modes of isomerization. One motional model which has been discussed in connection with conformational reorientation in situations like this (e.g., polymers) is the Boyer crankshaft motion[12] which may be represented by TTTGTG'TTT ⇄ TTTTTGTG'T. This motion, which is equivalent to the diffusion of a GTG' sequence by two units along the chain, leaves the ends of the chain in place during the isomerization. However, at specific carbon segments, G ⇄ T and T ⇄ G' conformational jumps occur, and these are "two-site" jumps which would produce the effects observed in the ^2H NMR line shapes.

It should also be mentioned that torsional oscilltions could contribute to averaging of the ^2H NMR spectra. In fact, if these oscillations are sufficiently large (±70°), they will result in an $\eta = 1$ spectrum of 120-kHz breadth. Since the maximum in the trans-gauche energy barrier occurs at ±60°, it appears that this mechanism would reduce to discrete isomerization if the bonds were rigidly coupled and the oscillations were constrained to a single carbon segment. However, this seems physically implausible; a more reasonable mechanism might involve smaller angular excursions at individual segments which would accumulate to ±70° excursions at the carbon of interest. Alternatively, torsional oscillations within discrete rotational isomers may be contributing to the averaging process. Thus, while the diamond lattice jumping model provides a convenient physical and mathematical framework to understand our results, it may represent an oversimplification of the motional processes which are actually present.

Finally, it is reasonable to inquire if this type of phenomenon is a general property of polymethylene chains in lipid bilayers, and there is some evidence that this is indeed the case. For example, we have shown in Figure 4 spectra of 1-myristoyl-2-[6,6-$^2H_2$]myristoyl-*sn*-glycero-3-phosphocholine (DMPC) and note that the spectra observed for this lipid at −20 and 0 °C are remarkably similar to the cerebroside spectra at 0 and 20 °C, respectively. Since lecithins undergo phase transitions at much lower temperature (23.5 °C in the case of DMPC), it is not possible to obtain a fast-limit $\eta = 1$ spectrum. Nonetheless, the similarities in the low-temperature line shapes, where axial diffusion is absent, suggest that the motional processes in both types of lipid bilayers are similar. Thus, we tentatively conclude that lecithins are also undergoing the type of restricted rotational isomerization discussed for glycolipids.[13]

In summary, we have observed for the first time axially asymmetric deuterium spectra from a specifically ^2H-labeled polymethylene chain. This special line shape suggests that the motional process responsible for it is discrete reorientation, and its breadth is only consistent with a two-site exchange process between trans and gauche isomers. At temperatures just below T_c, the jump rate is in the fast exchange limit and the two allowed diamond lattice sites are equally probable. As the temperature is lowered, both the jump rate and one of the site probabilities decrease. The similarity between line shapes in glycolipids and lecithins suggests that this mechanism may be common to polymethylene chains in lipid bilayers.

Acknowledgment. Thanks are accorded to M. G. Munowitz for his assistance in the early stages of the line-shape calculations and J. Schaefer for helpful comments regarding reorientation mechanisms in polymers. This work was supported in part by the National Institutes of Health (Grants CA-00245, GM-23289, GM-25505, and RR-00995), the National Science Foundation (Grant PCM 78-23021, Contract C-670), and the Alfred P. Sloan Foundation.

(12) Boyd, R. H.; Breitling, S. M. *Macromolecules* **1974**, *7*, 855. Helfand, E. *J. Chem. Phys.* **1971**, *54*, 4651. Skolnick, J.; Helfand, E. *Ibid.* **1980**, *72*, 5489. Pechold, W.; Blasenbrey, S.; Woerner, S. *Kollid-Z. Z. Polym.* **1963**, *189*, 14.

(13) DMPC spectra in the temperature range 10–23 °C are complicated by the presence of a pretransition (Ladbrooke, B. D.; Chapman, D. *Chem. Phys. Lipids* **1969**, *3*, 304). As a consequence, we believe they consist of a superposition of spectra from molecules which are undergoing slow axial diffusion and molecules which are not. These spectra will be discussed in a future publication.

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(15) Alfred P. Sloan Research Fellow, 1978–1980; USPHS Research Career Development Awardee, 1979–1984.
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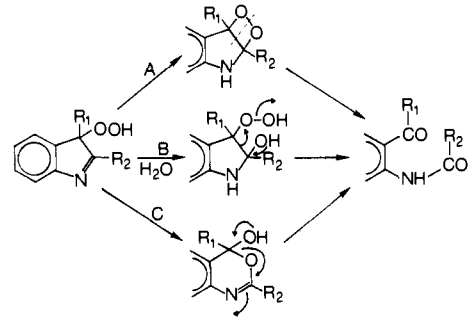
Received June 16, 1980

Differentiation between Criegee Rearrangement and Dioxetane Rearrangement Mechanisms for the Decomposition of α,β-Unsaturated Hydroperoxides

Sir:

There are three known mechanisms for the decomposition of α,β-unsaturated hydroperoxides which result in C—C bond scission and the formation of C=O bonds (for example, eq 1). Rearrangements by mechanism C received consideration in the 1940s and 1950s, but little since.[1,2] The involvement of pathway A in the decomposition of 3-(hydroperoxy)indolenines is supported by the chemiluminescence which accompanies this process.[3] However, Witkop[2] presented arguments for C rearrangement of the structurally related 11-(hydroperoxy)tetrahydrocarbazolenine, and Hamilton[4] has pointed out that path C should be favored over A due to the ring strain which accompanies dioxetane formation. It has been possible in several systems to determine the extent of competition between paths A and B.[5,6] Under the anhydrous and anerobic conditions of this study, path B cannot be operative. We report herein a means for determining the extent of competition between reaction A and another intramolecular rearrangement which we can only assume to be a Criegee-type reaction (path C).[7] This procedure depends upon the reductive trapping



(1)

(1) Criegee, R. *Ber.*, **1944**, *77*, 22, 722; *Liebigs Ann. Chem.*, **1948**, *560*, 127. Criegee, R.; Schnorrenberg, A. *Ibid.* **1948**, *560*, 141.
(2) Witkop, B. *J. Am. Chem. Soc.*, **1950**, 72, 1428. (b) Witkop, B.; Patrick, J. B., *Ibid.* **1951**, *73*, 2196. (c) Patchett, A. A.; Witkop, B. *J. Org. Chem.* **1957**, *22*, 1477. (d) Hayaishi, O.; Patchett, A. A.; Witkop, B. *Ann.* **1957**, *608*, 158. (e) Nakagawa, M.; Watanabe, H.; Kodato, S.; Okajima, H.; Hino, T.; Flippen, J. L.; Witkop, B. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 4730.
(3) (a) McCapra, F.; Chang, Y. C. *J. Chem. Soc., Chem Commun.* **1966**, 522. (b) McCapra, F.; Richardson, D. G.; Chang, Y. C. *Photochem. Photobiol.* **1965**, *4*, 111. (c) Sugiyama, N.; Yamamoto, H.; Omote, Y.; Akutagawa, M. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1917.
(4) G. A. Hamilton in "Oxidases and Related Redox Systems"; King, T. E., Mason, H. S., Morrison, M. Eds; University Park Press: Baltimore, MD, **1971**; Vol. I, p 136.
(5) Sawaki, Y.; Ogata, Y. *J. Am. Chem. Soc.* **1977**, *99*, 5412.
(6) Maskiewicz, R.; Sogah, D.; Bruice, T. C. *J. Am. Chem. Soc.* **1979**, *101*, 5347.

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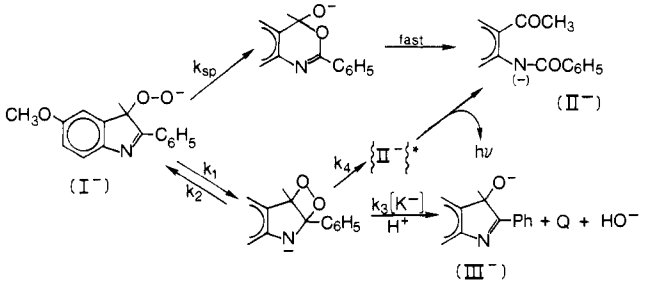
Scheme I



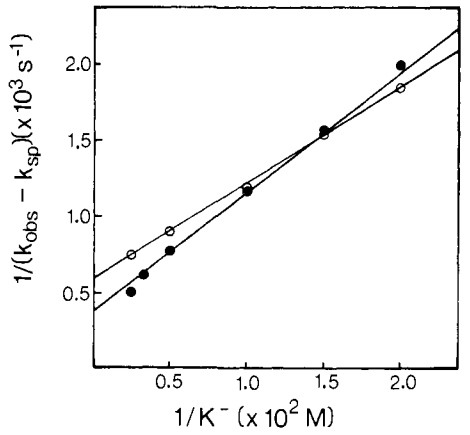
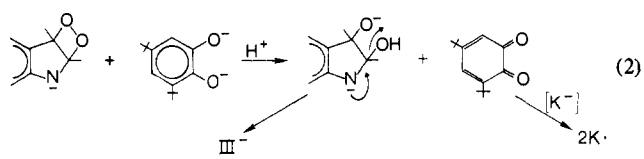


Figure 1. Plot of the reciprocal of the observed first-order rate constants (k_{obsd}) for appearance of 3,5-di-*tert*-butylcatechol semiquinone (K·) vs. the reciprocal of the concentration of 3,5-di-*tert*-butylcatechol dianion (K^-) (○). Plot of the reciprocal of the observed first order rate constants (k_{obsd}) for decrease in light emission intensity vs. $1/(K^-)$ (●). The observed pseudo-first-order rate constants (k_{obsd}) have been corrected for the rate constants of spontaneous decay of I^- (k_{sp}).

of the dioxetane intermediate of reaction A. The method may be of general utility, but the present study is of a preliminary nature and has been restricted to the decomposition of 3-(hydroperoxy)-5-methoxy-3-methyl-2-phenylindolenine (I)[8] in *anhydrous* and *oxygen-free* *t*-BuOH containing *t*-BuOK in excess of substrate.[9] Differentiation between A and C processes is of particular importance in the understanding of the mechanisms of mixed-function oxidase enzymes.[10]

Our results are discussed in terms of Scheme I (K^- = dianion of 3,5-di-*tert*-butylcatechol, Q = 3,5-di-*tert*-butyl-1,2-benzoquinone, and K· = 3,5-di-*tert*-butylcatechol semiquinone). In Scheme I dioxetane is at steady state and path C predominates (i.e., $k_2 > k_1 > k_{sp}$). Justifications for the scheme and assumptions follow. Decomposition of I^- in the absence of K^- provides a corrected[11] quantum yield (Φ) of only 5×10^{-6} while the yield of II^- is 94% of theory (~4% III^- is also obtained, probably due to reductive breakdown of dioxetane by *t*-BuOK). Even though pathway C predominates over A, the first-order rate constant, in the absence of K^-, for the falloff of the intensity of light emission will be (as found) identical with the rate constant for the disappearance of I^-. This is so because in the conversion of $I^- \rightarrow II^-$ the intensity of light emission is determined by $[I^-]$, which is in turn controlled by k_{sp} ($k_{sp} = 9 \times 10^{-4}\ s^{-1}$).[6] Under the conditions of $[t\text{-BuO}^-] = 9.0 \times 10^{-2}\ M > [K^-] > [I^-]$, increase in $[K^-]$ is accompanied initially by an increase in the first-order rate constant (k_{obsd}) for the appearance of K· (eq 2), but as $[K^-]$ is further



(2)

increased, k_{obsd} becomes independent of $[K^-]$ as the rate-determining step changes from $k_3[K^-]$ to k_1. In Figure 1 are plotted $1/k_{obsd}$ for the appearance of K· (corrected for the rate in the absence of K^-) vs. $1/[K^-]$.[12] Included in Figure 1 is a plot of $1/k_{obsd}$ vs. $1/K^-$ for the rates of chemiluminescent decay. Both plots should reflect the change in rate-determining step from $k_3[K^-]$ to k_1 for the disappearance of I^-.[6] The intercept values of Figure 1 are equal to $1/k_1$ (4.1×10^2 s by photon counting and 5.9×10^2 s by spectrophometry) and the slopes equal k_2/k_1k_3 (7.8 s M by photon counting and 6.3 s M by spectrophotometry). Thus, $k_1 \simeq 2.0 \times 10^{-3}\ s^{-1}$ and the partition coefficient $k_2/k_3 \simeq 1.4 \times 10^{-2}$ M. Also in accord with Scheme I are the findings that with increase in $[K^-]$, there is a decrease in the percent yield (%

Table I

$[K^-] \times 10^{-2}$, M	0	0.5	0.667	1.0	2.0	4.0	∞
[K·], %		73	85	96	111	142	~150
$[II^-]$, %	92	61	52	46	32	26	
$[III^-]$, %	4	33	38	49	62	69	~73

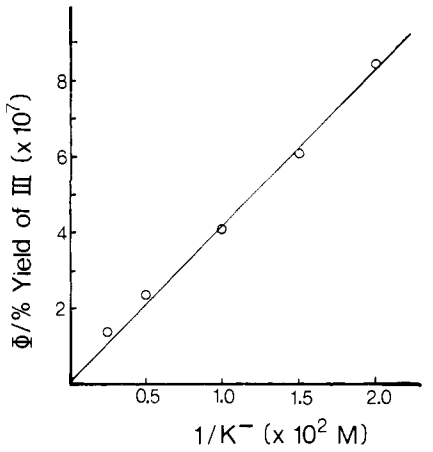
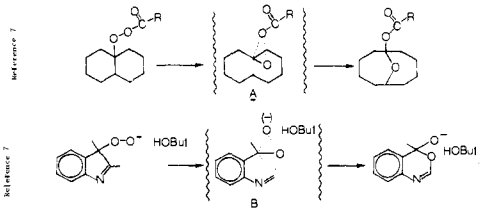


Figure 2. Plot of the quantum yield (Φ) divided by the % yield of III vs. the reciprocal of the concentration of 3,5-di-*tert*-butylcatechol dianion (K^-).

(7) The term Criegee rearrangement is applied herein to the rearrangements of such compounds as 9-*trans*-decyl hydroperoxide benzoate and 11-hydroperoxytetrahydrocarbazolenine studied by Criegee and Witkop, respectively.[1,2] For these, Witkop[2e] has recently suggested the transition states as A. Perhaps the transition state for the rearrangement of I^- by the pathway not involving an intermediary dioxetane may be represented by B.



(8) Beer, R. J. S.; Donavanik, T.; Robertson, A. *J. Chem. Soc.* **1954**, 4139.

(9) The kinetics of I^- decomposition in the presence of K^- were studied as follows: In a Thunberg cuvette a solution of I (2×10^{-4} M) was mixed with solutions of K (0.5 ~4×10^{-2} M) containing *t*-BuOK (9×10^{-2} M) in *t*-BuOH at 30 °C. The rates of K· appearance were followed at 730 nm. In a similar manner the rate of disappearance of I^- (1×10^{-4} M) in the absence of K^- was monitored at 339 nm. Photon counting was carried out with a quantum photometer Model 1140A (Princeton Applied Research) equipped with 1P 28A photomulitplier tubes. All reactions obeyed the first-order rate law to at least $3t_{1/2}$.

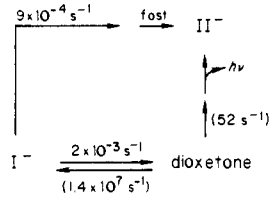
(10) King, T. E., Mason, H. S., Morrison, M., Eds. "Oxidases and Related Redox Systems"; University Park Press: Baltimore, MD, 1973; Vol I and II.

(11) The efficiency of fluorescence of $\{II^-\}^*$ was determined by using rhodamine B ($\Phi_s = 0.69$ in ethanol: Parker, C. A.; Rees, W. T. *J. Chem. Soc.* **1960**, 596) as a standard substance. The fluorescence quantum efficiency of II^- (Φ_f) in *t*-BuOH was calculated as 0.079 under the conditions of the kinetic study by comparing the fluorescent intensity of $\{II^-\}^*$ with that of {rhodamine B}*. The corrected quantum yield for chemiluminescence was obtained by dividing the quantum yields obtained in the hydroperoxide reaction by Φ_f.

(12) Kinetic equation for Scheme I is as follows: $k_{obsd} = k_{sp} + k_1 - k_1k_2/(k_2 + k_4 + k_3[K^-])$. When $k_4 \ll k_2 + k_3[K^-]$, $1/(k_{obsd} - k_{sp}) = 1/k_1 + k_2/k_1k_3[K^-]$.

Y) of II⁻ and an increase in that of III⁻ and the % Y of K· equals approximately twice that of III⁻ (Table I).[13] At saturation in K⁻, II⁻ and III⁻ form through competing parallel first-order reactions rate-controlled by k_{sp} and k_1, respectively. The maximum yield of III⁻ that may be obtained may then be calculated as 100 $k_1/(k_1 + k_{sp})$ = 73%. In the presence of K⁻, the dioxetane is partitioned to III⁻ and $\{II^-\}^*$ by parallel and competing (k_4 vs. $k_3[K^-]$) first-order reactions. Since the quantum yield (Φ) is proportional to the percent yield of $\{II^-\}^*$, it follows that % Y of II⁻/% Y of III⁻ = $\alpha\Phi$/% Y of III⁻ = $k_4/k_3[K^-]$. The fact that dioxetane partitions between $\{II^-\}^*$ and trapping by K⁻ is established by a plot (Figure 2) of Φ/(% Y of III⁻) vs. $1/[K^-]$ which is linear with the zero intercept as required. The slope of the plot of Figure 2 is equal to $k_4/\alpha k_3 = 4.1 \times 10^{-9}$ M.

In conclusion, we have established that the reactions of Scheme I account for the modes of decomposition of I⁻ in *t*-BuOH (anhydrous, O_2-free) in the presence of *t*-BuOK in excess over reactants. The constants k_{sp} and k_1 have been determined directly, and with the assumption that k_3 represents a thermodynamically favorable electron transfer ($k_3 \simeq 10^9$ M^{-1} s^{-1}) and a knowledge of the fluorescence quantum yield of $\{II^-\}^*$,[11] we arrive at the approximation of eq 3. In eq 3 the rate constants have not been



(3)

corrected for the extent of ionization of intermediates and pertain, therefore, to the experimental conditions employed.[9] Under the conditions of this study, the rate constant for dioxetane formation is twice that for the Criegee rearrangement (path C). Even though dioxetane formation involves an intramolecular nucleophilic attack by an α-effect base, the strain brought about by formation of a four-membered ring and the forcing of an unfavorable eclipsed conformation upon the nonbonding electrons of the peroxide oxygen atoms disfavor this process.[14] Thus, conversion of dioxetane back to I⁻ is associated with a rate constant of $\sim 10^7$ s^{-1}, so that the rate of rearrangement through the Criegee mechanism is $\sim 10^5$ faster than through the diioxetane pathway. It is our plan to extend this study to other solvent conditions and to other α,β-unsaturated hydroperoxides.

Acknowledgment. This work was supported by grants from the National Institutes of Health and the National Science Foundation.

(13) The yields of K·, II, and III were determined as follows: [K·] was quantified by using its absorbance at 730 nm (ϵ_{730} = 680 M^{-1} cm^{-1}: Muto, S.; Bruice, T. C. J. Am. Chem. Soc. **1980**, *102*, 4472). The yields of II and III were determined by high-performance LC. The LC analyses were carried out with a Du Pont Instruments reverse-phase column (Lichrosorb 5RP 8, 25 cm, 4.6 mm) with CH_3CN–H_2O, 40:60 (v/v), at a flow rate 1.2 mL/min. The products were monitored at 242 nm (=λ_{max} of I, II, and III). Retention times of authentic I, II, and III were 11.9, 25.2, and 10.1 min, respectively.

(14) O'Neal, H. E.; Richardson, A. H. *J. Am. Chem. Soc.* **1970**, *92*, 6553.

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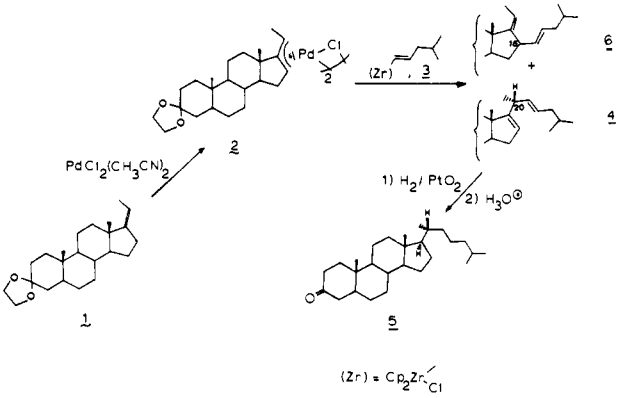
Regiocontrolled Coupling of (π-Allyl)palladium Complexes with Organozirconium Species: A New Steroid Synthesis

Sir:

Allylic functionalization of olefins, achieved through the intermediacy of (π-allyl)palladium complexes, has been elegantly applied in high-yield regio- and stereoselective syntheses of a variety of target molecules in which the key bond-forming step has been regarded as a direct attack by a nucleophile on the allylic ligand.[1] For carbon–carbon bond formation, the scope of these procedures is constrained by the limited range of permissible carbon nucleophiles: it is reported that, in general, only stabilized anions can be used.[2] Trost has applied this synthetic methodology to problems in steroid synthesis[3] in which the stabilized carbanion is the precursor of the steroid side chain formed by attack on a (π-allyl)palladium complex derived from a simpler olefin containing the steroid nucleus. Because of stereochemical preferences of substituents in this π-allylic complex and the requirement for trans attack of the nucleophile upon it, the steroidal products thus formed have the epi configuration at C-20.[4] Were it possible to utilize these simple olefin-derived (π-allyl)palladium complexes in a process involving attack by a carbon species *at the metal*, followed by C–C reductive elimination, steroids containing the natural *R* configuration at C-20 would result. Indeed, regiocontrolled attack (with respect to the termini of the allylic unit) to couple modifiable side chains with accessible π-allylic complexes derived from simple steroidal olefins would achieve convergent syntheses of a wide variety of steroidal analogues having the natural configuration at C-20. Alkenylzirconium complexes had been shown[5,6] to transfer alkenyl groups to Pd(II) salts, and we now report that these alkenylzirconium species couple with (π-allyl)palladium chloride complexes to give high yields of the resultant 1,4-dienes. We wish to describe these results in the context of regioselective synthesis of steroids possessing the natural configuration at C-20.

Olefin **1** was converted (90%) to (π-allyl)palladium chloride dimer **2**[7,8] by refluxing with excess $PdCl_2(CH_3CN)_2$ in methylene



chloride in the presence of sodium carbonate. Initial attempts at coupling **2** and **3**[9] did not proceed smoothly to give the desired diene **4**. Rather, a complex mixture was obtained consisting of **1**, **4**, and the regioisomer **6** corresponding to coupling at C-16. The combined yield of coupled product was 59% (**4**:**6** formed in a ratio 2:3).

It was hoped that formation of **1** could be suppressed and that regiocontrolled coupling could be obtained by equilibrating **2** with

(1) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615.

(2) Trost, B. M.; Weber, L.; Strege, P.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3426.

(3) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1978**, *100*, 3435.

(4) Transformation of $\Delta^{17(20)}$ olefin to an allylic acetate enabled preparation of steroidal material with the natural configuration at C-20 using a catalytic amount of $(PPh_3)_4Pd$.

(5) Yoshifuji, M.; Loots, M. J.; Schwartz, J. *Tetrahedron Lett.* **1977**, 1303.

(6) Okukado, N.; Van Horn, D. E.; Klima, W. L.; Negishi, E. I. *Tetrahedron Lett.* **1977**, 1027.

(7) ^1H NMR (C_6D_6) δ 3.59 (s, 4), 3.37 (q, 1, J = 7.6 Hz), 3.32 (br d, 1, J = 2.7 Hz), 1.20 (d, 3, J = 7.6 Hz), 0.9–2.1 (br m, 20), 0.62 (s, 6).

(8) ^{13}C NMR shows **2** to be a single compound. The data of D. N. Jones and S. D. Knox (*J. Chem. Soc., Chem. Commun.* **1977**, 165) suggest that strong shielding of the C-18 methyl group would be expected if the Pd were on the β face of the steroid. No such shift is observed. The pertinent features of the proton NMR are in good agreement with data reported by Trost for the syn isomer of bis[chloro[16,17,20-η^3-3-methoxy-19-norpregna-1,3,5-(10),17(20)-tetraene]palladium(II)].[3]

(9) For a general procedure to prepare this type of complex, see: Carr, D. B.; Schwartz, J. *J. Am. Chem. Soc.* **1979**, *101*, 3521.

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