ever, the results at both irradiation wavelengths support the view that the thermally equilibrated excited states of complexes may be distorted from their ground states.[2]

The most extensive kinetic measurements were made in acetonitrile. From the relaxation times and spectrophotometrically determined equilibrium constant[9] $K = k_s/k_t$, both measured over the temperature range 10-50°, the following kinetic and thermodynamic parameters were obtained

$$\underset{\text{(planar)}}{\text{Ni(dpp)Cl}_2} \underset{k_t}{\overset{k_s}{\rightleftharpoons}} \underset{\text{(tetrahedral)}}{\text{Ni(dpp)Cl}_2}$$

$K^{23°} = k_s/k_t = 0.75$; $\Delta H° = 7 \pm 1$ kJ mol$^{-1}$; $\Delta S° = 20 \pm 2$ J K$^{-1}$ mol$^{-1}$ $k_s^{23°} = 4.5 \times 10^5$ sec$^{-1}$, $k_t^{23°} = 6 \times 10^5$ sec$^{-1}$

Activation parameters, determined from a plot of log $k/T$ against $T^{-1}$, were $\Delta H_t^{\ddagger} = 35 \pm 1$ kJ mol$^{-1}$; $\Delta S_t^{\ddagger} = -15 \pm 4$ J K$^{-1}$ mol$^{-1}$. These rate constants are of the same order as have been reported[1] for related complexes investigated by NMR but much slower than for bischelate complexes.[1a] These systems, where $k_t^{298} > 10^7$ sec$^{-1}$ is expected, are outside the range of NMR but are likely to be within the scope of the present method where the principal limitation is the laser pulse duration.

Finally we note that a useful link is beginning to emerge between the reactivity of the photoexcited states of transition metal complexes and structural equilibria involving such complexes in their ground electronic states. Specific photodissociation[10] or electron transfer[11] processes or, as in the present case, an excited state distortion may provide convenient means of perturbing such equilibria and hence, through chemical relaxation,[12] of studying the kinetics of interconversions.

**Acknowledgment.** We wish to thank the Science Research Council for a grant in support of this work.

## References and Notes


(1) (a) L. H. Pignolet, W. DeW. Horrocks, and R. H. Holm, *J. Am. Chem. Soc.*, **92**, 1855, (1970); (b) G. N. LaMar and E. O. Sherman, *ibid.*, **92**, 2691 (1970); (c) L. Que and L. H. Pignolet, *Inorg. Chem.*, **12**, 156 (1973).

(2) (a) P. D. Fleischauer, A. W. Adamson, and G. Sartori, *Prog. Inorg. Chem.*, **17**, 1 (1972); (b) V. Balzani and V. Carassiti, "Photochemistry of Coordination Compounds", Academic Press, London and New York, 1970, Chapter 6.

(3) Reference 2b, p 313 summarizes previous observations on Ni(II) systems.

(4) G. Van Hecke and W. DeW. Horrocks, *Inorg. Chem.*, **5**, 1968 (1966).

(5) The effective symmetry is $C_{2v}$ but the spectra can be interpreted in terms of the point group $T_d$. See ref 6.

(6) (a) F. A. Cotton, O. D. Faut, and D. M. L. Goodgame, *J. Am. Chem. Soc.*, **83**, 344 (1961); (b) G. W. Everett and R. H. Holm, *ibid.*, **87**, 2117 (1965), especially p 2121 and 2123.

(7) Private discussion with Professor C. J. Ballhausen.

(8) C. J. Ballhausen, N. Bjerrum, R. Dingle, K. Eriks, and C. R. Hare, *Inorg. Chem.*, **4**, 514 (1965).

(9) Measured at 475 nm, assuming $\epsilon_{475}$ 1510 $M^{-1}$ cm$^{-1}$ for the planar isomer; this value of $\epsilon_{475}$ is that measured in acetonitrile for the complex Ni(dpe)Cl$_2$ which exists exclusively (ref 4) in the planar form. Dpe is 1,2-bis(diphenylphosphino)ethane.

(10) (a) K. J. Ivin, R. Jamison, and J. J. McGarvey, *J. Am. Chem. Soc.*, **94**, 1763 (1972); (b) H. Hirohara, K. J. Ivin, J. J. McGarvey, and J. Wilson, *ibid.*, **96**, 4435 (1974).

(11) C. R. Bock, T. J. Meyer, and D. G. Whitten, *J. Am. Chem. Soc.*, **96**, 4710 (1974).

(12) C. Creutz and N. Sutin, *J. Am. Chem. Soc.*, **95**, 7177 (1973).


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*Received November 23, 1974*

## Antiport Regulation of Carrier Mediated Chiroselective Transport through a Liquid Membrane[1]

*Sir:*

Selective transport of amino acids through a liquid membrane by lipophilic carrier molecules has been described.[2] Coupling to acid-base reactions and to cation gradients was used to pump the transport process. pH effects on transmembrane diffusion of weak acids has also been observed in biological model systems (see for instance ref 3 and references therein).

We wish to report regulatory effects of the counter transported (antiport) species on *chiroselective transport* by a chiral carrier molecule, i.e., on preferential transport of one optical antipode of a racemic substrate. The carrier was the optically active hydrochloride of (−)-*N*-(1-naphthyl)methyl α-methylbenzylamine[4,5] ((−)T$^+$Cl$^-$, $C_6H_5CH(CH_3)N^+H_2CH_2$-α-$C_{10}H_7$, Cl$^-$; $[\alpha]_D = -22.2 \pm 0.4°$, $c$ 3.565, $CHCl_3$) dissolved in chloroform, and the substrate was racemic sodium mandelate, S$^-$Na$^+$, in water.[6] This system displays partial resolution by extraction of S$^-$ by T$^+$ from water into chloroform.[4] The experiments were performed in a setup consisting of a stirred chloroform membrane M separating two stirred water phases IN and OUT,[2,7] which contained initially (±) sodium mandelate and the sodium salts of different acids, A$^-$Na$^+$, respectively. The amount and optical rotation of mandelate in all three phases was followed as a function of time.

(1) When the carrier T$^+$ is added to the membrane, mandelate S$^-$ and the antiport anion A$^-$ are taken up and exchanged across the interfaces, so that S$^-$ and A$^-$ appear simultaneously in the OUT and IN phases, respectively. In the absence of carrier in M the leakage of mandelate (or mandelic acid) through the membrane is negligible (<2 μmol/(hr cm$^2$)). Since both antipodes of mandelate are competing for the carrier, the transport process may be described as *competition flux* of (+)S$^-$ and (−)S$^-$ in *exchange diffusion* with A$^-$ (see for instance ref 8) mediated by the carrier T$^+$. It may present both flux stimulation, as is generally possible in exchange diffusion,[8] and substrate selectivity via the diastereomeric pairs [(−)T$^+$, (+)S$^-$] and [(−)T$^+$, (−)S$^-$] formed in M. Table I and Figure 1 give results for a variety of antiport anions.

(2) Sodium mandelate, initially racemic in IN, becomes optically active in all three phases. Thus, the transport process is *chiroselective*. Although the maximum optical resolution obtained (<10%) is at most equal to that of a two-

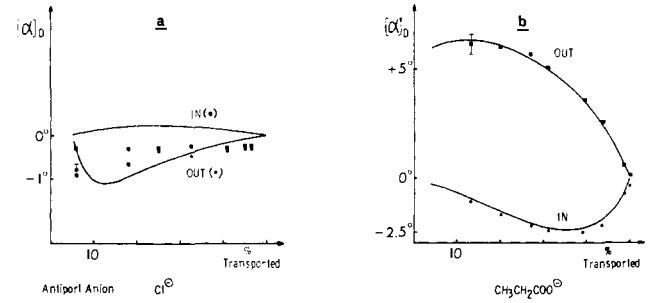


**Figure 1.** Variation of the specific optical rotation $[\alpha]_D$ of mandelate in the IN and OUT phases as a function of per cent mandelate transported when the antiport anion is chloride (a) or propionate (b) (see also footnote to Table I). The points are experimental results and the curves are computed as described in ref 11. Because resolution of the transport equations[11] would have been much more involved, the amount of mandelate extracted from IN into M was neglected. The calculated curves should be displaced toward the bottom of the figures (to about $[\alpha]_D = -0.3°$ for IN, Cl$^-$ case) leading to agreement with the experimental numbers.

Table I. Chiroselective Transport of (±) Mandelate Anion by (−)-*N*-(1-Naphthyl)methyl-α-methylbenzylamine Hydrochloride as a Function of Antiport Anion[a]

| Entry | Antiport anion, $A^-$ | % mandelate (in *M*) | Transport rate μmol/(hr cm²) | [α] D mandelate IN | [α] D mandelate M | [α] D mandelate OUT | % mandelate transported |
|---|---|---|---|---|---|---|---|
| 1 | $Cl^-$[b] | 83 ± 5 | 50 ± 5 | −0.30 ± 0.03 | +9.5 ± 0.5 | −0.8 ± 0.1 | 5 |
| 2 | $HCOO^-$ | 38 ± 3 | 30 ± 3 | −0.30 ± 0.03 | +10.7 ± 0.5 | +1.8 ± 0.3 | 8 |
| 3 | $CH_3COO^-$ | 5 ± 0.5 | 20 ± 2 | −0.40 ± 0.04 | +6.9 ± 1 | +6.4 ± 0.5 | 7 |
| 4 | $CH_3CH_2COO^-$ | 28 ± 3 | 100 ± 10 | −1.0 ± 0.05 | +8.4 ± 0.4 | +6.2 ± 0.4 | 11 |
| 5 | $CH_3(CH_2)_2COO^-$ | 22 ± 2[c] | 160 ± 16 | −0.75 ± 0.05 | +5.0 ± 0.3[c] | +5.3 ± 0.5 | 9 |
| 6 | $CH_3(CH_2)_4COO^-$ | 8 ± 2 | 70 ± 7 | −0.35 ± 0.05 | *d* | +2.6 ± 0.5 | 9 |
| 7 | $CH_3(CH_2)_6COO^-$ | 2.5 ± 0.5 | 9 ± 1 | ~0 | *d* | ~0 | 5 |

[a] Initial concentrations: IN and OUT, ca. 1 *M* solutions (40 ml) of racemic sodium mandelate and $Na^+A^-$, respectively, at pH 6–8; M, 0.12 *M* carrier $T^+Cl^-$ in chloroform (10 ml). Temperature was maintained at 20 ± 1. All phases were stirred at 300 rpm. Area of interface is 2 ± 0.2 cm². Mandelate concentrations (±5%) have been obtained from the uv absorption at 257 nm (Cary 118C spectrometer. [α] D is measured on a Perkin-Elmer 141 polarimeter (±0.008°); concentrations were in the range *c* ~14 (IN) and *c* ~2–4 (M, OUT). Percent mandelate is the amount of mandelate in M with respect to carrier (i.e., carrier saturation). Percent mandelate and [α] D listed have been measured after the fraction of total mandelate given in the last column has been transported from IN to OUT. Transport rates are obtained from the rate of appearance of mandelate in OUT. Transport rates are about ±10%. Carrier concentration in the aqueous phases is $<10^{-4}$ *M*/l. [b] Results similar to those obtained for $Cl^-$ have been obtained for $SO_4^{2-}$ back-transport. [c] Values corresponding to 20% mandelate transported. [d] Values were too small for accurate measurement.

phase extraction (about 10% in the chloroform layer) performed in the same conditions as between IN and M, the actual resolution in a given phase depends strongly on the conditions of a given experiment (see below).[9]

(3) Both the rate and the chiroselectivity of the transport display effects of *regulation by the antiport anion* $A^-$. Such phenomena are particularly interesting since they link the forward flux to the nature of the counter transported species. Changing A modifies the relative amounts of $S^-$ and $A^-$ in M, i.e., the effective affinity of the carrier for mandelate.

(4) The *rates* of transport are fastest when anions $A^-$ and mandelate $S^-$ have similar lipophilicity (Table I, entries 4 and 5) and are slower otherwise.

(5) The *sign* of the transport *chiroselectivity* is dependent on the nature of the antiport anion. In the case of $A^- = Cl^-$ the optical rotation of mandelate has the same (−) sign in IN and OUT whereas it is of (+) sign in M. The situation is different in all other cases where one has (−) IN, (+) M, (+) OUT.

(6) When $A^-$ = propionate (Figure 1b) the evolution of the specific rotations of the IN and OUT phases resembles respectively that of the starting material and the product of a *kinetic resolution* experiment. The optical purity of the IN phase becomes appreciably higher than achieved in an extraction experiment in the same conditions. It behaves like the starting compound in a chiral destruction experiment.[10] However, after about 30% transport, back-transport of mandelate is no more negligible and the optical purity of IN begins to decrease. At the end of the experiment both IN and OUT phases have the same slightly negative [α]D corresponding to the excess of (+) antipode in the membrane.

(7) A detailed analysis of the kinetics of the transport flux has been performed. The *calculated* curves shown in Figure 1 are in satisfactory agreement with the experimental results.[11] According to the present computations, the results obtained for both $A^- = Cl^-$ and $A^-$ = propionate require that the system be *asymmetrical*, with higher extraction efficiency and (+)/(−) selectivity at the M/OUT interface than at the M/IN interface.[12]

In a symmetrical membrane system (i.e., same (+)/(−) >1 selectivity on both sides) the computations show that, after 10% transport, OUT would display only slight (+) rotation in the chloride case but would have about the same (+) optical purity as M when $A^-$ = propionate.

When the system is made asymmetrical, with (+)/(−) selectivity higher on the M/OUT than on the M/IN side, the result is that the [α]D (OUT) curves are displaced in favor of the (−) antipode for both antipode anions. Thus, for chloride, OUT can change from weakly (+) (symmetrical) to weakly (−) (asymmetrical), whereas for propionate, OUT remains (+) but with lower optical purity than in the symmetrical case. Therefore, the striking inversion of transport selectivity observed may be ascribed to the effect of the lipophilicity difference (i.e., distribution constants, with respect to mandelate or $S^-$ in general) of the antiport anions $A^-$ in an asymmetrical membrane system.

In conclusion, the nature and the amount of transport chiroselectivity in an exchange diffusion process may be regulated to some extent via the antiport anion. This should hold not only for the separation of optical antipodes but also in the *regulation* of the selective transport of different substrates in artificial or biological systems.

The use of multiple consecutive membranes operating in the same or in opposite directions should allow high selectivities to be reached while retaining great flexibility. The design of more elaborate carriers will allow further refinements, for instance, by means of chiral polycyclic ligands[13,14] presenting marked chiral recognition.[13] Applications in various fields from analytical techniques to drug absorption may be envisaged.

## References and Notes


(1) Transport Processes in Organic Chemistry, Part II. Previous paper: see ref 2.
(2) J. P. Behr and J. M. Lehn, *J. Am. Chem. Soc.*, **95**, 6108 (1973).
(3) (a) J. Gutknecht and D. C. Tosteson, *Science*, **182**, 1258 (1973); (b) E. P. Bakker and K. Van Dam, *Biochim. Biophys. Acta*, **339**, 285 (1974).
(4) S. J. Romano, K. H. Wells, H. L. Rothbart, and W. Rieman III, *Talanta*, **16**, 581 (1969).
(5) R. C. Hutton, S. A. Salam, and W. I. Stephen, *J. Chem. Soc. A*, 1573 (1966).
(6) (+)-Mandelate has [α]D = +118 ± 2°, *c* 2.06, NaOH, pH 12.55.
(7) K. Sollner in "Diffusion Processes, Proceedings of the Thomas Graham Memorial Symposium", University of Strathclyde, Vol. 2, J. N. Sherwood, A. V. Chadwick, W. M. Muir, and F. L. Swinton, Ed., Gordon and Breach, London 1971, p 655.
(8) J. A. Jacquez, *Biochim. Biophys. Acta*, **79**, 318 (1964).
(9) Slight optical isomer separation has been reported for diffusion through optical active aqueous sugar or polymer solutions; V. Carassiti, *Ann. Chim. (Rome)*, **46**, 1112 (1956); **49**, 8, 17 (1959); *J. Inorg. Nucl. Chem.*, **8**, 227 (1958); J. Klein, J. A. Baker, and E. L. Cussler, *Ind. Eng. Chem., Fundam.*, **10**, 183 (1971). Much higher resolution has been achieved recently for amino acids; M. Newcomb, R. C. Helgeson, and D. J. Cram, *J. Am. Chem. Soc.*, **96**, 7367 (1974).
(10) G. Balavoine, A. Moradpour, and H. Kagan, *J. Am. Chem. Soc.*, **96**, 5152 (1974).
(11) For the present process of competition flux in exchange diffusion the transport rates are given by eq i and ii, where $C^+_{OUT}$, $C^-_{OUT}$, $C^+_{IN}$, and $C^-_{IN}$ are the concentrations of (+) and (−) antipodes in the OUT and IN phases, $C^0_{IN}$ is the initial total (±) mandelate concentration, $K^+_{IN}$, $K^+_{OUT}$, $K^-_{IN}$, and $K^-_{OUT}$ are the equilibrium constants for the two-phase distribution of mandelate into the membrane, M/IN and M/OUT, and

$$\frac{dC^*_{OUT}}{dt} = V_{max}[A - B] \quad \text{(i)}$$

$$A = \left[K^*_{IN}\left(\frac{C^0_{IN}}{2} - C^*_{OUT}\right)\right] / \left[K^*_{IN}\left(\frac{C^0_{IN}}{2} - C^*_{OUT}\right) + K^-_{IN}\left(\frac{C^0_{IN}}{2} - C^-_{OUT}\right) + C^*_{OUT} + C^-_{OUT}\right]$$

$$B = [K^*_{OUT}C^*_{OUT}] / [K^*_{OUT}C^*_{OUT} + K^-_{OUT}C^-_{OUT} + C^0_{IN} - C^*_{OUT} - C^-_{OUT}]$$

$V_{max}$ is the maximum transport rate. A similar equation (ii) holds for $dC^-_{OUT}/dt$, where in eq i all (+) exponents are exchanged against (−) and conversely. The coupled rate equations i and ii are solved simultaneously on a UNIVAC 1108 computer using the combined Runge-Kutta and Hammings numerical iteration methods. The parameters $K$ are iterated until the calculated curves are in satisfactory agreement with the experimental data. The set of values leading to agreement with experiment is not necessarily unique, but additional data (e.g., extraction coefficients) provide reference points for choosing a reasonable set.

(12) In extraction experiments[4] performed at different concentrations of sodium mandelate and sodium chloride the extraction selectivity (+)/(−) has been found to vary from 1.22 to 1.42; the extraction efficiency changes too. Although performed in different conditions, these extraction data foreshadow the transport results for the chloride case (D. J. Cram and M. Newcomb, private communication). The present analysis[11] of our data gives $K^+_{IN}/K^-_{IN} \sim 1.1$ and $K^+_{OUT}/K^-_{OUT} \sim 1.4$ and indicates that the extraction efficiency of mandelate increases when the concentration of antiport anion increases. A more detailed discussion of the experimental and theoretical results will be given in the final account of this work.

(13) D. J. Cram and J. M. Cram, *Science*, **183**, 803 (1974), and references therein.

(14) B. Dietrich, J. M. Lehn, and J. Simon, *Angew. Chem.*, **13**, 406 (1974), and unpublished results.

(15) E.R.A. No. 265 du C.N.R.S.

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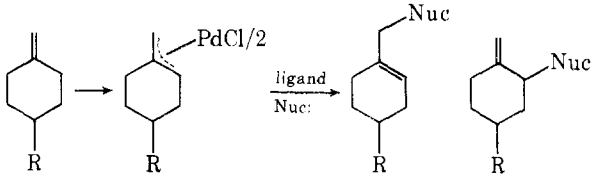
## On the Regio- and Stereoselectivity of Allylic Alkylation

*Sir:*

The utility of allylic alkylation via $\pi$-allylpalladium complexes stems from its control of the course of the carbon–carbon bond forming reaction.[1,2] We have established that the nucleophile bonds to the face of the $\pi$-allyl unit opposite to palladium.[3] In extending our studies to cyclic compounds, we discovered a remarkable regioselectivity and stereoselectivity in methylenecyclohexane derivatives.[4]




(1)

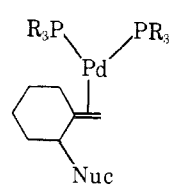
1

Treatment of **1** (R = H) with the anions derived from methyl methylsulfonylacetate, methyl phenylsulfonylacetate, methyl phenylthioacetate, and methyl malonate in the presence of hexamethylphosphorus triamide (**2**) leads to substitution at the primary rather than the secondary carbon atom (see eq 1 and Table I). On the other hand, utilizing a bulky activating ligand, such as tri-*o*-tolylphosphine (**3**) leads to predominate reaction at the secondary carbon atom.[5] At present, the reaction is best considered as a nucleophilic attack on $\eta^3$-allylpalladium cationic complexes.[2a,6] Thus, this selectivity may be attributed to the stability of the presumed initial product of alkylation—the olefin-palladium $\pi$ complexes **4** and **5**[7]—compared to the steric hindrance to the approach of the nucleophile. Normally, the

Table I. Regioselectivity of Allylic Alkylation[a]

| $\pi$-Allyl | Phosphine[b] | Alkylating agent[c] | Yield[d] | Attack at[i] Primary (%) | Attack at[i] Secondary (%) |
|---|---|---|---|---|---|
| 1 R = H | HMP | $CH_3SO_2CH_2CO_2CH_3$ | 58 | 100 | ... |
| 1 R = H | HMP | $CH_3SO_2CH_2CO_2CH_3$ | 90[e] | 100 | ... |
| 1 R = H | TOT | $CH_3SO_2CH_2CO_2CH_3$ | 90 | 15 | 85 |
| 1 R = H | HMP | $PhSO_2CH_2CO_2CH_3$ | 34 | 71 | 29 |
| 1 R = H | TOT | $PhSO_2CH_2CO_2CH_3$ | 83 | 26 | 74 |
| 1 R = H | HMP | $PhSCH_2CO_2CH_3$ | ..[f] | 57 | 47 |
| 1 R = H | TOT | $PhSCH_2CO_2CH_3$ | 18 | <1 | >99 |
| 1 R = H | HMP | $CH_2(CO_2CH_3)_2$ | 34 | 79 | 21 |
| 1 R = H | TOT | $CH_2(CO_2CH_3)_2$ | 57 | 26 | 74 |
| 1 R = $t$-$C_4H_9$ | HMP | $CH_3SO_2CH_2CO_2CH_3$ | 31 | 95 | 5 |
| 1 R = $t$-$C_4H_9$ | TOT | $CH_3SO_2CH_2CO_2CH_3$ | 52[g] | 45 | 55 |
| 1 R = $t$-$C_4H_9$ | HMP | $CH_2(CO_2CH_3)_2$ | 95 | 63 | 37 |
| 1 R = $t$-$C_4H_9$ | TOT | $CH_2(CO_2CH_3)_2$ | 83[h] | 21 | 79 |

[a] All reactions were carried out at room temperature in DMSO as solvent unless otherwise specified. [b] HMP = hexamethylphosphorus triamide. TOT = tri-*o*-tolylphosphine. [c] The anions were generated by treatment of the active methylene compound with sodium hydride in the solvent of the reaction. [d] Yields are for isolated purified compounds. [e] THF was employed as solvent in this run. [f] Not determined. [g] Ligand and complex were heated at 70° for 1.5 hr. [h] Ligand and complex were heated at 60° for 1.5 hr. [i] Ratio determined by NMR spectroscopy of the crude product as well as the purified product utilizing the ratio of the absorptions for the vinyl protons at $\delta$ 5.4–5.6 for the product of primary attack and $\delta$ 4.5–5.0 for the product of secondary attack.

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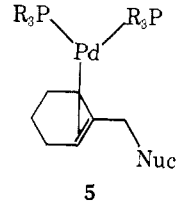


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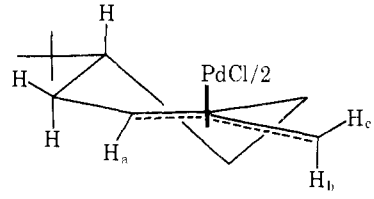
nucleophile prefers to approach at the less-hindered end of the $\pi$-allyl system to generate **5**.[2] However, if the palladium bears very bulky phosphines, the steric congestion that develops in the transition state for the formation of **5** increases the energy of this transition state such that the nucleophile is "directed" toward the more substituted carbon to generate the less congested olefin-palladium $\pi$ complex **4**.[8]

Complex **1** (R = $t$-$C_4H_9$) shows similar behavior. Furthermore, it allows determination of the stereochemistry of alkylation at a ring carbon. NMR data[9] indicate this complex to be approximately a 3:2 mixture of **6** and **7** (**6**, $H_a$ ($\delta$ 4.26, bs), $H_b$ (2.67, bs), $H_c$ (3.60, bs); **7**, $H_a$ ($\delta$ 4.18, d, $J$ = 7 Hz), $H_b$ (2.57, bs), $H_c$ (3.60, bs). The splitting of $H_a$ in these complexes is in accord with the major isomer having a dihedral angle between this proton and the adjacent methy-

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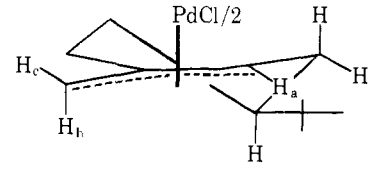


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