

Allylic Alkylation: Nucleophilic Attack on π -Allylpalladium Complexes

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Abstract: Allylic alkylation of alkyl substituted π -allylpalladium complexes requires enhancement of their electrophilicity by addition of ligands. Phosphines and phosphites are preferred. The regiochemistry of the alkylation as a function of ligand and π -allyl complex is explored. The stereochemistry of the reaction is determined.

Introduction

The ability to chemoselectively alkylate α to a carbonyl group via the intermediacy of enols and enolates constitutes one of the major applications of carbonyl compounds in synthesis. Extension of these reactions to olefins which are iso-electronic in a π sense with carbonyl compounds has been less successful. Specifically, the development of methods to replace an allylic C-H bond with an allylic C-C bond in the presence of other functional groups constitutes a fascinating challenge. The ene reaction represents one such case.¹ It has found surprisingly little use in synthesis.² Part of the difficulty resides in its limited scope. Metalation in the main group series provides a greater degree of flexibility.³ Unfortunately, it generally lacks chemoselectivity. On the other hand, metalation in the transition metal series potentially can overcome this limitation. In the first paper, we explored the palladation of olefins. In this paper, we explore the reaction of the resultant complexes to form carbon-carbon bonds. Ultimately, it is hoped that a catalytic reaction can evolve. The study of the stoichiometric reaction has relevance to determine the features of the reaction. Furthermore, there are many applications for which this chemistry will prove to be economically feasible especially since the palladium is so easily recycled.

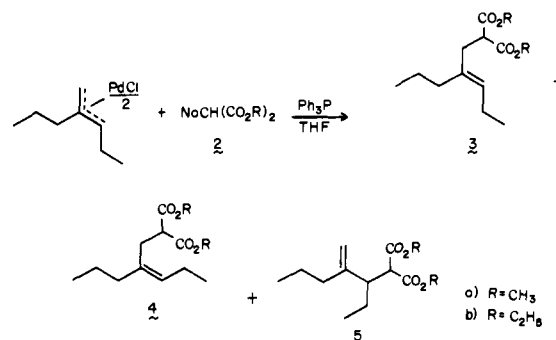
Formation of carbon-carbon bonds using π -allylpalladium complexes has largely focussed on carbonylations.⁴ Tsuji reported the reaction of dimethyl sodiomalonates⁵ and enamines⁶ with the parent complex, di- μ -chlorobis- π -allyldipalladium, and suggested initial coordination to palladium followed by migration to carbon.⁷ Unfortunately, attempts to expand the generality of the reaction failed since any but the parent complex was unreactive. We wish to report a new approach which indeed has proven general.⁸ Furthermore, we can show that our reaction does not proceed by initial bonding to palladium.

Results

Nucleophilic attack on π -allylpalladium complexes requires the complex to serve as an electrophile. Addition of alkyl substituents which increase the electron density of the π -allyl unit decrease the ability of the complex to serve as such. Since addition of ligands, especially phosphines, is known to ionize π -allylpalladium chloride complexes,⁹⁻¹⁷ it was anticipated that such ligands would activate the chloride bridged dimers toward nucleophilic attack. Indeed, this expectation is fully borne out.

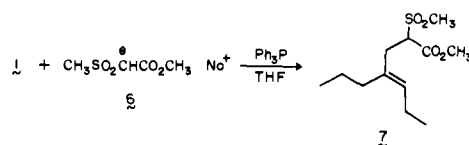
Initial work focused on di- μ -chlorobis(1-ethyl-2-propyl- π -allyl)dipalladium (**1**). Treatment of **1** with diethyl sodiomalonate (**2b**) in THF led to no reaction, even after prolonged refluxing. On the other hand, addition of 2 equiv of triphenylphosphine per palladium led to smooth alkylation at room temperature (22 °C) in 68% yield. The major alkylation

products derive from attack at the less substituted carbon ((3 + 4):5, ~8:1). Of the products resulting from attack at the less



hindered carbon, the ratio of *Z*:*E* (**4**:**3**) is 1.6. The assignment of stereochemistry rests upon the relative shifts of the vinyl protons upon addition of Eu(fod)₃. The major isomer shows the vinyl proton to shift 1.34 ppm, whereas this proton shifts 2.66 ppm in the minor isomer. This result is consistent with the vinyl proton being trans to the carbomethoxy substituents in the major isomer and cis in the minor isomer.

Much greater selectivity was observed using methyl methanesulfonysodiocetate (**6**) as the attacking nucleophile. In this case, a single product assigned structure **7** is obtained.



The structure rests upon spectroscopic data which clearly indicate attack occurred at the less substituted carbon. The stereochemistry is less secure. Based upon analogy (vide infra), the *E* configuration is expected. Eu(fod)₃-induced shifts tend to support that assumption since the vinyl proton shifts about the same amount as the allylic methylene of the propyl group (50 Hz vs. 44 Hz for the vinylic and allylic protons, respectively). Since these two groups are almost the same distance from the sulfone ester in the *E* isomer **7** but substantially different in the *Z* isomer, the assignment of the stereochemistry seems appropriate.

Reaction occurs at a cyclic carbon as well as an acyclic carbon as illustrated by the alkylation of complex **8** with **6** to give **9**.

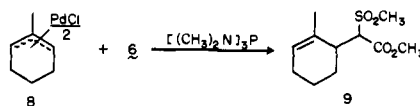
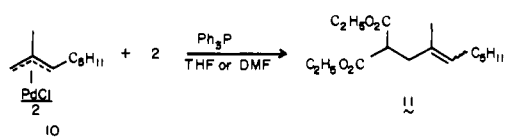


Table I. Dependence of Regioselectivity on Ligands in Alkylation of Di- μ -chlorobis(1,2-tetramethylene- π -allyl)dipalladium(II) with Methyl Methanesulfonylsodioacetate

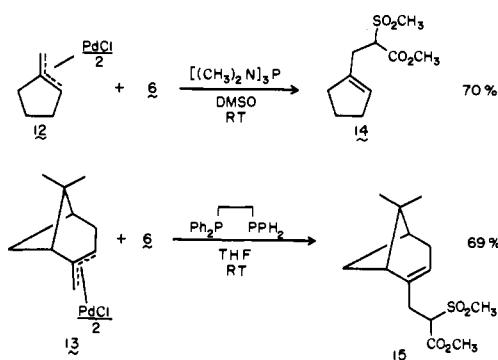
Entry	Ligand	Solvent	Yield, %	% 17 (X = CH ₃ SO ₂)(X = CH ₃ SO ₂)- _a	
				% 17 _a	% 18 _a
1	Triphenylphosphine	Me ₂ SO	75	62	38
2	Triphenylphosphine	THF ^b	81	89	11
3	Tri- <i>n</i> -butylphosphine	Me ₂ SO	100	100	
4	Tri- <i>n</i> -butylphosphine	THF	57	90	10
5	1,2-Bis(diphenylphosphino)ethane	Me ₂ SO	64	76	24
6	1,2-Bis(diphenylphosphino)ethane	THF	100	75	25
7	1,3-Bis(diphenylphosphino)propane	Me ₂ SO	100	75	25
8	1,3-Bis(diphenylphosphino)propane	THF	72	78	22
9	Diphenyl- <i>o</i> -tolylphosphine	Me ₂ SO	66	54	46
10	Diphenyl- <i>o</i> -tolylphosphine	THF	53	87	13
11	Tri- <i>o</i> -tolylphosphine	Me ₂ SO	90	18	82
12	Tri- <i>o</i> -tolylphosphine	Me ₂ SO	79	12	88
13	Tri- <i>o</i> -tolylphosphine	THF	0		
14	Tri- <i>o</i> -anisylphosphine	Me ₂ SO	80	70	30
15	Tri- <i>o</i> -trifluoromethylphosphine	Me ₂ SO	79	49	51
16	Hexamethylphosphorous triamide	Me ₂ SO	58	100	
17	Hexamethylphosphorous triamide	THF	90	100	
18	Trimethyl phosphite	Me ₂ SO	91	87	13
19	Trimethyl phosphite	THF	88	91	9
20	Triphenyl phosphite	Me ₂ SO	86	93	7
21	Triphenyl phosphite	THF	69	91	9
22	<i>N,N,N',N'</i> -Tetramethylethylenediamine	Me ₂ SO	12	66	34
23	<i>N,N,N',N'</i> -Tetramethylethylenediamine	THF	17	100	
24	Triphenylarsine	Me ₂ SO	45	62	38
25	Triphenylarsine	THF	86	100	
26	None	Me ₂ SO	0		
27	None	THF	0		
28	None	HMPA	0		

^a Ratios determined by NMR integration of olefin protons. ^b Tetrahydrofuran.

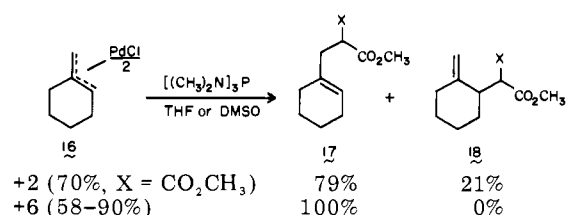
With the establishment of the alkylation reaction, we turned our attention to the selectivity exhibited by it. First arises the question of regioselectivity. As shown above, regioselectivity clearly depends upon the nature of the attacking nucleophile. It is also highly dependent upon structure of the π -allyl complex. For example, complex **10** led only to alkylation at the less substituted end to give **11** (stereochemistry undefined).



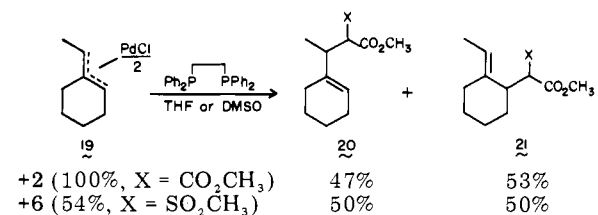
The cyclic cases were most studied. A strong preference normally exists for reaction at the less substituted carbon. Thus, complexes **12** and **13** only give products from reactions at the acyclic carbon, i.e., **14** and **15**, respectively.



Monocyclic cyclohexyl systems showed a propensity for reacting at either the exocyclic or endocyclic position. As seen previously, this ratio depends upon the choice of alkylating



agent with the sulfone ester **6** giving complete selectivity for reaction at the less substituted acyclic carbon. If the two systems are similarly substituted as in complex **19**, then a ratio more nearly equal to 1 is obtained. Part of the differences ob-



served between **16** and **19** result from the different ligands (vide infra). Nevertheless, part of the differences clearly also reflects the different substitution patterns since alkylation of **16** with **6** using 1,2-bis(diphenylphosphino)ethane (diphos) gave **17** and **18** (X = SO₂CH₃) in a 75:25 ratio compared with the 50:50 ratio for **19**.

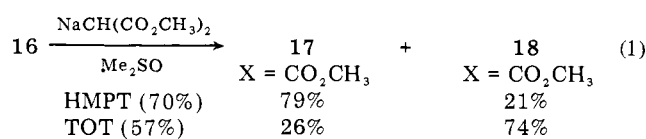
The most intriguing aspect of the regioselectivity is the dependence on activating ligands as outlined in Table I for the reaction of **6** with **16**. The solvent effect on this reaction appears to be minor as the ratios normally change little upon switching from THF to Me₂SO. The major effect seen is a change from a 100:0 (**17:18**, X = CH₃SO₂) with hexamethylphosphorous triamide (HMPT) to 15:85 with tri-*o*-tolyl-

Table II. Regioselectivity of Alkylation of Complex 19

Entry	Alkylating agent ^a	Ligand	Yield, %	%20	%21
1	CH ₃ SO ₂ CH ₂ CO ₂ CH ₃	HMPT ^b	48	100 ^c	
2	CH ₃ SO ₂ CH ₂ CO ₂ CH ₃	diphos ^d	54	50 ^c	50 ^c
3	PhSO ₂ CH ₂ CO ₂ CH ₃	HMPT	68	100 ^e	
4	PhSO ₂ CH ₂ CO ₂ CH ₃	diphos	N.D. ^f	50 ^e	50 ^e
5	CH ₂ (CO ₂ CH ₃) ₂	Ph ₃ P	90	85 ^g	15 ^g
6	CH ₂ (CO ₂ CH ₃) ₂	diphos	100	47 ^g	53 ^g

^a All reactions involve the sodium salt of the alkylating agent generated in Me₂SO or THF. ^b Hexamethylphosphorou triamide. ^c X = CH₃SO₂. ^d 1,2-Bis(diphenylphosphino)ethane. ^e X = PhSO₂. ^f Not determined. ^g X = CO₂CH₃.

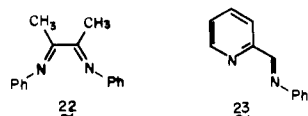
phosphine (TOT). No discernible trend is seen with respect to the ability of the ligand to serve as a σ donor or π acceptor. Thus, tri-*n*-butylphosphine, trimethyl phosphite, and triphenyl phosphite all give similar ratios. Triphenylphosphine and triphenylarsine show similar results. On the other hand, the series triphenylphosphine, diphenyl-*o*-tolylphosphine, and tri-*o*-tolylphosphine in Me₂SO show a progressively increasing amount of the product which results from reaction at the en-



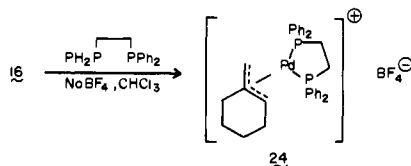
dicyclic carbon. Alkylations with dimethyl sodiomalonate show a similar dependency but not to the extremes seen for the sulfone **6** as the data in eq 1 illustrates.

A similar dependency is seen for complex **19** as the data in Table II indicates. Unfortunately, TOT was too weak an activating ligand to allow alkylation; however, HMPT leads to high selectivity for reaction at the exocyclic carbon even though both sites for attack are similarly substituted.

Attempts to explore nitrogen ligands in this regard were very restricted. As illustrated in Table I, *N,N,N',N'*-tetramethylethylenediamine does allow alkylation, but only in low yields. Similarly, the bidentate nitrogen ligand **22** led to low yields in Me₂SO and the ligand **23** led to no discernible reaction in either THF or Me₂SO.

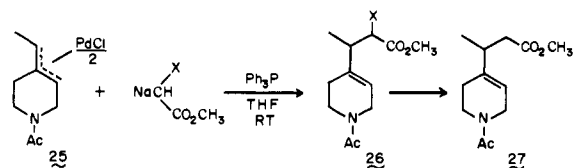


The ratio of exocyclic to endocyclic attack in complexes like **16** and **19** offers an opportunity to explore the nature of the reactive intermediate. The optimum ratio of activating phosphine ligand of 2 P per Pd suggested a cationic complex such as **24**.¹²⁻¹⁷ Alkylation of **24** with **6** under conditions identical



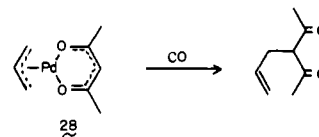
with those employed in the normal procedure led to **17** and **18** (X = CH₃SO₂) in a ratio of ~4:1, identical within experimental error with that obtained in the usual fashion.

The presence of a heteroatom in the ring does affect regioselectivity. Complex **25** reacts smoothly with the sodium salt of either dimethyl malonate or methyl phenylsulfonylacetate to give **26**. For the latter, **26** (X = PhSO₂) was isolated in 53% yield; for the former, **26** (X = CO₂CH₃) was isolated in 47% yield. The lower yields obtained in these cases relative to the all hydrocarbon system stem in large part from the isolation procedure. Alkylating **25** with **2** and subjecting the initial crude

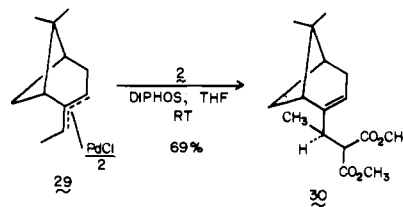


product to hydrolysis and decarboxylation led directly to **27** in 83% overall yield from **25**. This example illustrates several important features of the allylic alkylation procedure. Most significantly, the allylic amide unit remains inert. Oxidative addition of allylic substituted systems to palladium(0) complexes is a known reaction.¹⁸⁻²⁰ Since such palladium complexes are the products of the alkylation reaction, the decomposition of the product was a real concern. It is curious to note the exclusive alkylation at the acyclic position even with triphenylphosphine as the activating ligand.

With the establishment of the alkylation process and the potential control of regiochemistry, we examined the stereochemistry of alkylation. The work of Takahashi et al. suggested that a likely mechanism would involve initial bonding of the nucleophile to palladium followed by migration from palladium to carbon.⁷ In support of this concept, addition of CO to complex **28** led to allylacetate.



To examine this question, we alkylated the complex **29** derived from 2-ethylidenenorpinane whose stereochemistry was determined by NMR and x-ray crystallography. Alkylation with **2** proceeded smoothly at room temperature to give a single product which was regio- and stereochemically homogeneous. The regiochemical homogeneity stands in stark contrast to complex **19** which gave an ~1:1 mixture of exo- and endocyclic



attack. NMR spectroscopy (see Experimental Section) allows easy discernment of the regiochemistry.

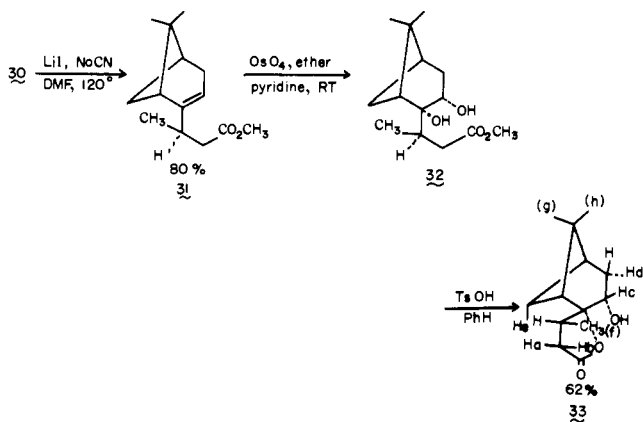
The establishment of stereochemistry was more complex. To facilitate the solution of this problem, acyclic geometry was converted to cyclic geometry. Decarbomethoxylation to **31**²¹ followed by hydroxylation should produce **32** which upon lactonization in the presence of acid should give lactone **33**. None of these subsequent reactions affects the concerned center of asymmetry. Reactions of α -pinenes (as well as β -pinenes) normally occur anti to the bridge bearing the *gem*-dimethyl groups. Since osmium tetroxide normally reacts on

Table III. $\text{Eu}(\text{fod})_3$ -Induced Shifts of Lactones **33** and **34**

% $\text{Eu}(\text{fod})_3$	Proton							
	H_a	H_b	H_c	H_d	H_e	H_f	H_g	H_h
	33							
0.0	2.89 ^a	2.20 ^b	4.52 ^c	1.73 ^d	1.47 ^e	1.23 ^f	1.30 ^g	0.98 ^g
3.0	3.11	2.43	5.56		1.81	1.59	1.41	1.12
6.6	3.46	2.83	7.12		2.42	2.11	1.57	1.34
9.8	3.83		8.61	4.74	3.07	2.66	1.74	1.56
12.7	4.09		9.84	5.40	3.55	2.96	1.85	1.76
15.8	4.53		11.20	6.18	3.94	3.40	2.00	2.00
	34							
0.0	2.80 ^h	2.08 ⁱ	5.57 ^j	1.66 ^k	1.61 ^e	1.09 ^f	1.31 ^g	1.04 ^g
4.6	3.09		6.10	~2.0	1.80	1.27	1.34	1.12
8.6	3.37	2.74	6.41	~2.6	1.99	1.45	1.39	1.20
13.0	3.83	3.25	7.14	3.2	2.30	1.75	1.45	1.33
19.2	4.12	3.58	7.60	3.8	2.49	1.97	1.50	1.42

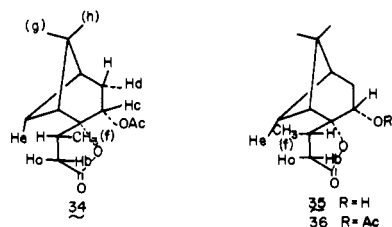
^a dd, $J = 17.4, 8$ Hz. ^b dd, $J = 17.4, 2$ Hz. ^c q, $J = 7$ Hz. ^d ddd, $J = 13.5, 7, 2$ Hz. ^e d, $J = 10$ Hz. ^f d, $J = 7$ Hz. ^g s. ^h dd, $J = 17, 8$ Hz. ⁱ dd, $J = 17, 2.5$ Hz. ^j dd, $J = 10, 7$ Hz. ^k ddd, $J = 13, 7, 2$ Hz.

the sterically less hindered side, that assumption is made here,²² thus assigning the α configuration to the diol **32**. The presence of a five-membered-ring lactone and a secondary hydroxyl group in **33** was inferred from the carbonyl stretching



frequency at 1780 cm^{-1} and the shift for the methine proton next to the hydroxyl group at $\delta 4.52$. The presence of the secondary hydroxyl group was further confirmed by smooth acetylation with acetic anhydride at room temperature in pyridine and by the concomitant shift of the adjacent methine proton to $\delta 5.57$ in **34**.

To differentiate **33** from the alternative **35**, we examined the $\text{Eu}(\text{fod})_3$ shifts on both **33** and **34** and the data are summarized in Table III. The protons α to the lactone carbonyl are clearly discernible at $\delta 2.89$ and 2.20 in **33** and $\delta 2.80$ and 2.08 in **34**. In a virtually planar five-membered-ring lactone, cis

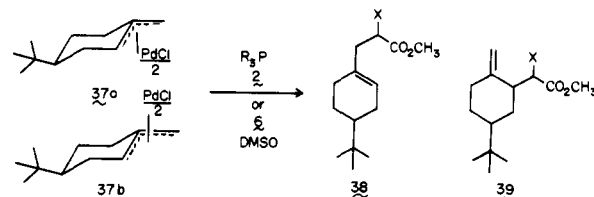


coupling is larger than trans coupling. The eclipsing of H_b by the methyl group also causes a net shielding effect due to the anisotropy associated with a C-C bond. Assignments of H_c , H_e , H_f , H_g , and H_h in **33** stem from their chemical shifts and multiplicities. In the case of H_e , assignment as the anti rather than syn proton with respect to the *gem*-dimethyl bridge rests upon the absence of observable coupling with the bridgehead

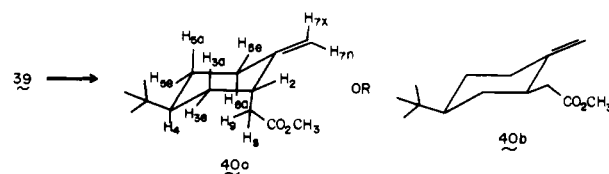
protons due to the nearly 90° dihedral angle and the substantial Eu^+ -induced shift ($\Delta\delta 1.47$) for such a distal proton. The assignment of H_d in **33** rests upon its coupling and the very large shift ($\Delta\delta 4.45$) suggesting a proximal position with respect to the hydroxyl group. Similar arguments allow the corresponding assignments in **34**.

The key in assigning stereochemistry arises from consideration of the relative shifts in **33** in which primary complexation to the hydroxyl group is anticipated.^{23,24} This anticipation is fully confirmed by comparison of the differential shifting observed for **33** and its acetate **34**. In the latter case, more nearly equal complexation at the lactone and ester is evident. In **33**, the methyl doublet shifts 217 Hz whereas H_a shifts 164 Hz. Where comparisons can be made for H_a , H_b , and H_f (i.e., at 6.6% shift reagent), the methyl doublet (H_f) shifts more than either H_a or H_b . These observations are consistent only with the methyl protons being closer to the hydroxyl group than either H_a or H_b . Thus, **35** can be eliminated.

The question of the stereochemistry of attack at the ring carbon was unanswered by this experiment. Attempts to direct attack to the ring carbon by use of TOT failed since no reaction occurred. Furthermore, the bias that the *gem*-dimethyl bridge introduces led us to consider a simpler system. We, therefore, examined the reactions of complex **37** which is a 3:2 mixture



of **37a** and **37b**. The regiochemistry of alkylation showed a dependence upon activating ligand as did complex **16** but not to as high a degree as summarized in Table IV. The obtention of major amounts of **39** allowed determination of its stereochemistry. In order to do so, **39** ($\text{X} = \text{CO}_2\text{CH}_3$) was decar-



bomethoxylated to **40**. VPC analysis indicated two peaks in the ratio of 18:1 with the major isomer eluting first.²⁵ Collection of this major peak and analysis of the 270-MHz NMR

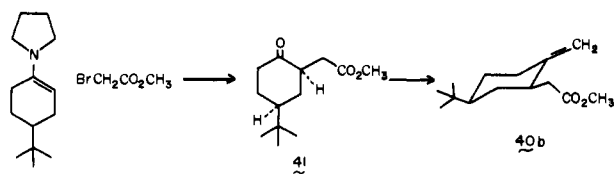
Table IV. Regiochemistry of Alkylation of Complex 37

Entry	Alkylating agent ^a	Ligand	Yield, %	%38	%39
1	CH ₂ (CO ₂ CH ₃) ₂	HMPT ^b	100	63 ^c	37 ^c
2	CH ₂ (CO ₂ CH ₃) ₂	TOT ^{d,e}	83	21 ^c	79 ^c
3	CH ₃ SO ₂ CH ₂ CO ₂ CH ₃	HMPT ^b	31	95 ^f	5 ^f
4	CH ₃ SO ₂ CH ₂ CO ₂ CH ₃	TOT ^{d,f}	52	45 ^f	55 ^b

^a All reactions involve the sodium salt of the alkylating agent generated in Me₂SO. ^b See Table I for abbreviations. ^c X = CO₂CH₃. ^d Tri-*o*-tolylphosphine. ^e The ligand and complex were heated at 60 °C for 1.5 h prior to performing the alkylation at room temperature. ^f The ligand and complex were heated at 70 °C for 1.5 h prior to performing the alkylation at room temperature. ^g X = SO₂CH₃.

spectrum aided by selective spin decoupling allowed the following assignments and coupling constants: H₂, δ 2.94; H_{3a}, 1.33; H_{3b}, 1.71; H₄, 1.31; H_{5e}, 1.85; H_{5a}, 1.03; H₆, 2.63–2.77; H_{7x}, 4.69; H_{7n}, 4.64; H₈, 2.46; H₉, 2.50 ($J_{2,8} = J_{2,9} = 7.7$; $J_{2,3a} = 2.3$, $J_{2,3e} = 1.2$; $J_{2,7x} = J_{2,7n} = 1.2$; $J_{3a,3b} = 12$; $J_{3a,4} = 12$; $J_{3e,4} = 2$; $J_{4,5a} = 12$; $J_{5a,5e} = J_{5a,6a} = 12.5$; $J_{5a,6e} = 5$ Hz). The coupling pattern observed for H₂ is consistent with this proton being equatorial and thus assigning structure **40a** to the major alkylation product.

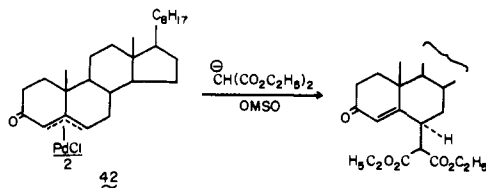
To confirm this assignment, an independent synthesis of **40b** was undertaken. Alkylation of the pyrrolidine enamine of 4-*tert*-butylcyclohexanone with methyl bromoacetate followed by hydrolytic workup gave **41**.²⁶ To ensure formation of the thermodynamically most stable isomer of **41**, the initial product



after hydrolysis was subjected to methanolic sodium methoxide. Methylation completed the sequence.²⁷ Based upon its method of synthesis and spectroscopic data, it can be assigned the stereochemistry depicted in **40b**. The subsequent work of Smith confirms the above assignments.²⁸ In addition to the points that Smith makes, it is noteworthy that the average chemical shift for the protons of the terminal methylene group in the axial isomer (δ 4.66) is at lower field than in the equatorial isomer (4.57) and their nonequivalence is less in the former (Δδ 0.05) than in the latter (0.20). Thus, allylic alkylation has a high preference for axial compared with equatorial attack on the cyclohexane ring.

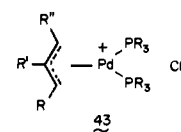
Discussion

The alkylation of π -allylpalladium complexes by nucleophiles generally requires enhancement of their electrophilicity. The parent complex^{5,6} and complexes bearing electron-withdrawing groups²⁹ are apparently sufficiently electrophilic to minimize their requirement for substantial activation. Thus, complex **42** undergoes alkylation in Me₂SO without additional



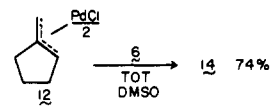
ligands.^{29b} It should be noted that Me₂SO is itself a ligand and has been reported to ionize π -allylpalladium chloride bridged dimers.³⁰

With alkyl substituents such activation is insufficient. Thus, complex **16** undergoes no alkylation with dimethyl sodiomalonate in THF even at reflux and only very little alkylation in Me₂SO (<10%). Phosphine and phosphite ligands are the best. Stibines and diamines are inferior. The optimum ratio

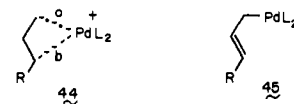


of ligand to palladium clearly implicates cationic complexes such as **43**.¹²⁻¹⁷ The fact that identical alkylation ratios are obtained by reacting preformed cationic complex **24** with the anion of methyl methanesulfonylacetate and by alkylating **16** with this anion in the presence of diphos supports this contention.

The most fascinating aspect of the role of ligand is its dramatic influence on regiochemistry of reaction of complexes like **16** and **37**. Such an effect is not seen for acyclic complexes nor for complexes of other ring sizes such as **12** which only gives acyclic attack even in the presence of TOT.

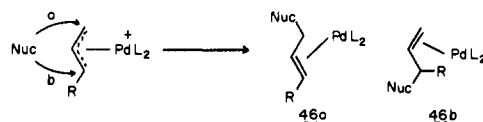


Two explanations can be proffered. Unsymmetrically substituted π -allyl complexes would be expected to be unsymmetrically bonded with respect to palladium and the π -allyl unit.³¹ In **44** distance a would be expected to be shorter than distance b and this asymmetry would be expected to be a function of ligand. The σ complex **45** is the extreme of this



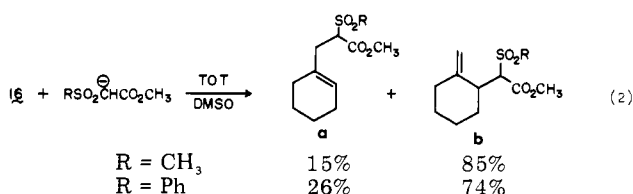
situation. Since TOT is a relatively poor ligand, electron donation from the π -allyl unit to palladium would be expected to be more important relative to other ligands, thereby increasing such asymmetry with preference for stronger bonding to the less substituted carbon. The steric bulk of the phosphine would reinforce this preference. Attack on **44** by nucleophile must then occur at the carbon of the π -allyl system sustaining less bonding to the metal. On the other hand, with more normal phosphines, the complex would be more nearly symmetrical (i.e., distances a and b more nearly equal) and the preference for attack at the less hindered carbon dominates. This explanation fails to take note of substrate specificity with respect to regio differentiation.

An alternative and more attractive explanation considers the initial product of alkylation, the olefin-palladium complex **46**. In terms of bonding to the metal in such olefin-metal(0) complexes,³² increasing alkyl substitution generally decreases the stability of the complex owing to steric congestion and decreased back-bonding from the metal to the olefin. Thus, as

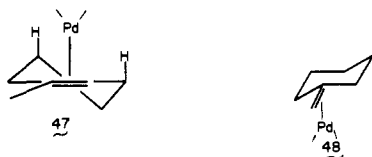


the transition state becomes more product-like, the importance of the stability of this type of complex increases which will tend to favor attack by path b to give **46b**. Steric bulk on the ligand would further enhance the preference for formation of **46b** relative to **46a**. TOT is a poorer activator and is sterically very demanding. Thus, the above effects should be maximized. With normal ligands, these effects are less important and the regiochemistry is determined by the least hindered approach of the nucleophile.

Such an explanation also suggests that the regiochemistry will be very dependent upon attacking nucleophile and π -allyl system. Increasing the steric bulk of the nucleophile should affect this ratio as supported by the results in eq 2. Most im-

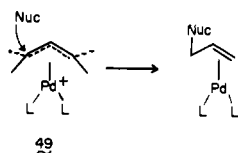


portantly this explanation accounts for the uniqueness of the cyclohexyl system relative to all other cyclic systems (for which only acyclic attack is always observed) and to acyclic systems. The conformational rigidity of the six-membered ring makes a complex such as **47** very crowded owing to the interactions of the metal and its ligands with the ring and especially the axial hydrogens indicated. In most all other cases, conformational flexibility allows such interactions to be minimized. Complex **48** does not suffer from such bad steric interactions.



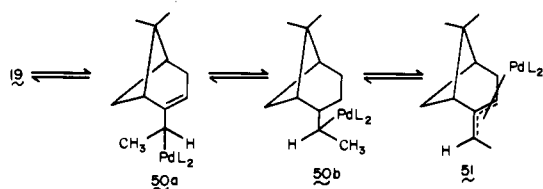
Thus, only in cases like **47** would the stability of the initial olefin-palladium complex come into serious question as observed experimentally.

The stereochemistry of attack is at first quite surprising especially in light of earlier suggestions.⁷ Obtention of **30** from **29** demands that the nucleophile approach on the face opposite to palladium—i.e., reductive elimination occurs with inversion at carbon as depicted in **49**. Depicting palladium as a leaving



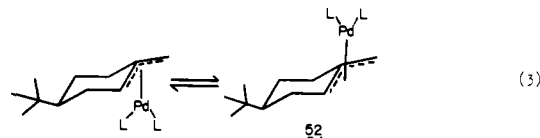
group in the classical organic sense makes such a result less surprising. Attack on olefin-palladium(+2) complexes has been shown to be predominantly with inversion.³³ Thus, this stereochemical event can be generalized to attack on allyl systems.

Complexes like **29** are potentially interconvertible with an alternative isomer **51** through σ complex **50** (**50a** and **50b** are rotamers).^{9,18} Such an equilibrium is undetectable in the alkylation of **29** since the relative stereochemistry of the acyclic

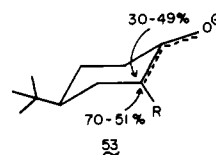


carbon with respect to palladium is unchanged. Thus, if attack occurs on the face opposite to palladium (henceforth referred to as distal attack), the identical product results from attack at the acyclic carbon of either **29** or **51**. On the other hand, stereochemistry of attack at the ring carbon is affected by the above equilibrium.

Alkylation of **37** broaches this question. The observation that **37** is a mixture of two complexes, but essentially only a single alkylation product emerges, suggests that the equilibration



represented in eq 3 is fast. Considering the alkylation involves distal attack, ring alkylation involves essentially only **52**. Thus, alkylation involves a strong preference for axial attack. This result may be compared with that of enolate **53** for which preference for axial attack has been noted.^{26a,34} Such a result may be rationalized on stereoelectronic grounds. In maximizing orbital overlap in the transition state of alkylation, axial attack allows the ring to adopt a chair conformation but equatorial attack requires distortion of the ring toward a boat. This explanation can be invoked to rationalize the preferred alkylation of **52**. The striking difference between **52** and the enolate **53** is the magnitude of the preference. The reaction



involving the transition metal exhibits a much greater stereoselectivity.

Allylic alkylation provides an unusual opportunity to elaborate an olefin. The transition metal can be considered a template upon which our substrate (olefin) is "absorbed" and subsequently activated in the allylic position. Reaction with the nucleophile effects "desorption" and gives the desired product. The template exerts a tremendous degree of chemo-, regio-, and stereocontrol on the reaction. The initial applications in synthesis further verify the utility of the method so documented in the accompanying manuscripts.

The question of the cost of the metal cannot be ignored. Ultimately a catalytic process would be most desirable. Nevertheless, palladium emerges as palladium black from these reactions and can be easily recycled. The uniqueness of the chemistry available plus the ability to recycle palladium makes this approach most attractive.

Experimental Section

General. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were determined on a Beckman IR-8 or Perkin-Elmer 267 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were determined on a Varian A-60A, Jeolco MH-100, or Bruker 270-MHz spectrometer. Chemical shifts are given in δ units in parts per million relative to tetramethylsilane as internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Coupling constants are given in hertz. Mass spectra were taken on an AEI-MS-902 mass spectrometer at an ionizing current of 98 ms and an ionization energy of 70 eV.

Column chromatography was performed on Grace silica gel, grade 62, mesh size 60-200 (Davidson Chemical). Thick layer chromatography was performed on 200 \times 400 \times 1.5 mm layers of Merck silica gel PF-254 (E. Merck, AG Darmstadt). Compounds were removed by repeated washings with ethyl ether. Solvent mixture chloroform, ether, and 2-propanol was 400:320:8.

Table V. Reaction Details for General Allylic Alkylations

Complex (mg, mmol)	Alkylating agent (mg, mmol)	NaH, ^a (mg, mmol)	Phosphine (mg, mmol)	Solvent	Time, h	Product, mg (% yield)	Rel % of products
1 (68, 0.134)	2b (86, 0.54)	17, 0.40	Ph ₃ P (148, 0.56)	THF	0.25	3 + 4 + 5, 49 (68) ^b	3:34%, 4:54%, 5:12%
8 (61, 0.129)	6 (78, 0.516)	22.6, 0.516	HMPT (84, 0.516)	Me ₂ SO (8 mL)	16	9, 30 (48) ^c	
10 (62, 0.115)	2b (42, 0.26)	5.1, 0.21	Ph ₃ P (122, 0.46)	DMF or THF	0.25	11, 41 (63) ^b	
12 (104, 0.233)	6 (142, 0.933)	39, 0.933	HMPT (152, 0.933)	Me ₂ SO (8 mL)	16	14, 76 (70) ^{c,d}	
13 (77, 0.139)	6 (84, 0.556)	23.6, 0.556	diphos (220, 0.278)	THF (8 mL)	12	15, 52 (69) ^c	
29 (98.5, 0.169)	2a (50.7, 0.686)	30.0, 0.686	diphos (136.5, 0.343)	THF (10 mL)	16	30, 64 (68) ^c	

^a Weights of sodium hydride are for 55% mineral oil dispersion. ^b Purified by TLC using chloroform. ^c Purified by TLC using a chloroform (400)-ether (320)-2-propanol (8) system. ^d Mp 62–63 °C (chloroform-hexane).

All reactions were carried out under an atmosphere of nitrogen. Tetrahydrofuran and 1,2-dimethoxyethane were distilled from sodium benzophenone ketyl. Dimethyl sulfoxide was distilled from calcium hydride. Sodium hydride was used as a 55% dispersion in mineral oil. Glassware for experiments requiring anhydrous conditions was dried with a flame under a stream of nitrogen. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich.

General Alkylation Procedure. Preparation of (*E*)-Methyl-2-methylsulfonyl-4-*n*-propyl-4-heptene (7). A solution of methyl sodio-2-methylsulfonylacetate was prepared by adding 65 mg (0.43 mmol) of methyl 2-methylsulfonylacetate to 13.5 mg of a 57% dispersion (0.32 mmol) of sodium hydride (washed free of mineral oil with *n*-pentane) in 1 mL of dry THF at room temperature. The resultant solution was added by syringe to a solution of 54 mg (0.11 mmol) of di- μ -chlorobis(1-ethyl-2-propyl- π -allyl)dipalladium and 1.26 mg (0.48 mmol) of triphenylphosphine in 1 mL of THF at room temperature. After the reaction mixture was stirred for 45 min, it was poured into ether and filtered through a pad of Celite to remove any metal. The supernatant was washed with water and dried (MgSO₄) to give an oil after concentration in vacuo. Preparative TLC (CHCl₃) gave a band for the product 7 (40 mg, 80% yield) which, upon extraction from the silica gel (ether) and evaporation, crystallized, mp 76 °C (carbon tetrachloride-pentane), in addition to 5 mg (10% recovery) of the starting π -allyl complex: NMR (CCl₄) δ 5.23 (t, *J* = 7.5 Hz, 1 H), 3.86 (dd, *J* = 11, 8 Hz, 1 H), 3.77 (s, 3 H), 2.98 (s, 3 H), 2.75 (m, 2 H), 1.98 (m, 4 H), 1.33 (m, 2 H), 0.90 (t, *J* = 7.0 Hz, 3 H), 0.89 (t, *J* = 7.0 Hz, 3 H); IR (CCl₄) 1737, 1642, 1327, 1115 cm⁻¹; mass spectrum *m/e* (rel %) 262 (3), 183 (34), 182 (56), 153 (96), 151 (20), 139 (36), 122 (100), 95 (40), 82 (46), 81 (54), 55 (50) (calcd for C₁₂H₂₂O₄S, 262.1239; found, 262.0940).

The ester was hydrolyzed by stirring 50 mg (0.19 mmol) of 7 with 90 mg (2.25 mmol) of sodium hydroxide in a water (1 mL)-methanol (10 mL) mixture at room temperature for 3 h. After evaporation of the methanol in vacuo, the aqueous layer was acidified to pH 1 with hydrochloric acid at 0 °C, extracted with ether, dried, and evaporated to give a crystalline solid (44 mg, 93%): mp 75–76 °C (carbon tetrachloride-*n*-pentane); NMR (CCl₄) δ 9.82 (s, 1 H), 5.26 (t, *J* = 7 Hz, 1 H), 3.95 (dd, *J* = 10, 4.5 Hz, 1 H), 3.03 (s, 3 H), 2.7 (m, 2 H), 2.0 (m, 4 H), 1.3 (m, 2 H), 0.95 (t, *J* = 7 Hz, 6 H); IR (CCl₄) 2700–3400, 1715, 1330, 1310, 1140, 1120 cm⁻¹; mass spectrum *m/e* (rel %) 203 (4), 139 (15), 127 (16), 125 (77), 124 (52), 123 (31), 109 (26), 95 (51), 81 (100), 67 (39), 55 (60). Anal. (C₁₁H₂₀O₄S) C, H.

Table V lists the reaction details for additional runs.

Spectral Data for Alkylation Products. 9: NMR (CDCl₃) δ 4.70 (m, 1 H), 4.0 (m, 1 H), 3.84 (s, 3 H), 3.16 and 3.06 (2s, 3 H), 2.9 (m, 1 H), 1.78 and 1.70 (2s, 3 H), 0.9–2.2 (m, 6 H); IR (CCl₄) 1739, 1328, 1122 cm⁻¹; mass spectrum *m/e* (rel %) 260 (1), 167 (27), 166 (76), 151 (20), 138 (88), 135 (36), 197 (48), 105 (21), 95 (40), 94 (100), 91 (50), 79 (70), 77 (34), 41 (30) (calcd for C₁₁H₁₈O₄S, 260.1081; found, 260.1084).

11: NMR (CCl₄) δ 5.17 (t, *J* = 7 Hz, 1 H), 4.12 (q, *J* = 7 Hz, 4 H), 3.37 (t, *J* = 7 Hz, 1 H), 2.50 (d, *J* = 7 Hz, 2 H), 0.8–1.4 (m, 20 H); IR (CCl₄) 1740 cm⁻¹; mass spectrum *m/e* (rel %) 284 (14), 160 (100), 124 (39), 85 (72) (calcd for C₁₆H₂₈O₄, 284.1987; found, 284.1936).

14: mp 62–63 °C; NMR (CDCl₃) δ 5.54 (m, 1 H), 4.07 (t, *J* = 7 Hz, 1 H), 3.88 (s, 3 H), 3.08 (s, 3 H), 2.94 (d, *J* = 7 Hz, 2 H), 2.3 (m, 4 H), 1.95 (m, 2 H); IR (CCl₄) 1738, 1435, 1330, 1117 cm⁻¹; mass spectrum *m/e* (rel %) 232 (2), 153 (71), 152 (100), 137 (25), 121 (40), 120 (50), 93 (73), 92 (20), 91 (33), 79 (27), 77 (30) (calcd for C₁₀H₁₆O₄S, 232.0769; found, 232.0766).

15 (mixture of diastereomers): NMR (CDCl₃) δ 5.35 (m, 1 H), 3.8 (m, 1 H), 3.78 (s, 3 H), 2.98 (s, 3 H), 2.74 (m, 2 H), 2.0–2.6 (m, 5 H), 1.28 (s, 3 H), 1.10 (m, 1 H), 0.80 and 0.75 (2s, 3 H); IR (CCl₄) 3049, 2841, 1748, 1332 cm⁻¹; mass spectrum *m/e* (rel %) 286 (2), 243 (11), 211 (82), 206 (21), 163 (29), 134 (23), 132 (87), 131 (36), 121 (25), 119 (25), 105 (39), 91 (100), 79 (29), 77 (24) (calcd for C₁₅H₂₂O₄S, 286.1238; found, 286.1242).

30: NMR (CDCl₃) δ 5.34 (m, 1 H), 3.75 (s, 3 H), 3.70 (s, 3 H), 3.45 (d, *J* = 10 Hz, 1 H), 2.88 (m, 1 H), 2.00–2.50 (m, 5 H), 1.24 (s, 3 H), 1.24 (m, 1 H), 1.04 (d, *J* = 7 Hz, 3 H), 0.76; IR (s, 3 H) (CHCl₃) 1758, 1735, 1633 cm⁻¹; mass spectrum *m/e* (rel %) 280 (3), 170 (20), 148 (28), 133 (20), 121 (11), 106 (14), 105 (100), 93 (13), 91 (14), 79 (11) (calcd for C₁₆H₂₄O₄, 280.1674; found, 280.1679).

General Experimental Procedure for Alkylation of Di- μ -chlorobis(1,2-tetramethylene- π -allyl)dipalladium (16). The ligand and complex were stirred for 15 min in 5 mL of solvent. In a separate flask, sodium hydride, washed free of mineral oil with pentane, was suspended in 5 mL of solvent and methyl methylsulfonylacetate or dimethyl malonate was added in one portion. After the mixture was stirred for 15–20 min, the solution of the anion was added under a stream of nitrogen to the solution of the complex and the resultant mixture stirred for 16 h at ambient temperature. The solution was filtered through Celite, poured into 100 mL of water, and extracted with ether (2 \times 100 mL). The combined organic layers were washed with water and saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. Filtration and removal of solvent in vacuo gave an oil which was purified by thick layer chromatography on silica gel (*R_f* 0.60 in chloroform-ether-2-propanol mixture) to give the products.

1-(2'-Carbomethoxy-2'-methylsulfonyl)ethyl)cyclohexene (17, X = SO₂CH₃): mp 72–73 °C; NMR (CDCl₃) δ 5.54 (m, 1 H), 3.84 (m, 1 H), 3.81 (s, 3 H), 3.00 (s, 3 H), 2.72 (~d, *J* = 8 Hz, 2 H), 1.96 (m, 4 H), 1.58 (m, 4 H); IR (CCl₄) 3021, 2959, 2882, 2857, 1748, 1330 cm⁻¹; mass spectrum *m/e* (rel %) 246 (2), 167 (23), 166 (100), 135 (30), 94 (35), 79 (45) (calcd for C₁₁H₁₈O₄S, 246.0935; found, 246.0934). 2-(Carbomethoxymethylsulfonylmethyl)methylene-cyclohexane (18, X = SO₂CH₃): NMR (CDCl₃) δ 4.91, 4.76, 4.72 (3s, 2 H), 4.3 (m, 1 H), 3.84, 3.74 (2s, 3 H), 3.05, 3.02 (2s, 3 H), 2.2 (m, 3 H), 1.6 (m, 6 H); IR (CCl₄) 3096, 3049, 2959, 2882, 1748, 1660, 1456, 1439, 1330 cm⁻¹. The two products cochromatographed under the above conditions and ratios of products were determined by NMR integration of the peaks at δ 5.54 vs. 4.91, 4.76, 4.72. Product ratios were determined on crude material as well as purified material and were consistent in all cases. Reaction details appear in Table VI and the ratios appear in Table I. 1-(2'-Dicarbomethoxyethyl)cyclohexene (17, X = CO₂CH₃): NMR (CDCl₃) δ 5.46 (m, 1 H), 3.75 (s, 6 H), 3.56 (t, *J* = 8 Hz, 1 H), 2.52 (d, *J* = 8 Hz, 2 H), 1.4–2.2 (m, 8 H); IR (CCl₄) 2862, 1764, 1742, 1648 cm⁻¹; mass spectrum *m/e* (rel %) 226 (20), 208 (1), 195 (20), 167 (12), 166 (42), 163 (15), 138 (16), 135 (23), 134 (20), 133 (47), 107 (20), 95 (27), 94 (100), 91 (22), 79 (57),

Table VI. Reaction Details for Alkylation of **16**

16 , mg, mmol	Ligand (mg, mmol)	Alkylating Agent (mg, mmol)	NaH, ^a mg, mmol	Solvent	Product, ^b mg (% yield)
198, 0.420	(PhO) ₃ P (520, 1.67)	6 (510, 3.35)	146, 3.35	Me ₂ SO	177 (86)
126, 0.266	(PhO) ₃ P (330, 1.07)	6 (325, 2.14)	93, 2.14	THF	87 (69)
143, 0.300	(CH ₃ O) ₃ P (150, 1.20)	6 (184, 1.2)	52.7, 1.2	Me ₂ SO	134 (91)
189, 0.380	(CH ₃ O) ₃ P (189, 1.52)	6 (231, 1.52)	66.3, 1.52	THF	163 (88)
152, 0.321	Ph ₃ P (337, 1.28)	6 (390, 2.57)	112, 2.57	Me ₂ SO	119 (75)
109, 0.230	Ph ₃ P (284, 0.920)	6 (140, 0.92)	40, 0.92	THF	92 (81)
133, 0.281	(C ₄ H ₉) ₃ P (227, 1.12)	6 (171, 1.12)	49, 1.12	Me ₂ SO	138 (100)
134, 0.283	(C ₄ H ₉) ₃ P (229, 1.13)	6 (343, 2.26)	98.6, 2.26	THF	79 (57)
117, 0.247	Ph ₂ P(CH ₂) ₃ PPh ₂ (203, 0.494)	6 (150, 0.988)	43.1, 0.988	Me ₂ SO	122 (100)
178, 0.376	Ph ₂ P(CH ₂) ₃ PPh ₂ (310, 0.752)	6 (229, 1.5)	65.6, 1.5	THF	134 (72)
102, 0.226	diphos (180, 0.453)	6 (138, 0.906)	39.5, 0.906	Me ₂ SO	66 (60)
108, 0.228	diphos (181, 0.456)	6 (139, 0.912)	40, 0.912	THF	72 (64)
83, 0.175	HMPT (114, 0.700)	6 (107, 0.700)	30.6, 0.700	Me ₂ SO	50 (58) ^c
70, 0.147	HMPT (96, 0.586)	6 (89, 0.586)	25.6, 0.586	THF	65 (90%) ^c
126, 0.266	TOT ^d (321, 1.06)	6 (162, 1.06)	47, 1.06	Me ₂ SO	118 (90) ^e
103, 0.216	TOT ^d (264, 0.866)	6 (132, 0.87)	38, 0.87	THF	N.A. ^f
105, 0.222	Ph ₂ PC ₆ H ₄ CH ₃ -2 (245, 0.888)	6 (135, 0.888)	39, 0.88	Me ₂ SO	72 (66)
96, 0.202	Ph ₂ PC ₆ H ₄ CH ₃ -2 (223, 0.808)	6 (123, 0.808)	35.3, 0.808	THF	53 (53)
80, 0.169	(2-CH ₃ OC ₆ H ₄) ₃ P (238, 0.676)	6 (128, 0.844)	36.8, 0.844	Me ₂ SO	66 (80)
168, 0.228	(2-CF ₃ C ₆ H ₄) ₃ P (425, 0.912)	6 (277, 1.82)	79.6, 1.82	Me ₂ SO	88 (79)
104, 0.219		6 (134, 0.88)	38.4, 0.88	Me ₂ SO	N.A. ^f
82, 0.173		6 (105, 0.692)	30.2, 0.692	THF	N.A. ^f
95, 0.20		6 (243, 1.60)	69.8, 1.60	HMPA	N.A. ^f
131, 0.276	TMEDA (64, 0.553)	6 (168, 1.11)	48.3, 1.11	Me ₂ SO	16 (12)
150, 0.317	TMEDA (74, 0.634)	6 (193, 1.27)	55.3, 1.27	THF	27 (17)
71, 0.150	Ph ₃ As (183, 0.599)	6 (199, 1.31)	57.2, 1.31	Me ₂ SO	33 (45)
210, 0.443	Ph ₃ As (543, 1.77)	6 (270, 1.77)	77.4, 1.77	THF	188 (86)
106, 0.223	HMPT (146, 0.893)	2a (118, 0.893)	38.2, 0.893	Me ₂ SO	3 (36) ^g
101, 0.213	HMPT (139, 0.853)	2a (252, 1.91)	83.2, 1.91	Me ₂ SO	67 (70) ^g
95, 0.200	TOT ^d (242, 0.801)	2a (196, 0.801)	34.9, 0.801	Me ₂ SO	54 (60) ^g
83, 0.175		2a (93, 0.701)	30.6, 0.701	Me ₂ SO	N.D. ^h

^a Weight refers to 57% mineral oil dispersion of sodium hydride. ^b The product is a mixture of **17** and **18** (X = SO₂CH₃) whose ratio is listed in Table I. ^c The product is pure **17** (X = SO₂CH₃), mp 72–73 °C (chloroform–hexane). ^d Complex and TOT are heated to 60 °C and then cooled to room temperature before addition of the nucleophile. ^e The product is mainly **18** (X = SO₂CH₃) from which a pure sample was obtained for characterization. ^f No alkylation product detected. ^g The product is a mixture of **17** and **18** (X = CO₂CH₃) whose ratio is listed in the results section. ^h Not determined. The alkylation went in very low yield. The ratio is listed in Table I.

77 (21), 67 (19), 41 (31), 39 (21) (calcd for C₁₂H₁₈O₄, 226.1205; found, 226.1198). 2-(Dicarbomethoxymethyl)methylidenecyclohexane (**18**, X = CO₂CH₃): NMR (CCl₄) δ 4.66, 4.57 (2s, 2 H), 3.76, 3.66 (2s, 6 H), 3.60 (d, *J* = 7 Hz, 1 H), 2.98 (m, 1 H), 1.4–2.6 (m, 8 H); IR (CCl₄) 1760, 1740, 1648, 900 cm⁻¹; mass spectrum *m/e* (rel %) 226 (4), 166 (35), 163 (17), 162 (16), 138 (15), 135 (22), 134 (19), 133 (51), 95 (27), 94 (100), 91 (12), 79 (38), 77 (18), 67 (19), 46 (22) (calcd for C₁₂H₁₈O₄, 226.12045; found, 226.12019). The ratio of products was determined by NMR integration of the peak at δ 5.46 vs. those at 4.66 and 4.57. Reaction details appear in Table VI and ratios in the Results section.

Alkylation of Di- μ -chlorobis(1-methyl-2,3-tetramethylene- π -allyl)dipalladium (19**).** Di- μ -chlorobis(1-methyl-2,3-tetramethylene- π -allyl)dipalladium(**19**) and ligand were stirred for 15 min in 5 mL of Me₂SO or THF. In a second flask, sodium hydride was washed with pentane and blown dry under a stream of nitrogen and 3–5 mL of Me₂SO or THF added. To this was added dimethyl malonate, methyl methylsulfonylacetate, or methyl phenylsulfonylacetate in one portion; the solution was stirred for 15 min and then added in one portion under a stream of nitrogen to the first solution. After the mixture was stirred for 12–16 h at ambient temperature, the solution was poured into water and extracted with ether (2 \times 75 mL). The combined ether layers were washed with water and saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. Filtration and concentration in vacuo gave an oil which was purified by preparative thick layer chromatography on silica gel (*R_f* 0.3, chloroform) to give the alkylation product. 1-(1'-Methyl-2',2'-dicarbomethoxyethyl)-cyclohexene and 2-(dicarbomethoxymethyl)ethylidenecyclohexane: NMR (CDCl₃) δ 5.47 (m) and 5.21 (q) (*J* = 7 Hz, 1 H), 3.69 and 3.62 (2s, 6 H), 2.90 (m, 1 H), 1.92 (m, 4 H), 1.57 (m) and 1.04 (d) (*J* = 7 Hz, 7 H); IR (CCl₄) 3025, 2950, 2845, 1750 (br), 1465, 1440 cm⁻¹;

mass spectrum *m/e* (rel %) 240 (10), 209 (5), 208 (6), 177 (14), 176 (18), 149 (13), 148 (21), 133 (48), 109 (39), 108 (100), 101 (8), 93 (25), 91 (9), 81 (10), 79 (41), 67 (20), 59 (9), 55 (10) (calcd for C₁₃H₂₀O₄, 240.13616; found, 240.13660). 1-(1'-Methyl-2',2'-dicarbomethoxyethyl)cyclohexene: NMR (CDCl₃) δ 5.46 (m, 1 H), 3.68 and 3.62 (2s, 2 H), 2.90 (m, 1 H), 1.8–2.1 (m, 4 H), 1.4–1.7 (m, 4 H), 1.04 (d, *J* = 7 Hz, 3 H); IR (CCl₄) 1750 (br), 1672 cm⁻¹. These compounds were further characterized by decarbomethoxylations and the resultant compounds separated by VPC and characterized.

1-(1'-Methyl-2'-carbomethoxy-2'-phenylsulfonyl)ethylcyclohexane and 2-(carbomethoxyphenylsulfonyl)ethylidenecyclohexane: NMR (CDCl₃) δ 7.4–8.0 (m, 5 H), 5.46 and 5.2 (m, 1 H), 4.58 and 4.46 (2d, *J* = 6 Hz, 0.5 H), 4.18 and 4.08 (2d, *J* = 7 Hz), 2.64 and 3.40 (2s, br, 3 H), 3.9–3.3 (m, 1 H), 1.1–2.6 (m) and 1.06 (d) (*J* = 7 Hz, 12 H); IR (CCl₄) 1745, 1585, 1335, 1140 cm⁻¹; mass spectrum *m/e* (rel %) 322 (0.5), 291 (2), 215 (10), 180 (53), 165 (52), 150 (7), 149 (35), 141 (11), 133 (6), 121 (23), 109 (25), 108 (100), 107 (10), 93 (24), 91 (23), 79 (40), 78 (16), 77 (60), 67 (21), 59 (16), 55 (22), 53 (12), 51 (17). These were fully and separately characterized after desulfonylation which gave the same products as obtained above.

1-(1'-Methyl-2'-carbomethoxy-2'-phenylsulfonyl)ethylcyclohexene: NMR (CDCl₃) δ 7.8–8.0 (m, 2 H), 7.4–7.7 (m, 3 H), 5.45 (m, 1 H), 4.19 and 4.08 (2d, *J* = 7 Hz, 1 H), 3.65 and 3.39 (2s, 3 H), 2.96 (m, 1 H), 1.7–2.1 (m, 4 H), 1.3–1.7 (m, 4 H), 1.37 and 1.06 (2d, *J* = 7 Hz, 3 H); IR (CCl₄) 1745, 1585, 1330, 1145 cm⁻¹.

1-(1'-Methyl-2'-carbomethoxy-2'-methylsulfonyl)ethylcyclohexene: NMR (CDCl₃) δ 5.68 and 4.62 (m, 1 H), 3.90 (m, 1 H), 3.88 and 3.80 (2s, 3 H), 3.10 and 3.06 (2s, 3 H), 2.9 (m, 1 H), 2.0 (m, 4 H), 1.64 (m, 4 H), 1.38 and 1.16 (2d, *J* = 8 Hz, 3 H); IR (CCl₄) 1748, 1670, 1330, 1135 cm⁻¹; mass spectrum *m/e* (rel %) 260 (6), 211 (10), 180 (40), 149 (28), 121 (46), 109 (28), 108 (100), 92 (38), 90 (27), 81

Table VII. Experimental Details for Alkylation of 19

19, mg, mmol	Ligand (mg, mmol)	Alkylating agent (mg, mmol)	NaH, mg, mmol	Solvent	Product, ^a mg (% yield)
110, 0.219	HMPT (143, 0.876)	6 (133, 0.876)	32.2, 0.876	THF	55 (48)
57, 0.114	diphos (90.7, 0.228)	6 (69.3, 0.46)	10.9, 0.46	THF	58 (98) ^b
94, 0.187	HMPT (122, 0.750)	PhSO ₂ CH ₂ CO ₂ CH ₃ (160.5, 0.750)	18, 0.750	THF	68 (56)
197, 0.339	diphos (270, 0.680)	PhSO ₂ CH ₂ CO ₂ CH ₃ (214, 1.0)	24, 1.0	THF	180 (83)
140, 0.279	Ph ₃ P (295, 1.13)	2a (132, 1.0)	24, 1.0	Me ₂ SO	120 (90)
117, 0.233	diphos (186, 0.466)	2a (123, 0.932)	22.4, 0.932	Me ₂ SO	112 (100)

^a The product and ratio are given in Table II. ^b A slight contamination of the product by diphos led to rechromatography and recovery of 32 mg (55%).

(23), 79 (58), 77 (21), 67 (27) (calcd for C₁₂H₂₀O₄S, 260.1082; found, 260.1084). Table VII summarizes the reaction details for each run.

Formation and Alkylation of the 1,2-Bis(diphenylphosphino)ethane-Tetrafluoroborate Cationic Complex of Di- μ -chlorobis(1,2-tetramethylene- π -allyl)dipalladium(II) (24) with Methyl Methylsulfonylacetate. Di- μ -chlorobis(1,2-tetramethylene- π -allyl)dipalladium(II) (353 mg, 0.745 mmol), 1,2-bis(diphenylphosphino)ethane (605 mg, 1.52 mmol), and sodium tetrafluoroborate (500 mg, 4.56 mmol) were stirred for 24 h at ambient temperature in 30 mL of chloroform. Filtration and removal of solvent in vacuo gave 980 mg (96%) of a light yellow powder which was used without purification: NMR (CDCl₃) δ 7.40 (m, 20 H), 4.70 (m, 1 H), 4.24 (br m, 1 H), 0.80–3.30 (m, 13 H); IR (CCl₄) 3086, 2967, 2920, 2874, 2762, 2732, 1727, 1678, 1637, 1613, 1442, 1377 cm⁻¹.

The complex (209 mg, 0.298 mmol) was dissolved in 5 mL of dry tetrahydrofuran. In a second flask *n*-butyllithium (0.47 mL, 0.60 mmol, 1.4 M in hexane) was added via syringe to methyl methylsulfonylacetate (1 mg, 0.60 mmol) in 3 mL of tetrahydrofuran. After the mixture was stirred for 15 min, the second solution was added in one portion under a stream of nitrogen to the first solution. After this was stirred for 12 h at ambient temperature, the solution was filtered and the filtrate poured into ether. The ether solution was washed with water and saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. Filtration and removal of solvent in vacuo gave 1-(2'-carbomethoxy-2'-methylsulfonyl)ethyl)cyclohexane and 2-(carbomethoxymethylsulfonylmethyl)methylene cyclohexane in 69% (47 mg) yield in a ratio of 4:1 as determined by NMR integration as previously described.

Alkylations of Bis[chloro(3,4,7-trihapto-N-acetyl-4-ethyl)denepiridine]palladium(II) (25). A. Preparation of 26 (X = CO₂CH₃). The π -allyl complex 25 (110 mg, 0.187 mmol), 195 mg (0.746 mmol) of triphenylphosphine, and the malonate anion generated from 98.4 mg (0.746 mmol) of dimethyl malonate and 17.9 mg (0.746 mmol) of sodium hydride in 9 mL of THF were reacted for 15 h at room temperature according to the general procedure. After the usual workup and preparative TLC (2:3 ether–chloroform), 49.3 mg (47% yield) of 26 (X = CO₂CH₃) was isolated: NMR (CDCl₃) δ 5.47 (m, 1 H), 3.2–4.0 (m, 5 H), 3.65 and 3.73 (2s, 6 H), 2.8–3.1 (m, 1 H), 2.05 and 2.09 (2s, 3 H), 2.10 (m, 2 H), 1.07 (d, *J* = 6.5 Hz, 3 H); IR (CHCl₃) 1758, 1735, 1633 cm⁻¹; mass spectrum *m/e* (rel %) 283 (3), 282 (5), 281 (7), 268 (10), 255 (25), 254 (41), 224 (16), 152 (60), 151 (27), 124 (21), 123 (27), 110 (50), 109 (20), 106 (20), 96 (20), 82 (20), 43 (100).

B. Direct Preparation of 27 via 26 (X = CO₂CH₃). The π -allyl complex 25 (100 mg, 0.17 mmol), 178 mg (0.680 mmol) of triphenylphosphine, and the malonate anion generated from 89.8 mg (0.68 mmol) of dimethyl malonate and 16.3 mg (0.680 mmol) of sodium hydride in 10 mL of THF were reacted for 20 h at room temperature according to the general procedure. Upon completion, the reaction was poured into 50 mL of ether and filtered through Celite to remove the precipitated palladium. Addition of 1 mL of water to quench any malonate anion, drying (Na₂SO₄), filtering, and evaporating in vacuo gave a brown tarry residue which was taken up in 20 mL of ether and filtered once more to remove additional palladium. Evaporation of the ether followed by Kugelrohr distillation (180–220 °C at 0.2 mm) gave 178.5 mg of crude product contaminated with triphenylphosphine and dimethyl malonate. The distillate was dissolved in 3 mL of degassed methanol and 84.5 mg (1.51 mmol) of potassium hydroxide added. After the mixture was stirred at room temperature for 5 h, the solvent was evaporated in vacuo and the residue dissolved in 20 mL

of water. Extraction with ether removed the triphenylphosphine. Acidification of the water layer with concentrated hydrochloric acid, saturation with sodium chloride, and extraction with ethyl acetate gave 79 mg of oil after drying (Na₂SO₄) and evaporating in vacuo. Decarboxylation was completed by heating the neat oil to 160 °C for 15 min. After cooling to room temperature and dissolution in 5 mL of ethyl acetate, the product was esterified with diazomethane. Evaporation in vacuo and Kugelrohr distillation (180–220 °C at 0.2 mm) gave 63.5 mg (83%) of pure product which showed one peak on VPC (5% Carbowax 20M on Chromosorb N column): NMR (CCl₄) δ 5.42 (m, 1 H), 3.90 (m, 2 H), 3.61 (s, 3 H), 3.48 (m, 2 H), 1.9–2.7 (m, 5 H), 2.00 (s, 3 H), 1.07 (d, *J* = 7 Hz, 3 H); IR (CCl₄) 1743, 1652 cm⁻¹; mass spectrum *m/e* (rel %) 225 (37), 194 (11), 182 (10), 152 (50), 151 (21), 149 (15), 124 (45), 110 (58), 109 (23), 82 (74), 72 (33), 71 (28), 69 (16), 43 (60), 42 (100), 41 (58) (calcd for C₁₂H₁₉NO₃, 225.1365; found, 225.1363).

C. Preparation of 26 (X = PhSO₂). According to the general alkylation procedure, 203.9 mg (0.346 mmol) of complex 25 and 363 mg (1.384 mmol) of triphenylphosphine were alkylated with 222 mg (1.04 mmol) of methyl phenylsulfonylacetate and 24.9 mg (1.04 mmol) of sodium hydride in 10 mL of THF for 14 h at room temperature. The reaction was quenched by addition of 1 mL of water, dried (Na₂SO₄), filtered to remove precipitate, and concentrated in vacuo. The resultant crude oil was directly purified by preparative TLC (1:9 methanol–ether) to give 221 mg (88%) of product as a brown oil. Dissolution in 20 mL of ether, filtration, evaporation in vacuo, and rechromatography led to recovery of 132.5 mg (52%) of pure product as a diastereomeric mixture: NMR (CDCl₃) δ 7.84 (m, 2 H), 7.57 (m, 3 H), 5.46 (m, 1 H), 2.0–4.2 (m, 8 H), 1.9–2.5 (m, 3 H), 2.07 (s, 3 H), 1.38 and 1.07 (2d, *J* = 7 Hz, 3 H); IR (CCl₄) 1750, 1660, 1652, 1332, 1143 cm⁻¹; mass spectrum *m/e* (rel %) 365 (0.2), 121 (30), 119 (93), 117 (100), 84 (15), 82 (25), 43 (20) (calcd for C₁₈H₂₃O₅NS, 365.1297; found, 365.1307).

D. Desulfonylation of 26 (X = PhSO₂) to 27. To a solution of 37.8 mg (0.104 mmol) of sulfone 26 in 8 mL of dry methanol at 0 °C was added 5.76 g of ground 6% sodium amalgam. After 80 min, the slurry was filtered and the amalgam washed with additional methanol and then water. The filtrate was evaporated in vacuo and the residue diluted with 30 mL of water. After extracting with ethyl acetate and drying (Na₂SO₄), Kugelrohr distillation (180–220 °C at 0.2 mm) gave 14.4 mg (62%) of 27, identical with the previously characterized sample.

Decarboxylation of 30. A solution of 237.4 mg (0.976 mmol) of 30, 48.3 mg (0.985 mmol) of sodium cyanide, and 1.00 g (5.32 mmol) of lithium iodide trihydrate in 3 mL of DMF was heated for 10 h at 120 °C. After cooling, the reaction was diluted with 50 mL of ether and washed with water. The organic layer was dried (MgSO₄), evaporated in vacuo, and purified by preparative TLC (CHCl₃) to give 173.9 mg (80%) of 31 as a colorless oil: NMR (CCl₄) δ 5.24 (m, 1 H), 3.64 (s, 3 H), 2.1–2.7 (m, 8 H), 1.27 (s, 3 H), 1.12 (d, *J* = 8 Hz, 1 H), 0.98 (d, *J* = 7 Hz, 3 H), 0.79 (s, 3 H); IR (CHCl₃) 1730, 1655 cm⁻¹; mass spectrum *m/e* (rel %) 222 (3), 147 (16), 133 (17), 121 (22), 105 (100), 93 (23), 91 (32), 79 (26), 77 (22) (calcd for C₁₄H₂₂O₂, 222.1620; found, 222.1620).

Hydroxylation of 31 and Lactonization to 33. To a solution of 173.9 mg (0.784 mmol) of 31 in 1 mL of ether was added a solution of 201.9 mg (0.795 mmol) of osmium tetroxide in 5 mL of ether containing 0.6 mL of pyridine. After 15 h at room temperature, addition of 364 mg (3.54 mmol) of sodium bisulfite in 6.25 mL of water and 4.16 mL of pyridine quenched the reaction. Stirring was continued for 3 h.

Table VIII. Experimental Details for Alkylation of Complex 37

37, mg, mmol	Ligand (mg, mmol)	Alkylating agent (mg, mmol)	NaH, ^a mg, mmol	Solvent	Product, ^b mg (% yield)
108, 0.185	TOT (224, 0.740)	2a (98, 0.740)	32.4, 0.740	Me ₂ SO	86 (83)
86, 0.147	HMPT (96, 0.588)	2a (155, 1.176)	49.0, 1.176	Me ₂ SO	83 (100)
65, 0.111	TOT (135, 0.444)	6 (68, 0.444)	19.5, 0.444	Me ₂ SO	35 (52)
104, 0.178	HMPT (116, 0.710)	6 (108, 0.710)	30.9, 0.710	Me ₂ SO	33 (31)

^a Weights listed are for 55% mineral oil dispersion. ^b Ratio of isomers are listed in Table IV.

Methylene chloride extracted the glycol. After drying (Na₂SO₄) and evaporation in vacuo, the residue was taken up in benzene and washed with cold dilute aqueous hydrochloric acid to remove pyridine. The benzene layer was concentrated to ~5 mL, a spatula tip of TsOH added, and the mixture refluxed 30 min with azeotropic removal of any water. Dilution with 20 mL of benzene, washing with saturated aqueous sodium bicarbonate solution, drying (MgSO₄), and evaporation in vacuo gave 176 mg of oil which was further purified by preparative TLC (ether) to give 109 mg (62%) of a viscous oil that solidified slowly; for NMR see Results and Discussion sections; IR (CHCl₃) 3595, 1780, 1392, 1376 cm⁻¹; mass spectrum *m/e* (rel %) 224 (1), 206 (5), 180 (65), 165 (29), 154 (53), 153 (100), 138 (40), 126 (55), 109 (24), 95 (53), 91 (26), 83 (80), 81 (35), 69 (33), 67 (30), 55 (30) (calcd for C₁₃H₂₀O₃, 224.1411; found, 224.1416). Anal. (C₁₃H₂₀O₃) C, H.

Alkylation of Bis[chloro-(7,1,2-trihapto-4-tert-butylmethylene-cyclohexane)palladium(II)] (37). **A. With TOT.** The complex 37 and TOT were heated in 5 mL of Me₂SO at 60–70 °C for 1.5 h and then cooled to room temperature. As usual, a solution of the anion was prepared in a separate flask. After addition of the anion to the complex, the reaction was stirred for 16 h at ambient temperature. It was poured into water and extracted with ether. The combined ether extracts were washed with water and then saturated aqueous sodium chloride solution, dried (MgSO₄), filtered, and evaporated in vacuo to give an orange oil. Addition of methanol and cooling induced precipitation of the tri-*o*-tolylphosphine which was removed by filtration. The filtrate was concentrated in vacuo and purified in the usual way. The reaction details are summarized in Table VIII.

B. With HMPT. The general procedure and workup previously outlined was employed for alkylations of 37 activated by this phosphine. Details are summarized in Table VIII.

1-(2'-Dicarbomethoxyethyl)-4-*tert*-butylcyclohexene and 2-(dicarbomethoxymethyl)-4-*tert*-butylmethylene-cyclohexane: NMR (CDCl₃) δ 5.41 (m), 4.74 (m), 3.74, 3.72, 3.66 (3s, 6 H), 3.1–3.7 (m, 1 H), 2.54 (m, 2 H), 1.0–2.2 (m), 0.83, 0.81, 0.79 (3s, 9 H); IR (CCl₄) 2960, 2930, 2870, 1760, 1743, 1436, 1395, 1368 cm⁻¹; mass spectrum *m/e* (rel %) 282 (10), 251 (8), 219 (12), 191 (8), 190 (7), 166 (23), 165 (27), 150 (41), 145 (40), 135 (27), 134 (28), 133 (53), 132 (22), 107 (18), 105 (20), 101 (17), 95 (19), 94 (100), 93 (60), 92 (40), 91 (25), 79 (37), 77 (20), 52 (55) (calcd for C₁₀H₂₆O₄, 282.18304; found, 282.18347). These compounds were separately characterized after decarbomethoxylation (vide infra).

(*E*)-2-(Carbomethoxymethyl)-4-*tert*-butylmethylene-cyclohexane (40a): for NMR (CDCl₃) see Results and Discussion sections; IR (CCl₄) 3094, 2970, 2784, 1750, 1656 cm⁻¹; mass spectrum *m/e* (rel %) 224 (1), 168 (33), 166 (13), 150 (17), 136 (27), 135 (21), 133 (28), 108 (19), 107 (23), 95 (21), 94 (70), 93 (77), 92 (35), 91 (17), 81 (13), 79 (23), 77 (12), 57 (100), 55 (16), 43 (12), 41 (45), 39 (11) (calcd for C₁₄H₂₄O; 224.1776; found, 224.1784).

1-(2'-Carbomethoxyethyl)-4-*tert*-butylcyclohexene (38, X = H): NMR (CDCl₃) δ 5.38 (m, 1 H); 3.64 (s, 3 H), 1.0–2.6 (br m, 11 H), 0.85 (s, 9 H); IR (CCl₄) 3080, 2960, 2870, 1740, 1435, 1368 cm⁻¹; mass spectrum *m/e* (rel %) 225 (1), 224 (1), 168 (47), 146 (33), 145 (20), 108 (41), 107 (38), 94 (64), 93 (88), 92 (28), 91 (22), 79 (32), 58 (100) (calcd for C₁₄H₂₄O₂, 224.17755; found, 224.17778).

1-(2'-Carbomethoxy-2'-methylsulfonyl)ethyl)-4-*tert*-butylcyclohexene (38, X = SO₂CH₃): NMR (CDCl₃) δ 5.56 (m, 1 H), 3.82 (s, 3 H), 3.84 (m, 1 H), 3.00 (s, 3 H), 2.72 (d, *J* = 9 Hz, 2 H); 1.68–2.12 (m, 4 H), 1.22 (m, 3 H), 0.86 (s, 9 H); IR (CCl₄) 1741, 1705, 1655, 1120 cm⁻¹. It was further characterized by desulfonylation to give 1-(2'-carbomethoxyethyl)-4-*tert*-butylcyclohexene. A mixture of 38 and 39 (X = SO₂CH₃) showed peaks at δ 4.99 and 4.79 which compared with the absorption at 5.56 allowed determination of the ratio

of 38 to 39. The spectral data for the mixture of 38 and 39 (X = CH₃SO₂) were as follows: NMR (CDCl₃) δ 5.6 (m), 4.99 and 4.79 (2s), 3.87, 3.84, 3.76 (3s, 3 H), 3.09, 3.02 (2s, 3 H), 2.76 (m), 1.1–2.4 (m), 0.88, 0.86, 0.89 (3s, 9 H); IR (CCl₄) 3067, 2967, 2874, 1742, 1650, 1538, 1437, 1368, 1330 cm⁻¹. Further characterization was achieved by desulfonylation and comparison with 38 and 39 (X = H) prepared above.

Decarbomethoxylation of 38 and 39 (X = CO₂CH₃). **A. Of 38 (X = CO₂CH₃).** 1-(2'-Dicarbomethoxyethyl)-4-*tert*-butylcyclohexene (83 mg, 0.294 mmol), lithium iodide trihydrate (225 mg, 1.2 mmol), and sodium cyanide (13.3 mg, 0.294 mmol) were heated to 120 °C for 12 h in 5 mL of dimethylformamide and then allowed to cool to room temperature. The cooled solution was poured into water and then extracted with ether (2 \times 75 mL). The combined ether layers were washed with water, 10% aqueous hydrochloric acid solution, and saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. After filtration and removal of solvent in vacuo, the crude oil was purified by preparative thick layer chromatography on silica gel (*R_f* 0.70, chloroform as eluting solvent) to give 38 (X = H) (66 mg, 100%) as a colorless oil. See above for spectral data.

B. Of 39 (X = CO₂CH₃). As outlined above, 118 mg (0.41 mmol) of 39 (X = CO₂CH₃), 391 mg (2.08 mmol) of lithium iodide trihydrate, and 20.4 mg (0.416 mmol) of sodium cyanide were reacted to produce 93 mg (100%) of 39 (X = H). See above for spectral data.

Preparation of (Z)-2-(Carbomethoxymethyl)-4-*tert*-butylmethylene-cyclohexane (40b). The pyrrolidine enamine of 4-*tert*-butylcyclohexanone (3.75 mg, 18.1 mmol) and methyl bromoacetate (5.54 g, 36.2 mmol) were refluxed for 3 h in 25 mL of absolute methanol and then 2 mL of water was added and reflux continued for an additional 3 h. After cooling to room temperature, the solution was poured into ether. The ether solution was washed with water and saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. After filtration and removal of solvent in vacuo, the product was purified by dry column chromatography on silica gel to give 2-(carbomethoxymethyl)-4-*tert*-butylcyclohexanone (2.5 g, 61%). The product was treated with 1 equiv of sodium methoxide in methanol at ambient temperature for 6 h, reisolated, and used without further purification.

n-Butyllithium (3.66 mL, 1.45 M, 5.3 mmol) was added over 5 min to methyltriphenylphosphonium bromide (1.89 g, 5.3 mmol) in 25 mL of ether. The yellow solution was allowed to stir at ambient temperature for 24 h and then the above product (1.20 g, 5.3 mmol) in 5 mL of ether was added over a 10-min period, maintaining a gentle reflux. The mixture was refluxed for 12 h, cooled to room temperature, and filtered to remove triphenylphosphine oxide. Additional ether was added to the filtrate and the combined ether solution washed with water and saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. After filtration and removal of solvent in vacuo, the crude product was purified on preparative thick layer chromatography on silica gel (*R_f* 0.70, chloroform as eluting solvent) to give 600 mg (50% yield) of 40b as a colorless oil: NMR (CDCl₃) δ 4.64, 4.45 (2s, 2 H), 3.65 (s, 3 H), 1–2.7 (m, 11 H), 0.85 (s, 9 H); IR (CCl₄) 3100, 2970, 2885, 1748, 1654 cm⁻¹; mass spectrum *m/e* (rel %) 224 (1), 168 (70), 136 (30), 108 (39), 107 (31), 104 (72), 163 (75), 57 (100) (calcd for C₁₄H₂₄O₂, 224.17763; found, 224.17340).

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Allylic Alkylation: Nature of the Nucleophile and Application to Prenylation

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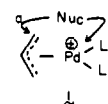
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Abstract: Alkylation of π -allylpalladium complexes requires a "soft" nucleophile. Successful alkylating agents include the anions derived from malonate, β -keto sulfones, β -keto sulfoxides, and β -keto sulfides. The regioselectivity as a function of nucleophile is considered. The use of sulfur stabilized anions has proven quite versatile. The sulfone ester can lead to the addition at an allylic position of an acetate by mild desulfonylation or an alkyl group by decarbomethoxylation followed by desulfonylation. The latter has led to a new prenylation sequence which allows direct conversion of lower terpenes into the higher terpenes as illustrated for the conversion of a monoterpene to a sesquiterpene and the latter to a diterpene. The use of β -keto sulfoxides allowed direct alkylation-elimination to a dienoate.

The ability to utilize the olefinic linkage as a point for structural elaboration depends upon carrying out reactions at that site in a specific manner. As shown in the previous two papers in this series, the allylic position of olefins can be selectively activated and alkylated via organopalladium chemistry.^{1,2} In this paper, we wish to explore the scope of this process and its application to acyclic terpenes.³

Results

The π -allyl cationic complexes are ambident electrophiles. Reaction can be envisioned to occur either at carbon (path a in **1**) or palladium (path b in **1**). With malonate anion, we have shown that reaction occurs via path a;¹ however, the divergency



of attack would be expected to be dependent upon the nucleophile. To explore this question, we examined a series of nucleophiles with complex **2** using triphenylphosphine as the

