are nonnucleophilic, the dimethyl compound I-OBs is faster. This observation is nicely in accord with the conclusion that in the dimethyl compound, internal return is faster than rearrangement.

The near constancy of the rate ratios of I-OBs to pinacolyl brosylate is also consistent with our mechanism. In both systems solvent is not involved nucleophilically before or during the rate-determining step (k_4 or k_{5s}), and therefore, the relative rates should not change with variation in solvent nucleophilicity. The rates are affected primarily by changes in the ionizing strength of the solvent and to nearly the same extent because of the similarities in charge separation in the two rate-determining transition states. For pinacolyl sulfonates, the rate-determining step is simple ionization to the tight ion pair and the transition state resembles the ion pair. In the case of 2,2-dimethylcyclopentyl brosylate, the rate-determining step is the exothermic rearrangement of the secondary to the tertiary cation, and according to the Hammond postulate, this transition state should also resemble the ion pair.

Experimental Section

Spectra. ^2H NMR spectra were recorded by using a Varian 220 spectrophotometer operating at 33.8 MHz. Chemical shifts were determined relative to tetramethylsilane-d_{12}. All solutions were approximately 0.1 M in the deuterated compound studied, and solutions were buffered with an equivalent of 2,6-lutidine. Chemical shifts were as follows: 3,3-dimethyl-2-deuteriocyclopentene (5.85 ppm), 2,3-dimethyl-3-deuteriocyclopentene (2.74 ppm), and 2,3-dimethyl-2-deuteriocyclopentanol (1.95 ppm). 1,2-Dimethylcyclopentene was determined from the amount of O-deuterated solvent (5.35 ppm).

2,2-Dimethylcyclopentyl *p*-Bromobenzenesulfonate (I). 2,2-Dimethylcyclopentanol was prepared by using the procedure of Wilcox and Mesirov.[9] The corresponding brosylate was prepared by using the Tipson procedure,[24] mp 48-50 °C.

Deuterated 2,2-Dimethylcyclopentanols. 1-Deuterio-2,2-dimethylcyclopentanol was prepared by treating 1.8 g of 2,2-dimethylcyclopentanone with 0.7 g of lithium aluminum deuteride. 5,5-Dideuterio-2,2-dimethylcyclopentanol was prepared by lithium aluminum hydride reduction of the corresponding ketone. 5,5-Dideuterio-2,2-dimethylcyclopentanone was prepared from the exchange reaction of 2,2-dimethylcyclopentanone and D_2O in the presence of anhydrous K_2CO_3. The exchange reaction was repeated 5 times.

Kinetic Measurements. Rate measurements were made by using a Cary 118A spectrophotometer. The reactions were carried out in stoppered 1-cm^2 quartz cells in a specially constructed, thermostated, brass block holder. The procedure and technique have been described previously.[16]

Acknowledgment. This material is based upon work supported by the National Science Foundation under Grant CHE 79-10015. M.A.I. also wishes to acknowledge The Robert A. Welch Foundation (Grant AD-506) for financial support.

Registry No. D_2, 7782-39-0; 2,2-dimethylcyclopentyl *p*-bromobenzenesulfonate, 94844-04-9; 2,2-dimethylcyclopentanol, 37617-33-7; 1-deuterio-2,2-dimethylcyclopentanol, 94844-05-0; 2,2-dimethylcyclopentanone, 4541-32-6; 5,5-dideuterio-2,2-dimethylcyclopentanol, 94844-06-1; 5,5-dideuterio-2,2-dimethylcyclopentanone, 94844-07-2.

Intramolecular Carbopalladation of Allylic Amines and Sulfides

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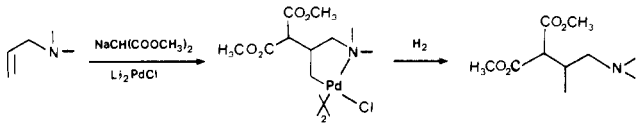
Contribution from the Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061. *Received May 14, 1984*

Abstract: β-Malonyl allyl sulfides and amines have been found to cyclize in the presence of lithium tetrachloropalladate and base to regiospecifically and stereospecifically provide fused bicyclic palladocycles which are converted to cyclopentanes upon hydrogenation. The cyclization may be extended to generate six- and seven-membered rings in high yield. Cyclization to provide cyclic ketones also occurs in high yield.

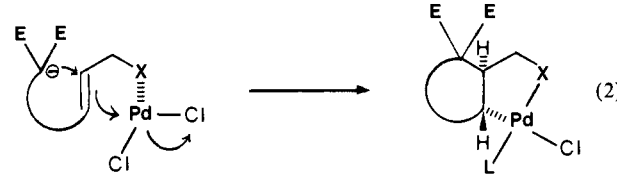
We have previously reported that allylic[1] and homoallylic[2] amines and sulfides undergo regiospecific carbopalladation in the presence of stabilized enolates and lithium tetrachloropalladate (LTP) to provide stable five-membered palladocyles (eq 1). The



(1)

palladium atom in these palladocycles may subsequently be replaced by carboxylate[3] (CO, CH_3OH), by hydrogen[1] (H_2, $NaBH_4$, or $NaBH_3CN$), or by a substituted vinyl group[4] (MVK, Et_3N). We have demonstrated that the carbopalladation process occurs in a stereospecific manner, introducing malonate and palladium in a trans fashion across the unsaturated linkage.[5,6]

We expected the intramolecular version of the carbopalladation reaction to provide a new method for the regiospecific construction of carbocyclic structures with concomitant stereochemical control at at least two contiguous carbon centers.[7] For example, allylic amines or sulfides should cyclize to provide bicyclic intermediates in which the ring juncture stereochemistry is governed by the stereochemistry of the allylic double bond (eq 2). We report



(2)

herein the successful realization of this objective, providing new methodology for the generation of carbocyclic compounds from acyclic allylic sulfides and amines.

The initial phase of this study required a variety of substrates encompassing both cis and trans allylic amines and sulfides potentially capable of cyclizing to provide carbocycles of several different sizes. For this purpose cis substrates **4a-g** and trans substrates **9a-f** (Scheme I) were prepared by using standard methodology. Preparation of these substrates was generally straightforward and, with one exception, requires no further comment.

We were fortunate to find that *cis*-olefins **7a** and **7b** (readily available by hydrogenation of **1a** and **1b**) served as convenient precursors of trans substrates **9a-f**. Conversion of **7a** or **7b** to the mesylate or dimesylate followed by treatment with excess sodium iodide led to formation of a ca. 3:1 equilibrium mixture

(1) Holton, R. A.; Kjonaas, R. A. *J. Am. Chem. Soc.* **1977**, *99*, 4177.
(2) Holton, R. A.; Kjonaas, R. A. *J. Organometal. Chem.* **1977**, *142*, C15.
(3) Kjonaas, R. A. Ph.D. Dissertation, Purdue University, 1978.
(4) Holton, R. A.; Kjonaas, R. A. *J. Organometal. Chem.* **1977**, *133*, C5.
(5) Holton, R. A. *J. Am. Chem. Soc.* **1977**, *99*, 8083. Also see: Kurosawa, H.; Asada, N. *Tetrahedron Lett.* **1979**, 255.
(6) For reviews, see: (a) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615. (b) Trost, B. M. *Pure Appl. Chem.* **1979**, *51*, 787. (c) Isuji, J. "Organic Synthesis with Palladium Compounds"; Springer-Verlag: New York, 1980. (d) Hegedus, L. S. *Tetrahedron* **1984**, *40*, 2415.
(7) A few examples of intramolecular palladium-promoted addition of nucleophiles to isolated olefins have been published. See: (a) Hayashi, T.; Hegedus, L. S. *J. Am. Chem. Soc.* **1977**, *99*, 7093. (b) Hegedus, L. S.; Allen, G. F.; Bozell, J. J.; Waterman, E. L. *Ibid.* **1978**, *100*, 5800.

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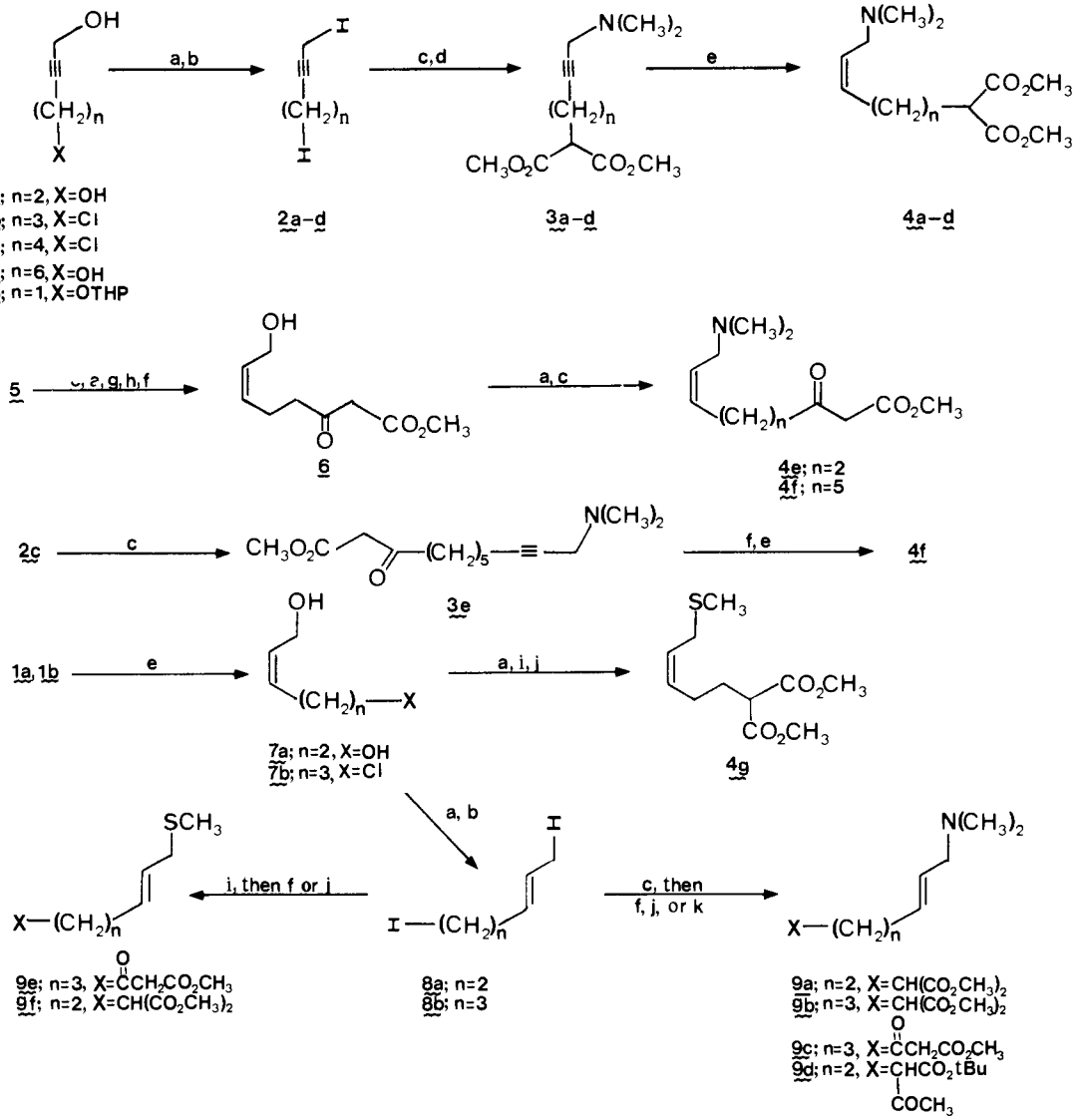
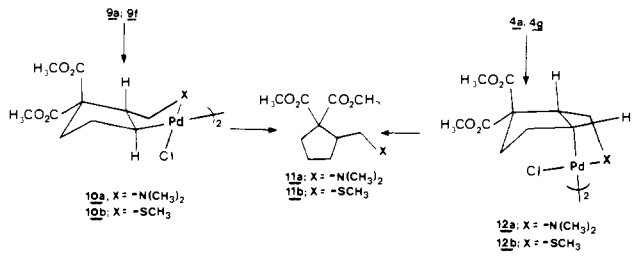
Scheme I. Preparation of Allylic Amines and Sulfides



(a) MsCl, Et_3N, THF, 0 °C; (b) NaI (4.0 equiv), acetone, reflux; (c) $HNMe_2$ (2.0 equiv), THF, 0 °C, (d) $NaCH(CO_2Me)_2$ (3.0 equiv), HMPA-THF, 25 °C; (e) 5% $Pd/BaSO_4$, H_2, MeOH; (f) Na,Li[$CH_2COCHCO_2Me$], THF, 0 °C; (g) NaI (1.0 equiv), THF, 25 °C, 20 min; (h) HCl, MeOH; (i) $NaSCH_3$ (1.0 equiv), 10% HMPA-THF, −78 °C → 0 °C; (j) $NaCH(CO_2CH_3)_2$ (4 equiv), NaI (0.1 equiv), HMPA-THF, 25 °C, 3 days; (k) $Na(CH_3COCHCO_2$-*t*-Bu)(3.0 equiv), HMPA-THF, 25 °C.

of trans/cis isomers of diiodide **8a** or **8b**.[8] The pure trans diiodide could, in each case, be obtained by low-temperature crystallization from the mixture in an ether–hexane solution. This procedure made available abundant quantities of **8a** and **8b**; we have found it to be vastly superior to other methodologies.[9]

Cyclization of the trans sulfide diester **9f**, via treatment of the sulfide with 1.0 mol equiv of LTP and 1.1 mol equiv of potassium *tert*-butoxide (KOtBU), gave rise to palladium complex **10b** after 15 h at 25 °C. The stereochemically homogeneous complex was



obtained in 53% yield after chromatography and is presumed to contain a trans ring fusion. When the cis sulfide diester **4g** was treated in a similar manner, a 65% yield of stereochemically pure palladocycle **12b** was obtained. Complex **12b** is believed to contain a cis ring fusion and exhibits spectral and chromatographic behavior different from that of complex **10b**.

Direct reduction of palladocycles **10b** and **12b** with sodium borohydride in methanol gave cyclic sulfide **11b** as the sole product in 71% yield from **9f** and 68% yield from **4g**. This is consistent with the structural assignments for stereoisomeric **10b** and **12b**.

The cyclizations of the amino diesters **9a** and **4a** proved to be considerably more facile. The palladocycles **10a** and **12a** were formed from **9a** and **4a** in 93% and 90% yields, respectively, in the presence of 1.0 mol equiv of LTP and 1.1 mol equiv of KOtBu at 0 °C for 0.5 h.

The kinetic difference between the cyclizations of sulfides and amines is noteworthy. Apparently the sulfide, being a stronger electron-donating ligand, reduces the charge on palladium, thus reducing the polarization of the olefin necessary to induce cyclization. This effect displays itself in both rate enhancement, when amine is used as ligand, and the much higher yields of aminopalladium complexes.

From the point of view of this study, the amines offered several other advantages. As with the sulfide diesters, direct reduction (hydrogenation) of complexes **10a** or **12a** yielded **11a** as the sole product in 95% and 93% yields, respectively. However, the

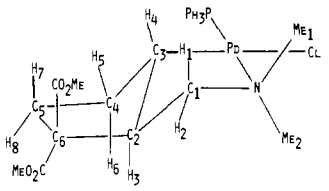
(8) The facile isomerization of allylic bromides and iodides is well-known; see, for example: de la Mare, P. B. D., de Mayo, P., Ed. "Molecular Rearrangements"; Wiley: New York, 1963, Part I; pp 27–110 and references cited therein.

(9) See, for example: Becher, J. *Acta Chem. Scand.* **1972**, *26*, 3627.

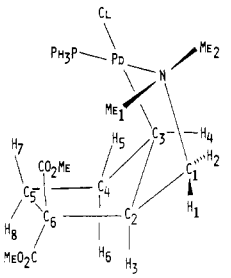
physical differences between the two complexes were much more pronounced. Complexes **10a** and **12a** exhibited distinctly different melting points, showed different chromatographic behavior, and were characterized by very different NMR spectra.

The ^{1}H NMR spectrum of palladocycle **10a** exhibits aminomethyl resonances as singlets at δ 2.73 and 2.80. Complex **12a** exhibits aminomethyl resonances at δ 2.39 and 2.88. The dramatic upfield shift of one nitrogen methyl resonance can be attributed to exceedingly strong shielding of the "endo" methyl group by the "endo" carbomethoxy group. The carbomethoxy proton resonances also differ significantly. The complex **10a** exhibits resonances at δ 3.66 and 3.73, whereas the palladocycle **12a** exhibits only a single methyl ester proton resonance at δ 3.80.

NMR assignments of the protons in complexes **10a** and **12a** depend upon comparison of the selectively decoupled ^{13}C NMR and ^{1}H NMR spectra. The complexity of the ^{13}C NMR spectra of complexes **10a** and **12a** made absolute assignments of the protons in these complexes impossible. However, when complexes **10a** and **12a** were converted to their corresponding triphenylphosphine derivatives, **10c** and **12c**, the ^{13}C NMR spectra were considerably simplified. Thus, comparison of the selectively decoupled ^{13}C NMR (50 MHz) and the proton ^{1}H NMR spectra (90, 200, 400, and 600 MHz) allowed the absolute assignment of protons in complexes **10c** and **12c** (Table I, Experimental Section). The 400-MHz ^{1}H NMR spectrum of palladocycle **10c** exhibits an 11.5-Hz coupling constant for the ring fusion hydrogens (H_3 and H_4 in Table I). Models indicate that these hydrogens are nearly antiperiplanar and, therefore, the 11.5-Hz coupling constant is consistent with a trans ring juncture.



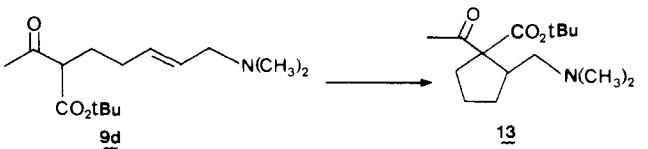
10c



12c

The 400-MHz ^{1}H NMR spectrum of palladocycle **12c** exhibits a 6-Hz coupling constant for the ring fusion hydrogens (H_3 and H_4 in Table I). This coupling constant is consistent with the ca. 40° dihedral angle estimated from models of palladocycle **12c**. The ^{1}H NMR spectrum of palladocycle **12c** also exhibits a 2-Hz coupling constant for the four-bond coupling between H_2 and H_4. This four-bond coupling constant is consistent with a cis fused ring juncture. The foregoing NMR studies firmly establish the stereoselectivity of these processes. The ^{1}H NMR spectra of palladocycles **10c** and **12c** can only be consistent with a trans addition of palladium and the carbon nucleophile to the olefin.

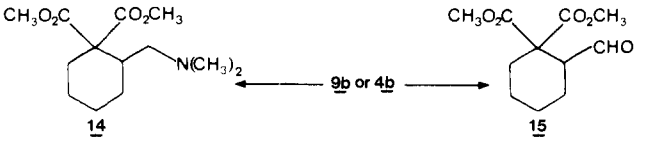
In the same manner as ring closures with diesters, exocyclic enolates could also be used to generate exocyclic ketones. Aminoketo ester **9d** gave cyclopentane **13** in 85% yield after direct reduction of the palladocycle with hydrogen.



9d **13**

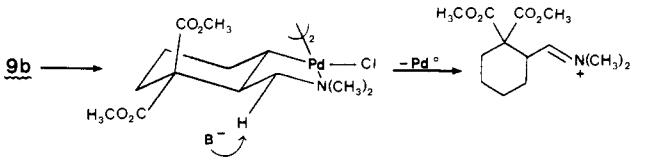
Cyclizations to produce larger ring systems also proceeded smoothly. However, the intermediate palladocycles proved too unstable to allow isolation. When trans amino diester **9b** was treated under the same reaction conditions employed in the cyclopentane ring closures and directly reduced with hydrogen gas, a ca. 3:1 mixture of amine **14** and aldehyde **15** was obtained.

Aldehyde **15** could arise from the iminum salt **17**, possibly formed by β-elimination of the intermediate palladium complex **16**. The iminium salt **17** could, subsequently, undergo either hydrogenation to give amine **14** or hydrolysis by adventitious water to give **15**.



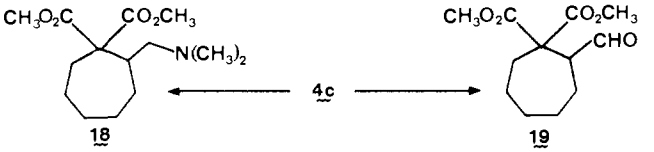
14 **15**

This hypothesis led to the development of conditions which yielded either cyclohexylamine **14** or cyclohexylaldehyde **15** exclusively. When 4-Å molecular sieves were added as a water scavenger prior to cyclization, direct reduction yielded only cyclohexylamine **14** in 91% yield. When the reaction mixture was warmed to 25 °C for 6 h and subsequently hydrolyzed with aqueous acetic acid, cyclohexylaldehyde **15** was obtained in 93% yield. The same sequence of events was repeated with the cis amino diester **4b**. Thus, cyclohexylamine **14** could be obtained from cis amino diester **4b** in 89% yield with molecular sieves, while cyclohexylaldehyde **15** could be obtained in 73% yield upon acetic acid hydrolysis.



16 **17**

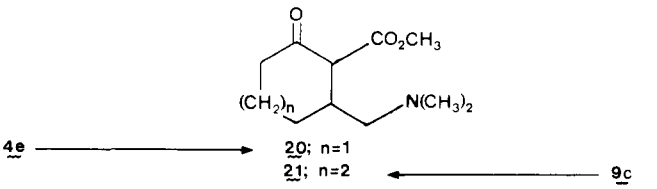
Seven-membered ring closures exhibited behavior which was analogous to the six-membered ring closures. In the absence of molecular sieves, a mixture of amine **18** and aldehyde **19** was obtained upon attempted cyclization of **4c**. Inclusion of molecular sieves in the reaction mixture allowed isolation of cycloheptylamine **18** in 71% yield, while acetic acid hydrolysis after 6 h at room temperature gave cycloheptylaldehyde **19** in 70% yield.



18 **19**

Although a rigorous kinetic study was not undertaken, the reactions to form five-, six-, and seven-membered rings with amine ligands were observed to proceed at distinctly different rates. The ring closures to form five-membered rings were found to be complete by gas chromatographic analysis in ca. 20 min at 0 °C, while the cyclohexyl rings were completely formed in ca. 30 min at 0 °C. The cycloheptyl systems were somewhat slower, requiring ca. 45 min to 1 h to reach completion at the same temperature.

To this point, only reactions in which an exocyclic enolate was employed have been discussed. Whereas the exocyclic enolates all cyclized smoothly, the endocyclic enolates proved somewhat more difficult to cyclize. When a solution of aminoketo ester **4e** in 1:1 methylene chloride/THF containing 1.0 equiv of LTP was treated with 1.1 equiv of KOtBu, a palladium complex could be observed to form (TLC analysis) over 1.5 h at room temperature. Reduction with hydrogen gas gave only a 35% yield of cyclohexanone **20**.



20; n=1
21; n=2

When aminoketo ester **9c** was cyclized under the same conditions, the reaction was cleaner (giving less side products), as fast, and gave a 65% yield of cycloheptanone **21**. However, allylic sulfide **9e** failed to undergo cyclization under these conditions. This is not surprising in view of the sluggishness with which both sulfides and endocyclic enolates undergo cyclization.

Attempts to extend these systems to medium-sized rings failed to proceed cleanly. The reactions of both **4d** and **4f** were exceedingly slow (1–2 weeks at 25 °C) and gave, upon hydrogenation, at lease nine products (TLC analysis).

We believe that these results demonstrate considerable potential

Table I. ^1H (400 MHz) and ^{13}C (50 MHz) NMR Assignments for Palladocycles **10c** and **12c**

	10C			**12C**		
		coupling constants ($J_{x,y}$)			coupling constants ($J_{x,y}$)	
atom no.	chemical shift (δ)	x, y	J, Hz	chemical shift (δ)	x, y	J, Hz
H_1	2.23	H_1, H_2	11.5	2.24	H_1, H_2	12
		H_1, H_3	11.5		H_1, H_3	14
H_2	2.60	H_2, H_3	4	2.72	H_2, H_3	6
		H_2, NCH_3	4		H_2, H_4	2
					H_2, NCH_3	2
H_3	2.55	H_3, H_4	11.5	3.41	H_3, H_4	6
H_4	2.16	H_4, H_5	4	1.90	H_4, H_5	10.5
		H_4, H_6	11.5		H_4, H_6	6
H_5	0.68	H_5, H_6	12	0.77	H_5, H_6	12
		H_5, H_7	8.5		H_5, H_7	8.5
		H_5, H_8	2.5		H_5, H_8	3.5
H_6	0.79	H_6, H_7	9.5	1.72	H_6, H_7	8.5
		H_6, H_8	10		H_6, H_8	12
H_7	2.07	H_7, H_8	12.5	2.07	H_7, H_8	12.5
H_8	1.72			1.72		
NCH_3	2.89			2.89		
	2.92			2.92		
CO_2CH_3	3.67			3.67		
	3.68			3.68		
C_1	63.1			65.3		
C_2	55.5			51.1		
C_3	46.0			48.6		
C_4	30.8			28.1		
C_5	33.7			31.9		
NCH_3	47.8			48.1		
	51.9			52.2		
OCH_3	52.3			52.6		
	52.6					
CO	171.5			171.1		
	172.7			172.6		

synthetic utility for cyclization via carbopalladation. We are currently investigating new methods for the replacement of σ-bound palladium by both carbon and heteroatomic moieties. Application of this methodology to the synthesis of natural products is also under way. The results of these endeavors will be reported in due course.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a Varian EM 390 spectrometer (90 MHz), a Bruker WP400 spectrometer (400 MHz, ^1H; 100 MHz, ^{13}C), or a Jeol FX200 spectrometer (200 MHz, ^1H; 50 MHz, ^{13}C). Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane as the internal standard.

Infrared spectra were recorded on a Perkin-Elmer 710B infrared spectrometer.

Mass spectra were run either on a Hitachi Perkin-Elmer RMU-7 mass spectrometer at 50 eV or on a Varian MAT 112 mass spectrometer at 70 eV.

Melting points were taken on a Bristol microscope equipped with a hot stage and are uncorrected.

Solvents, Reagents, and Chromatography. Tetrahydrofuran (THF) was stored under nitrogen at constant reflux over lithium aluminum hydride (LAH) in a recycling still. THF which had been added to the still was considered dry when 10 mL consumed no more than 50 μL of 1.6 M *n*-butyllithium at about 0 °C with triphenylmethane as an indicator. Hexamethylphosphoramide (HMPA) (Aldrich) was distilled at ca. 1 mmHg after being stirred overnight at ca. 100 °C over calcium hydride.

Acetone (Fisher) has dried by distillation from anhydrous potassium carbonate under nitrogen. All other solvents were obtained from Fisher Scientific and distilled prior to use.

Sodium hydride was purchased from Alfa Inorganics as a 50% oil dispersion and was washed with hexane in a frittred glass funnel immediately prior to use.

n-Butyllithium was purchased from Aldrich and titrated by addition to 10 mL of 10% HMPA–THF at −78 °C containing a trace of triphenylmethane as an indicator. *n*-Butyllithium was added until the solution turned red, ca. 5 mmol of an alcohol was then added and, finally, *n*-butyllithium was added until the red color reappeared.

Potassium *tert*-butoxide was obtained from Aldrich and sublimed at ca. 1 mmHg prior to use. Molecular sieves (4-Å) were obtained from Fisher Scientific and were predried at 170–200 °C at 1 mmHg for 24 h.

Plug filtration was performed with Silica Gel 60 (70–230 mesh, EM Reagents). Medium-pressure liquid chromatography (MPLC or flash chromatography) was performed by following the method of Still.[10]

Lithium Tetrachloropalladate. Lithium tetrachloropalladate (LTP) was prepared by the method of Cope and Friedrich.[11]

Diiodide 2a. General Procedure A. The preparation of diiodide **2a** is typical of the formation of diiodides from diols and chloroalcohols. To a solution of 6.583 g (65.8 mmol) of diol **1a**[9,12] in 200 mL of THF at 0 °C was added 19 mL (138 mmol) of triethylamine. To this mixture 10.2 mL (132 mmol) of methanesulfonyl chloride was added dropwise. The mixture was stirred for 0.5 h and then filtered, and the THF was evaporated. The residue was dissolved in 200 mL of dry acetone, and a solution of 10 g (66.6 mmol) of sodium iodide in 100 mL of dry acetone was added. The mixture was swirled for 10 min, filtered through celite, and washed with dry acetone. An additional 30 g (200 mmol) of sodium iodide in 300 mL of dry acetone was added, and the mixture was refluxed for 16 h. The mixture was filtered through celite and the acetone was evaporated. The crude diiodide was dissolved in ethyl ether. Partial evaporation of the ether and crystallization at −78 °C from 1:1 hexane/ethyl ether afforded 16.6 g (75%) of diiodide **2a**: ^1H NMR ($CDCl_3$) δ 2.67 (m, 2 H), 3.20 (t, 2 H, J = 7 Hz), 3.70 (t, 2 H, J = 2 Hz); IR ($CHCl_3$) 1140, 1170 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 320 (80), 193 (100), 66 (90).

Diiodide 2b. Following procedure A, with the exception that only half of the quantities of triethylamine and methanesulfonyl chloride were necessary, 15.7 g (0.118 mol) of chloroalcohol **1b**[13] was converted to 35.57 g (90%) of **2b** after trituration with hexane and subsequent crystallization at −78 °C from 1:2 ethyl ether/hexane: ^1H NMR ($CDCl_3$) δ 1.67–2.13 (m, 2 H), 2.17–2.43 (m, 2 H), 3.20 (t, 2 H, J = 7 Hz), 4.63 (t, 2 H, J = 2 Hz); IR ($CHCl_3$) 1140, 1170 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 334 (47), 207 (100), 80 (70).

Diiodide 2c. Following procedure A, with the exception that only half of the quantities of triethylamine and methanesulfonyl chloride were necessary, 10.1 g (68.9 mmol) of chloroalcohol **1c**[14] was converted to 20.2 g (84%) of diiodide **2c** after plug-filtration with hexane: ^1H NMR ($CDCl_3$) δ 1.33–2.07 (m, 4 H), 2.09–2.44 (m, 2 H), 3.20 (t, 2 H, J =

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7 Hz), 4.63 (t, 2 H, J = 2 Hz); IR ($CHCl_3$) 1140, 1170 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 348 (20), 221 (100), 94 (70), 80 (55).

Diiodide 2d. Following procedure A, 7.90 g (50.6 mmol) of diol **1d**[9,12] was converted to 12.58 g (66%) of diiodide **2d** after plug-filtration with hexane: ^1H NMR ($CDCl_3$) δ 1.37 (s br, 6 H), 1.57–1.97 (m, 2 H), 3.13 (t, 2 H, J = 6 Hz), 3.63 (t, 2 H, J = 2 Hz); IR ($CHCl_3$) 1140, 1170 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 376 (34), 249 (50), 122 (55), 94 (100).

Amino Diester 3a. General Procedure B. The preparation of amino diester **3a** is typical for the preparation of amino diesters from diiodides. To a solution of 14.42 g (45.1 mmol) of the diiodide **2a** in 200 mL of THF at 0 °C was added via syringe 5.7 mL (90.2 mmol) of chilled anhydrous dimethylamine. The mixture was stirred at 0 °C for 20 min and then filtered into a solution of sodium dimethylmalonate (prepared by adding 17.0 mL (148.8 mmol) of dimethyl malonate dropwise to a suspension of 3.25 g (135.3 mmol) of sodium hydride in 500 mL of THF). The volume of the solution was reduced to ca. 200 mL, and 20 mL of HMPA was added. Stirring was continued for 4 h at 25 °C, and the mixture was then partitioned between toluene and saturated aqueous sodium bicarbonate. The toluene layer was exhaustively extracted with water, dried over sodium sulfate, and concentrated to give a mixture of crude **3a** and dimethyl malonate. The mixture was heated in a Kugelrohr oven to 50 °C at 1 mmHg and distillate discarded. Kugelrohr distillation of the residue (95 °C at 1 mmHg) afforded 4.73 g (43%) of amino diester **3a**: ^1H NMR ($CDCl_3$) δ 2.04–2.51 (m, 4 H), 2.30 (s, 6 H), 3.17 (t, 2 H, J = 2 Hz), 3.63 (t, 1 H, J = 5 Hz), 3.77 (s, 6 H); IR ($CHCl_3$) 1730, 2770, 2810 cm^{-1}; mass spectrum (50 eV), m/e (rel intensity) 241 (3), 210 (6), 182 (11), 108 (28), 97 (100).

Anal. Calcd for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94; N, 5.81. Found: C, 59.69; H, 8.01; N, 5.93.

Amino Diester 3b. Following procedure B, 17.06 g (51.1 mmol) of diiodide **2b** was converted to 8.39 g (69%) of amino diester **3b** after Kugelrohr distillation (110 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.37–1.77 (m, 2 H), 1.83–2.13 (m, 2 H), 2.14–2.43 (m, 2 H), 2.27 (s, 6 H), 3.17 (t, 2 H, J = 2 Hz), 3.37 (t, 1 H, J = 7 Hz), 3.71 (s, 6 H); IR ($CHCl_3$) 1725, 2270, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 225 (5), 254 (20), 151 (100).

Anal. Calcd for $C_{13}H_{21}NO_4$: C, 61.16; H, 8.29; N, 5.49. Found: C, 61.02; H, 8.20; N, 5.59.

Amino Diester 3c. Following procedure B, 14.778 g (42.5 mmol) of diiodide **2c** was converted to 6.566 g (58%) of amino diester **3c** after Kugelrohr distillation (110 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.27 (s br, 2 H), 1.37–1.67 (m, 2 H), 1.77–2.10 (m, 2 H), 2.13–2.37 (m, 2 H), 2.27 (s, 6 H), 3.17 (t, 2 H, J = 2 Hz), 3.37 (t, 1 H, J = 7 Hz), 3.73 (s, 6 H); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 269 (10), 268 (30), 238 (40), 97 (100), calcd mass for $C_{14}H_{23}NO_4$ 269.161, found 269.162.

Amino Diester 3d. Following procedure B, 12.58 g (33.5 mmol) of diiodide **2d** was converted to 4.48 g (45%) of amino diester **3d** after Kugelrohr distillation (150 °C at 1 mm Hg): ^1H NMR ($CDCl_3$) δ 1.15–1.58 (m, 8 H), 1.70–1.95 (m, 2 H), 2.03–2.31 (m, 2 H), 2.26 (s, 6 H), 3.13 (t, 2 H, J = 2 Hz), 3.31 (t, 1 H, J = 7 Hz), 3.73 (s, 6 H); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 268 (70), 254 (53), 283 (74), 97 (100).

Anal. Calcd for $C_{16}H_{27}NO_4$: C, 64.62; H, 9.15; N, 4.71. Found: C, 64.98; H, 9.27; N, 4.72.

Aminoketo Ester 3e. General Procedure C. The preparation of aminoketo ester **3e** is typical of the preparation of aminoketo esters from diiodides. To a solution of 3.477 g (9.99 mmol) of diiodide **2c** in 50 mL of THF at 0 °C was added via syringe 1.32 mL (19.98 mmol) of chilled anhydrous dimethylamine. The solution was stirred for 20 min at 0 °C and then filtered under nitrogen through a dry, course fritted glass funnel into a THF solution of 1.5 equiv of methyl acetoacetate dianion (prepared from 1.74 g (14.98 mmol) of methyl acetoacetate according to the procedure of Weiler[15]). The reaction mixture was stirred at 0 °C for 1 h and then partitioned between chloroform and saturated aqueous sodium bicarbonate. (If the aqueous layer was basic, 1 M acetic acid was added to adjust the pH to 7–8.) The chloroform layer was dried over sodium sulfate, filtered, and concentrated to give 1.693 g (67%) of spectroscopically homogeneous aminoketo ester **3e** which was used in the next reaction without further purification: ^1H NMR ($CDCl_3$) δ 1.27–1.87 (m, 6 H), 2.10–2.40 (m, 2 H), 2.24 (s, 6 H), 2.53 (t, 2 H, J = 6 Hz) 3.13 (t, 2 H, J = 2 Hz), 3.41 (s, 2 H), 3.69 (s, 3 H); IR ($CHCl_3$) 1710, 1740, 2770, 2810 cm^{-1}.

Amino Diester 4a. General Procedure D. The preparation of olefinic amino diester **4a** is typical of the partial hydrogenation of acetylenes to give olefins. Hydrogen was introduced into a solution of 4.34 g (18.0 mmol) of amino diester **3a** in 75 mL of methanol containing 0.4 g of 5% palladium on barium sulfate. Hydrogen uptake was monitored via a gas buret. After 1.0 mol equiv (405 mL) of hydrogen was consumed, increments of 0.1 mol equiv (40 mL) of hydrogen were allowed to enter the vessel until the reaction was complete by gas chromatographic analysis. The catalyst was filtered off by filtration through celite to give an orange solution. The methanol was evaporated, and the residue was dissolved in ethyl ether. Refiltration and solvent removal gave crude amino diester **4a**. Kugelrohr distillation (95 °C at 1 mmHg) afforded 3.42 g (78%) of amino diester **4a**: ^1H NMR ($CDCl_3$) δ 1.79–2.39 (m, 4 H), 2.20 (s, 6 H), 2.87 (d, 2 H, J = 6 Hz), 3.37 (t, 1 H, J = 7 Hz), 3.75 (s, 6 H), 5.37–5.60 (m, 2 H); IR ($CHCl_3$) 1730, 2770, 2810 cm^{-1}; mass spectrum (50 eV), m/e (rel intensity) 243 (10), 212 (19) 112 (22), 98 (22), 84 (100).

Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.15; H, 8.85; N, 5.82.

Amino Diester 4b. Following procedure D, 7.270 g (28.51 mmol) of amino diester **3b** was converted to 6.724 g (92%) of amino diester **4b** after Kugelrohr distillation (110 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.17–2.57 (m, 8 H), 2.23 (s, 6 H), 2.90 (d, 2 H, J = 6 Hz), 3.37 (t, 1 H, J = 7 Hz), 3.73 (s, 6 H), 5.50 (t, 2 H, J = 5 Hz); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (60 eV), m/e (rel intensity) 257 (13), 126 (23), 99 (12), 59 (100).

Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.45; H, 9.33; N, 5.23.

Amino Diester 4c. Following procedure D, 4.743 g (17.63 mmol) of amino diester **3c** was converted to 4.543 g (95%) of amino diester **4c** after Kugelrohr distillation (110 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.25–1.45 (m, 4 H), 1.73–2.27 (m, 4 H), 2.23 (s, 6 H), 2.90 (d, 2 H, J = 6 Hz), 3.34 (t, 1 H, J = 7 Hz), 3.74 (s, 6 H), 5.40–5.47 (t, 2 H, J = 6 Hz); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 271 (30), 270 (25), 240 (80), 85 (60), 58 (100).

Anal. Calcd for $C_{14}H_{25}NO_4$: C, 61.97; H, 9.29; N, 5.16. Found: C, 62.00; H, 9.34; N, 5.09.

Amino Diester 4d. Following procedure D, 3.928 g (13.23 mmol) of amino diester **3d** was converted to 2.974 g (75%) of amino diester **4d** after MPLC (0.5% NH_3(aq)/4.5% MeOH/$CHCl_3$) and subsequent Kugelrohr distillation (120 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.32 (s br, 10 H) 1.77–2.20 (m, 4 H), 2.23 (s, 6 H), 2.91 (d, 2 H, J = 6 Hz), 3.33 (t, 1 H, J = 7 Hz), 3.74 (s, 6 H), 5.40–5.60 (m, 2 H); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 299 (65), 298 (30), 85 (93), 58 (100).

Anal. Calcd for $C_{16}H_{29}NO_4$: C, 64.19; H, 9.76; N, 4.68.

Found: C, 64.07; H, 10.02; N, 4.87.

Aminoketo Ester 4e. To a solution of 1.009 g (5.42 mmol) of hydroxyketo ester **6** in 50 mL of THF at 0 °C was added 0.94 mL (6.7 mmol) of triethylamine followed by dropwise addition of 0.50 mL (6.5 mmol) of methanesulfonyl chloride. The mixture was stirred for 0.5 h and filtered. To the filtrate was added 7.2 mL (109 mmol) of chilled anhydrous dimethylamine. The mixture was stirred overnight, filtered, and concentrated to give 1.225 g of crude aminoketo ester **4e**. Preparative thin-layer chromatography (0.7% NH_3(aq)/6.3% MeOH/$CHCl_3$) afforded 0.520 g (45%) of aminoketo ester **4e**: ^1H NMR ($CDCl_3$) δ 2.10–2.70 (m, 4 H), 2.23 (s, 6 H), 2.93 (d, 2 H, J = 6 Hz), 3.62 (s, 2.25 H), 3.73 (s, 0.75 H), 4.55 (s, 0.75 H), 5.45–5.67 (m, 2 H); IR ($CHCl_3$) 1610 (s), 1660 (s), 1715 (w), 1735 (w), 2770, 2810, 3325, 3580 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 213 (3), 136 (13), 97 (100) calcd for $C_{11}H_{19}NO_3$ 213.139, found 213.139.

Aminoketo Ester 4f. Following procedure D, 1.693 g (6.683 mmol) of aminoketo ester **3e** was converted to 0.900 g (53%) of aminoketo ester **4f** after MPLC with 0.6% NH_3(aq)/5.4% MeOH/$CHCl_3$: ^1H NMR ($CDCl_3$) δ 1.17–1.80 (m, 6 H), 1.90–2.13 (m, 2 H), 2.22 (s, 6 H), 3.46 (t, 2 H, J = 7 Hz), 2.91 (d, 2 H, J = 6 Hz), 3.40 (s, 2 H), 3.70 (s, 3 H) 5.39–5.53 (m, 2 H); IR ($CHCl_3$) 1710, 1745, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 255 (11), 234 (19), 98 (33), 84 (61), 58 (100), calcd for $C_{14}H_{25}NO_3$ 255.182, found 255.185.

Sulfide Diester 4g. To a solution of 4.058 g (39.7 mmol) of diol **7a** in 200 mL of THF at 0 °C was added 11.6 mL (83.4) mmol of triethylamine. To this mixture 6.15 mL (79.4 mmol) of methanesulfonyl chloride was added dropwise. The mixture was stirred 0.5 h and then filtered. To the filtrate was added 20 mL of HMPA followed by 2.78 g (39.7 mmol) of powdered sodium methylmercaptide. Stirring was continued for 30 h, and the mixture was added to a solution of sodium dimethylmalonate in THF (prepared by adding 20 mL (175 mmol) of dimethyl malonate dropwise to a suspension of 3.81 g of NaH (159 mmol) in 600 mL of THF). The volume of the solution was reduced to approximately 300 mL, and 0.60 g (4.0 mmol) of sodium iodide was added. The solution was stirred at 25 °C for 3 days and partitioned between toluene and saturated sodium bicarbonate. The toluene layer was dried over sodium sulfate and concentrated to give crude sulfide diester **4g**. MPLC with 25% ethyl ether/hexane afforded 2.933 g (30%) of sulfide diester **4g**: ^1H NMR ($CDCl_3$) δ 2.03 (s, 7 H), 3.10 (d, 2 H,

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J = 7 Hz), 3.38 (t, 1 H, J = 7 Hz), 3.76 (s, 6 H), 5.50 (m, 2 H); IR ($CHCl_3$) 1725 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 246 (56), 198 (92), 138 (55), 80 (83), 68 (100).

Anal. Calcd for $C_{11}H_{18}O_4S$: C, 53.64; H, 7.37. Found: C, 53.59; H, 7.30.

Hydroxyketo Ester 6. Following procedure D, 7.913 g (46.5 mmol) of tetrahydropyranyl alcohol **5**[16] was converted to 6.162 g (77%) of the corresponding *cis*-tetrahydropyranyl alcohol[17] after Kugelrohr distillation (125 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.20–1.97 (m, 6 H), 2.87 (s br, 1 H), 3.33–4.10 (m, 2 H), 4.17 (d, 4 H, J = 6 Hz), 4.63 (s, 1 H), 5.72 (d of t, J = 6, 10 Hz); IR ($CHCl_3$) 3400 (b), 3575 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 171 (7), 155 (96), 101 (43), 85 (100).

Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.51; H, 9.38.

To a solution of 4.563 g (26.5 mmol) of the *cis*-tetrahydropyranyl alcohol in 100 mL of THF at 0 °C was added 3.87 mL (27.8 mmol) of triethylamine followed by dropwise addition of 2.05 mL (26.5 mmol) of methanesulfonyl chloride. Stirring was continued for 0.5 h, and the mixture was then filtered. The filtrate was added to a solution of 4.37 g (29.1 mmol) of *freshly recrystallized* (from methanol) sodium iodide in 500 mL of THF. The mixture was stirred for 20 min at 25 °C, filtered, and concentrated to give a crude *cis*-allylic iodide intermediate which was used *immediately*.

The crude iodide was dissolved in 50 mL of THF and added to a THF solution of 1.5 mol equiv of methyl acetoacetate dianion (prepared from 3.38 g (29.1 mmol) of methyl acetoacetate by the method of Weiler[15]). After stirring at 0 °C for 30 min, the solution was partitioned between ethyl ether and sodium bicarbonate. The ether layer was dried over sodium sulfate and concentrated. MPLC with 1:1 ethyl ether/hexane afforded 5.763 g (80%) of tetrahydropyranyl keto ester: ^1H NMR ($CDCl_3$) δ 1.37–1.97 (m, 6 H), 2.20–2.51 (m, 2 H), 2.52–2.73 (m, 2 H), 3.37–4.00 (m, 2 H), 3.45 (s, 2 H), 3.83 (s, 3 H), 4.06–4.27 (m, 2 H), 4.60 (s, 1 H), 5.46–5.70 (m, 2 H); IR ($CHCl_3$) 1715, 1740 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 170 (20), 104 (100), 101 (30), 67 (75).

Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 62.09; H, 8.37.

To a solution of tetrahydropyranyl keto ester (4.274 g, 15.81 mmol) in 250 mL of methanol at 25 °C was added 2 drops of concentrated hydrochloric acid. The solution was stirred at 25 °C for 20 h and then excess solid sodium bicarbonate was added, and the methanol was evaporated. The crude product was dissolved in THF. Filtration and evaporation of the THF solution gave hydroxyketo ester **6** (2.211 g, 75%, after MPLC with ether): ^1H NMR ($CDCl_3$) δ 2.10–2.70 (m, 4 H), 3.18 (s, 1.33 H), 3.27 (s, 0.67 H), 3.43 (s, 1 H), 3.67 (s, 1 H), 3.72 (s, 2 H), 4.17 (d, 2 H, J = 6 Hz), 5.33–5.83 (m, 2 H); IR ($CHCl_3$) 1715, 1740, 3450 (b), 3600 cm^{-1} (s); mass spectrum (70 eV), m/e (rel intensity) 186 (4), 169 (40), 168 (50), 147 (100), 101 (88), calcd for $C_9H_{14}O_4$ 186.088, found 186.090.

***cis*-1,5-Pentenediol (7a).** In a manner similar to the procedure of Borch,[18] 28.1 g (0.281 mol) of alcohol **1a** was hydrogenated according to procedure F to afford 25.9 g (89%) of (*Z*)-1,5-pentenediol (**7a**)[18] after distillation.

Diiodide 8a. Following procedure A, 12.6 g (0.123 mol) of *cis*-1,5-pentenediol (**7a**) was converted to 23.8 g (60%) of diiodide **8a** after plug-filtration with hexane and crystallization from 3:1 hexane/ethyl ether at −78 °C: ^1H NMR ($CDCl_3$) δ 2.61 (m, 2 H), 3.27 (t, 2 H, J = 7 Hz), 3.91 (d, 2 H, J = 7 Hz), 5.61 (d of t, 1 H, J = 7, 16 Hz), 5.89 (d of t, 1 H, J = 7, 16 Hz); IR ($CHCl_3$) 1145, 960 cm^{-1}; mass spectrum (50 eV), m/e (rel intensity) 322 (1), 195 (100).

Diiodide 8b. Following procedure D, 20.0 g (0.151 mol) of chloro-alcohol **1b** was converted to 12.1 g (60%) of (*Z*)-1-hydroxy-6-chloro-2-pentene (**7b**)[13b] after distillation: bp 54–58 °C (1 mmHg); ^1H NMR ($CDCl_3$) δ 1.67–2.06 (m, 2 H), 2.13–2.47 (m, 2 H), 2.88 (s, 1 H), 3.56 (t, 2 H, J = 7 Hz), 4.23 (d, 2 H, J = 6 Hz), 5.47 (d of t, 1 H, J = 6, 10 Hz), 5.68 (d of t, 1 H, J = 6, 10 Hz); IR ($CHCl_3$) 3400 (b), 3580 cm^{-1} (s).

Anal. Calcd for $C_6H_{11}C_{10}$: C, 53.54; H, 8.24. Found: C, 53.41; H, 8.26.

Following procedure A, with the exception that only half of the quantities of triethylamine and methanesulfonyl chloride were required, 10.6 g (78.7 mmol) of (*Z*)-1-hydroxy-6-chloro-2-pentene (**7b**) was converted to 15.6 g (59%) of diiodide **8b** after plug-filtration and crystallization from 10% ether–hexane: ^1H NMR ($CDCl_3$) δ 1.89–2.33 (m, 4 H), 3.19 (t, 2 H, J = 7 Hz), 3.85 (d, 2 H, J = 7 Hz), 5.60 (d of t, 1 H, J = 7, 16 Hz), 5.85 (d of t, 1 H, J = 7, 16 Hz).

Amino Diester 9a. Following procedure B, 19.972 g (62.04 mmol) of diiodide **8a** was converted to 7.98 g (53%) of amino diester **9a** after Kugelrohr distillation (110 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.9–2.1 (m, 4 H), 2.21 (s, 6 H), 2.89 (d, J = 6 Hz), 3.38 (t, 1 H, J = 7 Hz), 3.74 (s, 6 H), 5.44–5.60 (m, 2 H); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 243 (40), 212 (43), 113 (20), 85 (100).

Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.25; H, 8.74; N, 5.92.

Amino Diester 9b. Following procedure B, 12.288 g (38.17 mmol) of diiodide **8b** was converted to 5.561 g (59%) of amino diester **9b** after Kugelrohr distillation (120 °C at 1 mmHg): ^1H NMR ($CDCl_3$) δ 1.16–1.53 (m, 2 H), 1.70–2.04 (m, 4 H), 2.14 (s, 6 H), 2.78 (d, 2 H, J = 6 Hz), 3.28 (t, 1 H, J = 7 Hz), 3.68 (s, 6 H), 5.38–5.53 (m, 2 H); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 257 (45), 226 (34), 99 (25), 85 (100).

Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.45; H, 9.03; N, 5.68.

Aminoketo Ester 9c. Following procedure C, 6.033 g (18.74 mmol) of diiodide **8a** was converted to 1.752 g (41%) of **9c** after MPLC with 0.7% NH_3(aq)/6.3% methanol/chloroform: ^1H NMR ($CDCl_3$) δ 1.53–1.87 (m, 2 H), 1.90–2.17 (m, 2 H), 2.22 (s, 6 H), 2.53 (t, 2 H, J = 7 Hz), 2.83 (d, 2 H, J = 6 Hz), 3.41 (s, 2 H), 3.72 (s, 3 H), 5.40–5.57 (m, 2 H); IR ($CHCl_3$) 1710, 1740, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 227 (45), 196 (5), 110 (20), 83 (100).

Anal. Calcd for $C_{12}H_{21}NO_3$: C, 63.41; H, 9.31; N, 6.16. Found: C, 63.82; H, 9.14; N, 6.09.

Aminoketo Ester 9d. Following procedure B, with the exception that *tert*-butyl acetoacetate was used in place of dimethyl malonate, 8.426 g (26.17 mmol) of diiodide **8a** was converted to 3.566 g (51%) of amino diester **9d** after MPLC with 0.5% NH_3(aq)/4.5% methanol/chloroform: ^1H NMR ($CDCl_3$) δ 1.48 (s, 9 H), 1.80–2.10 (m, 4 H), 2.19 (s, 9 H), 2.83 (d, 2 H, J = 6 Hz), 3.33 (t, 1 H, J = 7 Hz), 5.43–5.60 (m, 2 H); IR ($CHCl_3$) 1700, 1720, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 269 (66), 196 (30), 99 (52), 85 (100).

Anal. Calcd for $C_{15}H_{27}NO_3$: C, 55.74; H, 5.46; N, 2.17. Found: C, 55.66; H, 5.59; N, 2.11.

Sulfide Keto Ester 9e. To a solution of 19.23 g (59.7 mmol) of diiodide **8a** in 200 mL of 10% HMPA–THF at −78 °C was added 4.187 g (59.8 mmol) of solid sodium methylmercaptide. The solution was allowed to slowly warm to 25 °C and then recooled to −78 °C. To this mixture at −78 °C was added a solution of the dianion of methyl acetoacetate in THF (prepared from 7.63 g (65.7 mmol) of methyl acetoacetate by the method of Weiler[15]). The solution was allowed to slowly warm to 25 °C and was then partitioned between toluene and saturated aqueous sodium bicarbonate. The toluene layer was dried over sodium sulfate, filtered, and concentrated. The concentrate was heated in a Kugelrohr oven at 60 °C at 1 mmHg, and the distillate was discarded. The residue was purified by MPLC (20% ether–hexane) to afford 6.202 g (45%) of sulfide keto ester **9e**: ^1H NMR ($CDCl_3$) δ 1.56–1.90 (m, 2 H), 2.02 (s, 3 H), 2.00–2.23 (m, 2 H), 2.56 (t, 2 H, J = 7 Hz), 3.03 (d, 2 H, J = 6 Hz), 3.43 (s, 2 H), 3.73 (s, 3 H), 5.36–5.57 (m, 2 H); IR ($CHCl_3$) 1710, 1740 cm^{-1}, mass spectrum (70 eV), m/e (rel intensity) 212 (60), 183 (54), 151 (58), 109 (65), 82 (63), 68 (100).

Anal. Calcd for $C_{11}H_{18}O_3S$: C, 57.36; H, 7.88. Found: C, 57.29; H, 7.71.

Sulfide Diester 9f. To a solution of 3.428 g (10.65 mmol) of diiodide **8a** in 100 mL of 10% HMPA–THF at −78 °C was added 0.7462 g (10.65 mmol) of solid sodium methylmercaptide. The solution was slowly warmed to 0–10 °C. This solution was added to a THF solution of sodium dimethylmalonate (prepared by dropwise addition of 4.0 mL (350 mmol) of dimethyl malonate to a suspension of 0.767 g (32.0 mmol) of sodium hydride in 200 mL of THF). After stirring for 1 h at 25 °C, the mixture was partitioned between toluene and saturated aqueous sodium bicarbonate. The toluene layer was dried over sodium sulfate, filtered, and concentrated. The concentrate was heated in a Kugelrohr oven at 60 °C at 1 mmHg. The distillate was discarded and the residue purified by MPLC (20% ethyl ether/hexane) to afford 0.7903 g (31%) of sulfide diester **9f**: ^1H NMR ($CDCl_3$) δ 2.00 (s, 3 H), 2.07 (m, 4 H), 3.03 (d, 2 H, J = 6 Hz), 3.37 (t, 1 H, J = 7 Hz), 3.74 (s, 6 H), 5.39–5.50 (m, 2 H); IR ($CHCl_3$) 1730 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 246 (23), 200 (35), 199 (100), 138 (47), 79 (35).

Anal. Calcd for $C_{11}H_{18}O_4S$: C, 53.64; H, 7.37. Found: C, 53.59; H, 7.30.

Palladocycle 10a. General Procedure E. The formation of palladocycle **10a** is typical for the intramolecular carbopalladation of amines. To a solution of 125 mg (0.477 mmol) of LTP in 5 mL of THF at 0 °C was added a solution of 115 mg (0.473 mmol) of trans amino diester **9a** in 2.5 mL of THF. The color of the initial solution immediately lightened

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from dark red to light orange. After the addition was complete, stirring was continued for 10 min at 0 °C, and 58 mg (0.52 mmol) of powdered potassium *tert*-butoxide was added. The mixture was stirred at 0 °C for 30 min and then partitioned between water and chloroform. The chloroform layer was dried over sodium sulfate and concentrated to give crude complex **10a**. Plug-filtration with ethyl acetate, followed by crystallization from ethyl acetate, gave complex **10a** contaminated with ethyl acetate. Slow concentration of an ether–hexane solution of these crystals, under a stream of nitrogen, afforded 193 mg (93%) of **10a**: mp 96.5–98.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.1–1.3 (m, 1 H), 1.8–2.7 (m, 7 H), 2.73 (s, 3 H), 2.80 (s, 3 H), 3.66 (s, 3 H), 3.73 (s, 3 H); IR ($CHCl_3$) 1725 cm^{-1}.

An analytical sample was prepared by flash chromatography with ethyl ether.

Anal. Calcd for $(C_{12}H_{20}ClNO_4Pd)_2$: C, 37.52; H, 5.25; N, 3.65. Found: C, 37.54; H, 5.11; N, 3.52.

Preparation of Palladocycle 10b. General Procedure F. The preparation of palladocycle **10b** is typical for the intramolecular carbopalladation of sulfides. To a solution of 108 mg (0.412 mmol) of LTP in 5 mL of THF at 25 °C was added a solution of 101 mg (0.410 mmol) of **9f** in 2.5 mL of THF. The color of the initial solution lightened from dark red to light orange. After the addition was complete, stirring was continued for 10 min at 25 °C before addition of 51 mg (0.454 mmol) of powdered potassium *tert*-butoxide. The mixture was stirred at 25 °C for 15 h and then partitioned between water and chloroform. The chloroform layer was dried over sodium sulfate, filtered, and concentrated to give crude complex **10b**. Plug filtration with ethyl acetate gave 85 mg (54%) of **10b** as a yellow oil. The oil could be crystallized after MPLC with ethyl ether and recrystallized by precipitation from methylene chloride with hexane: mp 74–76 °C; ^{1}H NMR ($CDCl_3$) δ 1.2–2.7 (m, 8 H), 2.45 (s, 3 H), 3.61 (s, 3 H), 3.65 (s, 3 H); IR ($CHCl_3$) 1730 cm^{-1}.

Anal. Calcd for $(C_{11}H_{17}O_4PdS)_2{\cdot}5(C_2H_5)O_2$: C, 35.52; H, 4.84. Found: C, 35.25; H, 4.90.

Palladocycle 10c. Following procedure E, with the exception that 319 mg (1.22 mmol) of powdered triphenylphosphine was added 10 min prior to workup, 270 mg (1.11 mmol) of trans amino diester **9a** was converted to 563 mg (79%) of palladocycle **10c** after flash chromatography with ethyl ether: mp 147.5–148.5 °C; ^{1}H NMR ($CDCl_3$), ^{13}C NMR, see Table I; IR ($CHCl_3$) 1725 cm^{-1}.

Anal. Calcd for $C_{30}H_{35}ClNO_4PPd$: C, 55.74; H, 5.46; N, 2.71. Found: C, 55.66; H, 5.11; N, 3.52.

Cyclopentane 11a from Trans Amino Diester 9a. General Procedure G. The formation of cyclopentane **11a** is typical for the formation of carbocyclic amines. Following procedure E, palladocycle **10a** was prepared in situ from 106 mg (0.436 mmol) of trans amino diester **9a**. Hydrogen was bubbled through the solution at 0 °C for 1 h. The solution was partitioned between ether and saturated sodium bicarbonate. The combined ether layers were dried over sodium sulfate and concentrated to give crude cyclopentane **11a**. Kugelrohr distillation of the crude material (100 °C at 1 mmHg) gave 101 mg (95%) of **11a**: ^{1}H NMR ($CDCl_3$) δ 1.21–2.54 (m, 8 H), 2.20 (s, 6 H), 2.64–2.97 (m, 1 H), 3.64 (s, 3 H), 3.71 (s, 3 H); IR ($CHCl_3$) 1720, 2770, 2810 cm^{-1}; mass spectrum (50 eV), *m/e* (rel intensity) 243 (100), 212 (89), 84 (24), 58 (96).

Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.06; H, 8.77; N, 5.65.

Cyclopentane 11a from Cis Amino Diester 4a. With the exception of the addition of 1 mL of methanol prior to hydrogenation, procedure G was followed to convert 99 mg (0.407 mmol) of amino diester **4a** to 92 mg (93%) of cyclopentane **11a** after Kugelrohr distillation. The product from **4a** was spectroscopically and chromatographically identical with that obtained from **9a**.

Cyclopentane 11b from Trans Sulfide Diester 9f. General Procedure H. The preparation of cyclopentane **11b** is typical for the formation of carbocyclic sulfides. Following procedure F, palladocycle **10b** was prepared in situ from 100 mg (0.405 mmol) of trans sulfide diester **9f**. To this solution was added 153 mg (4.04 mmol) of powdered sodium borohydride, followed by 1 mL of methanol. After stirring for 1 h, the mixture was partitioned between 1 M aqueous hydrochloric acid and ethyl ether. The ether layers were dried over sodium sulfate and concentrated to give crude cyclopentane **11b**. Kugelrohr distillation (100 °C at 1 mmHg) afforded 71 mg (71%) of cyclopentane **11b**: ^{1}H NMR ($CDCl_3$) δ 1.00–3.73 (m, 9 H), 1.93 (s, 3 H), 3.51 (s, 3 H), 3.53 (s, 3 H); IR ($CHCl_3$) 1720 cm^{-1}; mass spectrum (70 eV), *m/e* (rel intensity) 246 (47), 215 (28), 199 (95) 78 (100).

Anal. Calcd for $C_{11}H_8O_4S$: C, 53.64; H, 7.37. Found: C, 53.97; H, 7.68.

Cyclopentane 11b from Cis Sulfide Diester 4g. Following procedure H, 108 mg (0.438 mmol) of cis sulfide diester **4g** was converted to 73 mg (68%) of cyclopentane **11b** after Kugelrohr distillation. The cyclopentane **11b** obtained from cis sulfide diester **4g** was spectroscopically and chromatographically identical with that obtained from trans sulfide diester **9f**.

Palladocycle 12a. According to procedure E, 108 mg (0.444 mmol) of cis amino diester **4a** was converted to 141 mg (90%) of palladocycle **12a**: mp 151.5–153.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.55–3.50 (m, 8 H) 2.39 (s, 3 H), 2.88 (s, 3 H), 3.80 (s, 6 H); IR ($CHCl_3$) 1725 cm^{-1}.

An analytical sample was prepared by flash chromatography with ethyl ether.

Anal. Calcd for $(C_{12}H_{20}ClNO_4Pd)_2$: C, 37.52; H, 5.25; N, 3.65. Found: C, 37.68; H, 5.32; N, 3.58.

Palladocycle 12b. Following procedure F, cis sulfide diester **4g** (118 mg, 0.479 mmol) was converted to 125 mg (64%) of the etherate of palladocycle **12b** after flash chromatography with ethyl ether; mp 78.5–81 °C; ^{1}H NMR ($CDCl_3$) δ 1.73–3.73 (m, 8 H), 2.70 (s), 2.73 (s), 3.85 (s, 6 H); IR ($CHCl_3$) 1725 cm^{-1}.

Anal. Calcd for $(C_{11}H_{17}O_4PdS)_2{\cdot}5(C_2H_5)_2O$; C, 35.52; H, 4.84. Found: C, 35.31; H, 4.87.

Palladocycle 12c. Following procedure E, with the exception that 285 mg (1.09 mmol) of powdered triphenylphosphine was added and the mixture was stirred for 10 min prior to workup, 240 mg (0.986 mmol) of cis amino diester **4a** was converted to 516 mg (81%) of palladocycle **12c** after flash chromatography with ethyl ether: mp 155.5–157 °C; ^{1}H NMR ($CDCl_3$), ^{13}C NMR, see Table I; IR ($CHCl_3$) 1725 cm^{-1}.

Anal. Calcd for $C_{30}H_{35}ClNO_4PPd$: C, 55.74; H, 5.46; N, 2.17. Found: C, 55.88; H, 5.59; N, 2.13.

Cyclopentane 13. Following procedure G, 100 mg (0.371 mmol) of aminoketo ester **9d** was converted to 86 mg (86%) of cyclopentane **13** as a mixture (ratio undetermined) of diastereomers: ^{1}H NMR ($CDCl_3$) δ 1.20–2.26 (m, 8 H), 1.48 (s, 9 H), 2.14 (s, 6 H), 2.23 (s, 3 H), 2.5–3.0 (m, 1 H); IR ($CHCl_3$) 1705, 2760, 2810 cm^{-1}; mass spectrum (70 eV), *m/e* (rel intensity) 269 (34), 213 (7), 196 (33), 84 (14), 58 (100).

Anal. Calcd for $C_{14}H_{27}NO_3$: C, 66.88; H, 10.10; N, 5.20. Found: C, 66.94; H, 10.35; N, 5.10.

Cyclohexane 14 from Trans Amino Diester 9b. Procedure G was followed with the exception that 250 mg of molecular sieves (4 Å) was added prior to the addition of amino diester **9b**. By this method, 104 mg (0.404 mmol) of trans amino diester **9b** was converted to 95 mg (91%) of cyclohexane **14** after Kugelrohr distillation (110 °C at 1 mmHg): ^{1}H NMR ($CDCl_3$) δ 1.10–2.70 (m, 11 H), 2.22 (s, 6 H), 3.67 (s, 3 H), 3.70 (s, 3 H); IR ($CHCl_3$) 1725, 2770, 2810 cm^{-1}; mass spectrum (70 eV), *m/e* (rel intensity) 257 (53), 226 (49), 198 (95), 194 (92), 58 (100).

Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.53; H, 9.25; N, 5.36.

Cyclohexane 14 from Cis Amino Diester 4b. Procedure G was followed with the exception that 250 mg of molecular sieves (4 Å) was added prior to the addition of the cis amino diester **4b**. In this way, 109 mg (0.424 mmol) of cis amino diester **4b** was converted to 97 mg (89%) of cyclohexane **14** after Kugelrohr distillation. The cyclohexane **14** obtained from cis amino diester **4b** was chromatographically and spectroscopically identical with that obtained from trans amino diester **9b**.

Cyclohexane 15 from Trans Amino Diester 9b. General Procedure I. The formation of cyclohexane **15** from trans amino diester **9b** is typical of the formation of carbocyclic aldehydes. The initial palladocycle **16** was formed from 103 mg (0.400 mmol) of the trans amino diester **9b** following procedure G. The mixture was then stirred at 25 °C for 6 h. The intermediate iminium salt was hydrolyzed by addition of 5 mL of 1 M aqueous acetic acid and stirring for 0.5 h. The mixture was partitioned between ethyl ether and water. Exhaustive extraction of the aqueous layer, followed by drying over sodium sulfate, gave a crude yellow ether solution to which hydrogen was added to reduce any remaining soluble palladium salts. Filtration through celite, concentration, and Kugelrohr distillation (110 °C at 1 mmHg) afforded 85 mg (94%) of cyclohexane **15**: ^{1}H NMR ($CDCl_3$) δ 1.2–3.2 (m, 9 H), 3.80 (s, 6 H), 9.77 (d, 1 H, J = 2 Hz); IR ($CHCl_3$) 1725 cm^{-1}; mass spectrum (50 eV), *m/e* (rel intensity) 196 (23), 169 (19), 132 (45), 113 (100), 59 (94).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 58.23, H, 7.32.

Cyclohexane 15 from Cis Amino Diester 4b. Following procedure I, 103 mg (0.400 mmol) of cis amino diester **4b** was converted to 66 mg (72%) of cyclohexane **15**. The cyclohexane **15** obtained from cis amino diester **4b** was chromatographically and spectroscopically identical with that obtained from trans amino diester **9b**.

Cycloheptane 18. Procedure G was followed with the exception that 250 mg of molecular sieves (4 Å) was added prior to the addition of the amino diester **4c**. The solution was stirred for 1 h prior to hydrogenation. In this manner, 103 mg (0.382 mmol) of amino diester **4c** was converted to 73 mg (71%) of cycloheptane **18** after Kugelrohr distillation (120 °C at 1 mmHg): ^{1}H NMR ($CDCl_3$) δ 1.2–2.9 (m, 13 H), 2.20 (s, 6 H), 3.74 (s, 6 H); IR ($CHCl_3$) 1730, 2770, 2810 cm^{-1}; mass spectrum (70 eV), *m/e* (rel intensity) 271 (28), 240 (30), 212 (100), 59 (70), 58 (96).

Anal. Calcd for $C_{14}H_{25}NO_4$: C, 61.97; H, 9.29; N, 5.16. Found: C, 61.92; H, 9.50; N, 5.05.

Cycloheptane 19. Procedure I was followed to convert 113 mg (0.420

mmol) of amino diester **4c** to 71 mg (70%) of cycloheptane **19** after Kugelrohr distillation (120 °C at 1 mmHg): ^{1}H NMR ($CDCl_3$) δ 1.20–3.0 (m, 11 H), 3.68 (s, 3 H), 3.70 (s, 3 H), 9.79 (d, 1 H, J = 2 Hz); IR ($CHCl_3$) 1720 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 242 (13), 215 (37), 150 (49), 145 (100), 113 (38), calcd for $C_{12}H_{18}O_5$ 242.115, found 242.113.

Cyclohexanone 20. General Procedure J. To a solution of 129 mg (0.477 mmol) of LTP in 8 mL of 1:1 methylene chloride/THF was added 250 mg of molecular sieves (4 Å) at 25 °C. To this mixture was added a solution of 105 mg (0.492 mmol) of aminoketo ester **4g** in 2 mL of 1:1 methylene chloride/THF. After the solution was stirred for 10 min at 25 °C, 61 mg of powdered potassium *tert*-butoxide was added. The mixture was stirred for 1.5 h at 25 °C, 1 mL of methanol was added, and hydrogen was bubbled through the mixture for 1.5 h. The solution was immediately placed on an MPLC column and chromatographed with 0.7% aqueous ammonia/6.3% methanol/chloroform to afford 37 mg (35%) of cyclohexanone **20**: ^{1}H NMR ($CDCl_3$) δ 1.20–1.87 (m, 3 H), 1.90–3.40 (m, 6 H), 2.27 (s, 6 H), 3.67 (s, 3 H), 6.20 (s, very br, 1 H); IR ($CHCl_3$) 1600, 1645, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 213 (20), 154 (100), 122 (55), calcd for $C_{11}H_{19}NO_3$ 213.136, found 213.139.

Cycloheptanone 21. Following procedure J, 108 mg (0.475 mmol) of aminoketo ester **9c** was converted to 70 mg (65%) of cycloheptanone **21**: ^{1}H NMR ($CDCl_3$) δ 1.17–2.03 (m, 5 H), 2.07–3.00 (m, 7 H), 2.20 (s, 5.4 H), 2.25 (s, 0.6 H), 3.07–3.60 (m, 1 H), 3.69 (s, 0.3 H), 3.75 (s, 2.7 H); IR ($CHCl_3$) 1600, 1640, 1705, 1735, 2770, 2810 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 227 (47), 200 (8), 151 (19), 125 (10), 58 (100), calcd for $C_{12}H_{21}NO_3$ 227.151, found 227.145.

Attempted Intramolecular Carbopalladation of Sulfide Keto Ester 9e. Following procedure H, 100 mg of sulfide keto ester **9e** failed to cyclize. TLC and ^{1}H NMR analysis indicated the presence of starting olefin complex only, even after 1 month at 25 °C.

Attempted Carbopalladation of 4c. Procedure G was followed with the exception that the solution was diluted to 0.01 M in amino diester **4d** and molecular sieves (4 Å) were added prior to the addition of the amino diester **4d**. Gas chromatographic analysis after reduction of a small aliquot of the reaction mixture failed to show even traces of a new product until the solution had been stirred for 48 h at 25 °C. Within 2 weeks at 25 °C, the starting material was completely consumed. TLC analysis of the reduced reaction mixture revealed a minimum of nine materials.

Attempted Carbopalladation of Aminoketo Ester 4f. Procedure J was followed with the exception that the solution was diluted to 0.01 M in aminoketo ester **4f**. TLC analysis showed that the starting material was completely consumed in ca. 1 week. After reduction with hydrogen, as in procedure J, TLC analysis revealed at least nine products.

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Registry No. 1a, 36697-88-8; **1b**, 1002-37-5; **1c**, 1002-50-2; **1d**, 94517-78-9; **2a**, 94517-79-0; **2b**, 94517-80-3; **2c**, 94517-81-4; **2d**, 94517-82-5; **3a**, 94517-83-6; **3b**, 94517-84-7; **3c**, 94517-85-8; **3d**, 94517-86-9; **3e**, 94517-87-0; **4a**, 94517-88-1; **4b**, 94517-89-2; **4c**, 94517-90-5; **4d**, 94517-91-6; **4e**, 94517-92-7; **4f**, 94517-93-8; **4g**, 94517-94-9; **5**, 64244-47-9; **6**, 94517-95-0; **7a**, 27354-43-4; **7b**, 76047-81-9; **8a**, 94517-96-1; **8b**, 94517-97-2; **9a**, 94517-98-3; **9b**, 94517-99-4; **9c**, 94518-00-0; **9d**, 94518-01-1; **9e**, 94518-02-2; **9f**, 94518-03-3; **10a**, 94518-17-9; **10b**, 94518-18-0; **10c**, 94518-19-1; **11a**, 94518-04-4; **11b**, 94518-05-5; **12a**, 94596-00-6; **12b**, 94596-01-7; **12c**, 94596-02-8; **13** (isomer 1), 94518-06-6; **13** (isomer 2), 94518-07-7; **14**, 94518-08-8; **15**, 94518-09-9; **16**, 94518-20-4; **17**, 94518-10-2; **18**, 94518-11-3; **19**, 94518-12-4; **20**, 94518-13-5; **21**, 94518-14-6; LTP, 15525-45-8; Na-($CH_3COCHCO_2$-*t*-Bu), 64770-14-5; $NaCH(CO_2Me)_2$, 18424-76-5; $CH_2(CO_2Me)_2$, 108-59-8; $(CH_2COCHCO_2Me)^{2-}$, 30568-00-4; *cis*-tetrahydropyranyl alcohol, 57323-06-5; *cis*-allylic iodide, 94518-15-7; tetrahydropyranyl keto ester, 94518-16-8.

Alkoxide Triggered Ligand Substitution. Highly Stereoselective Formation of Unsaturated Phosphinite Ester—$Mo(CO)_4$ Chelates and the X-ray Crystal Structure of $(PMe_2OCHPhCH{=}CH_2)Mo(CO)_4$

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Abstract: Treatment of $(L)Mo(CO)_4$ (L = η^2-pyridyl dimethylphosphinite) at 0 °C in diethyl ether with 1.1 equiv of lithium alkoxides (ROLi) derived from unsaturated alcohols affords $(\eta^3$-$PMe_2OR)Mo(CO)_4$ chelates. The reaction involves nucleophilic attack at the phosphorus with cleavage of the chelate bridge and subsequent rapid extrusion of the alkoxide of 2-hydroxypyridine. The procedure is illustrated by using a number of allylic, homoallylic, 1°, 2°, and 3° alkoxides. When the alkoxides contain asymmetric centers, disastereofacial coordination selectivities of 3 → 30:1 are observed. A molecular structure determination of $(\eta^3$-$PMe_2OR)Mo(CO)_4$ (**10**; R = 1-phenylallyl) was effected. Crystals of $(PMe_2OCPhCH{=}CH_2)Mo(CO)_4$ belong to the centrosymmetric triclinic space group $P\bar{1}$ with cell parameters a = 7.416 (1) Å, b = 8.649 (1) Å, c = 13.572 (2) Å, α = 98.48 (1)°, β = 94.08 (1)°, γ = 97.29 (1)°, and Z = 2. Diffraction data (Mo Kα, 2θ = 4.5–45.0°) were collected with a Syntex $P2_1$ automated diffractometer and the structure refined to R_F = 2.3% for all 2223 reflections (R_F = 1.8% for those 1984 data with $|F_o| > 6\sigma|F_o|$. The complex has a central Mo(0) atom that is octahedrally coordinated to four carbonyl ligands and with the other two (mutually cis) sites being taken up by the phosphorus atom and the terminal olefin function of the chelating $PMe_2OCHPhCH{=}CH_2$ ligand; the Mo—P distance is 2.446 (1) Å, Mo—C (olefin) distances are Mo—C(1) = 2.430 (3) Å and Mo—C(2) = 2.399 (3) Å, and the bond length of the coordinated olefin is C(1)–C(2) = 1.370 (4) Å.

It has become clear that transition-metal-mediated processes will play an increasingly important role in natural products synthesis.[1] Despite the often elegant work in this area, however, a surprisingly small percentage of this methodology has successfully reached the stage of being used *routinely* by the average organic synthesis practitioner. This derives in part from the paucity of information pertaining to relative stereocontrol, that is, the in-

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