until the alkyl halide was consumed (the addition of 1 in the coupling of 0.05–0.15 mol of alkyl halide takes ca. 1.5 h). The reaction mixture was poured into a separatory funnel containing saturated ammonium chloride and diethyl ether. The ethereal layer was separated, and the aqueous layer was again extracted with diethyl ether. The ethereal solutions were combined, washed with brine, and dried over magnesium sulfate. Filtration, evaporation of volatiles, and distillation provided the desired acetals.

B. Acetal Hydrolysis. The reaction flask was equipped with a liquid–liquid continuous extractor that was designed to return the bottom aqueous layer to the reaction flask. The upper layer in the continuous extractor consisted of an organic solvent such as hexane or ethyl acetate. For small-scale reactions (<20 mmol), a Dean–Stark trap[11] was modified to serve as the extractor. A 0.45 M solution of acetal in water containing benzoic acid (0.1 equiv) was heated to reflux with stirring for 1.25 h,[22] during which time the product, in most cases, steam distilled into the trap. After cooling, the contents of the trap and reaction flask were combined and extracted with ethyl acetate (2×). The combined organic extracts were washed with aqueous sodium bicarbonate followed by brine and dried over magnesium sulfate. Filtration, evaporation of volatiles, and distillation gave the desired aldehydes.

Registry No. **2** (n = 4; R = CH_3), 110-53-2; **2** (n = 4; R = OCH_3), 4457-67-4; **2** (n = 5; R = Cl), 54512-75-3; **2** (n = 4; R = CN), 5414-21-1; **2** (n = 2; R = CO_2Et), 539-74-2; **2** (n = 3; R = CO_2Et), 2969-81-5; **2** (n = 4; R = CO_2Et), 14660-52-7; **2** (n = 7; R = CO_2Et), 29823-21-0; **3** (n = 4; R = CH_3), 4359-57-3; **3** (n = 4; R = OCH_3), 85318-81-6; **3** (n = 5; R = Cl), 85318-82-7; **3** (n = 4; R = CN), 13050-10-7; **3** (n = 2; R = CO_2Et), 56741-64-1; **3** (n = 3; R = CO_2Et), 85318-83-8; **3** (n = 4; R = CO_2Et), 85318-84-9; **3** (n = 7; R = CO_2Et), 85318-85-0; **4** (n = 4; R = CH_3), 124-13-0; **4** (n = 4; R = OCH_3), 85318-86-1; **4** (n = 5; R = Cl), 72359-96-7; **4** (n = 4; R = CN), 13050-09-4; **4** (n = 2; R = CO_2Et), 27983-42-2; **4** (n = 3; R = CO_2Et), 3990-05-4; **4** (n = 4; R = CO_2Et), 1540-83-6; **4** (n = 7; R = CO_2Et), 85318-87-2; Li_2CuCl_4, 15489-27-7; 2-(2-bromoethyl)-1,3-dioxolane, 18742-02-4.

(22) In general, aldehydes that steam distill are formed in ca. 1–2 h. The generation of aldehydes that do not steam distill is much slower. The period required for each acetal hydrolysis is shown in Table I.

Communications

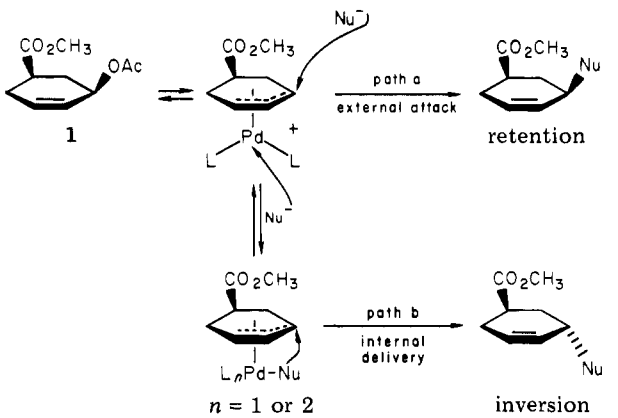
Regioselectivity in Organo-Transition-Metal Chemistry. A New Indicator Substrate for Classification of Nucleophiles

Summary: A new model for the characterization of nucleophiles is proposed, based on the regioselectivity of the reaction of a given nucleophile with 3-acetoxy-3-cyano-1-phenylpropene (14) in the presence of Pd(0) catalyst. A general correlation between regioselectivity using this indicator substrate and literature data on stereospecificity of nucleophilic substitution in other model compounds is apparent.

Sir: The characterization of nucleophilic reactivity is, in general, a difficult task. While there have been significant advances in the classification both of leaving groups[1a] and of nucleophiles,[1b] much work remains to be done, especially with respect to the latter. There is a growing need for a reliable criterion for predicting nucleophilic reactivities, especially with respect to electrophilic transition-metal complexes. It would allow one to employ transition metals in organic synthesis in a more rational manner to provide high degrees of chemoselectivity, regioselectivity, and stereochemical control. These benefits are probably best exemplified by palladium-catalyzed nucleophilic allylic substitution reactions that have been extensively used in organic synthesis for obtaining carbon–carbon or carbon–heteroatom bonds.[2]

Nucleophiles can be qualitatively classified via the mechanism by which they attack (π-allyl)palladium species. The two distinct mechanistic pathways are shown in Scheme I. Path a (usually attributed to "soft" nucleophiles[3]) involves external attack at carbon, resulting in retention of its configuration, while path b (usually

Scheme I



(1) (a) Stirling, C. J. M. *Acc. Chem. Res.* **1980**, *12*, 198. (b) Hirsch, J. A. "Concepts in Theoretical Organic Chemistry"; Allyn and Bacon: Boston, 1974; Chapter 8, (Nucleophilic Character).

(2) (a) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (b) Trost, B. M.; Verhoeven, T. R. In "Comprehensive Organometallic Chemistry"; Pergamon Press: Oxford, England, 1982, Vol. 8, pp, 799–938. (c) Tsuji, J. "Organic Synthesis with Palladium Compounds"; Springer: New York, 1980.

(3) (a) Pearson, R. G. "Symmetry Rules for Chemical Reactions"; Wiley: New York, 1976. (b) Ho, T.-L. *Chem. Rev.* **1975**, *75*, 1.

(4) (a) Trost, B. M.; Verhoeven, T. R. *J. Org. Chem.* **1976**, *41*, 3215. (b) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

(5) Fiaud, J. C.; Malleron, J. L. *Tetrahedron Lett.* **1980**, 4437.

(6) Fiaud, J. C.; Malleron, J. L. *J. Chem. Soc., Chem. Commun.* **1981**, 1159.

(7) Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, 2591.

(8) Trost, B. M.; Rivers, G. T., unpublished results. See: Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, 2595.

(9) Trost, B. M.; Keinan, E. *J. Am. Chem. Soc.* **1978**, *100*, 7779.

(10) (a) Trost, B. M.; Verhoeven, T. R.; Fortunak, J. M. *Tetrahedron Lett.* **1979**, 2301. (b) See also: Backvall, J. E.; Nordberg, R. E.; Bjorkaman, E. E.; Moberg, C. *J. Chem. Soc., Chem. Commun.* **1980**, 943. (c) Backvall, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 4959.

(11) Matsushita, H.; Negishi, E. *J. Chem. Soc., Chem. Commun.* **1982**, 160.

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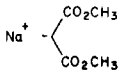
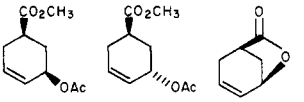
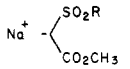
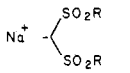
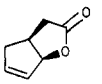
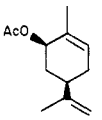
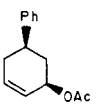
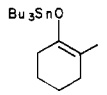
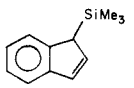
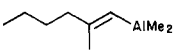
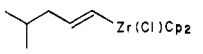
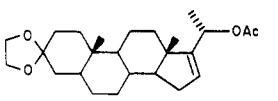
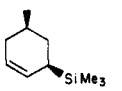
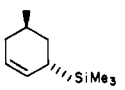
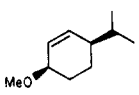
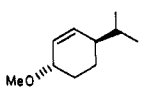
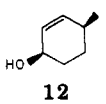
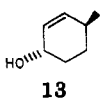
(13) Kumada, M. 10th International Conference on Organometallic Chemistry, Toronto, Canada, Aug 1981.

(14) Gendreau, Y.; Normant, J. F. *Tetrahedron* **1979**, *25*, 1517.

(15) Consiglio, G.; Morandini, F.; Piccolo, O. *J. Am. Chem. Soc.* **1981**, *103*, 1846.

0022-3263/83/1948-1769$01.50/0

Table I. Stereochemical Classification of Nucleophiles

nucleophile	model compounds	stereochemical classification	ref
	 1 2 3	retention	4
	1, 2	retention	4b
	3,  4	retention	4b
	 6	retention	5
	 5	retention	6
	1	retention	7
	1	retention	8
R_2NH	1, 2, 3	retention, inversion	9
$CH_3CO_2^-$	1, 2	retention, inversion	10, 4b
	1, 3	inversion	11
	 7	inversion	12
PhZnCl	3	inversion	11
PhMgBr	 8  9	inversion	13
BuMgCl[a]	 10  11	inversion	14
CH_3MgI[b]	 12  13	inversion	15
$NaBH_4$	1, 2	inversion	16

[a] Cu^I as catalyst. [b] Ni^{II} as catalyst.

attributed to "hard" nucleophiles) procedes by initial attack at the palladium atom, followed by reductive elimination, resulting in inversion of the configuration.

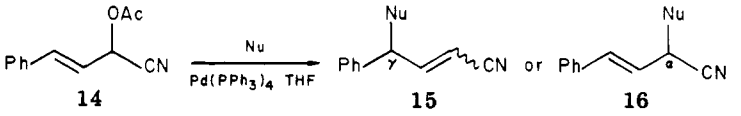
The character of a given nucleophile, in this regard, can be experimentally verified by allowing it to react with a model compound possessing a defined stereochemical structure. The stereochemical relationship between the reactant and product is thus used to distinguish between the two modes of nucleophilic attack (Scheme I).

Table I lists representative examples of nucleophiles classified on the basis of stereospecificity results reported in the literature.

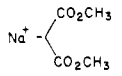
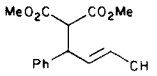
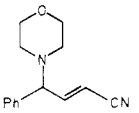
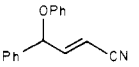
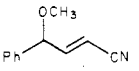
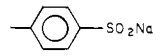
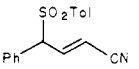
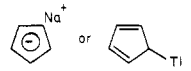
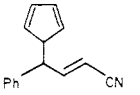
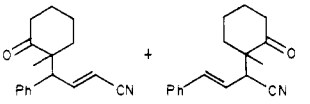
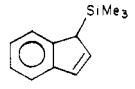
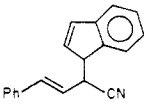
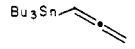
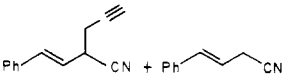
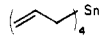
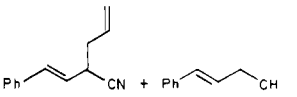
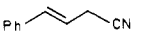
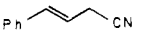
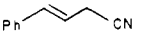
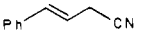
It is conceivable that in π-allyl complexes where the two ends of the allylic unit differ substantially from one an-

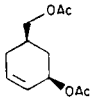
(16) Keinan, E.; Greenspoon, N. *Tetrahedron Lett.* **1982**, 241.

Table II. Regiochemical Classification of Nucleophiles



14 15 16

entry	nucleophile	product	regiochemical class	sterochemical[a] course
1[b]			A	retention
2			A	retention (major), inversion
3	Bu_3SnOPh or NaOPh		A	retention (major), inversion
4	Bu_3SnOCH_3		A	retention (major), inversion
5			A	retention
6[c]			A	retention
7[d]			A, B	retention
8			B	retention
9[e]		 17	B	*f*
10			B	*f*
11	$NaBH_4$ or Bu_3SnH		B or C	inversion
12	MeLi, Me_2CuLi		C	inversion
13	PhLi, $PhSnBu_3$, PhHgOAc, PhZnCl		C	inversion
14	$CH_3C{\equiv}CSnBu_3$		C	*f*

[a] Data taken from Table I except for entries 3-5 where the stereochemical course was determined by using model compound 1 or its derivative: 

[b] Reference 17b. [c] Reference 19. The product shown is one of three cyclopentadiene ring isomers obtained. [d] Reference 20, 37:63. [e] Reference 21. [f] Unknown.

other, the two modes of nucleophilic attack will be reflected not only in differing stereospecificity but also in characteristic regioselectivity. The possibility of using regioselectivity as a mechanistic probe rather than stereospecificity is quite attractive as it involves much simpler and easier experimental procedures.

In this communication we suggest a mechanistic probe for palladium-catalyzed allylic substitution, based on regiochemical selectivity. The chosen indicator substrate, 3-acetoxy-3-cyano-1-phenylpropene (**14**),[17] was indeed found to be an efficient tool for classifying nucleophiles. It is a convenient, readily available substrate that is also highly reactive, allowing all reactions to be carried out at room temperature. It is free of complications such as β-hydride elimination or epimerization of stereodefined centers.[6b] Moreover, product analysis is simple and convenient by using either ^1H NMR or IR spectroscopy.

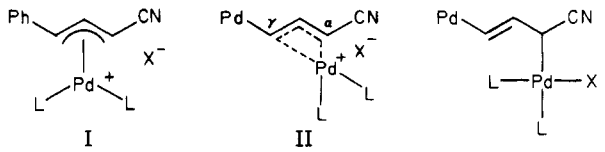
When **14** was allowed to react with a variety of nucleophilic reagents in the presence of catalytic $Pd(PPh_3)_4$, a highly regioselective substitution occurred at either the γ or α positions, leading to **15** or **16**, respectively (see Table II). Except in the case of enol stannane (entry 7), all products were regioisomerically pure, as verified by proton NMR (270 MHz).[18]

(17) (a) Nudelman, A.; Keinan, E. *Syntheses* **1982**, 687. (b) Tsuji, J.; Ueno, H.; Kobayashi, Y.; Okumoto, H. *Tetrahedron Lett.* **1981**, 2573. (c) Mandai, T.; Hashio, S.; Goto, J.; Kawada, M. *Ibid.* **1981**, 2187.

A general correlation between regioselectivity and stereospecificity phenomena is apparent from the results given in Table II, although the change in mode of reactivity for each of the two parallel series occur at slightly different points.

It seems that characterizing nucleophiles with indicator substrate **14** is even more informative than stereochemical characterization, as nucleophiles can be divided into three categories correlating with increasing "hardness": (A) "soft" nucleophiles that attack at the γ position, (B) "intermediate" nucleophiles that attack at the α position, (C) "hard" nucleophiles that fail to substitute at either the γ or α positions but give rise to reduced product **17** instead.

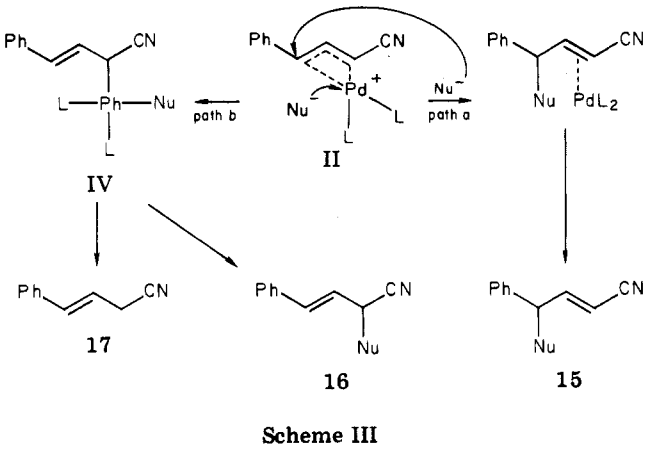
This three-fold behavior may be explained by kinetic arguments. The palladium atom in the η^3 palladium intermediate is probably unsymmetrically positioned with respect to the two ends of the allylic system, lying closer to the α-carbon atom (structure II rather than structure I).[22,23]



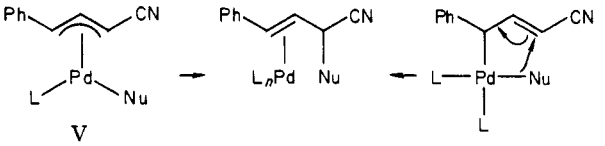
I II III

Consequently, external nucleophilic attack must occur at the γ carbon, which is less strongly bound to the metal (path a in Scheme II).

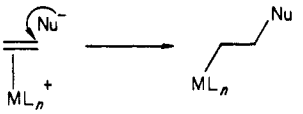
Scheme II



Scheme III



Path a is analogous to the more thoroughly investigated nucleophilic attack on electrophilic η^2 metal complexes (eq 1), which was studied both experimentally[25] and theoretically.[26]



(1)

The direct attack of the nucleophile at the metal (path b) may lead to formation of a (σ-allyl)palladium complex IV, which upon a subsequent reductive elimination will form the α-substituted product **16**. The formation of reduced product **17** in most reactions involving "hard" nucleophiles is more intriguing. One may envision the involvement of some electron-rich intermediate evolving from a one-electron or two-electron transfer from the nucleophile to neutral complex IV, or even a palladium–carbene complex related to IV.[21]

Assuming two alternative structures (V and VI) for intermediate complex IV suggests the possible existence of two other mechanistic pathways along which the reductive elimination may procede (Scheme III). Studies to explore these possibilities are currently in progress.

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Registry No. (*E*)-**14**, 79311-09-4; **14**·$Pd(Ph_3)_4$ complex, 85235-08-1; (*E*)-**15** (Nu = $CH(CO_2CH_3)_2$), 79311-10-7; (*Z*)-**15** (Nu = $CH(CO_2CH_3)_2$), 79328-42-0; (*E*)-**15** (Nu = morpholino), 85234-92-0; (*Z*)-**15** (Nu = morpholino), 85235-02-5; (*E*)-**15** (Nu = PhO), 85234-93-1; (*Z*)-**15** (Nu = PhO), 85235-03-6; (*E*)-**15** (Nu = CH_3O), 85234-94-2; (*Z*)-**15** (Nu = CH_3O), 85235-04-7; (*E*)-**15** (Nu = $TolSO_2$), 85234-95-3; (*Z*)-**15** (Nu = $TolSO_2$), 85235-05-8; (*E*)-**15** (Nu = 2,4-cyclopentadienyl), 85234-96-4; (*Z*)-**15** (Nu = 2,4-cyclopentadienyl), 85235-06-9; **15** (Nu = 1-methyl-2-cyclohexanonyl), 85234-97-5; **16** (Nu = 1-methyl-2-cyclohexanonyl), 85234-98-6; **16** (Nu = 1-indenyl), 85234-99-7; (*E*)-**16** (Nu = propargyl), 85235-00-3; (*E*)-**16** (Nu = 2-propenyl), 85235-01-4; (*E*)-**17**, 20068-10-4; $Pd(PPh_3)_4$, 14221-01-3; $CH_2(COOCH_3)$·Na, 18424-76-5; Bu_3SnOPh, 3587-18-6; p-$CH_3C_6H_4SO_2Na$, 824-79-3; $Bu_3SnCH{=}C{=}CH_2$, 53915-69-8; $(CH_2{=}CHCH_2)_4Sn$, 7393-43-3; $PhSnBu_3$, 960-16-7; PhHgOAc, 62-38-4; $CH_3{\equiv}CSnBu_3$, 64099-82-7; Bu_3SnOCH_3, 1067-52-3; $NaBH_4$, 16940-66-2; Bu_3SnH, 688-73-3; MeLi, 917-54-4; Me_2CuLi, 15681-48-8; PhLi, 591-51-5; PhZnCl, 28557-00-8; morpholine, 110-91-8; (η^5-2,4-cyclopentadien-1-yl)thallium, 34822-90-7; sodium cyclopentadiene, 4984-82-1; 1-trimethylsilylindene, 18053-75-3; (2-methyl-1-cyclohexen-1-yloxy)tributylstannane, 21750-52-7.

(18) In all experiments, **16** was formed as a single stereoisomer *E*, whereas **15** was obtained as a mixture of *E* and *Z* isomers at about 4:1 ratio, respectively.

(19) Corey, E. J.; Koelliker, U.; Neuffer, J. *J. Am. Chem. Soc.* **1971**, *93*, 1489.

(20) Keinan, E.; Sahai, M., unpublished results.

(21) Keinan, E.; Peretz, M. *J. Org. Chem.*, submitted for publication.

(22) Several crystalline π-allyl palladium complexes related to **14** are currently being analyzed by X-ray difraction in order to verify this hypothesis.

(23) An allylic σ-complex such as III was recently suggested to be the active intermediate in the nucleophilic substitution of dimeric (π-allyl)-palladium chloride complexes in the presence of phosphine ligands: Akermark, B.; Akermark, G.; Hegedus, L. S.; Zetterberg, K. *J. Am. Chem. Soc.* **1981**, *103*, 3037.

(24) Such arguments were suggested earlier: Trost, B. M.; Weber, L.; Strege, P. E.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3416.

(25) Chang, T. C. T.; Foxman, B. M.; Rosenblum, M.; Stockman, C. *J. Am. Chem. Soc.* **1981**, *103*, 7361.

(26) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4308.

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Thermal Rearrangement of *syn*-7-(1,2-Butadienyl)bicyclo[2.2.1]hept-2-ene: Evidence of Concertedness

Summary: *syn*-7-(1,2-Butadienyl)bicyclo[2.2.1]hept-2-ene (**1**) has been found to thermally rearrange to 1-ethylidene-3a,4,5,7a-tetrahydroindene (**4**) under conditions for which the corresponding anti epimer (**2**) is completely stable. These results are interpreted as supporting a

