

(eq 7, path b). Alternatively, synthesis of the vinyl epoxide by selective epoxidation of a diene<sup>16</sup> translates into a 1,4 addition of the elements of OH and Nu across the termini of the diene (eq 7, path c). The characteristics of the reaction also clearly demonstrate that, in contrast to the reaction of vinyl epoxides with iron(0) complexes which involve C-O insertion<sup>17</sup> and in contrast to a similarly proposed pathway for the palladium-catalyzed isomerization,<sup>2</sup> this reaction presumably involves an ionization to a zwitterion with *inversion* in which the epoxide oxygen serves as a leaving group (see eq 3). A new appreciation for the potential of transition-metal-catalyzed alkylations emerges from this reaction.

**Acknowledgment.** We wish to thank the National Science Foundation for their generous support of our work. G.M. thanks NIH for a postdoctoral fellowship and Brian Peterson for preparation of some of the substrates utilized in this study. Johnson-Matthey and Englehard Industries made available a generous supply of palladium chloride.

**Supplementary Material Available:** Spectral and analytical data for compounds (3 pages). Ordering information is given on any current masthead page.

(16) Potassium carbonate buffered MCPBA epoxidations were employed. See: Crandall, J. K.; Banks, D. B.; Colyer, R. A.; Watkins, R. J.; Arrington, J. P. *J. Org. Chem.* **1968**, *33*, 423.

(17) Aumann, R.; Fröhlich, K.; Ring, H. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 275.

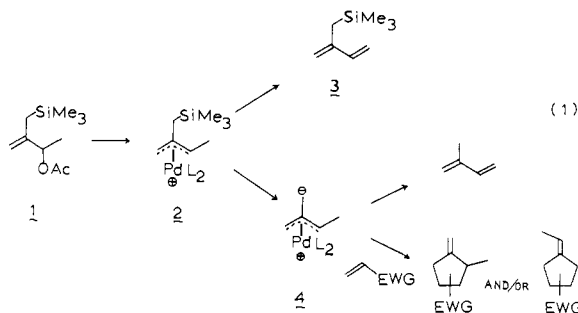
## Regiochemistry of the Cycloaddition of a Substituted Trimethylenemethanepalladium Complex

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The utility of the cycloaddition of transition-metal complexed trimethylenemethanes in synthesis depends upon the availability of substituted systems.<sup>1-3</sup> However, substitution does not represent a simple structural change. Consider the case of introduction of a methyl group using the silicon based bifunctional conjunctive reagent **1** as the precursor (reaction 1). At the first intermediate



**2**, competition exists between deprotonation<sup>4</sup> to form the stable

† Standard Oil of Ohio Fellow, 1980.

(1) (a) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6429, 6432. (b) Trost, B. M.; Chan, D. M. T. *Ibid.* **1980**, *102*, 6359.

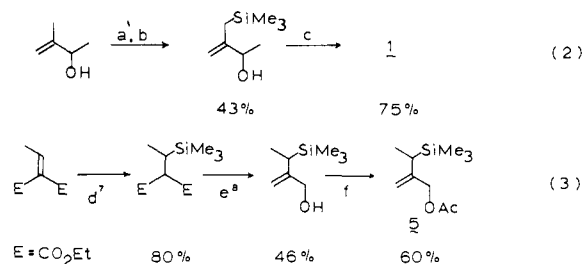
(2) For codimerizations of olefins with methylenecyclopropanes, see: Binger, P. *Synthesis* **1973**, 427. Binger, P.; Schuchardt, U. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 249. *Chem. Ber.* **1980**, *113*, 3334.

(3) Also see: Balavoine, G.; Eskenazi, C.; Guillemot, M. *J. Chem. Soc., Chem. Commun.* **1979**, 1109. Dallas, B. K.; Hughes, R. P. *J. Organomet. Chem.* **1980**, *184*, C67. Inoue, Y.; Hibi, T.; Kawashima, Y.; Hashimoto, H. *Chem. Lett.* **1980**, 1521.

(4) Pd-catalyzed elimination to dienes is well precedented. Trost, B. M.; Verhoeven, T. R.; Fortunak, J. *Tetrahedron Lett.* **1979**, 2301. Tsuji, J.; Yamakawa, T.; Kaito, M.; Mandai, T. *Ibid.* **1978**, 2075.

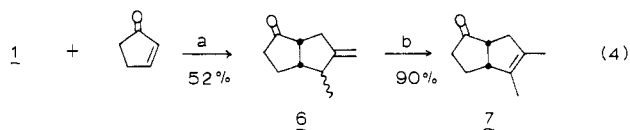
molecule **3** and desilylation to form a reactive intermediate **4**. In the latter, a competition exists between simple tautomerism to isoprene vs. a bimolecular trapping to give the cycloadduct. For cycloaddition to be successful, it must compete with two apparently highly favorable reaction pathways. In addition, the question of regioselectivity of any cycloaddition exists.

Two isomeric methyl substituted precursors **1**<sup>5,6</sup> [bp 70–73 °C (4.5 mm)] and **5**<sup>5,6</sup> [bp 70–75 °C (4.5 mm)] are available as summarized in reactions 2 and 3. For cycloaddition, we chose



(a) *n*-BuLi, THF, ether, TMEDA, room temperature, then Me<sub>3</sub>SiCl; (b) 1 N H<sub>2</sub>SO<sub>4</sub>, THF, room temperature; (c) AcCl, C<sub>5</sub>H<sub>5</sub>N, catalytic (dimethylamino)pyridine, 0 °C; (d) Me<sub>3</sub>SiLi, HMPA, THF, -78 °C; (e) NaH, THF, then LAH, reflux; (f) AcCl, C<sub>5</sub>H<sub>5</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C

cyclopentenone as our key trap. With the parent TMM-PdL<sub>2</sub> and this enone, cycloaddition proceeds in 56% yield—a fact which can be contrasted with an unsuccessful attempt to synthesize the same adduct by a titanium tetrachloride catalyzed reaction of [2-(chloromethyl)allyl]silane with this trap.<sup>9</sup> As illustrated in reaction 4, not only did cycloaddition proceed—a fact that in-



(a) 3.8 mol % (Ph<sub>3</sub>P)<sub>4</sub>Pd, 1.3 mol % Ph<sub>3</sub>P, reflux; (b) 15 mol % TsOH·H<sub>2</sub>O, CDCl<sub>3</sub>, 50 °C

dedicated our fears for competing reactions to be unwarranted—but essentially a single product **6**<sup>5</sup> (as a 1:1 stereoisomeric mixture) arises. By VPC and 270-MHz NMR analysis, very small amounts (<5%) of other products were observed, one of which appears to be a regioisomer of **6**.<sup>10</sup> Thus, in this case, the regioselectivity is >20:1. Mild acid-catalyzed double-bond migration converted **6** to **7**<sup>5</sup> and confirms the stereoisomeric nature of **6**.

While a detailed analysis of the Eu-induced shifts in the 270-MHz NMR spectrum initially allowed assignment of the regiochemistry, in order to confirm this critical assignment and illustrate the synthetic potential, we converted **6** into **8**, mp 57.5–58.0 °C (lit.<sup>11</sup> mp 58.5–59.0 °C) (reaction 5), a precursor of chrysolmelidial **9**, the larval defensive secretion of a chrysolmelide beetle.<sup>12,13</sup>

(5) This compound has been fully characterized by IR, NMR, and mass spectroscopy, and elemental composition established by high-resolution mass spectrometry and/or combustion analysis. Yields of adducts are normally based on recovered trap.

(6) **1**: IR (neat) 1739, 1637, 850 cm<sup>-1</sup>; NMR (270 MHz, CDCl<sub>3</sub>) δ 0.05 (s, 9 H), 1.31 (d, *J* = 6.6 Hz, 3 H), 1.46 (dd, *J* = 14.2, 1.1 Hz, 1 H), 1.60 (dd, *J* = 14.2, 1.1 Hz, 1 H), 2.06 (s, 3 H), 4.67 (br s, 1 H), 4.90 (t, *J* = 1.1 Hz, 1 H), 5.20 (q, *J* = 6.6 Hz, 1 H). **5**: IR (neat) 1745, 1640, 840 cm<sup>-1</sup>; NMR (270 MHz, CDCl<sub>3</sub>) δ 0.01 (s, 9 H), 1.14 (d, *J* = 7.5 Hz, 3 H), 1.56 (q, *J* = 7.5 Hz, 1 H), 2.09 (s, 3 H), 4.45 (dm, *J* = 13 Hz, 1 H), 4.46 (dm, *J* = 13 Hz, 1 H), 4.73 (m, 1 H), 4.97 (m, 1 H).

(7) Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063.

(8) Marshall, J. A.; Andersen, N. H.; Hochstetler, A. R. *J. Org. Chem.* **1967**, *32*, 113.

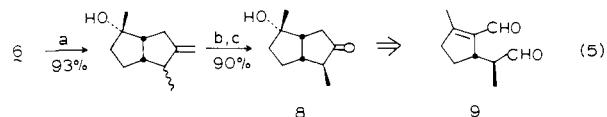
(9) Knapp, S.; O'Connor, U.; Mobilio, D. *Tetrahedron Lett.* **1980**, 4557.

(10) A very small absorption at δ 1.56 (dm, *J* = 6.5 Hz) was assigned to an isomer of **6** bearing the methyl group on the double bond.

(11) Kon, K.; Isoe, S. *Tetrahedron Lett.* **1980**, 3399.

(12) Meinwald, J.; Hones, T. H.; Eisner, T.; Hicks, K. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 2189.

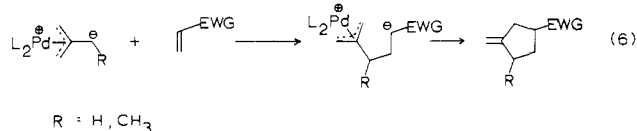
(13) Meinwald, J.; Johnes, T. H. *J. Am. Chem. Soc.* **1978**, *100*, 1883. Jones, T. H.; Blum, M. S.; Fales, H. M. *Tetrahedron Lett.* **1980**, 1701.



(a) MeLi, ether,  $-78\text{ }^\circ\text{C}$ ; (b)  $\text{O}_3$ ,  $\text{CH}_2\text{Cl}_2$ , MeOH,  $-78\text{ }^\circ\text{C}$ ; (c) 42 mol % NaOMe, MeOH, room temperature

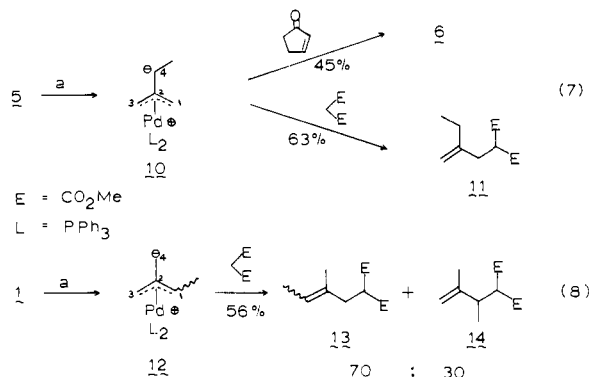
Spectroscopic comparison with an authentic sample of **8** also confirms their identity. Considering that the previous synthesis of **8** involves 14 steps,<sup>11</sup> this 6-step route (which includes the synthesis of **1**) represents an attractive alternative. A loganin synthesis may also be envisioned from **6**.<sup>14</sup>

Since previous work on the parent system suggested a dipolar structure for these complexes in which the cycloaddition involves a Michael-type addition followed by ring closure (reaction 6),<sup>1</sup>



the above results demonstrate that the carbon bearing the methyl group initiates attack on the acceptor. Assuming that the most electron-rich carbon initiates this attack leads to the incredible conclusion that the normally electron-releasing methyl group prefers to be on the most electron-rich carbon of the TMM complex!

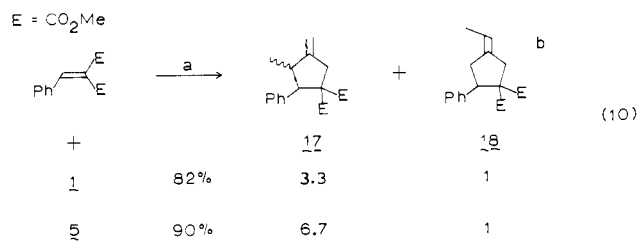
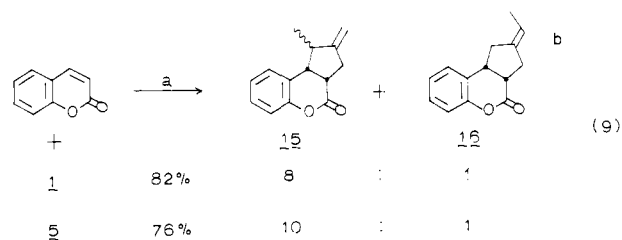
To illustrate that the regioselectivity is not an artifact of the structure of the TMM precursor, the isomeric precursor **5** was also reacted with cyclopentenone and gave the same results as did **1**. However, initially, the two different precursors produce two different TMM complexes, **10** and **12**. Reaction of dimethyl malonate with **5** leads only to **11**<sup>5</sup> (reaction 7), whereas, a similar



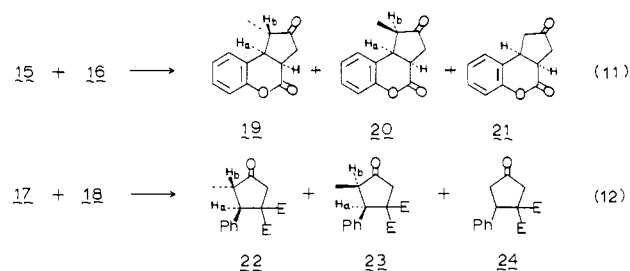
(a) catalytic  $(\text{Ph}_3\text{P})_4\text{Pd}$ , THF, reflux

reaction of **1** leads only to **13**<sup>5</sup> and **14**<sup>5</sup> (reaction 8). Thus, protonation of the TMM complexes is faster than equilibration.<sup>1b</sup> On the other hand, equilibration of **10** and **12** is faster than cycloaddition. Equally important, the site of protonation supports the interpretation that C(4) in both **10** and **12** is the most electron-rich carbon.

Extension of these observations to other traps confirms their generality. Coumarin (reaction 9) and dimethyl benzylidene-malonate (reaction 10) produce selectively the isomers **15**<sup>5</sup> and **17**<sup>5</sup>, respectively, in which reaction is initiated by the carbon of the complex bearing the methyl group regardless of the Me-TMM precursor.<sup>15</sup> The ratio of the stereoisomeric mixture of **15** (stereoisomers, 1.5:1) to **16** was determined by integration of the methyl doublets in 270-MHz NMR spectrum (**15**,  $\delta$  1.16 and 0.67; **16**,  $\delta$  1.56) and confirmed by ozonolysis (MeOH,  $\text{CH}_2\text{Cl}_2$ ,  $-78\text{ }^\circ\text{C}$ ) to **19**–**21** (reaction 11). Equilibration (DBU, THF, room



(a) catalytic  $(\text{Ph}_3\text{P})_4\text{Pd}$ , catalytic  $\text{Ph}_3\text{P}$ , THF, reflux; (b) only one isomer detected, although exact stereochemical assignment is uncertain



$\text{E} = \text{CO}_2\text{Me}$

temperature) converts the stereoisomeric mixture of **19** and **20** to essentially one isomer, **19**.<sup>5</sup> The presence of **21** as a very minor product was confirmed by comparison of the 270-MHz NMR spectrum of the mixture with an authentic sample of **21**.<sup>5,16</sup> and TLC. Similarly, the ratio of the stereoisomeric mixture of **17**<sup>5</sup> (stereoisomers 1.4:1) to **18**<sup>5</sup> was determined by integration of the olefinic signals in the 270-MHz NMR spectrum (**17**,  $\delta$  5.0 and 4.86; **18**,  $\delta$  5.44) and confirmed by ozonolysis (MeOH,  $\text{CH}_2\text{Cl}_2$ ,  $-78\text{ }^\circ\text{C}$ ) to **22**,<sup>5</sup> **23**, and **24**<sup>5</sup> (reaction 12), which, upon equilibration (NaOMe, MeOH, room temperature) of **22** and **23**, produces predominantly **22**. In this case too, the minor product **24**.<sup>5,17</sup> was compared to an authentic sample. NMR analysis confirms the regiochemistry of **19** and **22** [**19**,  $\text{H}_a$   $\delta$  3.13, dd,  $J = 12.5, 7.6$  Hz;  $\text{H}_b$   $\delta$  2.08, dq,  $J = 12.5, 6.6$  Hz. **22**,  $\text{H}_a$   $\delta$  3.76, d,  $J = 13$  Hz;  $\text{H}_b$   $\delta$  2.94, dq,  $J = 13, 7$  Hz].

The degree of regioselectivity depends upon the nature of the catalyst. For example, switching to  $(\text{dpep})_2\text{Pd}$  as the catalyst for the reaction in reaction 10 diminishes the ratio of **17** to **18** from 6.7 to 1.0. Further discussion of this point is deferred. The results reported herein clearly indicate that substituted as well as the parent TMM complexes are useful synthetic intermediates. This cycloaddition-like method becomes a regiocontrolled synthesis of substituted cyclopentenes and cyclopentanones in addition to methylenecyclopentanes. Most astonishing is the degree and the nature of the regioselectivity.<sup>18</sup> While intuition might have led to the prediction that products should have derived from **26** (EDG = electron-donating group), the simplest interpretation of the observations implies the products derive from **25**.<sup>19</sup> Because of

(16) An authentic sample of **21** was prepared by ozonolysis of the adduct derived from coumarin and the parent TMM system. See ref 1.

(17) An authentic sample of **24** was prepared by ozonolysis of the adduct derived from dimethyl benzylidene-malonate and the parent TMM system. See ref 1.

(18) The results reported herein may be contrasted to the codimerization of 2-(methylmethylene)cyclopropane with dimethyl maleate. Germer, A. Ph.D. Thesis, Ruhr-Universität, Bochum, West Germany. We thank Professor P. Binger for a copy of this thesis.

(14) Kon, K.; Ise, S. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu*, 23rd 1980, 49.

(15) In the case of dimethyl benzylidene-malonate, the difference in ratio of products from the two separate precursors may reflect incomplete equilibration relative to cycloaddition.



such an extraordinary suggestion, detailed MO calculations on such complexes and on those possessing an electron-withdrawing group on the TMM were performed and are reported in the accompanying manuscript.<sup>20</sup> Nevertheless, the remarkable regioselectivity demonstrates the extraordinary control by transition metals in changing the rules of selectivity and reactivity of organic molecules.<sup>21</sup>

**Acknowledgment.** We thank the National Science Foundation and the National Institutes of Health for their generous support of our programs. We also extend our gratitude for generous supplies of palladium salts to Johnson Matthey and Co. and Englehard Industries. D.M.T.C. acknowledges the receipt of a Standard Oil of Ohio fellowship. Professor Isoe graciously provided comparison spectra for compound 8.

**Supplementary Material Available:** Spectral data for both stereoisomers of 6, 7, 19, 21, 22, and 24 (3 pages). Ordering information is given on any current masthead page.

(19) The question of mechanism is clouded by the relative reactivity of 25 vs. 26 and the nature of the bond forming steps. From the protonation results reported herein and our previous studies,<sup>1</sup> this interpretation represents a reasonable working hypothesis.

(20) Gordon, D.; Nanninga, T.; Fenske, R. F.; Trost, B. M. *J. Am. Chem. Soc.*, following paper in this issue.

(21) Trost, B. M. *Acc. Chem. Res.* 1980, 13, 385.

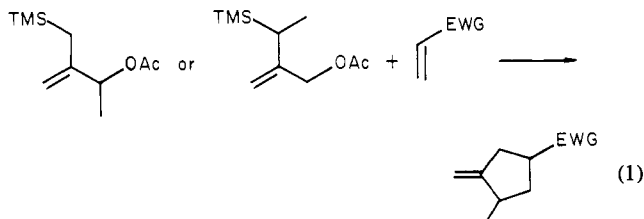
### A Molecular Orbital Study of Substituted Trimethylenemethane-Bis(phosphine)palladium Complexes

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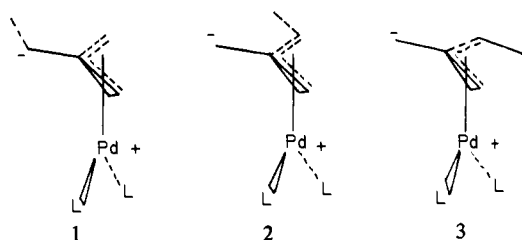
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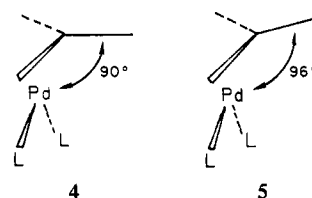
The chemistry of substituted trimethylenemethane-metal complexes remains almost unexplored from both an experimental and a theoretical point of view. In the preceding paper, a most striking regiochemistry in the cycloaddition reaction was observed for the methyl substituted derivative of  $\eta^3$ -trimethylenemethane-bis(triphenylphosphine)palladium (reaction 1). If one



considers possible rationales for this most unexpected observation, the question of the relative stabilities of the three isomers of this complex 1-3 arises. While intuitively one might think that 2 or 3 would be more stable since they place the electron-releasing substituent on the least electron-rich carbon, the product would most easily be rationalized to arise from 1. In this communication, this question as well as the question of the effect of electron-withdrawing groups is probed—a study which reveals the extraordinary level of control exerted by the transition metal.



Albright<sup>1</sup> has recently undertaken a theoretical investigation of the most stable geometry of  $d^{10}$  trimethylenemethane-metal bis(phosphine) complexes, and concluded that the preferred structure is 4, in which the trimethylenemethane (TMM) is coordinated to the metal in an allylic fashion. We have previously



reported results of Fenske-Hall calculations, a nonparametrized approximate molecular orbital method,<sup>2</sup> on TMM-Pd(PH<sub>3</sub>)<sub>2</sub>,<sup>3</sup> using structure 5 where the dihedral angle between the P-Pd-P and TMM planes is not 90° as in 4, but 96°, chosen by analogy to known  $\pi$ -allyl complexes.<sup>4,5</sup> Since it appeared that Albright failed to consider a geometry of type 5, we undertook a systematic reinvestigation of the preferred geometry for TMM-Pd(PH<sub>3</sub>)<sub>2</sub> using the Fenske-Hall method. The results of our calculations do indeed lead us to predict that 5 is more stable than 4.

We have performed molecular orbital calculations on methyl substituted trimethylenemethane complexes 1-3 using the tipped geometry calculated to be the most stable. Figure 1 presents molecular orbital diagrams for these three isomers. The highest occupied molecular orbital (HOMO) is indicated by two arrows representing a pair of electrons. The symmetry labels for the metal fragment basis orbitals in the left column are taken from the  $C_{2v}$  point group, while those of the Me-TMM fragment orbitals in the right column are from the  $D_{3h}$  symmetry of the unsubstituted trimethylenemethane.<sup>6</sup> The orbitals involved in the metal-trimethylenemethane bonding level are the 4b<sub>2</sub> on the metal (composed of a combination of palladium 4d and 5p orbitals pointing toward the end carbons in the allylic portion of the TMM) and an appropriate combination of  $1e_{g'}$  and  $1e_{g''}$  on the Me-TMM which is localized on those end carbons. The 2a<sub>2</sub>, 2b<sub>1</sub>, 4a<sub>1</sub>, and

(1) Albright, T. A. *J. Organomet. Chem.* 1980, 198, 159-168.

(2) Hall, M. B.; Fenske, R. F. *Inorg. Chem.* 1972, 11, 768-775.

(3) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* 1980, 102, 6359-6361.

(4) (a) Smith, A. E. *Acta Crystallogr.* 1965, 18, 331-340. (b) Oberhansli, W. F.; Dahl, L. F. *J. Organomet. Chem.* 1965, 3, 43-54. (c) Mason, R.; Wheeler, A. G. *J. Chem. Soc. A* 1968, 2543-2549, 2549-2554. (d) Kuli-Zade, T. S.; Kukina, G. A.; Poraj-Košic, M. A. *Z. Strukt. Khim.* 1969, 10, 149-151 (*J. Struct. Chem.* 1969, 10, 141-143). (e) Broadbent, T. A.; Pringle, G. E. *J. Inorg. Nucl. Chem.* 1971, 33, 2009-2014. (f) Mason, R.; Whimp, P. O. *J. Chem. Soc. A* 1969, 2709-2717. (g) Hendriks, P.; Olie, K.; Vrieze, K. *Cryst. Struct. Commun.* 1975, 4, 611-616.

(5) The possibility that the dihedral angle in the TMM-Pd(PH<sub>3</sub>)<sub>2</sub> complex should be different from 90° was suggested by the dihedral angles in ref 4. The value of 96° used in the present calculations is not the result of a rigorous geometry optimization, but rather it comes from the geometric constraints of a planar TMM, fixed Pd-C bond distances, and the PdL<sub>2</sub> unit being situated very near the axis formed by the two methylene carbons. We have performed other calculations on TMM-Pd(PH<sub>3</sub>)<sub>2</sub> in which the Pd-C bond distances were fixed, but the dihedral angle was as large as 110° and the PdL<sub>2</sub> unit was much closer to the central carbon than to the line connecting the methylene carbons. The geometry used in the calculations presented here was the lowest in energy of all of those considered and the geometry in which the dihedral angle was 90° was the highest in energy.

(6) The energies of the metal and Me-TMM fragment orbitals before mixing are not identical in Figure 1a-c because these values reflect the energies of the orbitals in the changing molecular environment, as derived from the diagonal elements of the approximate Fock matrix.