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Thermodynamic and Kinetic Effects of the Double Coordination of Carbonyl Groups by Bidentate Lewis Acids

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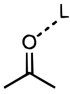
Abstract: Treatment of 1,2,3,4-tetrahexylbenzene or 1,2,4,5-tetrahexylbenzene with $Hg(OOCCF_3)_2$ produces 1,2-phenylenedimercury bis(trifluoroacetate) **7** or its 1,4-isomer **9**, which are bidentate Lewis acids. IR studies in CH_2Cl_2 established that 1,2-isomer **7** forms doubly coordinated 1:1 complexes with amides in which both atoms of mercury interact simultaneously with the carbonyl oxygen atom of the bound amide, whereas 1,4-isomer **9** forms more weakly bound singly coordinated complexes. Variable-temperature IR studies revealed that for the double coordination of diethylformamide (DEF) by 1,2-isomer **7**, $\Delta H° = -4.5 \pm 0.2$ kcal mol^{-1} and $\Delta S° = -6.9 \pm 1.0$ eu, whereas for the single coordination of DEF by 1,4-isomer **9**, $\Delta H° = -3.4 \pm 0.2$ kcal mol^{-1} and $\Delta S° = -8.1 \pm 1.0$ eu. These measurements establish that double coordination is significantly more exothermic than single coordination. In addition, variable-temperature NMR studies showed that $\Delta G^‡$ for rotation around the N−C(O) bond of dimethylpivalamide (normally 12.2 ± 0.1 kcal mol^{-1} in $CDCl_3$) is increased more by the addition of an equimolar amount of 1,2-isomer **7** (12.9 ± 0.1 kcal mol^{-1}) than by the addition of an equimolar amount of 1,4-isomer **9** (12.3 ± 0.1 kcal mol^{-1}). This demonstrates that the double coordination of carbonyl compounds by bidentate Lewis acids can have measurable effects on the rates of subsequent chemical transformations.

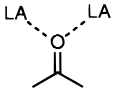
Introduction

Lewis acids are useful because they can bind complementary basic molecules and thereby modify their reactivity. An example of particular practical importance is the activation of carbonyl compounds by the formation of complexes **1** with Lewis acids.[2]



1

LA = Lewis acid



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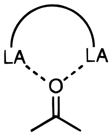

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By reducing the electron density on the carbonyl carbon, further polarizing the carbon−oxygen double bond, and lowering the energy of the lowest unoccupied molecular orbital, the complexation of carbonyl compounds by Lewis acids can have dramatic kinetic effects. For example, the Diels−Alder reaction of methyl acrylate with butadiene at 20 °C in benzene is 10^5 times faster in the presence of an equimolar amount of $AlCl_3$.[3,4] Furthermore, Lewis acids can also have beneficial effects on regioselectivity and stereoselectivity.[5] For all of these reasons, Lewis acids play a major role as catalysts and stoichiometric reagents in contemporary organic synthesis.

The precise geometries of adducts **1** vary, depending on the Lewis acid and the substrate. In general, neutral main-group Lewis acids favor $\eta^1(\sigma)$ complexes in which the Lewis acid lies close to the carbonyl plane along the direction of one of the formal sp^2 lone pairs on oxygen.[2,6] In contrast, Lewis acids incorporating late transition metals tend to prefer $\eta^2(\pi)$ complexes in which the metal lies above the carbonyl plane and interacts simultaneously with both the carbon atom and the oxygen atom of the carbonyl group.[2] In principle, either mode of complexation leaves one or more sp^2 lone pairs free and available for binding a second Lewis acid, which would produce doubly coordinated termolecular complexes **2**. Such adducts are potentially valuable in synthesis because they promise to be even more highly activated than their singly coordinated analogues **1**.

Unfortunately, doubly coordinated termolecular complexes **2** are presently unknown.[7,8] However, we have shown in previous work that closely related doubly coordinated bimolecular complexes **3** can be formed when two sites of Lewis acidity are joined to create single bidentate reagents.[9,10] Furthermore, recent reports suggest that the double coordination

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[1] Fellow of the Natural Sciences and Engineering Council of Canada, 1988−1992.

[2] Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 256. Hay, R. W. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: New York, 1987; Vol. 6, Chapter 61.4.

[3] Inukai, T.; Kojima, T. *J. Org. Chem.* **1966**, *32*, 872.

[4] For related work, see: Angus, P. M.; Fairlie, D. P.; Jackson, W. G. *Inorg. Chem.* **1993**, *32*, 450.

[5] For example, see: Narasaka, K. *Synthesis* **1991**, 1.

[6] Wiberg, K. B.; Marquez, M.; Castejon, H. *J. Org. Chem.* **1994**, *59*, 681.

[7] Related complexes are known in which carbonyl compounds are doubly protonated or doubly hydrogen bonded. For references, see: Saied, O.; Simard, M.; Wuest, J. D. *J. Org. Chem.* **1998**, *63*, 3756.

[8] Doubly coordinated termolecular complexes **2** have been postulated as activated intermediates or transition states in additions of organometallic reagents to carbonyl compounds. For example, see: Evans, D. A. *Science* **1988**, *240*, 420.

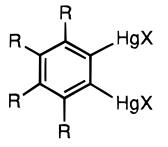
10.1021/ja982725x CCC: $15.00

of carbonyl compounds by bidentate Lewis acids increases their reactivity,[11,12] although in none of the reported cases have the structures of the intermediate complexes and the origin of the activation been determined unambiguously.

This earlier work establishes that the double coordination of carbonyl groups by Lewis acids is possible and may have useful consequences. Nevertheless, many fundamental questions about double coordination remain unanswered. In particular, no detailed thermodynamic comparison of single and double coordination has been made, and no values of $\Delta H°$ and $\Delta S°$ for double coordination are available. Furthermore, in no chemically well-defined case has double coordination been shown to have special effects on the rates of subsequent chemical transformations. We now provide this important information by describing the thermodynamic and kinetic effects of the double coordination of the carbonyl group of amides by bidentate Lewis acids derived from 1,2-phenylenedimercury.

Results and Discussion

Syntheses of 3,4,5,6-Tetrahexyl-1,2-phenylenedimercury Bis(trifluoroacetate) (7), 2,3,5,6-Tetrahexyl-1,4-phenylenedimercury Bis(trifluoroacetate) (9), and Related Compounds. Various derivatives of 1,2-phenylenedimercury, including 1,2-phenylenedimercury dichloride (**4**) and 3,4,5,6-tetramethyl-1,2-phenylenedimercury bis(trifluoroacetate) (**5**), are known to hold two Lewis acidic atoms of mercury in an orientation that favors the double coordination of carbonyl compounds and other simple Lewis bases.[9] In particular, cocrystallization of bidentate Lewis acids **4** and **5** with various *N*,*N*-dialkylformamides gives doubly coordinated complexes that can be represented by structure **6**. In these complexes, the two sites of Lewis acidity do not both lie in the carbonyl plane but instead occupy widely varying positions with respect to the plane, suggesting that carbonyl oxygen atoms do not have very strong steric or electronic preferences for dative bonding to mercury along specific directions. This observation is consistent with the expectation that the association of carbonyl compounds with Lewis acidic organomercury compounds is inherently weak.[13]

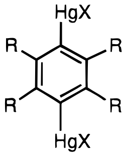


4 (R = H, X = Cl)

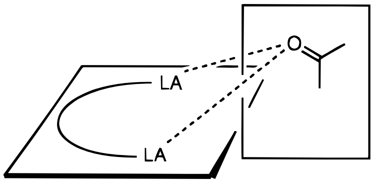
5 (R = CH_3, X = $OOCCF_3$)

7 (R = hexyl, X = $OOCCF_3$)

16 (R = tetradecyl, X = $OOCCF_3$)



9 (R = hexyl, X = $OOCCF_3$)



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For this reason, the double coordination of carbonyl compounds by bidentate Lewis acids derived from 1,2-phenylenedimercury is unlikely to find important applications in organic synthesis. However, these reagents offer practical advantages that compensate for their weak Lewis acidity and make them attractive for thermodynamic and kinetic studies of double coordination. In particular, (1) effective methods exist for their synthesis;[9] (2) unlike many other organometallic reagents, they do not react with the carbonyl groups of potential substrates by nucleophilic addition; (3) in general, they are not highly sensitive to H_2O or O_2; and (4) the structures of their complexes with *N*,*N*-dialkylformamides and other basic organic molecules are well-established, at least in the solid state, and reveal a consistent preference for double coordination. As a result, we decided to use bidentate Lewis acids derived from 1,2-phenylenedimercury in the first quantitative thermodynamic and kinetic comparison of the single and double coordination of carbonyl compounds. In making this choice, we were conscious of the specialized nature and limited practical value of reagents derived from 1,2-phenylenedimercury; however, we were optimistic that our comparisons would be feasible and would provide fundamental information of general significance.

Unfortunately, the solubilities of 1,2-phenylenedimercury dichloride (**4**) and 3,4,5,6-tetramethyl-1,2-phenylenedimercury bis(trifluoroacetate) (**5**) in common noncoordinating organic solvents are too low to allow convenient study of double coordination in solution. To make more soluble derivatives, we prepared 3,4,5,6-tetrahexyl-1,2-phenylenedimercury bis(trifluoroacetate) (**7**) in 81% yield by treating 1,2,3,4-tetrahexylbenzene (**8**) with $Hg(OOCCF_3)_2$. Its 1,4-phenylenedimercury isomer **9**, a closely related bidentate Lewis acid that cannot form a doubly coordinated complex **6**, was made similarly from 1,2,4,5-tetrahexylbenzene (**10**) in 52% yield. The required tetrahexylbenzenes were synthesized from 1,2,4,5-tetraiodobenzene (**11**)[14] according to Scheme 1. The synthesis of 1,2,3,4-tetrahexylbenzene (**8**) features a modified version of the Jacobsen reaction, in which sulfonation of highly substituted alkylbenzenes by concentrated sulfuric acid normally induces the alkyl groups to migrate to positions remote from the site of sulfonation.[15,16] Although 1,2,4,5-tetrahexylbenzene (**10**) did not undergo the normal Jacobsen reaction, we found that treatment with chlorosulfonic acid produced the rearranged 2,3,4,5-tetrahexylbenzenesulfonyl chloride (**13**),[17] which was subsequently converted into 1,2,3,4-tetrahexylbenzene (**8**) according to Scheme 1.

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[9] Wuest, J. D. *Acc. Chem. Res.* **1998**, in press. Vaugeois, J.; Simard, M.; Wuest, J. D. *Coord. Chem. Rev.* **1995**, *145*, 55.

[10] For recent related studies of multidentate Lewis acids, see: Antonisse, M. M. G.; Reinhoudt, D. N. *J. Chem. Soc., Chem. Commun.* **1998**, 443. Tschinkl, M.; Schier, A.; Riede, J.; Mehltretter, G.; Gabbaï, F. P. *Organometallics* **1998**, *17*, 2921. Hawthorne, M. F.; Zheng, Z. *Acc. Chem. Res.* **1997**, *30*, 267. Beer, P. D.; Smith, D. K. *Prog. Inorg. Chem.* **1997**, *46*, 1. Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609. Chistyakov, A. L.; Stankevich, I. V.; Gambaryan, N. P.; Struchkov, Yu. T.; Yanovsky, A. I.; Tikhonova, I. A.; Shur, V. B. *J. Organomet. Chem.* **1997**, *536*–*537*, 413. Altmann, R.; Jurkschat, K.; Schürmann, M.; Dakternieks, D.; Duthie, A. *Organometallics* **1997**, *16*, 5716. Grdenić, D.; Korpar-Čolig, B.; Matković-Čalogović, D. *J. Organomet. Chem.* **1996**, *522*, 297. Tamao, K.; Hayashi, T.; Ito, Y. *J. Organomet. Chem.* **1996**, *506*, 85.

[11] For example, see: Ooi, T.; Takahashi, M.; Maruoka, K. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 835. Reilly, M.; Oh, T. *Tetrahedron Lett.* **1995**, *36*, 221.

[12] For an earlier related study of the activation of thiocarbonyl compounds by bidentate Lewis acids, see: Wuest, J. D.; Zacharie, B. *J. Am. Chem. Soc.* **1985**, *107*, 6121.

[13] Laszlo, P.; Teston, M. *J. Am. Chem. Soc.* **1990**, *112*, 8750.

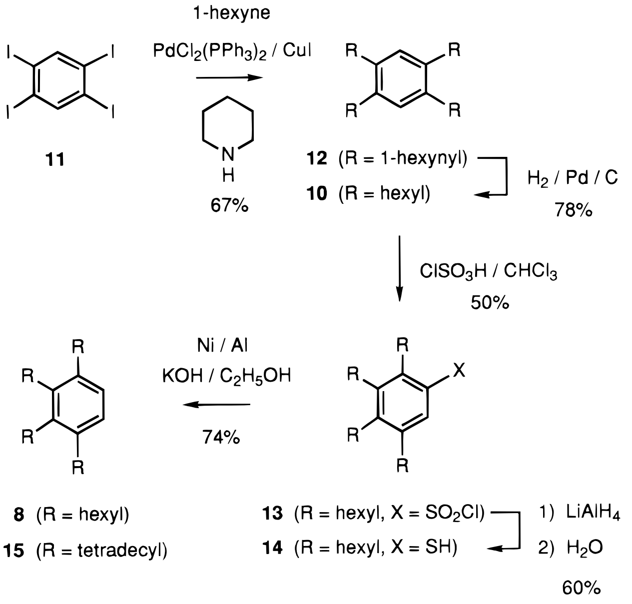
[14] Mattern, D. L. *J. Org. Chem.* **1984**, *49*, 3051.

[15] Suzuki, H. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 1642. Smith, L. I. *Org. React.* **1942**, *1*, 370.

[16] Koeberg-Telder, A.; Cerfontain, H. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 85.

[17] It is noteworthy that the Jacobsen reaction has not previously been used to synthesize simple tetraalkylbenzenes with substituents other than methyl or ethyl, and chlorosulfonic acid has been reported to be incapable of promoting the reaction.[16]

Scheme 1



As expected, hexyl-substituted phenylenedimercury bis(trifluoroacetates) **7** and **9** both showed much higher solubilities in organic solvents such as CH_2Cl_2 than their methyl-substituted analogue **5**. The corresponding 3,4,5,6-tetrakis(tetradecyl)-1,2-phenylenedimercury bis(trifluoroacetate) (**16**), prepared in an analogous way via 1,2,3,4-tetrakis(tetradecyl)benzene (**15**), proved to have similar solubility, and thus we decided to use hexyl-substituted derivatives in subsequent thermodynamic and kinetic studies of the coordination of carbonyl compounds.

Thermodynamic Effects of the Single and Double Coordination of Carbonyl Compounds by Lewis Acids. For the following reasons, we elected to use *N*,*N*-dialkylformamides as the carbonyl substrates in our studies: (1) Amides are among the most basic carbonyl compounds,[18] allowing them to associate with Lewis acids that are intrinsically weak; and (2) simple *N*,*N*-dialkylformamides are known to form well-characterized multiply coordinated adducts with 3,4,5,6-tetramethyl-1,2-phenylenedimercury bis(trifluoroacetate) (**5**) in the solid state, and we could reasonably expect its tetrahexyl analogue **7** to behave similarly, possibly even in solution.

IR spectroscopy permitted an initial assessment of the association of bidentate Lewis acid **7** or its 1,4-isomer **9** with DEF in CH_2Cl_2 at various concentrations. The carbonyl regions of typical spectra showed peaks at 1696 and 1668 cm^{-1} corresponding to terminal trifluoroacetate and free amide, respectively. In addition, characteristic bands appeared at 1633 cm^{-1} for DEF bound by 1,2-isomer **7** and at 1647 cm^{-1} for DEF bound by 1,4-isomer **9**. The distinctly different stretching frequencies observed for bound DEF immediately suggested that 1,2-isomer **7** forms a doubly coordinated complex in solution, as related compounds do in the solid state, whereas 1,4-isomer **9** forms a singly coordinated complex. Double coordination causes a significantly larger shift relative to free DEF (35 cm^{-1}) than single coordination does (21 cm^{-1}), suggesting that double coordination is stronger than single coordination and that it weakens the carbon−oxygen double bond more substantially. In neither case do our data provide information about the precise geometry of coordination, but the consistent behavior of the closely related bidentate Lewis acids 1,2-phenylenedimercury dichloride (**4**) and 3,4,5,6-tetramethyl-1,2-phenylenedimercury bis(trifluoroacetate) (**5**) in the solid state suggests that tetrahexyl analogue **7** behaves similarly in solution and favors doubly coordinated adducts **6** in which one or more atoms of mercury lie out of the carbonyl plane.

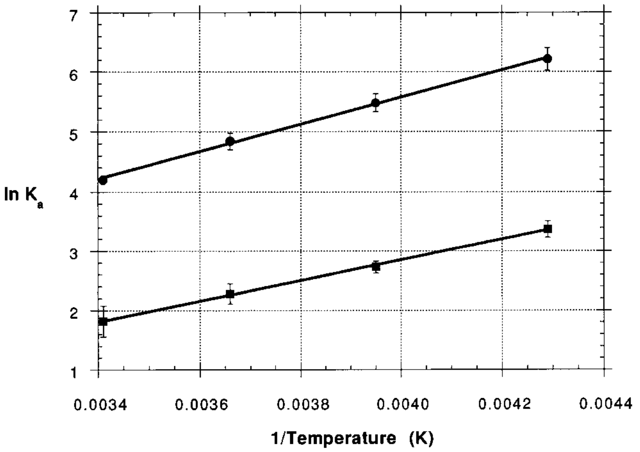


Figure 1. van't Hoff plots for the association of bidentate Lewis acids **7** (●) and **9** (■) with *N*,*N*-diethylformamide in CH_2Cl_2. The lines provide the best fit to the van't Hoff equation ($\ln K_a = -\Delta H°/RT + \Delta S°/R$), with $\Delta H° = -4.5 \pm 0.2$ kcal mol^{-1} and $\Delta S° = -6.9 \pm 1.0$ eu for 1,2-isomer **7**, and with $\Delta H° = -3.4 \pm 0.2$ kcal mol^{-1} and $\Delta S° = -8.1 \pm 1.0$ eu for 1,4-isomer **9**.

Quantitative analysis of IR spectra recorded at −40, −20, 0, and 20 °C yielded association constants (K_a) for the binding of DEF by bidentate Lewis acids **7** and **9**,[19] and van't Hoff plots (Figure 1) revealed that for the double coordination of DEF by 1,2-isomer **7**, $\Delta H° = -4.5 \pm 0.2$ kcal mol^{-1} and $\Delta S° = -6.9 \pm 1.0$ eu, whereas for the single coordination of DEF by 1,4-isomer **9**, $\Delta H° = -3.4 \pm 0.2$ kcal mol^{-1} and $\Delta S° = -8.1 \pm 1.0$ eu. As expected, both values of $|\Delta H°|$ are very small, and they provide quantitative confirmation that the association of carbonyl compounds with Lewis acidic organomercury compounds is inherently weak.[13] Nevertheless, our measurements are noteworthy because they provide the first quantitative demonstration that double coordination is significantly more exothermic than single coordination. Specifically, our results suggest that conversion of a singly coordinated complex into a doubly coordinated complex is exothermic by 1.1 ± 0.2 kcal mol^{-1} in this particular system, or approximately 32% as exothermic as initial formation of the singly coordinated adduct itself. This provides experimental support for earlier ab initio calculations of $\Delta H°$ for formation of the singly and doubly coordinated 1:1 and 1:2 σ complexes of formaldehyde with BH_3 in the gas phase, which suggested that $\Delta H°$ for addition of the second equivalent of BH_3 (−2.3 kcal mol^{-1}) is 32% of the value of $\Delta H°$ for addition of the first (−7.3 kcal mol^{-1}).[20] It is noteworthy that a similar thermodynamic relationship between single and double coordination governs two widely different Lewis acids that form complexes likely to have distinctly different geometries. This encourages us to believe that our thermodynamic and kinetic studies of the effects of double coordination in a special system may have broader significance. The double coordination of carbonyl compounds by two sites of Lewis acidity may be enthalpically feasible in other systems as well, and $\Delta H°$ for coordination of the second site may be a significant fraction of $\Delta H°$ for coordination of the first.

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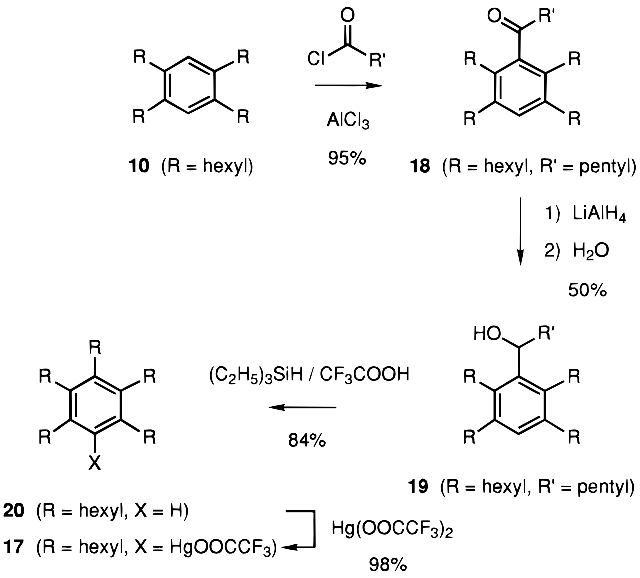
(18) Gal, J.-F.; Maria, P.-C. *Prog. Phys. Org. Chem.* **1990**, *17*, 159.

(19) For an instructive related study that used variable-temperature IR spectroscopy for the quantitative evaluation of weak association, see: Gellman, S. H.; Dado, G. P.; Liang, G.-B.; Adams, B. R. *J. Am. Chem. Soc.* **1991**, *113*, 1164.

(20) LePage, T. J.; Wiberg, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 6642. Deschatelets, P.; Wuest, J. D., unpublished results.

Scheme 2



As expected, the observed values of $\Delta S°$ for single and double coordination are both consistent with the formation of 1:1 complexes. The two values are not significantly different, even though it is likely that the doubly coordinated adduct is somewhat more highly ordered. In part, the similarity of the values is presumably due to the rigid orientation of the Lewis acidic atoms of mercury in 3,4,5,6-tetrahexyl-1,2-phenylenedimercury bis(trifluoroacetate) (**7**). Furthermore, previously reported structural data indicate that dative bonds between oxygen and mercury are characteristically long, weak, and deformable,[9] so the values of $|\Delta S°|$ associated with their formation should be unusually small. In such cases, desolvation may make an important contribution to the observed values of $\Delta S°$.

We believe that the observed values of $\Delta H°$ are different primarily because 3,4,5,6-tetrahexyl-1,2-phenylenedimercury bis(trifluoroacetate) (**7**) forms a doubly coordinated complex with DEF, whereas its 1,4-isomer **9** forms a singly coordinated complex. For the following reasons, we doubt that subtle steric differences between bidentate Lewis acid **7** and its 1,4-isomer **9** have important effects on $\Delta(\Delta H°)$. Steric effects are likely to be negligible because of the deformable nature of dative bonds between oxygen and mercury; in addition, the characteristically long Hg−C bonds in phenylmercury compounds make the sites of coordination remote from the potential steric influence of adjacent alkyl substituents.

To assess possible electronic differences between 3,4,5,6-tetrahexyl-1,2-phenylenedimercury bis(trifluoroacetate) (**7**) and its 1,4-isomer **9**, we synthesized a soluble monodentate analogue, (2,3,4,5,6-pentahexylphenyl)mercuric trifluoroacetate (**17**), by the route summarized in Scheme 2. The Lewis acidities of bidentate Lewis acid **9** and its monodentate analogue **17** were evaluated qualitatively by recording their ^{199}Hg NMR spectra in CD_2Cl_2 (70 mM, 20 °C) and then by comparing the values of $\Delta(\delta\ ^{199}\mathrm{Hg})$ caused by the addition of equimolar amounts of DEF. As expected, these experiments indicated that monodentate Lewis acid **17** is intrinsically less Lewis acidic than either of its bidentate analogues. This confirms that electronic factors increase the Lewis acidity of a phenylmercuric trifluoroacetate when a second $Hg(OOCCF_3)$ group is introduced, at least in the ortho or para positions. We conclude that 3,4,5,6-tetrahexyl-1,2-phenylenedimercury bis(trifluoroacetate) (**7**) and its 1,4-isomer **9** provide a pair of bidentate Lewis acids that are carefully matched and fully suitable for assessing the thermodynamic and kinetic effects of single and double coordination. Because the two bidentate Lewis acids are structurally similar and have two ortho or para $Hg(OOCCF_3)$ groups, any comparisons of their reactivity are likely to be free of significant steric or electronic bias.

If it is true that the coordination chemistry of bidentate Lewis acids derived from 1,2-phenylenedimercury is insensitive to steric effects, then amides more highly substituted than DEF and DMF should also form similar doubly coordinated complexes **6**. This was confirmed by an X-ray crystallographic study of the 1:1 complex of 3,4,5,6-tetramethyl-1,2-phenylenedimercury bis(trifluoroacetate) (**5**) with *N*,*N*-diethylacetamide (DEA). The results of this study, which are summarized in Figure 2, establish that both Lewis acidic atoms of mercury bind the carbonyl oxygen atom of DEA and that both lie out of the carbonyl plane, creating the partial structures shown in Figure 2. All four carbonyl O•••Hg distances are much shorter than the sum of the van der Waals radii of oxygen (1.40 Å)[21] and mercury (1.73 Å),[22] and the average distance (2.68(2) Å) is similar to the one measured for doubly coordinated DEF in its 3:2 complex with bis(trifluoroacetate) **5** (2.75(2) Å).[23] Simultaneously, the two atoms of mercury in the 1:1 complex of bis(trifluoroacetate) **5** with DEA retain enough Lewis acidity to doubly bind the carbonyl oxygen atom of a trifluoroacetate group in a neighboring molecule.[24] However, this additional double coordination is much weaker than that of DEA, and the average carbonyl O•••Hg distance is 2.94(2) Å.

In the 1:1 complex of bis(trifluoroacetate) **5** with DEA, the average carbonyl C−O bond length in the bound amide (1.27(2) Å) is longer than the generally accepted value for free tertiary amides (1.23(1) Å), and the N−C(O) bond length (1.32(3) Å) is slightly shorter than the normal value (1.35(1) Å).[25] These differences are consistent with the hypothesis that double coordination weakens the carbon−oxygen double bond but they are not large enough to be considered crystallographically significant.

Highly substituted amides are complexed by bidentate Lewis acids derived from 1,2-phenylenedimercury in solution, as well as in the solid state. For example, we found that variable-temperature IR spectra of solutions of *N*,*N*-dimethylpivalamide (DMP) in $CHCl_3$ (0.093 M) containing equimolar amounts of either 3,4,5,6-tetrahexyl-1,2-phenylenedimercury bis(trifluoroacetate) (**7**) or its 1,4-isomer **9** resemble analogous spectra of *N*,*N*-dialkylformamides such as DEF. Specifically, the carbonyl regions show a band at 1609 cm^{-1} characteristic of free DMP and an additional band at either 1569 or 1577 cm^{-1}, corresponding to DMP that is doubly or singly coordinated, respectively. In contrast, similar IR studies showed that ketones and other less basic carbonyl compounds are bound more weakly or not at all by bidentate Lewis acid **7** or its 1,4isomer **9**.

Kinetic Effects of the Single and Double Coordination of Carbonyl Compounds by Lewis Acids. Collectively, our structural, spectroscopic, and thermodynamic studies suggest that the double coordination of amides by bidentate Lewis acids derived from 1,2-phenylenedimercury is a general phenomenon and that it weakens the carbon−oxygen double bond more than single coordination does. If so, double coordination should have

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[21] Pauling, L. *The Nature of the Chemical Bond*; Cornell University Press: Ithaca, NY, 1960; p 514.

[22] Canty, A. J.; Deacon, G. B. *Inorg. Chim. Acta* **1980**, *45*, L225.

[23] Simard, M.; Vaugeois, J.; Wuest, J. D. *J. Am. Chem. Soc.* **1993**, *115*, 370.

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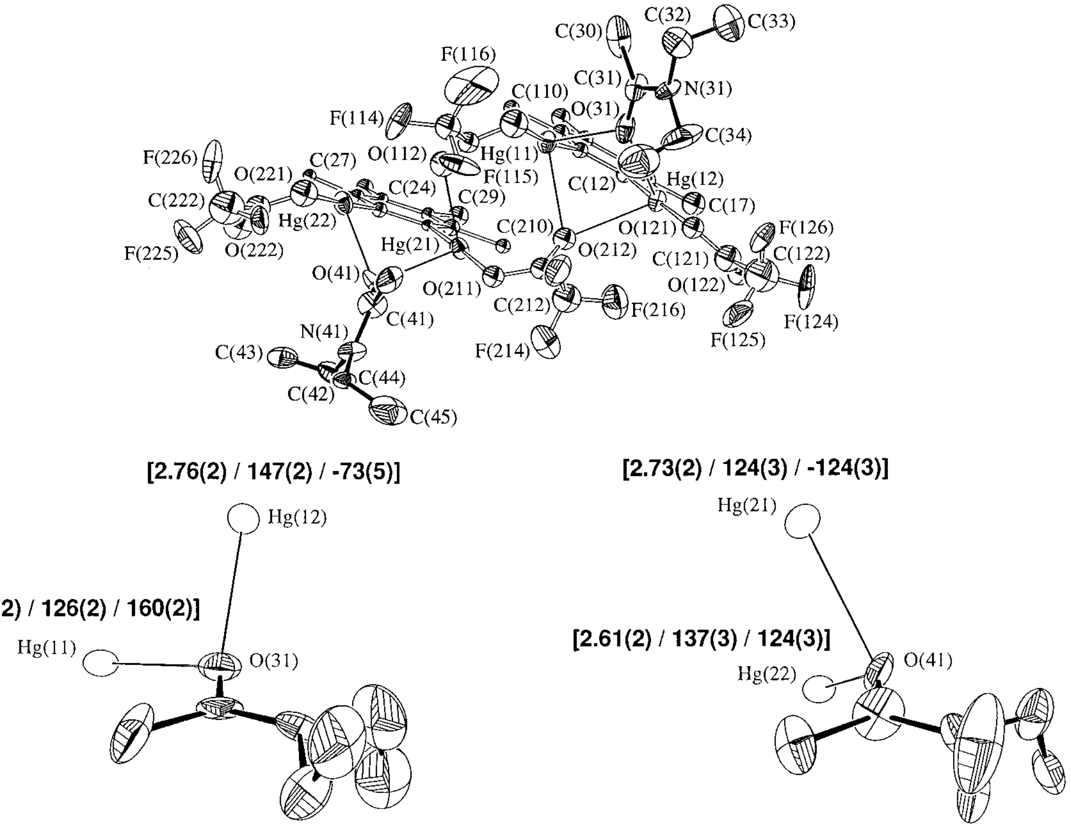

Figure 2. ORTEP views of the structure of the 1:1 complex of μ-(3,4,5,6-tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**5**) with *N,N*-diethylacetamide (DEA). (a) The upper view provides the atomic-numbering scheme. Non-hydrogen atoms are represented by ellipsoids corresponding to 30% probability, hydrogen atoms are omitted for clarity, dative bonds to mercury are indicated using narrow lines, and bonds in DEA are represented by solid lines. Important bond lengths include Hg(11)−O(31) = 2.63(2), Hg(12)−O(31) = 2.76(2), Hg(21)−O(41) = 2.73(2), Hg(22)−O(41) = 2.61(2), C(31)−O(31) = 1.26(2), C(41)−O(41) = 1.28(2), C(31)−N(31) = 1.31(3), C(41)−N(41) = 1.33(3), Hg(11)−O(212) = 2.82(2), Hg(12)−O(212) = 2.89(2), Hg(21)−O(112) = 2.82(2), and Hg(22)−O(112) = 3.21(2) Å. (b) The lower views show only the bound amides and the two associated atoms of mercury. To facilitate comparison, each structure is viewed along the carbonyl C═O axis from slightly above the carbonyl plane. All hydrogen atoms are omitted for simplicity. The three geometric parameters that appear next to each mercury atom correspond to the carbonyl O···Hg distance (Å)/C═O···Hg angle (deg)/N−C═O···Hg dihedral angle (deg).

unique effects on the reactivity of bound amides. Because bidentate Lewis acids derived from 1,2-phenylenedimercury are weak, any special kinetic effects of double coordination will be small and hard to detect. For this reason, initial comparisons of the effects of 3,4,5,6-tetrahexyl-1,2-phenylenedimercury bis(trifluoroacetate) (**7**) and its 1,4-isomer **9** on various bimolecular reactions of amides proved inconclusive. As an alternative, we decided to compare the effects of bidentate Lewis acids **7** and **9** on barriers for rotation around the N−C(O) bond in amides,[26] using values of $\Delta G^\ddagger$ determined by variable-temperature ^{1}H NMR spectroscopy. To maximize the percentage of amide bound by the weakly Lewis acidic reagents **7** and **9**, we needed to conduct these experiments at the lowest possible temperatures, and therefore we required an amide substrate in which rotation is especially fast. Highly substituted amides such as DMP satisfy this condition; in addition, we had already established that DMP is doubly coordinated in solution by bidentate Lewis acid **7** and singly coordinated by 1,4-isomer **9**.

Coalescence of the methyl signals of DMP occurred at $T_c = -1.5, -14$, or -16 ± 1 °C, respectively, in solutions containing an equimolar amount of 1,2-isomer **7**, an equimolar amount of 1,4-isomer **9**, or DMP alone (0.093 M in $CDCl_3$). The corresponding values of $\Delta G^\ddagger$ are 12.9, 12.3, and 12.2 ± 0.1 kcal mol^{-1}.[27] As expected, the differences are small; nevertheless, they are significant, and they establish for the first time that the double coordination of carbonyl compounds can have measurable effects on the rates of subsequent chemical transformations. In this particular case, the effects presumably arise because the association constant for double coordination is higher than that for single coordination, and because double coordination further weakens the carbon−oxygen double bond of amides, further strengthens the N−C(O) bond, and thereby inhibits rotation more effectively.

Conclusions

Our results establish that (1) the double coordination of carbonyl compounds by two sites of Lewis acidity is enthalpically feasible in the solid state and in solution, (2) $\Delta H°$ for coordination of the second site is a significant fraction of $\Delta H°$ for coordination of the first, and (3) the double coordination of carbonyl compounds by Lewis acids can have measurable effects on the rates of subsequent chemical transformations. Our results are based on the special case of the complexation of amides by weak Lewis acids derived from phenylenedimercury; nevertheless, our conclusions may prove to have general validity, and significant thermodynamic and kinetic effects may be observed in other cases when basic molecules are bound by suitable bidentate Lewis acids.

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Bidentate Lewis acids remain poorly studied, but it is increasingly difficult to dismiss them as esoteric reagents of mere academic interest. Recent studies have shown that they can bind and activate organic substrates in genuinely useful ways,[11,12] and our present results provide fundamental new information that should accelerate development of this field of research. Moreover, strongly encouraging analogies exist between the activation induced by bidentate Lewis acids and catalytic processes that are already known to play important roles in nature. In particular, double coordination of the oxygen atom of carbonyl groups is similar to double coordination of the oxygen atom of phosphoryl groups by two metal cations, which is believed to be a crucial step in various enzyme-catalyzed phosphoryl transfers.[28,29] As a result, we believe that bidentate Lewis acids will eventually find broad applications in chemistry, particularly as catalytic or stoichiometric reagents in organic synthesis.

Experimental Section

Tetrahydrofuran (THF) and ether were dried by distillation from the sodium ketyl of benzophenone, and piperidine, CS_2, and CH_2Cl_2 were dried by distillation from CaH_2. *N*,*N*-Diethylformamide and *N*,*N*-dimethylformamide were purified by distillation at 0.2 Torr and then dried over 4 Å molecular sieves. $PdCl_2(PPh_3)_2$ was prepared in the normal way.[30] All other reagents were commercial products that were used without further purification. Flash chromatography was performed in the usual manner.[31]

1,2,4,5-Tetra-1-hexynylbenzene (12). A solution of 1,2,4,5-tetraiodobenzene (**11**; 30 g, 52 mmol),[14] $PdCl_2(PPh_3)_2$ (2.6 g, 3.7 mmol), and CuI (3.5 g, 18 mmol) in piperidine (1.0 L) was stirred at 25 °C under dry Ar, 1-hexyne (21 g, 260 mmol) was added, and the resulting mixture was stirred at 25 °C for 12 h. Volatiles were then removed by evaporation at 50 °C under reduced pressure, and the solid residue was extracted with hexane. The extracts were filtered, solvent was removed by evaporation under reduced pressure, and the residue was purified by flash chromatography (silica, hexane (98%)/ethyl acetate (2%)) to give 1,2,4,5-tetra-1-hexynylbenzene (**12**; 14 g, 35 mmol, 67%) as an analytically pure yellow solid: IR (melt) 2220 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, 12H, $^3J = 7.1$ Hz), 1.45−1.65 (m, 16H), 2.45 (t, 8H, $^3J = 6.8$ Hz), 7.38 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.6, 19.2, 21.8, 30.6, 78.8, 95.3, 125.0, 135.0. HRMS (EI) calcd for $C_{30}H_{38}$ *m*/*e* 398.2974, found 398.2970. Anal. Calcd for $C_{30}H_{38}$ C, 90.39; H, 9.61. Found C, 90.16; H, 9.75.

1,2,4,5-Tetrahexylbenzene (10).[32] A suspension containing 10% Pd/C (22 g) and 1,2,4,5-tetra-1-hexynylbenzene (**12**; 36 g, 90 mmol) in a mixture of hexane (600 mL) and C_2H_5OH (600 mL) was stirred at 25 °C under H_2 (6.9 atm) in a Parr reactor. After 96 h, the mixture was filtered, and volatiles were removed from the filtrate by evaporation under reduced pressure. Kugelrohr distillation (195 °C/0.5 Torr) of the residue gave 1,2,4,5-tetrahexylbenzene (**10**; 29 g, 70 mmol, 78%) as an analytically pure colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, 12H, $^3J = 6.9$ Hz), 1.30−1.50 (m, 24H), 1.50−1.65 (m, 8H), 2.53 (t, 8H, $^3J = 7.7$ Hz), 6.92 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.0, 22.6, 29.5, 31.4, 31.7, 32.3, 129.7, 137.6. Anal. Calcd for $C_{30}H_{54}$ C, 86.88; H, 13.12. Found C, 86.53; H, 12.58.

2,3,4,5-Tetrahexylbenzenesulfonyl Chloride (13). A solution of 1,2,4,5-tetrahexylbenzene (**10**; 1.0 g, 2.4 mmol) in $CHCl_3$ (7 mL) was stirred at 25 °C and treated cautiously with neat chlorosulfonic acid (15 mL). After a vigorous reaction, the mixture was stirred at 25 °C for 1 h, and then H_2O (25 mL) was added slowly. The resulting mixture was extracted with $CHCl_3$, and volatiles were removed from the combined extracts by evaporation under reduced pressure. Flash chromatography (silica, hexane (90%)/$CHCl_3$ (10%)) of the residue provided an analytically pure sample of 2,3,4,5-tetrahexylbenzenesulfonyl chloride (**13**; 0.60 g, 1.2 mmol, 50%) as a pale yellow oil: IR ($CHCl_3$) 1365, 1161 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85−0.95 (m, 12H), 1.25−1.70 (m, 32H), 2.55−2.70 (m, 6H), 2.95−3.05 (m, 2H), 7.75 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.0 (4C), 22.5, 22.5, 22.6 (2C), 29.0, 29.4, 29.6, 29.7, 29.9, 30.0 (2C), 30.7, 31.0, 31.1, 31.3, 31.3, 31.4 (2C), 31.5, 32.9, 127.5, 137.9, 139.8, 140.9, 142.7, 147.8. Anal. Calcd for $C_{30}H_{53}ClO_2S$ C, 70.20; H, 10.41. Found C, 70.37; H, 10.36.

2,3,4,5-Tetrahexylbenzenethiol (14). A solution of 2,3,4,5-tetrahexylbenzenesulfonyl chloride (**13**; 3.1 g, 6.0 mmol) in THF (50 mL) was stirred at 25 °C under dry Ar, solid $LiAlH_4$ (1.9 g, 50 mmol) was added in portions, and the mixture was heated at reflux for 12 h. The resulting mixture was cooled to 0 °C and treated dropwise with H_2O. Solids were then dissolved by adding 6 N aqueous HCl, and volatiles were partially removed by evaporation under reduced pressure. The aqueous residue was extracted with $CHCl_3$, solvent was removed from the combined extracts by evaporation under reduced pressure, and the residue was purified by flash chromatography (silica, hexane). This yielded 2,3,4,5-tetrahexylbenzenethiol (**14**; 1.6 g, 3.6 mmol, 60%) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.90−1.00 (m, 12H), 1.30−1.64 (m, 32H), 2.45−2.62 (m, 6H), 2.62−2.71 (m, 2H), 3.21 (s, 1H), 6.97 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.0 (4C), 22.5, 22.6 (3C), 29.0, 29.5, 29.6, 29.7, 29.8, 30.0, 30.0, 31.3, 31.4, 31.5 (5C), 31.6, 32.8, 127.3, 129.4, 136.8, 137.0, 139.2, 139.8. HRMS (FAB, thioglycerol) calcd for $C_{30}H_{54}S$ *m*/*e* 446.3973, found 446.3946.

1,2,3,4-Tetrahexylbenzene (8). A solution of 2,3,4,5-tetrahexylbenzenethiol (**14**; 12 g, 27 mmol) in a mixture of hexane (250 mL) and C_2H_5OH (250 mL) was stirred at 25 °C and treated with solid KOH (1.8 g, 32 mmol) and then with an aqueous slurry of Raney nickel (55 g, 50 wt %). After 12 h, a second portion of Raney nickel (12 g) was added. After an additional period of 24 h, the mixture was filtered, the filtered solid was rinsed with hexane, and volatiles were removed from the combined filtrates by evaporation under reduced pressure. Kugelrohr distillation (200 °C/0.5 Torr) of the residue provided an analytically pure sample of 1,2,3,4-tetrahexylbenzene (**8**; 8.5 g, 20 mmol, 74%) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.86−0.96 (m, 12H), 1.24−1.69 (m, 32H), 2.50−2.60 (m, 8H), 6.94 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.0, 14.0, 22.6, 22.6, 29.1, 29.6, 30.1, 31.3, 31.5, 31.6, 31.7, 33.0, 126.5, 138.3, 138.6. Anal. Calcd for $C_{30}H_{54}$ C, 86.88; H, 13.12. Found C, 86.80; H, 12.79.

***μ*-(3,4,5,6-Tetrahexyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (7).** A solution of 1,2,3,4-tetrahexylbenzene (**8**; 1.1 g, 2.7 mmol) in CH_2Cl_2 (30 mL) was stirred at 25 °C and treated with $Hg(OOCCF_3)_2$ (2.8 g, 6.6 mmol) and then with CF_3COOH (20 mL). The resulting mixture was stirred at 25 °C for 12 h, and then volatiles were removed by evaporation under reduced pressure. The residue was dried in vacuo for 12 h and then extracted with hexane, and the extracts were passed through a 0.2-*μ*m Millipore filter. Cooling of the filtrate to −78 °C caused the precipitation of *μ*-(3,4,5,6-tetrahexyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**7**; 2.3 g, 2.2 mmol, 81%), which was isolated as an analytically pure colorless solid: mp 149−150 °C; IR (CH_2Cl_2) 1695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.82−0.98 (m, 12H), 1.25−1.65 (m, 32H), 2.50−2.67 (m, 8H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.8, 14.0, 22.4, 22.5, 29.5, 30.0, 30.2, 31.3, 31.4 (2C), 33.3, 38.9, 118.0 (q, $^1J_{C-F} = 288$ Hz), 141.9, 143.8, 152.0, 162.0 (q, $^2J_{C-F} = 40$ Hz); ^{199}Hg NMR (71.6 MHz, CD_2Cl_2) δ −1535. Anal. Calcd for $C_{30}H_{52}F_6Hg_2O_4$ C, 39.27; H, 5.04; F, 10.96. Found C, 38.49; H, 5.15; F, 10.75.

***μ*-(2,3,5,6-Tetrahexyl-1,4-phenylene)bis(trifluoroacetato-*O*)dimercury (9).** A solution of 1,2,4,5-tetrahexylbenzene (**10**; 0.12 g, 0.29 mmol) in CH_2Cl_2 (10 mL) was stirred at 25 °C and treated with $Hg(OOCCF_3)_2$ (0.32 g, 0.75 mmol) and then with CF_3COOH (10 mL). The resulting mixture was stirred at 25 °C for 3 h, and then volatiles were removed by evaporation under reduced pressure. The residue was dried at 70 °C in vacuo for 12 h and then extracted with hot hexane, and the extracts were passed through a 0.2-*μ*m Millipore filter. Cooling of the filtrate to −78 °C caused the precipitation of *μ*-(2,3,5,6-tetrahexyl-1,4-phenylene)bis(trifluoroacetato-*O*)dimercury (**9**; 0.16 g, 0.15 mmol,

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52%), which was isolated as an analytically pure colorless solid: mp 105−107 °C; IR (KBr) 1714, 1693 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.91 (t, 12H, ^3J = 6.9 Hz), 1.28−1.40 (m, 16H), 1.40−1.55 (m, 8H), 1.55−1.69 (m, 8H), 2.69 (t, 8H, ^3J = 7.9 Hz); ^{13}C NMR (100.6 MHz, CDCl$_3$) d 13.8, 22.4, 29.4, 31.4, 33.4, 39.3, 118.9 (q, $^1J_{C-F}$ = 288 Hz), 143.5, 151.2, 161.7 (q, $^2J_{C-F}$ = 39 Hz); ^{199}Hg NMR (71.6 MHz, CD$_2$Cl$_2$) δ −1366. Anal. Calcd for $C_{30}H_{52}F_6Hg_2O_4$ C, 39.27; H, 5.04. Found C, 40.17; H, 5.38.

Variable-Temperature IR Studies of the Binding of *N*,*N*-Diethylformamide by *μ*-(3,4,5,6-Tetrahexyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (7) and *μ*-(2,3,5,6-Tetrahexyl-1,4-phenylene)bis(trifluoroacetato-*O*)dimercury (9). These studies employed a Perkin-Elmer model 1650 FT-IR spectrometer equipped with a Specac model 21500-6 variable-temperature cell and a Specac model 20426 temperature controller. All cell windows in contact with solutions of bidentate Lewis acids **7** and **9** were made of CaF$_2$.[33] At each temperature, values of K_a were determined using multiple nominal concentrations of DEF and either bidentate Lewis acid **7** or **9**. Each experiment was performed in triplicate. In studies of the association of 1,2-isomer **7** with DEF, the nominal concentrations of DEF ranged from 4.5 mM to 18 mM, and the nominal concentrations of compound **7** ranged from 4.8 mM to 9.6 mM. In studies involving the 1,4-isomer **9**, the nominal concentrations of DEF varied from 31 mM to 94 mM, and the nominal concentrations of compound **9** varied from 31 mM to 62 mM. At each temperature, the amount of free DEF was estimated using calibration curves measured at the same temperature.

A Job plot confirmed that 1,2-isomer **7** forms a 1:1 complex, and for both isomers the formation of higher-order aggregates is negligible under the conditions described. At temperatures below −40 °C and at higher concentrations (19 mM), spectra of solutions containing DEF and 1,2-isomer **7** revealed a minor peak at 1645 cm^{-1} in addition to those at 1633 and 1668 cm^{-1} associated with doubly coordinated DEF and free DEF, respectively. It is possible that the additional peak corresponds to a 1:2 complex in which bidentate Lewis acid **7** doubly coordinates two molecules of DEF.[34] To minimize complications caused by higher-order association, we avoided temperatures below −40 °C and concentrations of bidentate Lewis acid **7** above 9.6 mM.

1:1 Complex of *μ*-(3,4,5,6-Tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (5) with *N*,*N*-Diethylacetamide. *μ*-(3,4,5,6-Tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**5**; 185 mg, 0.244 mmol)[35] was dissolved in hot *N*,*N*-diethylacetamide (100 mL). The solution was cooled to 60 °C, pentane (1.0 mL) was added, the mixture was shaken vigorously, and the phases were separated. The 1:1 complex of *μ*-(3,4,5,6-tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**5**) with *N*,*N*-diethylacetamide separated from the pentane phase as colorless crystals suitable for X-ray crystallographic study: ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.99 (t, 3H, ^3J = 7.2 Hz), 1.08 (t, 3H, ^3J = 7.2 Hz), 1.95 (s, 3H), 2.17 (s, 6H), 2.37 (s, 6H), 3.16−3.30 (m, 4H).

X-ray Crystallographic Study of the 1:1 Complex of *μ*-(3,4,5,6-Tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (5) with *N*,*N*-Diethylacetamide. Crystals of the 1:1 complex of *μ*-(3,4,5,6-tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**5**) with *N*,*N*-diethylacetamide belong to the orthorhombic space group *Pbca* with a = 15.098(5) Å, b = 17.281(7) Å, c = 39.52(2) Å, a = 90°, b = 90°, g = 90°, V = 10311(8) Å^3, D_{calcd} = 2.254 g cm^{-3}, and Z = 8. Data were collected at 225 K, and the structure was refined to R1 = 0.066, wR2 = 0.148 for 5295 reflections with $I > 2.00\,\sigma(I)$. A detailed description of the structure and its determination is provided in the Supporting Information.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada, the Ministère de l′Éducation du Québec, and Merck Frosst for financial support. In addition, acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. We also thank Professor Samuel H. Gellman and Dr. Gregory P. Dado for helpful advice about variable-temperature IR spectroscopy. In addition, we are grateful to Dr. Michel Simard of the Laboratoire de Diffraction des Rayons-X, Département de Chimie, Université de Montréal, for having determined the structure of the 1:1 complex of *μ*-(3,4,5,6-tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**5**) with *N*,*N*-diethylacetamide.

Supporting Information Available: Full experimental details for the synthesis and characterization of *μ*-(3,4,5,6-tetrakis(tetradecyl)-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**16**), (2,3,4,5,6-pentahexylphenyl)(trifluoroacetato-*O*)mercury (**17**), and their precursors; tables of atomic coordinates and isotropic thermal parameters, complete bond lengths and angles, anisotropic thermal parameters, hydrogen atom coordinates and thermal parameters, and distances to weighted least-squares planes for the 1:1 complex of *μ*-(3,4,5,6-tetramethyl-1,2-phenylene)bis(trifluoroacetato-*O*)dimercury (**5**) with *N*,*N*-diethylacetamide (29 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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