Kato, T.; Iwasawa, N. *Chem. Lett.* **1990**, 1271–1274. Dohmeier, C.; Mattes, R.; Schnöckel, H. *J. Chem. Soc., Chem. Commun.* **1990**, 358–359. Kaufmann, D.; Boese, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 545–546. Chujo, Y.; Tomita, I.; Saegusa, T. *Macromolecules* **1990**, *23*, 687–689. Layh, M.; Uhl, W. *Polyhedron* **1990**, *9*, 277–282. Jurkschat, K.; Rühlemann, A.; Tzschach, A. *J. Organomet. Chem.* **1990**, *381*, C53–C56. Kelly, T. R.; Meghani, P. *J. Org. Chem.* **1990**, *55*, 3684–3688. Tamao, K.; Hayashi, T.; Ito, Y.; Shiro, M. *J. Am. Chem. Soc.* **1990**, *112*, 2422–2424. Newcomb, M.; Horner, J. H.; Blanda, M. T.; Squattrito, P. J. *Ibid.* **1989**, *111*, 6294–6301. Jurkschat, K.; Kuivila, H. G.; Liu, S.; Zubieta, J. A. *Organometallics* **1989**, *8*, 2755–2759. Katz, H. E. *J. Org. Chem.* **1989**, *54*, 2179–2183. Schmidbaur, H.; Öller, H.-J.; Wilkinson, D. L.; Huber, B.; Müller, G. *Chem. Ber.* **1989**, *122*, 31–36. Jung, M. E.; Xia, H. *Tetrahedron Lett.* **1988**, *29*, 297–300. Kaufmann, D. *Chem. Ber.* **1987**, *120*, 901–905. Khan, M. A.; Peppe, C.; Tuck, D. G. *Organometallics* **1986**, *5*, 525–530.

(3) (a) Phan Viet, M. T.; Sharma, V.; Wuest, J. D. *Inorg. Chem.*, in press. (b) Bélanger-Gariépy, F.; Hoogsteen, K.; Sharma, V.; Wuest, J. D. *Inorg. Chem.*, in press (c) Bachand, B.; Bélanger-Gariépy, F.; Wuest, J. D. *Organometallics* **1990**, *9*, 2860–2862. (d) Sharma, V.; Simard, M.; Wuest, J. D. *Inorg. Chem.* **1991**, *30*, 579–581. (e) Galeffi, B.; Simard, M.; Wuest, J. D. *Ibid.* **1990**, *29*, 955–958. (f) Galeffi, B.; Simard, M.; Wuest, J. D. *Ibid.* **1990**, *29*, 951–954.

(4) Wuest, J. D.; Zacharie, B. *J. Am. Chem. Soc.* **1985**, *107*, 6121–6123.

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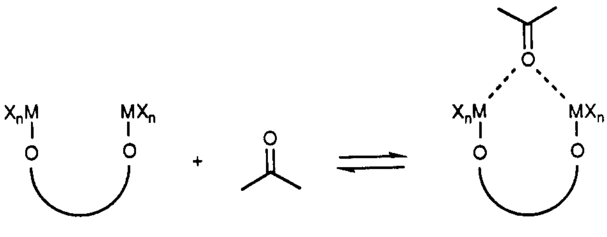

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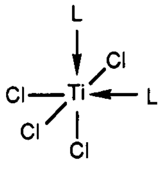
promote asymmetric additions when the bidentate Lewis acids 1 are chiral. In this paper, we describe a series of bidentate titanium trichloroalkoxides prepared by the simple procedure of eq 1, and we show how these compounds and their simple monodentate analogues bind and activate ketones.

Previous work has established that $TiCl_4$ is a strong Lewis acid able to form 1:2 adducts with a variety of monodentate Lewis bases.[5] We have extended these studies by examining the interaction of $TiCl_4$ with simple ketones in greater detail. At −85 °C in CD_2Cl_2, the ^1H NMR spectrum of a 0.30 M solution of $TiCl_4$ containing 3 equiv of acetone showed two singlets at δ 2.63 and 2.14 in a 2:1 ratio. The downfield signal corresponds to bound acetone in the cis octahedral 1:2 complex **3** (L = acetone),[5] while the upfield signal corresponds to free acetone. The coalescence temperature for exchange of free and bound acetone is −55 °C, so $\Delta G^{\ddagger}_{218}$ is approximately 10.1 ± 0.2 kcal/mol.[6] This value indicates that acetone is strongly bound and suggests that the rate-limiting step for exchange is dissociation of a single acetone from the 1:2 complex.[7] A similar experiment with 3 equiv of 3,3-dimethyl-2-butanone (pinacolone) also showed that two were bound, giving a single major 1:2 adduct with peaks at δ 2.72 and 1.22 shifted downfield by 0.59 and 0.14 ppm, respectively, from those of free pinacolone. Under similar conditions, the ^{13}C NMR spectrum showed one carbonyl carbon at δ 234.2 and one methyl carbon at δ 46.7 in addition to the corresponding signals of free pinacolone at δ 215.6 and 43.8. We propose that the adduct has the cis octahedral geometry of structure **3** (L = pinacolone), since $ZrCl_4$ also forms a cis 1:2 complex with pinacolone.[3f] In general, a cis orientation of the bound ketones is favored because it places chlorines trans to the more weakly π-donating ketone ligands and thereby maximizes chlorine-p metal-d π-bonding.[5,8] Variable-temperature ^1H NMR spectra of a 0.40 M solution of $TiCl_4$ in CD_2Cl_2 containing 3 equiv of pinacolone have shown that the coalescence temperature for exchange of the downfield methyls of free and bound ketone is −60 °C, so $\Delta G^{\ddagger}_{213}$ is approximately 9.7 ± 0.2 kcal/mol.[6] This indicates that $TiCl_4$ binds pinacolone almost as strongly as it binds acetone.



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Since $TiCl_4$ normally favors nonlinear σ-bonded adducts of carbonyl compounds in the solid state,[9] we expected its ketone complexes **3** to have a similar structure in solution. This would differentiate the two methyl groups of each bound acetone in adduct **3** (L = acetone). In fact, they could not be distinguished by ^1H NMR spectroscopy, even in spectra recorded at temperatures as low as −140 °C in 3:1 mixtures of CHF_2Cl and CD_2Cl_2. We conclude that syn–anti isomerization is extremely rapid (eq 3). The transition state for this process is presumably a linear σ-complex stabilized by significant oxygen-p titanium-d π-bonding or by an important electrostatic contribution to the energy of complexation.[10,11]

(3)

Like $TiCl_4$, titanium trichloroalkoxides are powerful Lewis acids. To obtain detailed information about their coordination chemistry, we used variable-temperature NMR spectroscopy to study the interaction of titanium trichloroisopropoxide [$TiCl_3OCH(CH_3)_2$ (**4**)][12] with ketones. At −25 °C in CD_2Cl_2, the ^1H NMR spectrum of a 0.066 M solution of pure compound **4** showed only the expected doublet at δ 1.56 (6 H) and septet at δ 5.19 (1 H). At −70 °C, however, the spectrum became more complex and consisted of two doublets at δ 1.46 and 1.55 in a 1:3 ratio, as well as two broad signals at δ 4.78 and 5.27 in a similar ratio. Since cryoscopic studies have established that titanium trichloroalkoxides are normally monomeric in benzene at concentrations up to 0.2 M,[13] we doubt that changes in the NMR spectrum can be attributed to association of titanium trichloroisopropoxide (**4**). Instead, we suggest that compound **4** undergoes partial redistribution in solution to give titanium dichlorodiisopropoxide (**5**)[12b] and $TiCl_4$ (eq 4).[13] Compounds **4** and **5** appear to form

$$\underset{\mathbf{4}}{2TiCl_3OCH(CH_3)_2} \rightleftharpoons \underset{\mathbf{5}}{TiCl_2[OCH(CH_3)_2]_2} + TiCl_4 \qquad (4)$$

mixed aggregates with $TiCl_4$,[14] since low-temperature ^{47}Ti and ^{49}Ti NMR spectra of solutions of titanium trichloro-

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[5] Turin, E.; Nielson, R. M.; Merbach, A. E. *Inorg. Chim. Acta* **1987**, *134*, 79–85, 67–78.

[6] $\Delta G^{\ddagger}$ (kcal/mol) was calculated by using the equation $\Delta G^{\ddagger} = aT_c \times (9.97\ aT_c(9.97 + \log T_c/\delta\nu)$, where T_c is the coalescence temperature (K), $a = 4.575 \times 10^{-3}$, and $\delta\nu$ is the shift difference (Hz) between the two exchanging sites in the limiting low-temperature spectrum. See: Gunther, H. *NMR Spectroscopy, An Introduction*; Wiley: New York, 1973; p 243.

[7] For thermodynamic studies of the complexation of carbonyl compounds by $TiCl_4$, see: Elegant, L.; Pagliardini, A.; Torri, G.; Azzaro, M. *Bull. Soc. Chim. Fr.* **1972**, 4422–4424. Osipov, O. A.; Kletenik, Yu. B. *Zh. Neorg. Khim.* **1960**, *5*, 2220–2222. Osipov, O. A.; Lysenko, Yu. A. *Ibid.* **1960**, *5*, 1840–1845.

[8] Borden, R. S.; Loeffler, P. A.; Dyer, D. S. *Inorg. Chem.* **1972**, *11*, 2481–2484. Borden, R. S.; Hammer, R. N. *Ibid.* **1970**, *9*, 2004–2009. Dyer, D. S.; Ragsdale, R. O. *Ibid.* **1969**, *8*, 1116–1120.

[9] (a) Sobota, P.; Utko, J.; Lis, T. *J. Organomet. Chem.* **1990**, *393*, 349–358. (b) Oppolzer, W.; Rodriguez, I.; Blagg, J.; Bernardinelli, G. *Helv. Chim. Acta* **1989**, *72*, 123–130. (c) Maier, G.; Seipp, U.; Boese, R. *Tetrahedron Lett.* **1987**, *28*, 4515–4516. (d) Poll, T.; Metter, J. O.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 112–114. (e) Bassi, I. W.; Calcaterra, M.; Intrito, R. *J. Organomet. Chem.* **1977**, *127*, 305–313. (f) Brun, L. *Acta Crystallogr.* **1966**, *20*, 739–749.

[10] (a) Huffman, J. C.; Moloy, K. G.; Caulton, K. G. *Inorg. Chem.* **1988**, *27*, 2190–2192. (b) Chisholm, M. H.; Rothwell, I. P. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: New York, 1987; Vol. 2, Chapter 15.3. Latesky, S. L.; Keddington, J.; McMullen, A. K.; Rothwell, I. P.; Huffman, J. C. *Inorg. Chem.* **1985**, *24*, 995–1001.

[11] LePage, T. J.; Wiberg, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 6642–6650.

[12] (a) Rasuwajew, G. A.; Bobinowa, L. M.; Etlis, V. S. *Tetrahedron* **1959**, *6*, 154–160. (b) Bradley, D. C.; Hancock, D. C.; Wardlaw, W. *J. Chem. Soc.* **1952**, 2773–2778.

[13] Martin, R. L.; Winter, G. *J. Chem. Soc.* **1961**, 2947–2957.

[14] (a) Simple titanium dichlorodialkoxides are known to be dimeric in benzene at concentrations as low as 0.04 M.[13] (b) For structural studies of dimeric titanium dichlorodialkoxides, see: Haase, W.; Hoppe, H. *Acta Crystallogr., Sect. B* **1968**, *B24*, 281–282. Watenpaugh, K.; Caughlan, C. N. *Inorg. Chem.* **1966**, *5*, 1782–1786.

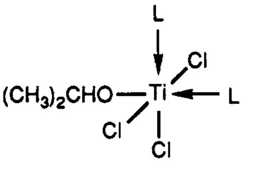
isopropoxide (4) in CD_2Cl_2 consisted of extremely broad, poorly defined signals, and did not reveal a sharp peak at δ 0 characteristic of free $TiCl_4$.[15]

The redistribution of simple titanium trichloroalkoxides has important chemical consequences, since it helps explain earlier observations that metal haloalkoxides MX_nOR^* derived from metal halides MX_{n+1} and simple optically active alcohols R^*OH are inefficient catalysts for a variety of asymmetric processes, including Diels-Alder reactions.[16] Partial redistribution of a chiral monoalkoxide catalyst MX_nOR^* may produce kinetically significant amounts of the corresponding chiral dialkoxide $MX_{n-1}(OR^*)_2$ and the achiral halide MX_{n+1} (eq 5), which then

$$2MX_nOR^* \rightleftharpoons MX_{n-1}(OR^*)_2 + MX_{n+1} \qquad (5)$$

competes effectively with the chiral reagent MX_nOR^*. This possibility raises disturbing questions about the ability of a chiral bidentate derivative 1 to play its intended role as an efficient catalyst for asymmetric reactions.

At −100 °C in 3:1 CHF_2Cl/CD_2Cl_2, the ^1H NMR spectrum of a 0.16 M solution of titanium trichloroisopropoxide (4) containing 5 equiv of acetone showed three sharp singlets at δ 2.57, 2.53, and 2.12 in a 1:1:3 ratio. The first two correspond to bound acetone and the third to free acetone. In addition, the spectrum showed one isopropyl doublet at δ 1.51 and a corresponding septet at δ 5.46, and no peak characteristic of the 1:2 adduct 3 of $TiCl_4$ and acetone could be detected. Under similar conditions, the proton-decoupled ^{13}C NMR spectrum of a 0.46 M solution containing 3 equiv of acetone revealed signals at δ 226.8, 224.8, 31.8, and 31.7 corresponding to two different bound acetones, signals at δ 211.6 and 30.8 derived from free acetone, and signals at δ 96.4 and 22.5 attributable to a single isopropyl group. These observations suggest that redistribution is negligible and that the major product is a single *mer* octahedral 1:2 adduct 6 (L = acetone) with nonequivalent molecules of acetone. This structure is favored because chlorine and the strongest π-donor, the alkoxy group,[10] are trans to the more weakly π-donating ketone ligands, and oxygen-p titanium-d π-bonding and chlorine-p titanium-d π-bonding are therefore maximized.[17] Both acetones are presumably σ-bonded, since adducts of $TiCl_4$ show a similar preference.[9] However, the two nonequivalent methyl groups of each acetone could not be distinguished by ^1H NMR spectroscopy even at −120 °C, so syn–anti isomerization must be very rapid (eq 3). In ^1H NMR spectra, the methyls of free acetone coalesce with those of both bound acetones of complex 6 at approximately −70 °C, so $\Delta G^{\ddagger}_{203}$ is close to 9.3 kcal/mol for both.[6] Since the coalescence temperature proved to be independent of the concentration of free acetone, the mechanism of exchange must be dissociative.



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Similar low-temperature ^1H NMR spectra of solutions of titanium trichloroisopropoxide (4) in CD_2Cl_2 containing 3 equiv of pinacolone showed three methyl singlets of equal intensity at δ 2.65, 2.57, and 2.13 corresponding to the two bound pinacolones of adduct 6 (L = pinacolone) and free pinacolone. At −130 °C in 3:1 CHF_2Cl/CD_2Cl_2, the proton-decoupled ^{13}C NMR spectrum of a 0.34 M solution of titanium trichloroisopropoxide (4) containing 3 equiv of pinacolone revealed signals at δ 232.8, 231.3, 46.8, and 46.7 corresponding to two different bound pinacolones, as well as signals at δ 218.6 and 44.8 derived from free pinacolone. Single peaks at δ 95.6 and 22.7 confirmed that only one isopropyl group was present, and no peak at δ 236.5 corresponding to the 1:2 adduct 3 of $TiCl_4$ and pinacolone could be detected. We conclude that redistribution is unimportant under these conditions, and that the quantitative formation of *mer* octahedral 1:2 ketone complexes is a general feature of the coordination chemistry of simple titanium trichloroalkoxides. In similar ^{13}C NMR spectra in CD_2Cl_2 (Figure 1), coalescence of the carbonyl carbons occurred at −54 °C, so $\Delta G^{\ddagger}_{219}$ for the exchange of free and bound pinacolone is approximately 9.2 ± 0.2 kcal/mol.[6]

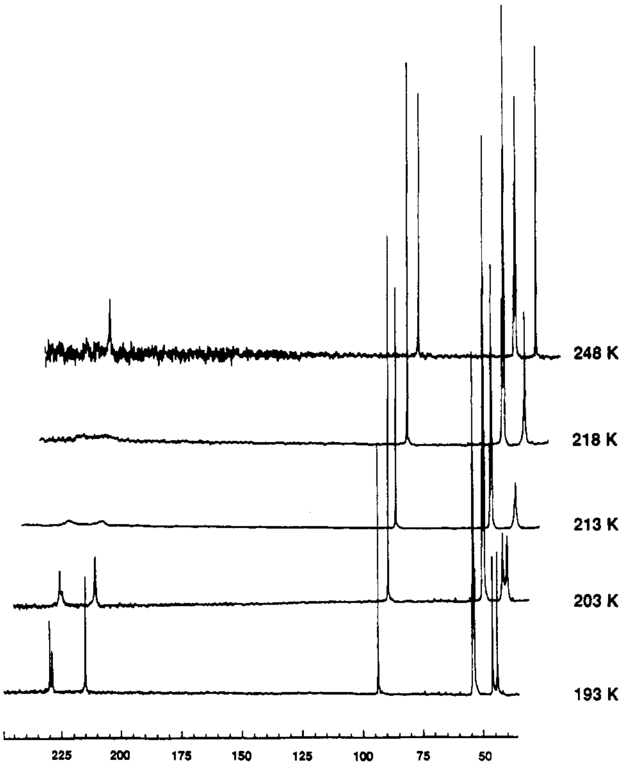

Figure 1. Variable-temperature proton-decoupled ^{13}C NMR spectra of a 0.45 M solution of titanium trichloroisopropoxide (4) in CD_2Cl_2 containing 4 equiv of pinacolone.

Both $TiCl_4$ and titanium trichloroisopropoxide (4) favor 1:2 ketone adducts, and both have similar free energies of activation for the exchange of free and bound ketones. In addition, the carbonyl carbon of bound pinacolone has comparable ^{13}C chemical shifts in the $TiCl_4$ adduct (δ 236.5) and in the titanium trichloroisopropoxide adduct (δ 232.8, 231.3).[18] We conclude that the Lewis acidities of $TiCl_4$ and titanium trichloroalkoxides are not dramatically different. This is critically important, because it suggests that carbonyl compounds doubly activated by well-designed bidentate titanium trichloroalkoxides (eq 2)

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[15] Hao, N.; Sayer, B. G.; Dênès, G.; Bickley, D. G.; Detellier, C.; McGlinchey, M. J. *J. Magn. Reson.* **1982**, *50*, 50–63.

[16] Takemura, H.; Komeshima, N.; Takahashi, I.; Hashimoto, S.-i.; Ikota, N.; Tomioka, K.; Koga, K. *Tetrahedron Lett.* **1987**, *28*, 5687–5690. Quimpère, M.; Jankowski, K. *J. Chem. Soc., Chem. Commun.* **1987**, 676–677.

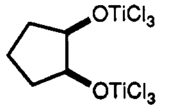
[17] Related zirconium trichloroalkoxides show a similar preference for *mer* octahedral 1:2 adducts.[3e]

[18] NMR chemical shifts have been used to establish relative Lewis acidities: Childs, R. F.; Mulholland, D. L.; Nixon, A. *Can. J. Chem.* **1982**, *60*, 801–808. See also: Laszlo, P.; Teston, M. *J. Am. Chem. Soc.* **1990**, *112*, 8750–8754.

may be substantially more reactive than singly activated adducts of any monodentate Lewis acids that are present, even if small amounts of $TiCl_4$ are produced by redistribution.[4] In fact, doubly activated adducts **2** may be able to play a kinetically significant role even if other adducts are favored thermodynamically. If so, it may be possible to use catalytic amounts of suitably designed diols in conjunction with stoichiometric or catalytic amounts of $TiCl_4$ to accelerate reactions of basic substrates.

Although monodentate titanium trichloroalkoxides should be effective Lewis acidic catalysts, naive attempts to use optically active derivatives $TiCl_3OR^*$ to promote asymmetric reactions of simple carbonyl compounds are not likely to give high enantiomeric excesses, even if redistribution can be controlled. This is because each molecule of titanium trichloroalkoxide will be coordinatively saturated under typical catalytic conditions and will bind two carbonyl ligands at stereochemically dissimilar sites. The two ligands will therefore react differently, and the one trans to the alkoxy group OR^* may be too remote to experience the full effects of its chirality. Furthermore, the barrier to rotation about the donor–acceptor bond is presumably low,[11] and adducts of monodentate titanium trichloroalkoxides should be able to adopt various conformations with different reactivities.

With these generalizations as a guide, we then began to study more complex Lewis acids containing two $OTiCl_3$ groups in close juxtaposition. Our initial objective was to prepare bidentate titanium trichloroalkoxides **7** and **8** derived from *cis*- and *trans*-1,2-cyclopentanediol and then to compare their coordination chemistry. Unfortunately, all attempts to prepare cis compound **7** by treating the diol or the corresponding bis(trimethylsilyl) ether[19] with 2 equiv of $TiCl_4$ were unsuccessful. The mass of the solid remaining after removal of solvent and volatile products showed immediately that only 1 equiv of $TiCl_4$ had been consumed. We believe that the ultimate product is the pentacyclic titanium chloroalkoxide **9** or its centrosymmetric isomer, which are formally derived from hypothetical bicyclic titanium dichlorodialkoxide **10** by dimerization. This hypothesis is reasonable, since simple titanium dichlorodialkoxides are known to exist as dimers in solution and in the solid state, and their structures incorporate central Ti_2O_2 rings containing pentacoordinate, trigonal-bipyramidal titaniums.[14b]



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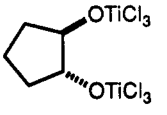

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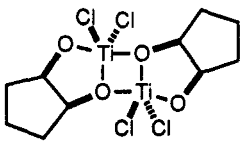

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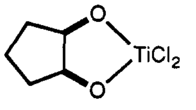

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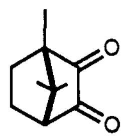
Direct evidence for the formation of a dimer came from a study of closely related titanium chloroalkoxides derived from optically active and racemic diols.[20] Optically pure (1*S*)-camphorquinone (**11**) and racemic quinone were converted by published procedures into the corresponding 2-*exo*,3-*exo*-camphanediols.[21] Direct treatment of optically pure diol **12** with 1 equiv of $TiCl_4$, followed by evaporation of solvent and volatile products, yielded a titanium chloroalkoxide. Its ^1H NMR spectrum in $CDCl_3$ at 25 °C showed characteristic doublets at δ 5.18 (1 H) and 5.91 (1 H) for the hydrogens at C_2 and C_3. The spectrum of the racemic mixture was dramatically different and consisted of the same pair as well as an approximately equal amount of a second pair at δ 5.18 and 5.79. Similarly, the spectrum of the optically pure material contained three methyl singlets, while that of the racemic mixture showed the same three signals plus three additional methyl singlets. We conclude that the optically pure [1*S*-(*exo*,*exo*)] titanium chloroalkoxide exists in solution as a single homochiral dimer **13**, and that the racemic material forms homochiral dimer **13** and its enantiomer, as well as approximately equal amounts of heterochiral dimer **14** and its enantiomer. In both cases, the hypothetical monomeric titanium dichlorodialkoxides from which these dimers are formed are linked by interactions involving titanium and the unique, less hindered oxygen at C_3. This specificity explains the large differences in chemical shift between the hydrogens at C_2 and C_3, since one oxygen is bonded to a single titanium while the other bridges two titaniums. Dimeric structures **9**, **13**, and **14** incorporating central Ti_2O_2 rings therefore account for our observations, whereas more symmetric alternatives like structure **15** do not.[22]



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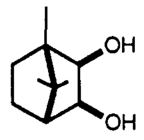

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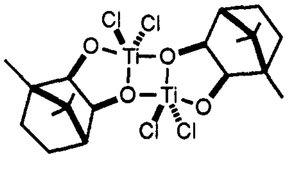

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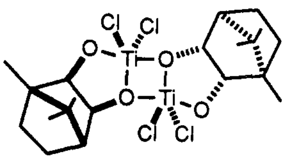

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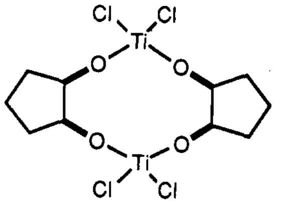

15

Dimers **13** and **14** are strongly associated and not easily cleaved by heat or weak bases. In toluene-d_8, ^1H NMR spectra of a saturated solution of a racemic mixture retained the two characteristic pairs of downfield doublets even at 95 °C, so ΔG^* for dissociation is at least 17.6

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(19) (a) Lasocki, Z. *Synth. Inorg. Met.-Org. Chem.* **1973**, *3*, 29–35. (b) For related work, see: Hwu, J. R.; Anderson, D. A.; Wang, N.; Buchner, M. M.; Gani, P.; Tsay, S.-C. *Chem. Ber.* **1990**, *123*, 1667–1671.

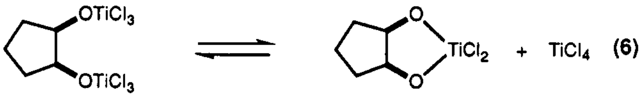
(20) For related studies, see: Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028–4036. Iwasawa, N.; Hayashi, Y.; Sakurai, H.; Narasaka, K. *Chem. Lett.* **1989**, 1581–1584.

(21) (a) Partanen, T.; Mälkönen, P. J.; Vainiotalo, P.; Vepsäläinen, J. *J. Chem. Soc., Perkin Trans. 2* **1990**, 777–782. (b) Angyal, S. J.; Young, R. J. *J. Am. Chem. Soc.* **1959**, *81*, 5467–5472. (c) Takeshita, T.; Kitajima, M. *Bull. Chem. Soc. Jpn.* **1959**, *32*, 985–991. (d) Trevoy, L. W.; Brown, W. G. *J. Am. Chem. Soc.* **1949**, *71*, 1675–1678. (e) Rupe, H.; Thommen, W. *Helv. Chim. Acta* **1947**, *30*, 933–947.

(22) In contrast, related dimeric (cyclopentadienyl)titanium chlorodialkoxides are known to favor structures with 10-membered $C_4O_4Ti_2$ rings.[10a]

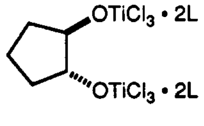
kcal/mol.[6] Furthermore, the dimers were not cleaved in $CDCl_3$ at 25 °C by the addition of 4 equiv of acetone. In contrast, in DMSO-d_6 the two pairs of doublets were replaced by a single pair of more closely spaced doublets at δ 5.30 and 5.49. This suggests that suitably strong bases can cleave the dimers and yield adducts of the monomers.

Formation of derivatives of bicyclic titanium dichlorodialkoxide **10** is a predictable consequence of the close proximity of the hydroxyl groups in *cis*-1,2-cyclopentanediol and the stability of dimeric motif **9**. Nevertheless, attempts to make cis bidentate titanium trichloroalkoxide **7** cannot be dismissed as naive. This is because simple titanium chloroalkoxides favor C–O–Ti angles near 180°,[10] which implies that formation of bicyclic compound **10** directly from the diol or by the hypothetical unimolecular redistribution of eq 6 is enthalpically problematic. We hoped that these factors would permit the formation and kinetic stabilization of target **7** at the expense of bicyclic monomer **10**. Although this did not occur, it is possible that significant amounts of free monomer **10** are never present and that the observed product **9** arises not by direct dimerization but by a more circuitous route, perhaps involving bimolecular reactions of the elusive cis bidentate titanium trichloroalkoxide **7**.



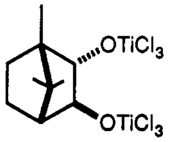
7 **10**

In contrast, treatment of racemic *trans*-1,2-cyclopentanediol with 2 equiv of $TiCl_4$, followed by evaporation of solvent and volatile products, provided the desired trans bidentate titanium trichloroalkoxide **8** in nearly quantitative yield. Its infrared spectrum (Nujol mull) revealed strong bands for Ti–Cl stretching near 430, 390, and 330 cm^{-1}, which are closely similar to those of simple monodentate titanium trichloroisopropoxide (**4**) itself. We conclude that the two $OTiCl_3$ groups of bidentate analogue **8** do not interact intramolecularly or intermolecularly by oxygen or chloride bridging. These groups are therefore freely available for the cooperative binding of suitable Lewis bases. At −85 °C in CD_2Cl_2, the ^1H NMR spectrum of a 0.050 M solution of compound **8** containing 5 equiv of acetone showed three methyl singlets at δ 2.59, 2.55, and 2.14 in a 2:2:1 ratio. Acetone (4 equiv) is therefore bound in two distinct environments, so we propose that the major species in solution is symmetric 1:4 complex **16** (L = acetone). Each $OTiCl_3$ group operates independently and forms a normal *mer* octahedral 1:2 complex containing two nonequivalent molecules of acetone. The coalescence temperature for exchange of free acetone and both bound acetones is −65 °C and is independent of the concentration of free acetone, so the rate and mechanism of exchange are similar to those determined for analogous processes involving $TiCl_4$ and titanium trichloroisopropoxide (**4**). These observations demonstrate that no dramatic chemical effects can be attributed to the presence of two neighboring electrophilic sites in bidentate Lewis acid **8**. The likely preference for C–O–Ti angles close to 180° causes the electrophilic sites to diverge and helps disfavor cooperative binding of a single basic atom by both metals. In addition, the unwillingness of the sites to cooperate is reinforced by their trans disposition on a five-membered ring.



16

Other bidentate titanium trichloroalkoxides derived from *trans*-1,2-cyclopentanediols behaved similarly. The bis(trimethylsilyl) ether of optically pure [1*S*-(2-*endo*,3-*exo*)]-camphanediol[21] could be prepared by the normal method[19a] and converted into bidentate titanium trichloroalkoxide **17** by the addition of 2 equiv of $TiCl_4$. At −85 °C in CD_2Cl_2, the ^1H NMR spectrum of 0.048 M solution containing 5 equiv of acetone showed that only one remained free, so the major species in solution is the expected 1:4 complex **18** (L = acetone). Although cooperative binding of a single carbonyl oxygen by both electrophilic sites seemed unlikely, we nevertheless attempted to use bidentate Lewis acid **17** to promote asymmetric reactions of hydrocinnamaldehyde ($PhCH_2CH_2CHO$). The addition of allyltrimethylsilane (1 equiv) to a solution of hydrocinnamaldehyde (1 equiv) and $TiCl_4$ (0.5 equiv) in CH_2Cl_2 at 25 °C, followed by an aqueous workup, has been shown to produce 1-phenyl-5-hexen-3-ol in 96% yield.[23] When $TiCl_4$ was replaced in this procedure by an equimolar amount of optically pure compound **17**, the alcohol was formed in 87% yield. Unfortunately, analysis by the method of Mosher[24] revealed that the product was racemic. Although these experiments establish that titanium trichloroalkoxides are effective Lewis acids, they also confirm that chiral bidentate derivatives prepared from optically active *trans*-1,2-cyclopentanediols will not normally be useful reagents for promoting asymmetric reactions of carbonyl compounds. In general, these compounds will fail to give useful enantiomeric excesses because cooperative binding cannot be achieved, because kinetically significant amounts of activated, achiral adducts of $TiCl_4$ may be produced by redistribution, and because 1:4 adducts with carbonyl ligands bound at two stereochemically dissimilar sites are favored under typical catalytic conditions.



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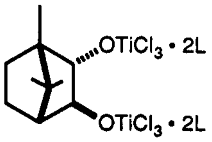

18

Our studies of titanium chloroalkoxides derived from 1,2-cyclopentanediols illustrate the promise and peril of direct attempts to make useful multidentate Lewis acids by attaching electrophilic sites to preexisting organic frameworks. The syntheses of trans bidentate titanium trichloroalkoxides **8** and **17** are attractively simple, but the electrophilic sites are too far apart to cooperate; in contrast, closer juxtaposition makes cooperative effects more likely but incurs the risk of cyclization. We hoped that frameworks derived from *trans*-1,2-cyclohexanediol would provide a suitable compromise. Treatment of the corresponding racemic bis(trimethylsilyl) ether[19a] with 2 equiv of $TiCl_4$, followed by evaporation of solvent and volatile products, provided crude bidentate titanium trichloroalkoxide **19** in nearly quantitative yield. The free Lewis acid could not be purified by sublimation or crystallization, and ^1H NMR spectra of saturated solutions in $CDCl_3$ invariably showed small extraneous signals. The solubility of compound **19** is low, so these signals may simply arise from small amounts of redistribution or accidental hydrolysis in dilute solution. Nevertheless, since

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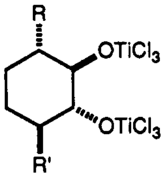
[23] Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295–1298.

[24] Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512–519.



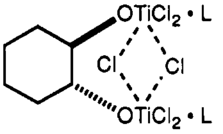
19 (R = R' = H)

20 (R = CH$_3$, R' = H)

21 (R = R' = CH$_3$)

we could not establish the purity of compound **19** and did not want to be misled by spurious signals, we did not study its interaction with ketones directly. After much effort, we obtained glassy yellow crystals of a pinacolone complex when pentane was added to a toluene solution of crude compound **19** containing 3 equiv of pinacolone. Elemental analysis and ^{1}H NMR spectroscopy revealed that the crystalline complex incorporated only 2 equiv of ketone. Since monodentate titanium trichloroalkoxides normally bind two, the OTiCl$_3$ groups of bidentate derivative **19** must be equatorial and must engage in some form of cooperative behavior in the 1:2 pinacolone complex. This dramatic change in stoichiometry is an intrinsic preference of bidentate Lewis acid **19** and related compounds, and it demonstrates that the close juxtaposition of electrophilic sites can have significant chemical consequences.

At −130 °C in 3:1 CHF$_2$Cl/CD$_2$Cl$_2$, the proton-decoupled ^{13}C NMR spectrum of a 0.15 M solution of the crystalline 1:2 pinacolone complex of compound **19** showed a single carbonyl carbon at δ 235.6 and one carbinolic carbon at δ 101.0, in addition to a minor signal at δ 236.5 characteristic of the 1:2 adduct **3** of TiCl$_4$ and pinacolone. At −85 °C in CD$_2$Cl$_2$, the ^{1}H NMR spectrum of a 0.17 M solution revealed a methyl singlet at δ 2.63 (6 H) for two equivalent bound pinacolones, a broad signal at δ 5.33 (2 H) for two equivalent carbinolic hydrogens, and a small peak at δ 2.72 assigned to the 1:2 adduct **3** of TiCl$_4$ and pinacolone. Under these conditions, the extent of redistribution is less than 5%, and the major species in solution is a 1:2 pinacolone adduct of bidentate titanium trichloroalkoxide **19** with an axis of real or effective C_2 symmetry. Possible structures include symmetric adducts **22** and **23** (L = pinacolone) with hexacoordinate titaniums and bridging chlorides or carbonyl oxygens, or symmetric adduct **24** with pentacoordinate titaniums and no bridging groups. In addition, the data are consistent with various unsymmetric adducts, including structure **25**, singly bridged adduct **26**, and related structures with bridging chlorides, if they undergo rapid symmetrization by ketone exchange even at temperatures as low as −130 °C. Our studies of ketone adducts of titanium trichloroisopropoxide (**4**) show that *inter*molecular exchange by the normal mechanism of dissociation and reassociation is slow under these conditions, so the symmetrization of hypothetical adducts **25** and **26** would have to occur by a more rapid *intra*molecular associative process involving intermediates or transition states with bridging carbonyl oxygens. Unfortunately, crystals of the 1:2 pinacolone adduct of compound **19** proved to be disordered and the structure could not be solved, so alternatives **22**–**26** could not be distinguished by X-ray crystallography.



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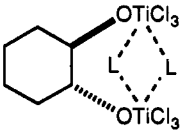

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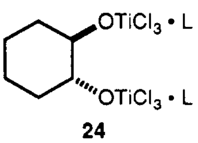

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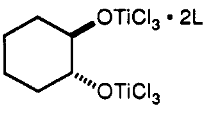

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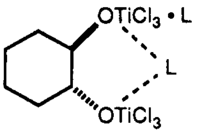
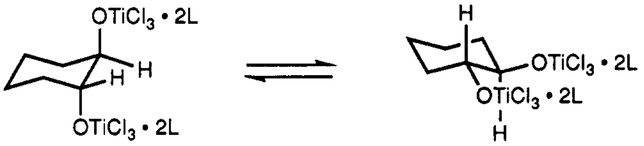


26

At −130 °C in 3:1 CHF$_2$Cl/CD$_2$Cl$_2$, the proton-decoupled ^{13}C NMR spectrum of a 0.17 M solution of the crystalline 1:2 adduct containing an additional 2 equiv of pinacolone showed four carbonyl carbons of similar intensity at δ 233.2, 233.1, 232.1, and 231.2 as well as two carbinolic carbons of similar intensity at δ 100.4 and 95.0. Only traces of pinacolone and its 1:2 complex **3** with TiCl$_4$ could be detected, so complexation is quantitative and redistribution is negligible under these conditions. At −85 °C in CD$_2$Cl$_2$, the ^{1}H NMR spectrum of a similar solution confirmed that 4 equiv of pinacolone were bound. Together, these observations suggest that similar amounts of two 1:4 adducts with axes of real or effective C_2 symmetry are formed when bidentate titanium trichloroalkoxide **19** interacts with 4 equiv of pinacolone in solution. We believe that one product is diaxial adduct **27a** (L = pinacolone), since its carbinolic carbon has an upfield shift characteristic of axial derivatives of cyclohexanol,[25] and we assign diequatorial structure **27b** (L = pinacolone) to the other 1:4 adduct. Formation of diaxial structure **27a** is presumably permitted because it separates the electrophilic sites and easily accommodates the normal complement of four ketones, even when they are as bulky as pinacolone. Although the 1:2 pinacolone adduct of titanium trichloroalkoxide **19** crystallizes preferentially in the presence of excess ketone, it is not the major species in solution under these conditions. This suggests that although the two adjacent OTiCl$_3$ groups can show cooperative effects, they are not powerful enough to prevent each titanium from becoming coordinatively saturated.



27a **27b**

The behavior of bidentate titanium trichloroalkoxide **19** in the presence of 3 equiv of pinacolone proved to be exceedingly complex. At −130 °C in 3:1 CHF$_2$Cl/CD$_2$Cl$_2$, the proton-decoupled ^{13}C NMR spectrum of a 0.17 M solution of the crystalline 1:2 adduct containing an additional 1 equiv of pinacolone showed the five characteristic carbonyl carbons of the 1:2 adduct and both 1:4 adducts, as well as additional signals that presumably correspond to 1:3 adducts. The complexity of this spectrum demonstrates that the particular arrangement of electrophilic sites in bidentate Lewis acid **19** does not favor the exclusive formation of symmetric 1:3 adduct **28** (L = pinacolone) with a bridging carbonyl ligand.

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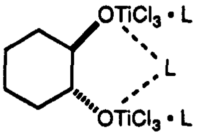
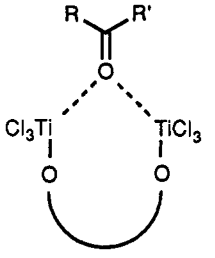
[25] Schneider, H.-J.; Freitag, W.; Weigand, E. *Chem. Ber.* **1978**, *111*, 2656–2664. Ziffer, H.; Seeman, J. I.; Highet, R. J.; Sokoloski, E. A. *J. Org. Chem.* 1974, *39*, 3698–3701.

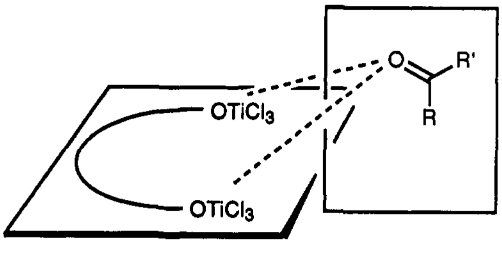


28

Cooperative binding of carbonyl compounds by bidentate titanium trichloroalkoxides can occur in two distinct ways. In structure **29a**, both titaniums lie near the carbonyl plane and interact formally with the two sp^2 lone pairs of the carbonyl oxygen, creating a purely σ-bonded adduct. In alternative **29b**, the planes of the carbonyl compound and the bidentate Lewis acid are nearly perpendicular, and both titaniums interact with a single lone pair. The bonding can then be described as a σ–π hybrid, or as a three-center, two-electron bond formed by the interaction of one sp^2 lone pair with two empty orbitals provided by titanium. Bridging of either type is extremely rare,[26] presumably because carbonyl compounds are only weakly basic and because a suitable juxtaposition of strongly electrophilic sites is hard to achieve. Motif **29b** can accommodate highly unsymmetric ketones such as pinacolone, since both OTiCl$_3$ groups can be placed syn to the smaller substituent R. In contrast, formation of σ-adduct **29a** would be problematic, so our exclusive use of pinacolone to probe the coordination chemistry of bidentate titanium trichloroalkoxide **19** introduces a bias. Unfortunately, we could not readily substitute small, symmetric ketones, since only pinacolone yielded an adduct that could be purified by crystallization and fully characterized.



29a



29b

To avoid the problems of crystalline disorder and conformational mobility encountered in our work with bidentate titanium trichloroalkoxide **19**, we decided to prepare an analogous compound from a substituted derivative of *trans*-1,2-cyclohexanediol. Standard procedures[19a] transformed racemic (1α,2β,3α)-3-methyl-1,2-cyclohexanediol[27] into the corresponding bis(trimethylsilyl) ether, which was then converted into bidentate titanium trichloroalkoxide **20** by the addition of 2 equiv of TiCl$_4$. Like analogue **19**, compound **20** formed a crystalline 1:2 adduct with pinacolone even in the presence of excess ketone. An X-ray crystallographic study, reported earlier,[3c] has shown that the complex has the partially disordered structure shown in Figure 2. The cyclohexane ring has a normal chair conformation with equatorial substituents,[28] and the OTiCl$_3$ groups are held in close proximity. Unfortunately, this juxtaposition promotes the adoption of motif **30** (X = Cl) with doubly bridging chlorides, not the desired motif **31** with doubly bridging carbonyl oxygens.

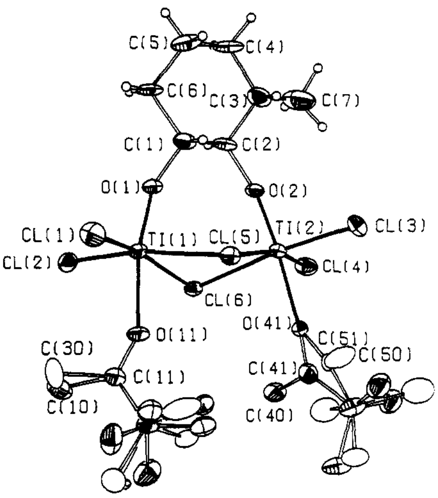
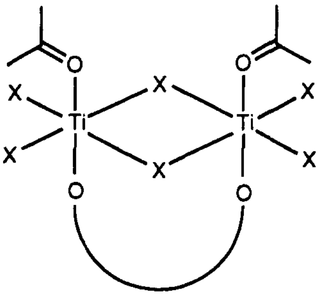


Figure 2. ORTEP drawing of the structure of the 1:2 pinacolone adduct of bidentate titanium trichloroalkoxide **20**.[3c] The ellipsoids correspond to 33% probability, and selected hydrogen atoms are shown as spheres of arbitrary size.



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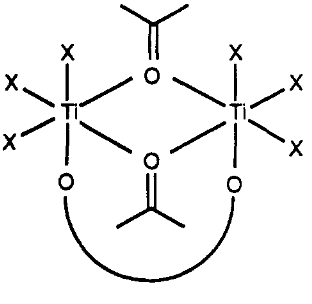

31

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(26) For examples of complexes in which a carbonyl oxygen bridges two metals, see: Beauchamp, A. L.; Olivier, M. J.; Wuest, J. D.; Zacharie, B. *Organometallics* **1987**, *6*, 153–156. Adams, H.; Bailey, N. A.; Gauntlett, J. T.; Winter, M. J. *J. Chem. Soc., Chem. Commun.* **1984**, 1360–1361. Rao, C. P.; Rao, A. M.; Rao, C. N. R. *Inorg. Chem.* **1984**, *23*, 2080–2085. Verbist, J.; Meulemans, R.; Piret, P.; Van Meerssche, M. *Bull. Soc. Chim. Belg.* **1970**, *79*, 391–395. Palm, J. H.; MacGillavry, C. H. *Acta Crystallogr.* **1963**, *16*, 963–968.

(27) Lepoittevin, J.-P.; Benezra, C. *J. Med. Chem.* **1986**, *29*, 287–291. Robinson, P. L.; Evans, S. A., Jr. *J. Org. Chem.* **1985**, *50*, 3860–3863. Klein, J.; Dunkelblum, E. *Tetrahedron* **1968**, *24*, 5701–5710.

(28) The structure of *trans*-1,2-cyclohexanediol has been studied: Jones, P. G.; Edwards, M. R.; Kirby, A. J. *Acta Crystallogr., Sect. C* **1989**, *C45*, 244–246.

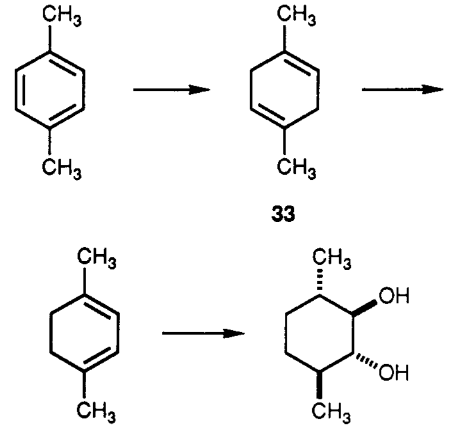
The disordered 1:2 pinacolone complex of analogue **19** presumably has a similar structure with bridging chlorides, so alternatives **23**–**26** (L = pinacolone) can be rejected. Each titanium binds a single pinacolone, creating adjacent octahedral complexes joined by a common edge. Both pinacolones are trans to an alkoxy group and are primarily σ-bonded. The average lengths of terminal Ti—Cl bonds (2.261 (3) Å), bridging Ti—Cl bonds (2.494 (3) Å), alkoxy Ti—O bonds (1.713 (5) Å), and carbonyl Ti$\cdots$O bonds (2.106 (6) Å) are closely similar to those found in related compounds.[3c] Furthermore, strong oxygen-p titanium-d π-bonding helps produce a typically large average alkoxy C—O—Ti angle (158.4 (5)°) and carbonyl C=O$\cdots$Ti angle (150.2 (11)°).[10] In general, the structure resembles those of dimeric, chloride-bridged 1:1 adducts of $TiCl_4$ with esters, except that bidentate acids **19** and **20** force substrates to be bound on the same side of the Ti_2Cl_6 plane.[9a,e,f]

At −85 °C in CD_2Cl_2, the ^1H NMR spectrum of a 0.13 M solution of the 1:2 pinacolone adduct of bidentate titanium trichloroalkoxide **20** showed a multiplet at δ 5.37 (1 H) and a sharp triplet at δ 4.98 (1 H, J = 9.1 Hz) for the carbinolic hydrogens at C_1 and C_2 (see Figure 2 for numbering). In addition, distinct singlets appeared at δ 2.63 (3 H) and 2.62 (3 H) for the methyl groups of two nonequivalent bound pinacolones, and an extremely small signal due to the 1:2 pinacolone complex **3** of $TiCl_4$ could be detected at δ 2.72. Under these conditions, redistribution occurs to an extent of less than 5%, but it is significant at 0.013 M. At −85 °C in CD_2Cl_2, the proton-decoupled ^{13}C NMR spectrum of a 0.099 M solution contained singlets at δ 99.5 and 105.1 for the carbinolic carbons at C_1 and C_2, as well as two carbonyl carbon signals at δ 233.6 and 233.4. Together, these data demonstrate that a single major 1:2 adduct is present in solution, that the two pinacolones are bound in similar but distinct environments, and that each $OTiCl_3$ group is equatorial and binds a single pinacolone. We conclude that the structures in solution and in the solid state are closely similar.

Methyl-substituted bidentate titanium trichloroalkoxide **20** proved to be less willing than unsubstituted analogue **19** to bind a full 4 equiv of pinacolone. At low temperatures in CD_2Cl_2, ^1H and proton-decoupled ^{13}C NMR spectra of solutions of the crystalline 1:2 pinacolone adduct containing an additional 2 equiv of pinacolone were highly complex and showed major signals attributable to free ketone. Spectra of mixtures containing a total of 3 equiv of pinacolone were similar, but no signals derived from free ketone could be detected. Since even the diequatorial conformer of compound **19** can bind 4 equiv of pinacolone, failure of analogue **20** to accept a full complement cannot simply be due to its strong preference for an all-equatorial conformation. Instead, the equatorial methyl must exert a specific steric effect on the nearby $OTiCl_3$ group at C_2 that allows formation of 1:3 pinacolone adducts but disfavors 1:4 adducts.

A well-designed bidentate titanium trichloroalkoxide must be able to bind carbonyl ligands cooperatively. In addition, it should resist the intrinsic preference for 1:4 adducts, which will be less strongly activated and will incorporate ligands bound in stereochemically diverse environments. The special effect of the methyl group in compound **20** was therefore intriguing, because it showed that the normal preference for 1:4 adducts could be successfully resisted even under typical catalytic conditions of excess ligand. We reasoned that addition of an equatorial methyl at C_6 would impose further restrictions and would create symmetry that would simplify the interpretation of NMR spectra, so we prepared bidentate titanium trichloroalkoxide **21**. This compound could be made by adding 2 equiv of $TiCl_4$ to the bis(trimethylsilyl) ether of racemic ($1\alpha,2\beta,3\alpha,6\beta$)-3,6-dimethyl-1,2-cyclohexanediol (**32**). After exploring various routes to diol **32**, including equilibration[29] of the stereoisomeric mixture of diols formed by hydroboration/oxidation of 3,6-dimethyl-2-cyclohexenone,[30] we chose the sequence of reactions summarized in Scheme I. Birch reduction of *p*-xylene, followed by isomerization of nonconjugated diene **33**, yielded a mixture of dienes enriched in conjugated isomer **34**.[31] Hydroboration/oxidation then provided compound **32** as the major component of a mixture of diols. Partial purification was achieved by chromatography, and remaining amounts of stereoisomeric *cis*-1,2-diols were selectively removed by acetalization with benzaldehyde. Further chromatography then provided pure diol **32** in 11% overall yield from *p*-xylene.

Scheme I



33

34 **32**

Like less substituted analogues **19** and **20**, bidentate titanium trichloroalkoxide **21** formed crystalline 1:2 ketone adducts, even in the presence of excess ketone. At −130 °C in 3:1 CHF_2Cl/CD_2Cl_2, the proton-decoupled ^{13}C NMR spectrum of a 0.14 M solution of the 1:2 pinacolone adduct showed a single carbonyl carbon at δ 235.6 and one carbinolic carbon at δ 106.2, in addition to a very minor signal at δ 236.5 characteristic of the 1:2 adduct **3** of $TiCl_4$ and pinacolone (Figure 3a). We conclude that a single, symmetric, chloride-bridged 1:2 adduct analogous to structure **22** (L = ketone) is favored in solution.

At −130 °C in 3:1 CHF_2Cl/CD_2Cl_2, the proton-decoupled ^{13}C NMR spectrum of a 0.14 M solution of the crystalline 1:2 pinacolone adduct containing an additional 1 equiv of pinacolone showed three carbonyl carbons at δ 234.7, 233.8, and 232.6 and two carbinolic carbons at δ 106.3 and 104.7 (Figure 3b). A similar spectrum of a mixture of the crystalline 1:2 diisopropyl ketone adduct and an additional 1 equiv of diisopropyl ketone showed corresponding signals at δ 240.6, 239.6, 237.6, 106.7, and 104.7. In neither case was free ketone present, and only traces of the 1:2 ketone complexes **3** with $TiCl_4$ could be detected. These data demonstrate that complexation is essentially quantitative, that redistribution is minor, and that single, unsymmetric 1:3 ketone adducts are favored in solution. Significant amounts of symmetric 1:3 complexes with a single bridging

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(29) Feghouli, G.; Vanderesse, R.; Fort, Y.; Caubere, P. *Tetrahedron Lett.* **1988**, *29*, 1383–1384. Slemon, C. E.; Yates, P. *Can. J. Chem.* **1979**, *57*, 304–313. McMurry, J. E.; Choy, W. *J. Org. Chem.* **1978**, *43*, 1800–1803. Eliel, E. L.; Ro, R. S. *J. Am. Chem. Soc.* **1957**, *79*, 5992–5994.

(30) Dreux, J. *Bull. Soc. Chim. Fr.* **1954**, 1443–1446.

(31) Brady, W. T.; Norton, S. J.; Ko, J. *Synthesis* **1985**, 704–705.

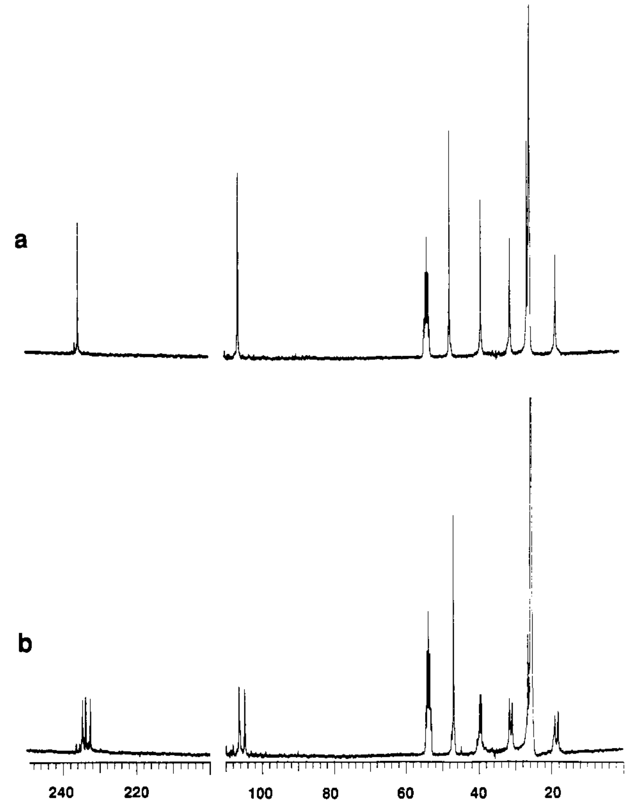
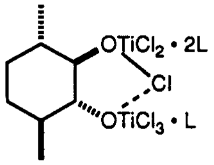


Figure 3. (a) Proton-decoupled ^{13}C NMR spectrum of a 0.14 M solution of the 1:2 pinacolone adduct of bidentate titanium trichloroalkoxide **21** in 3:1 CHF_2Cl/CD_2Cl_2 at −130 °C. (b) Spectrum of a similar solution containing an additional 1 equiv of pinacolone.

carbonyl oxygen are not present, even when the ketone is symmetric. None of the carbonyl carbons in the 1:3 adducts is abnormally deshielded, so none of the three ketones is bound cooperatively. Instead, we propose that the 1:3 adducts have structure **35** (L = ketone), in which one OTiCl$_3$ group binds two nonequivalent ketones and the other binds a single ketone. In addition, a single bridging chloride donated by the 1:2 site allows the other titanium to achieve octahedral coordination. Formation of adduct **35** presumably occurs by replacement of a bridging chloride in precursor **30** (X = Cl) with a ketone, giving motif **36** (X = Cl) or a closely related isomer. This structure is reasonable, since it maximizes π-bonding by placing the terminal chlorides and alkoxy groups trans to the more weakly π-donating ketones and bridging chloride.[17]



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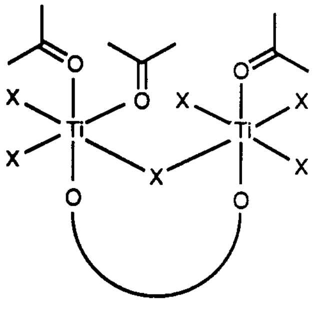

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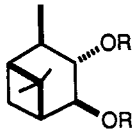
Disubstituted bidentate titanium trichloroalkoxide **21** could not be induced to bind more than 3 equiv of diisopropyl ketone. At −130 °C in 3:1 CHF_2Cl/CD_2Cl_2, the proton-decoupled ^{13}C NMR spectrum of a mixture containing a total of 4 equiv of ketone showed signals at δ 240.6, 239.6, 237.6, 106.7, and 104.7 characteristic of the 1:3 adduct, as well as signals corresponding to free diisopropyl ketone. No new signals corresponding to a symmetric 1:4 adduct could be detected. These observations establish that the buttressing effect of methyl substituents at C_3 and C_6, the rigid all-equatorial geometry, and the bulk of diisopropyl ketone restrict the ability of bidentate titanium trichloroalkoxide **21** to accept the normal complement of four ketones.

Although our detailed examination of the coordination chemistry of potentially bidentate titanium trichloroalkoxides **19–21** provided no evidence for complexes with cooperatively bound ketones, we nevertheless hoped that small amounts of these elusive, activated adducts were present and could play a kinetically important role in asymmetric additions. We therefore converted enantiomerically pure (1*R*)-*trans*-1,2-cyclohexanediol and pinanediol **37a**[32] into the corresponding bidentate titanium trichloroalkoxides **19** and **37b** by the normal procedure. Stoichiometric amounts of these compounds promoted the addition of allyltrimethylsilane to hydrocinnamaldehyde, but in both cases the resulting alcohol was racemic. Bidentate titanium trichloroalkoxides derived from *trans*-1,2-cyclohexanediols place two strongly electrophilic sites in close proximity, but we are forced to conclude that they cannot form kinetically significant amounts of adducts containing ketones that are cooperatively bound, doubly activated, and rigidly oriented.



37a (R = H)

37b (R = TiCl$_3$)

Moreover, adducts with bridging carbonyl oxygens are also disfavored as intermediates or transition states for ketone exchange. In a crucial experiment, we studied the symmetrization of unsymmetric 1:3 complex **35** (L = pinacolone) by recording variable-temperature proton-decoupled ^{13}C NMR spectra of a 0.13 M solution in 3:1 CHF_2Cl/CD_2Cl_2. Coalescence of the characteristic carbinolic carbons at δ 106.3 and 104.7 occurred at −50 °C, so $\Delta G^{\ddagger}_{223}$ is approximately 10.4 ± 0.2 kcal/mol.[6] An identical value was measured in pure CD_2Cl_2. This is slightly greater than the free energy of activation for dissociation of pinacolone from its 1:2 complex with $TiCl_4$ (9.7 kcal/mol) and from its 1:2 complex with titanium trichloroisopropoxide (9.2 kcal/mol). We conclude that symmetrization of 1:3 adduct **35** occurs by a normal dissociative mechanism and that intermediates or transition states **38** (X = Cl) with a bridging carbonyl oxygen do not provide a low-energy intramolecular pathway for ketone exchange.

*Although the electrophilic sites of bidentate titanium trichloroalkoxide **21** fail to interact simultaneously with a single carbonyl oxygen, they nevertheless show rigorously cooperative behavior.* Dissociation of pinacolone from the 1:2 site in 1:3 complex **35** (L = pinacolone) requires approximately 1.2 kcal/mol more energy than closely analogous dissociations from 1:2 complexes of comparable monodentate Lewis acids. We propose that the bidentate acid binds ketones more strongly because

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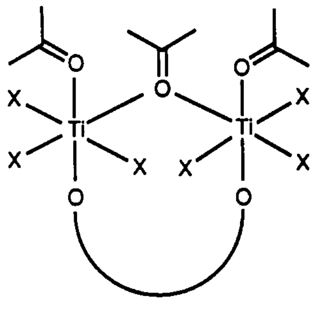
[32] Chrétien-Bessière, Y. *Bull. Soc. Chim. Fr.* **1964**, 2182–2185.



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the special juxtaposition of electrophilic sites favors the formation of a complex with a single chloride bridge, thereby enhancing the Lewis acidity of one titanium at the expense of the other.

Our work with titanium trichloroalkoxides has general significance because it establishes that strong, potentially bidentate Lewis acids can be made easily from simple precursors, and that clever juxtaposition of electrophilic sites can have striking chemical consequences, including modification of the normal kinetics and stoichiometry of complexation. We are optimistic that what we have learned about the synthesis and coordination chemistry of bidentate titanium trichloroalkoxides can be used to devise reagents able to achieve the double activation of carbonyl compounds and promote asymmetric additions. If so, organic synthesis will have a powerful new tool.

Experimental Section

Infrared (IR) spectra were recorded on a Perkin-Elmer Model 783 spectrometer. A Varian VXR-300 spectrometer was used to obtain ^{1}H nuclear magnetic resonance (NMR) spectra at 300 MHz and proton-decoupled ^{13}C NMR spectra at 75.4 MHz. In addition, a Bruker WH-400 instrument was used to record ^{1}H NMR spectra at low temperatures. ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million downfield from internal tetramethylsilane (δ). High-resolution mass spectra were recorded on a Kratos MS-50 TATC instrument using electron impact (EI) mass spectrometry. Melting points were recorded on a Thomas-Hoover capillary apparatus. Galbraith Laboratories, Knoxville, TN, performed all elemental analyses.

CH_2Cl_2 and CD_2Cl_2 were dried by distillation from CaH_2, $CDCl_3$ was dried by distillation from P_2O_5, CHF_2Cl was dried by passage over 3-Å molecular sieves and then over P_2O_5, pentane and toluene were dried over Na and distilled, tetrahydrofuran (THF) was dried by distillation from the sodium ketyl of benzophenone, acetone was dried over 3-Å molecular sieves and then distilled, and pinacolone, diisopropyl ketone, and 2-propanol were dried over $MgSO_4$ and 3-Å molecular sieves and were then distilled. $TiCl_4$ was purified by distillation. All other reagents were commercial products of the highest purity available.

Titanium Trichloroisopropoxide (4). At 25 °C under dry Ar, a stirred solution of $TiCl_4$ (17.3 g, 91.2 mmol) in CH_2Cl_2 (200 mL) was treated dropwise during 15 min with a solution of 2-propanol (4.7 g, 78.2 mmol) in CH_2Cl_2 (150 mL). The resulting mixture was stirred for 5 min, and volatiles were then removed by evaporation in vacuo. Sublimation of the solid residue (90 °C/0.5 Torr) provided yellow needles of titanium trichloroisopropoxide (12.6 g, 59.1 mmol, 76%): mp 85.0–86.5 °C (lit.[12a] 78–79 °C); IR (Nujol mull, CsI) 1400, 1100, 1020, 470, 410, 330 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 1.60 (d, 6 H, J = 6.2 Hz), 5.17 (septet, 1 H, J = 6.2 Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) δ 24.7, 96.2.

Reaction of the Bis(trimethylsilyl) Ether of *cis*-1,2-Cyclopentanediol with $TiCl_4$. At -78 °C under dry Ar, a stirred solution of the bis(trimethylsilyl) ether[19a] of *cis*-1,2-cyclopentanediol (452 mg, 1.83 mmol) in CH_2Cl_2 (5 mL) was treated dropwise with $TiCl_4$ (360 mg, 1.9 mmol). The mixture was stirred at -78 °C for 30 min, brought to 25 °C, and stirred for an additional 30 min. Removal of volatiles by evaporation in vacuo left an analytically pure sample of putative titanium chloroalkoxide **9** as a beige solid (393 mg, 1.80 mmol, 98%): mp 190–197 °C dec; IR (Nujol mull, CsI) 1100, 1050, 1020, 980, 810, 680, 600, 480, 430, 410, 340, 260 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.3–1.9 (m, 6 H), 5.65 (b s, 2 H). Anal. Calcd for $C_{10}H_{16}Cl_4O_4Ti_2$: C, 27.43; H, 3.68. Found: C, 27.41; H, 3.88.

Reaction of Racemic 2-*exo*,3-*exo*-Camphanediol (12) with $TiCl_4$. At 0 °C under dry Ar, a stirred solution of racemic 2-*exo*,3-*exo*-camphanediol (**12**; 205 mg, 1.20 mmol)[21] in CH_2Cl_2 (5 mL) was treated dropwise with $TiCl_4$ (260 mg, 1.4 mmol). The mixture was brought to 25 °C and stirred for 30 min. Removal of volatiles by evaporation in vacuo left a nearly pure residue of a racemic mixture of titanium chloroalkoxide dimers **13** and **14** as a yellow solid (371 mg, 1.29 mmol, 100%): mp 183–187 °C dec; IR (Nujol mull, CsI) 1080, 1040, 1020, 1010, 990, 960, 860, 840, 800, 780, 730, 690, 650, 620, 585, 550, 530, 500, 450, 400, 380 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (s, 6 H), 0.93 (s, 3 H), 0.95 (m, 4 H), 0.96 (s, 3 H), 1.19 (s, 3 H), 1.27 (s, 3 H), 1.50 (m, 2 H), 1.82 (m, 2 H), 2.82 (d, 2 H, J = 5.1 Hz), 5.18 (d, 2 H, J = 6.4 Hz), 5.79 (d, 1 H, J = 6.4 Hz), 5.91 (d, 1 H, J = 6.4 Hz). Anal. Calcd for $C_{20}H_{32}Cl_4O_4Ti_2$: C, 41.84; H, 5.62. Found: C, 41.10; H, 5.57.

Reaction of *trans*-1,2-Cyclopentanediol with $TiCl_4$. At 0 °C under dry Ar, a stirred solution of $TiCl_4$ (1.7 g, 9.0 mmol) in CH_2Cl_2 (13 mL) was treated dropwise with a solution of *trans*-1,2-cyclopentanediol (0.45 g, 4.4 mmol) in CH_2Cl_2 (15 mL). The mixture was stirred for 15 min, brought to 25 °C, and stirred for 45 min. Removal of volatiles by evaporation in vacuo left an analytically pure residue of bidentate titanium trichloroalkoxide **8** as a beige solid (1.8 g, 4.4 mmol, 100%): mp 133–137 °C dec; IR (Nujol mull, CsI) 1080, 1030, 1015, 430, 390, 330 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11 (quintet, 2 H, J = 7.9 Hz), 2.36 (m, 2 H), 2.45 (m, 2 H), 5.6 (m, 2 H). Anal. Calcd for $C_5H_8Cl_6O_2Ti_2$: C, 14.70; H, 1.97. Found: C, 14.75; H, 2.15.

1:2 Pinacolone Complex of Bidentate Titanium Trichloroalkoxide 19. At -78 °C under dry Ar, $TiCl_4$ (1.3 g, 6.8 mmol) was added dropwise to a stirred solution of the bis(trimethylsilyl) ether[19a] of *trans*-1,2-cyclohexanediol (0.867 g, 3.33 mmol) in toluene (14 mL). The mixture was brought to 25 °C, stirred for 30 min, and treated with pinacolone (1.0 g, 10 mmol). A layer of pentane (20 mL) was carefully added, and the two phases were allowed to diffuse at 25 °C. This procedure yielded yellow crystals of a toluene solvate (0.5 equiv) of the 1:2 pinacolone complex of bidentate titanium trichloroalkoxide **19** (1.82 g, 2.72 mmol, 82%): mp 85–97 °C dec; IR (Nujol mull, CsI) 1650, 1080, 1050, 725, 715, 410, 350 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 1.28 (s, 18 H), 1.32 (m, 2 H), 1.78 (m, 4 H), 2.36 (s, toluene), 2.46 (m, 2 H), 2.67 (s, 6 H), 5.38 (m, 2 H), 7.2 (m, toluene); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) 21.2, 22.9, 25.5, 26.1, 31.2, 46.6, 99.9, 125.1, 128.0, 128.8, 137.6, 231.4. Anal. Calcd for $C_{18}H_{34}Cl_6O_4Ti_2\cdot0.5C_7H_8$: C, 38.60; H, 5.73. Found: C, 37.91; H, 5.95.

Bis(trimethylsilyl) Ether of (1α,2β,3α)-3-Methyl-1,2-cyclohexanediol. This compound was prepared from (1α,2β,3α)-3-methyl-1,2-cyclohexanediol[27] in 88% yield by the procedure of Lasocki:[19a] IR (liquid film) 2950, 2870, 1460, 1250, 1170, 1110, 1060, 1040, 990, 970, 920, 900, 880, 840, 760, 740, 680 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.13 (s, 9 H), 0.14 (s, 9 H), 0.95 (d, 3 H, J = 6.5 Hz), 0.99 (m, 1 H), 1.26 (m, 2 H), 1.35 (m, 1 H), 1.60 (m, 2 H), 1.87 (m, 1 H), 2.98 (dd, 1 H, J = 8.4 Hz, J = 9.7 Hz), 3.36 (m, 1 H). HRMS (EI): calcd for $C_{13}H_{30}O_2Si_2$, 274.1784; found, 274.1757.

1:2 Pinacolone Complex of Bidentate Titanium Trichloroalkoxide 20. A procedure similar to the one used to prepare the 1:2 pinacolone complex of compound **19** converted the bis(trimethylsilyl) ether of (1α,2β,3α)-3-methyl-1,2-cyclohexanediol (0.760 g, 2.77 mmol), $TiCl_4$ (1.1 g, 5.8 mmol), and pinacolone (0.99 g, 9.9 mmol) into yellow crystals of a toluene solvate (0.5 equiv) of the 1:2 pinacolone complex of bidentate titanium trichloroalkoxide **20** (1.54 g, 2.25 mmol, 81%): mp 95–115 °C dec; IR (Nujol mull, CsI) 1655, 1140, 1085, 1045, 1030, 730, 395, 350 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 1.11 (m, 1 H), 1.29 (s, 18 H), 1.30 (m, 1 H), 1.41 (d, 3 H, J = 6.4 Hz), 1.74 (m, 3 H), 2.00 (m, 1 H), 2.36 (s, toluene), 2.46 (m, 1 H), 2.65 (s, 6 H), 4.99 (t, 1 H, J = 10 Hz), 5.45 (m, 1 H), 7.2 (m, toluene); ^{13}C NMR (75.4 MHz, CD_2Cl_2, 0 °C) δ 18.5, 21.6, 22.6, 26.1, 26.3, 31.7, 32.4, 39.0, 47.1, 100.3, 106.1, 125.4, 128.4, 129.2, 138.2, 232.6. Anal.

Calcd for $C_{19}H_{36}Cl_6O_4Ti_2{\cdot}0.5C_7H_8$: C, 39.56; H, 5.91. Found: C, 39.43; H, 6.03.

(1α,2β,3α,6β)-3,6-Dimethyl-1,2-cyclohexanediol (32). At −78 °C under dry Ar, a stirred solution of a mixture containing 53% dimethylcyclohexadiene **34** (2.41 g, 22.3 mmol)[31] in THF (5 mL) was treated dropwise during 15 min with $BH_3{\cdot}THF$ (60 mL, 1.0 M, 60 mmol). The mixture was stirred at −78 °C for 4 h and at 25 °C for 19 h and was then cooled to 0 °C and kept below 30 °C while 10% NaOH (10 mL) and 30% H_2O_2 (10 mL) were added. The resulting mixture was stirred at 25 °C for 3 h, cooled to 0 °C, and treated with H_2O (30 mL) and $Na_2S_2O_3{\cdot}5H_2O$ (20 g). Additional water was added, and the mixture was extracted thoroughly with ether. The combined extracts were dried ($MgSO_4$), and solvent was removed by evaporation under reduced pressure. Purification of the residue by flash chromatography (silica, hexane (50%)/ethyl acetate (50%))[33] yielded a crude sample of diol **32**. A solution of this material in benzene (15 mL) was treated with benzaldehyde (0.101 g, 0.952 mmol) and camphorsulfonic acid (9 mg) and heated at reflux for 2 h in an apparatus fitted with a Dean-Stark trap. The solution was then partitioned between saturated aqueous $NaHCO_3$ and ether, and the aqueous layer was extracted thoroughly with additional ether. The combined extracts were dried ($MgSO_4$), and solvent was removed by evaporation under reduced pressure. Flash chromatography of the residue (silica, hexane (50%)/ethyl acetate (50%))[33] provided (1α,2β,3α,6β)-3,6-dimethyl-1,2-cyclohexanediol (**32**) as a colorless solid (0.678 g, 4.70 mmol, 21%). Crystallization from hexane yielded an analytically pure sample: mp 91.0–92.5 °C; IR (melt) 3300, 2900, 1450, 1380, 1370, 1290, 1100, 1060, 1020, 980, 860 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (d, 6 H, J = 6.4 Hz), 1.06 (m, 2 H), 1.42 (m, 2 H), 1.61 (m, 2 H), 2.83 (s, 2 H), 2.96 (m, 2 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 18.3, 32.3, 37.6, 80.5. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.93; H, 11.42.

Bis(trimethylsilyl) Ether of (1α,2β,3α,6β)-3,6-Dimethyl-1,2-cyclohexanediol. This compound was prepared from the diol in 84% yield by the procedure of Lasocki:[19a] IR (liquid film) 2900, 1460, 1300, 1260, 1250, 1160, 1110, 1060, 1040, 1000, 910, 880, 860, 840 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.17 (s, 18 H), 0.95 (d, 6 H, J = 6.6 Hz), 1.06 (m, 2 H), 1.42 (m, 2 H), 1.59 (m, 2 H), 3.03 (m, 2 H). HRMS (EI): calcd for $C_{14}H_{32}O_2Si_2$, 288.1941; found, 288.1911.

1:2 Pinacolone Complex of Bidentate Titanium Trichloroalkoxide 21. A procedure similar to the one used to prepare the 1:2 pinacolone complex of compound **19** converted the bis(trimethylsilyl) ether of (1α,2β,3α,6β)-3,6-dimethyl-1,2-cyclohexanediol (711 mg, 2.46 mmol), $TiCl_4$ (930 mg, 4.9 mmol), and pinacolone (750 mg, 7.5 mmol) into yellow crystals of the 1:2 pinacolone complex of bidentate titanium trichloroalkoxide **21** (991 mg, 1.52 mmol, 62%): mp 150–160 °C dec; IR (Nujol mull, CsI) 1650, 1150, 1090, 1040, 730, 400, 360 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 1.13 (m, 2 H), 1.28 (s, 18 H), 1.41 (d, 6 H, J = 6.5 Hz), 1.71 (m, 2 H), 2.00 (m, 2 H), 2.65 (s, 6 H), 5.07 (m, 2 H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) δ 18.3, 25.5, 26.1, 31.4, 38.6, 46.6, 105.3, 231.4. Anal. Calcd for $C_{20}H_{38}Cl_6O_4Ti_2$: C, 36.90; H, 5.88; Cl, 32.68. Found: C, 37.77; H, 6.02; Cl, 32.89.

1:2 Diisopropyl Ketone Complex of Bidentate Titanium Trichloroalkoxide 21. A similar procedure converted the bis(trimethylsilyl) ether of diol **32** (238 mg, 0.825 mmol), $TiCl_4$ (310 mg, 1.6 mmol), and diisopropyl ketone (282 mg, 2.47 mmol) into yellow crystals of a toluene solvate (0.5 equiv) of the 1:2 diisopropyl ketone complex of bidentate titanium trichloroalkoxide **21** (498 mg, 0.687 mmol, 83%): mp 80–110 °C dec; IR (Nujol mull, CsI) 1665, 1090, 1040, 985, 730, 400, 350 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 1.17 (m, 2 H), 1.26 (d, 24 H, J = 6.9 Hz), 1.41 (d, 6 H, J = 6.4 Hz), 1.72 (m, 2 H), 2.01 (m, 2 H), 2.36 (s, toluene), 3.25 (septet, 4 H, J = 6.9 Hz), 5.06 (m, 2 H), 7.2 (m, toluene); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) δ 18.4, 18.7, 21.2, 31.6, 38.8, 39.5, 105.7, 125.1, 128.0, 128.8, 137.6, 234.1. In addition, minor peaks assigned to the products of redistribution could be seen in the ^{1}H and ^{13}C NMR spectra. Anal. Calcd for $C_{22}H_{42}Cl_6O_4Ti_2{\cdot}0.5C_7H_8$: C, 42.24; H, 6.39; Cl, 29.34. Found: C, 42.05; H, 6.67; Cl, 28.69.

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[33] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.