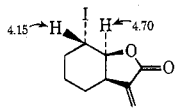
References and Notes

(1) P. A. Grieco, *Synthesis*, 67 (1975), and references therein.
(2) F. E. Ziegler, A. F. Marino, O. A. C. Petroff, and W. Studt, *Tetrahedron Lett.*, 2035 (1974).
(3) J. P. Marino and J. S. Farina, *Tetrahedron Lett.*, 3901 (1975).
(4) J. Ficini and J. C. Depezay, *Tetrahedron Lett.*, 4795 (1969).
(5) The upper limit for the thermal stability of reagents **3–6** has been estimated by us and others[4] to be approximately −40 °C. Reaction mixtures kept above −40 °C for any period of time darkened and the yields of products were diminished.
(6) The 3,4-epoxycyclohexene reaction with reagent **3** at −40 °C yielded about 7% 1,2 adduct. The reaction of **3** with 3,4-epoxycycloheptene failed to yield any adducts at −40 °C for 6–8 h.
(7) G. H. Posner, *Org. React.*, **22**, 253 (1975).
(8) B. Rickborn and J. Starosick, *J. Am. Chem. Soc.*, **93**, 3046 (1971).
(9) D. M. Wieland and C. R. Johnson, *J. Am. Chem. Soc.*, **93**, 3047 (1971).
(10) All of the chemical shifts cited here are given in ppm downfield from internal tetramethylsilane (60 MHz). The specific protons cited as well as the particular compounds were chosen because they were the most informative and definitive in making structural assignments. The multiplicities of the protons cited are not easily described without an actual spectrum but they are consistent with the assigned structures.
(11) The chemical shifts of the methine protons on carbons bearing the lactone oxygen in *cis*-α-methylene butyrolactone of cyclohexane and the corresponding trans isomer are δ 4.46 and 3.65 respectively [J. Marshall and N. Cohen, *J. Org. Chem.*, **30**, 3475 (1965)]. Also see ref 2 for spectral data for compound **10.**
(12) Lactone **14** was independently prepared by dehydrohalogenation of iodolactone i with DBN in benzene at room temperature. The preparation of i has been previously reported by us [J. P. Marino and D. M. Floyd, *J. Am. Chem. Soc.*, **96**, 7138 (1974)].



i

(13) Acetal **15** distilled between 95 and 100 °C (0.05 mmHg).
(14) Yields reported are isolated yields but they have not necessarily been maximized.
(15) The literature (see reference cited in 11) value for the chemical shifts of the lactone methines for *cis*- and *trans*-α-methylene-γ-butyrolactones of the cycloheptane series are δ 4.72 and 4.10, respectively. The absorptions that we have observed for the *trans*-lactone **17** (3.91) and the *cis*-lactone **18** (4.85) are most consistent for the assignments made.
(16) The 60-MHz NMR spectrum of **21** clearly showed coupling constants and chemical shifts for all of the methine hydrogens which were most consistent for the stereochemistry shown. Iodolactone **21** also failed to give an epoxide when treated under basic conditions. The preparation of **21** and analysis of its NMR spectrum were carried out by D. M. Floyd in this laboratory and full details will be published in a full paper.

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Allylic Substitutions with Retention of Stereochemistry

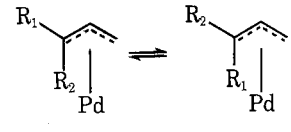
Summary: The "net SN2 displacements" of allylic acetates catalyzed by palladium proceed with complete retention of configuration at the carbon undergoing displacement and without loss of olefin geometry in a trisubstituted double bond.

Sir: The ability to perform displacements with inversion of configuration constitutes one of the most fundamental synthetic reactions in organic chemistry. Alkylations utilizing allylic halides, allylic sulfonate esters, etc., suffer from their high reactivity and consequently make stereochemical control difficult. With cyclohexenyl derivatives, the problems are further confounded by a tendency toward elimination reactions competing with the desired substitution reaction. The use of palladium-catalyzed allylic alkylations,[1,2] which allows use of the configurationally stable and easily handled allylic acetates, overcomes these limitations. Furthermore, these processes proceed with a net retention of configuration in contrast to the usual inversion which is observed in normal alkylations. Surprisingly, even though these reactions presumably involve π-allylpalladium intermediates[3] the stereochemistry of a trisubstituted double bond is retained in the alkylations.

In a previous paper, we suggested that the "net SN2 displacement" catalyzed by palladium(0) complexes proceeded with retention of configuration.[2] In order to establish this point unambiguously, we examined the alkylations of the cis (**1**) and trans (**2**) isomers of 3-acetoxy-5-carbomethoxycyclohexene[4] (see Scheme I). The cis isomer **1** is available by the methanolysis and acetylation of lactone **3**,[5] whereas the trans isomer **2** is available by acetylation of the hydroxy ester which, in turn, was isolated from a cis-trans mixture[6] by selective lactonization of the cis isomer. Whereas **1** was isomerically pure, VPC analysis[7a] of **2** indicated contamination to the extent of 7% by **1.**

Alkylation of **1** with the sodium salt of dimethyl malonate [catalytic amount of $(Ph_3P)_4Pd$, Ph_3P, THF; reflux; 92% yield] gave a single product **4**[4] which was assigned the cis stereochemistry.[8] At 270 MHz, the requisite coupling constants could be determined—$J_{AD} = J_{BD} = J_{CD} = 12.5$ Hz, $J_{BC} = 6.0$, $J_{AC} \sim 5$ Hz—which clearly indicate that both H_A and H_B are pseudoaxial. Alkylation of **2** under identical conditions gave **5**[4] (80% yield) which VPC analysis[7b] indicated was contaminated by **4** to the same extent (7%) that **2** was contaminated by **1.** The trans stereochemistry was indicated by the coupling constants obtainable at 270 MHz—$J_{AC} = 5.7$, $J_{AD} = 4$, $J_{BC} = 10$, $J_{BD} = 4$, $J_{CD} = 13.5$ Hz—which clearly suggest that H_A is pseudoequatorial and H_B is pseudoaxial. The assignment is further confirmed by the base-catalyzed isomerization [$KOC(CH_3)_3$, CH_3OH, reflux] of the less stable trans isomer **5** to the more stable cis isomer **4.** Both isomers were decarbomethoxylated[4] [$(CH_3)_4NOAc$, HMPA, 100 °C, 75% yield] without loss of configurational purity. Compounds of this type have been utilized as intermediates to ibogamine.[9] *Thus, within experimental error, these "net SN2 displacements" of allylic acetates proceed with complete retention of configuration at the carbon undergoing displacement.* Furthermore, no evidence for elimination competing with substitution is seen.

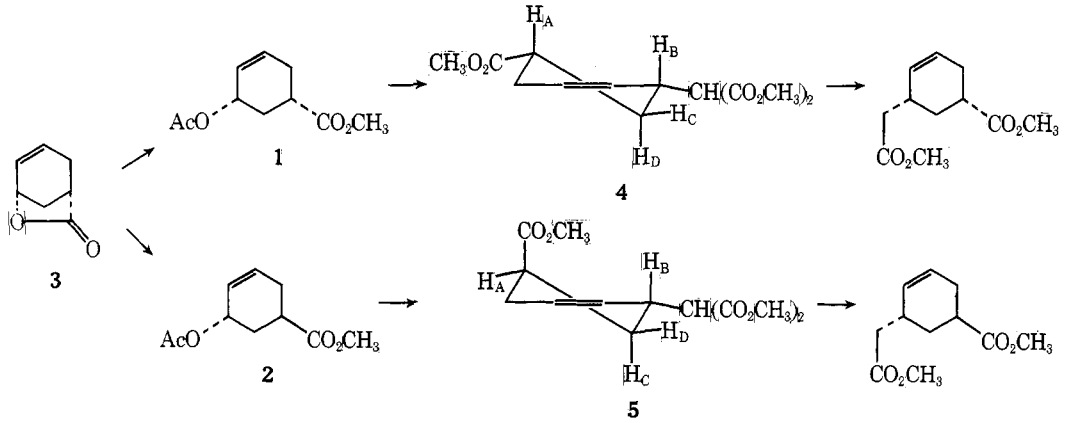
The question of the stereochemical integrity of the double bond in these reactions is crucial for their applications in synthesis. The well-known isomerization of π-allylpalladium complexes[10] makes interconversions of olefin isomers highly



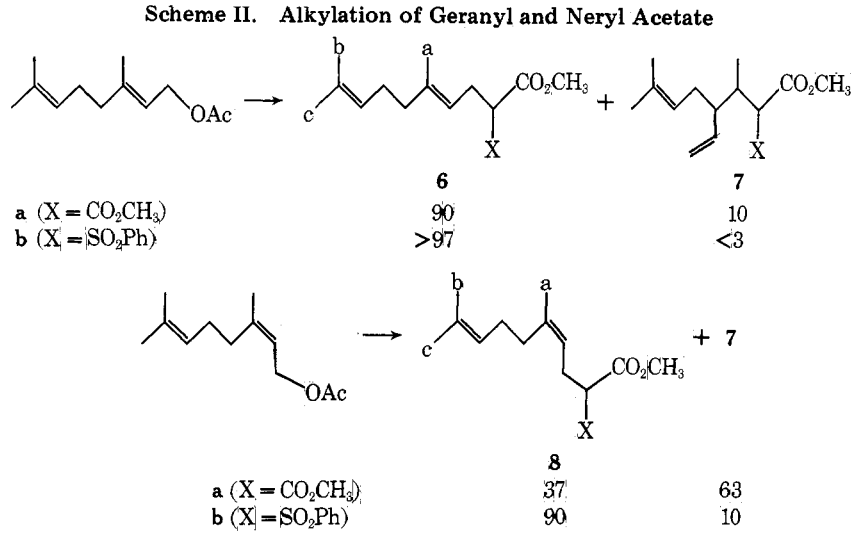
likely. Thus, to probe this question, alkylation of geranyl and neryl acetate was examined (see Scheme II). Alkylation of geranyl acetate with the sodium salt of either dimethyl malonate or methyl phenylsulfonylacetate under conditions identical with the above led to the product of substitution at the primary carbon, i.e., **6a**[4] and **6b**,[4] with complete retention of olefin geometry (VPC[7c] and NMR analysis) in 84–92% isolated yield. The *E* stereochemistry was confirmed by the ^{13}C NMR spectrum which showed a high field absorption for C_a compared (**6a**, δ_{C_a} 15.97, δ_{C_b} 17.63, δ_{C_c} 25.52; **6b**, δ_{C_a} 15.84, δ_{C_b} 17.40, δ_{C_c} 25.39) with the absorption for this methyl carbon in the *Z* isomer (vide infra). Unlike π-allylpalladium complexes from methylenecyclohexanes,[11] this alkylation reaction was insensitive to the nature of the phosphine present. On the other hand, it did show a sensitivity to the nature of the anion in which the sulfonyl anion led to attack only at the primary carbon atom.

Neryl acetate showed an even greater sensitivity to the nature of the anion. Alkylation under the usual conditions

Scheme I. Alkylation of *cis*- and *trans*-3-Acetoxy-5-carbomethoxycyclohexene



Scheme II. Alkylation of Geranyl and Neryl Acetate



	6	7
a ($X = CO_2CH_3$)	90	10
b ($X = SO_2Ph$)	>97	<3

	8	
a ($X = CO_2CH_3$)	37	63
b ($X = SO_2Ph$)	90	10

gave 7[4] and 8[4] in 74–78% isolated yield. As in the above case, the stereochemistry of the internal olefin derived from attack at the terminal carbon was exclusively *Z* (VPC[7c] and NMR analysis) as indicated by the ^{13}C NMR spectrum (**8a**, δ_{C_a} 23.33, δ_{C_b} 17.53, δ_{C_c} 25.52; **8b**, δ_{C_a} 23.12, δ_{C_b} 17.40, δ_{C_c} 25.32). In contrast to the geranyl case, the major product of the alkylation with malonate was attack at the tertiary carbon atom, whereas switching to the anion of the sulfonyl acetate gave a high regioselectivity for attack at the primary carbon atom.

The completely different product distribution clearly attests to the fact that the alkylation reaction is much faster than the syn–anti isomerization of the π-allylpalladium complexes. Thus, palladium-catalyzed allylic alkylations are kinetically controlled processes. As a result of this fact, stereochemistry is completely retained at both the carbon undergoing substitution and the trisubstituted double bond—obviously of tremendous importance in the application of these processes in syntheses.

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(3) While explanations involving σ complexes as intermediates can be invoked, these do not account for the identical product mixtures seen for regioisomeric allylic acetates nor for the reactivity order 1-(1′-acetoxyethyl)cyclopentene > 1-(1′-acetoxyethyl)cycloheptene ≫ 1-(1′-acetoxyethyl)-cyclohexene. The latter parallels the trends observed for palladium-catalyzed carbonylations of olefins [see D. E. James and J. K. Stille, *J. Am. Chem. Soc.*, **98**, 1810 (1976).

(4) All new compounds have been fully characterized by spectral means and elemental composition.

(5) M. Kato, M. Kageyma, R. Tanaka, K. Kuwahara, and A. Yoshikoshi, *J. Org. Chem.*, **40**, 1932 (1975).

(6) A 1:1 mixture of *cis*- and *trans*-3-acetoxy-5-carbomethoxycyclohexenes was obtained by solvolysis of lactone **3** in glacial acetic acid. For easy separation via selective lactonization of *cis*-3-hydroxy-5-carbomethoxycyclohexene, the acetate mixture was subjected to methanolysis.

(7) (a) Column: 2.44 m × 0.64 cm 10% UCON polar on 60/80 mesh Chromosorb W at a column temperature of 135 °C. (b) Column: 2.44 m × 0.64 cm 10% XE-60 on 60/80 mesh Chromosorb W at a column temperature of 175 °C. (c) Same as column b but with a column temperature of 155 °C.

(8) In a typical experimental procedure, 229.5 mg (1.27 mmol) of geranyl acetate, 30.4 mg (0.116 mmol) of triphenylphosphine, and 48 mg (0.04 mmol) of tetrakis(triphenylphosphinepalladium) in 2 ml of dry THF were stirred for 15 min. A solution of the sodium salt of methyl phenylsulfonylacetate in 8 ml of dry THF, generated from 948 mg (4.42 mmol) of methyl phenylsulfonylacetate and 168.5 mg of sodium hydride (57% mineral oil dispersion, 4.0 mmol), was added all at once and the resultant mixture refluxed 36 h. The reaction was partitioned between ether and water, and the water layer extracted with additional ether. After drying and evaporation of the solvent in vacuo, the oil was subjected to chromatographic purification on silica gel (2.5:1 hexane–ethyl acetate) to give 345.1 mg (84%) of pure methyl 5,9-dimethyl-2-phenylsulfonyldeca-(*E*)-4,8-diene.

(9) M. E. Kuehne, J. E. Saavedra, and P. J. Reider, Abstracts of the First Chemical Congress of the North American Continent, Mexico City, Mexico, 1975, Orga. 126.

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