There are several pathways that the mechanism of the cycloaddition may follow. The simplest would be a concerted thermal [2 + 4] cheletropic addition. Alternatively, the reaction may proceed via a two-step addition involving an unstable 1,2 adduct (vinyl phosphiranium ion) which rearranges to give the 1,4 adduct. The former mechanism has been shown to predominate in the case of R_2Ge[13] while the latter holds for R_2Si,[2] both of which are expected to exist as ground-state singlets.[14] There is also the possibility of a nonconcerted addition that passes through a biradical intermediate and is expected for the addition of a triplet species. However, since R_2P^+ is almost certainly a ground-state singlet,[3d,4] this last mechanism is unlikely. At this time, both the [2 + 4] cheletropic and the stepwise addition remain as equally viable candidates.

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Registry No. 1a, 61788-01-0; **1b**, 84240-84-6; **2a**, 78-79-5; **2b**, 513-81-5; **3a**, 87712-52-5; **3b**, 87729-01-9; **3c**, 87729-02-0.

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Reaction of Phosphenium Ions with 1,3-Dienes: A Rapid Synthesis of Phosphorus-Containing Five-Membered Rings

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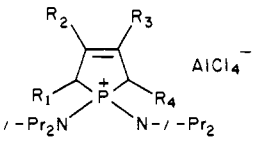
In the singlet state, phosphenium ions (R_2P^+) feature both a lone pair and a vacant orbital at the cationic center. The anticipated amphoterism of these cations is evidenced by the fact that they interact with Lewis bases,[1] undergo C-H oxidative addition reactions,[2] and function as ligands.[3] We now report that phosphenium ions react readily with a variety of 1,3-dienes.

Typically, 0.290 g (3.5 mmol) of 2,3-dimethyl-1,3-butadiene was added to a solution of 0.720 g (1.8 mmol) of $[(i\text{-}Pr_2N)_2P]^+[AlCl_4]^-$ (**1**)[4] in 50 mL of CH_2Cl_2 at 0 °C. $^{31}P\{^1H\}$ NMR monitoring of the product, **2a** (δ ^{31}P + 69.6), indicated that the reaction was complete in ~12 h.[5,6] The 3-phospholenium



2a, $R_1 = R_4 = H$; $R_2 = R_3 = Me$ (95% yield, mp 132 °C)
b, $R_2 = Me$; $R_1 = R_3 = R_4 = H$ (92% yield, mp 144 °C)
c, $R_1 = R_2 = R_3 = R_4 = H$ (73% yield, mp 153 °C)
d, $R_1 = Me$; $R_2 = R_3 = R_4 = H$ (64% yield, mp 175 °C)
e, $R_1 = R_4 = Me$; $R_2 = R_3 = H$ (55% yield, mp 167 °C)

cation structure for **2a** was deduced from the following NMR data: $^{13}C\{^1H\}$ (CH_2Cl_2) (20.0 MHz) δ 16.0 (Me (ring), d, J_{PCCC} = 14.5 Hz), 22.6 (Me (*i*-Pr), s), 37.1 (CH_2, d, J_{PC} = 76.5 Hz), 47.9 (CH (*i*-Pr), d, J_{PNC} = 4.1 Hz), 127.3 (C (ring), J_{PCC} = 11.5 Hz); ^1H NMR (90.0 MHz) (CH_2Cl_2) δ 1.3 (Me (*i*-Pr), d, 12 H, J_{HCCH} = 7.5 Hz), 1.8 (Me (ring), br, 6 H), 3.1 (CH_2, d, 4 H, J_{PCH} = 11.1 Hz), 3.7 (CH (*i*-Pr), m, 4 H). The structure was confirmed by a single-crystal X-ray diffraction study[7] and shows that the double bond is located between C(2) and C(3) (1.313 (5) Å), the other C-C bond lengths averaging 1.517 (5) Å (Figure 1). The $[(i\text{-}Pr_2N)_2P]^+$ unit[4] changes little on coordination: the P-N bond lengths increase by an average of 0.013 (4) Å while the N-P-N angles widen by 1.3 (2)°. The nitrogens remain trigonal planar.

The times for reaction completion for the other 1,3-dienes are dependent upon steric and electronic factors. Thus, the less activated dienes, isoprene and 1,3-butadiene, require ~24 h at 25 °C and afford the 3-phospholenium cations **2b** (δ ^{31}P + 76.5) and **2c** (δ ^{31}P + 76.0), respectively. The more sterically hindered dienes *trans*-1,3-pentadiene and *trans*-2,*trans*-4-hexadiene produce **2d** (δ ^{31}P + 79.7) and **2e** (δ ^{31}P +88.7) in 3 and 9 days, respectively. Reaction times can be decreased even further by using the less bulky phosphenium ion $[(Me_2N)_2P]^+$. For example, $[(Me_2N)_2P]^+$ reacts with 2,3-dimethyl-1,3-butadiene and isoprene in ~1 h (upon warming) from -78 to 25 °C) affording **3a** (δ ^{31}P +82.7) and **3b** (δ ^{31}P +89.6), respectively. The structures of **3a** and **3b** were shown to be analogous to those of **2a** and **2b** by ^1H and ^{13}C NMR spectroscopy.[6] The chlorophosphenium ion $[(i\text{-}Pr_2N)(Cl)P]^+$ also reacts very cleanly and rapidly (~30 min) with 2,3-dimethyl-1,3-butadiene to afford the corresponding 3-phospholenium cation, **4a** (δ ^{31}P +93.4).

It was first recognized by McCormack[9] that dihalophosphines react with 1,3-dienes and upon hydrolysis produce phospholene oxides. However, the McCormack reactions require several days or weeks for completion. The dramatic reduction in reaction times for the corresponding phosphenium ion reactions is due to their electrophilic nature.

Finally, we note that phosphenium cations are computed to be ground-state singlets.[10] The reactions of these cations with, in particular *trans*-2,*trans*-4-hexadiene show only one product according to ^{31}P NMR spectroscopy, thus suggesting the anticipated stereospecificity of the addition reaction. Further studies of the

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(5) After reactions were complete all volatiles were removed via vacuum. The phospholenium salts were dissolved in a minimum amount of CH_2Cl_2, and about twice the volume of hexane was layered over the CH_2Cl_2. The two-phase solution was placed at -20 °C. After a few days crystals resulted.

(6) Satisfactory elemental analyses were obtained for all new compounds. These data will be published in a full paper along with ^{13}C and ^1H NMR data.

(7) Crystal data for **2a**: $AlC_{18}Cl_4H_{38}N_2P$ M_r = 482.29, monoclinic, space group $P2_1/c$ (No. 14), a = 9.005 (1) Å, b = 16.134 (4) Å, c = 18.271 (2) Å, β = 96.94 (2)°, U = 2633 (3) Å^3, D_c = 1.216 g cm^{-3}, Z = 4, λ (Mo Kα) (graphite monochromator) = 0.71069 Å, μ (Mo Kα) = 5.5 cm^{-1}. From a total of 5869 unique reflections measured on an Enraf-Nonius CAD-4 diffractometer in the range $2.0 \le 2\theta \le 50.0°$, 3214 ($I > 3\sigma(I)$) were used to solve (MULTAN[8] and difference Fourier) and refine (full matrix, least squares) the structure of **2a**. Due to extensive disorder in the $AlCl_4^-$ anion, the structure did not refine well and gave final residuals R = 0.1046 and R_w = 0.1471. The cation was essentially well-behaved during the refinement, and its structure is adequately determined by this experiment. The $AlCl_4^-$ unit was refined as two tetrahedra except for one Cl atom, which did not refine. Positional parameters, occupancy factors, and thermal parameters were refined independently to obtain the best fit. Full details will be published in due course.

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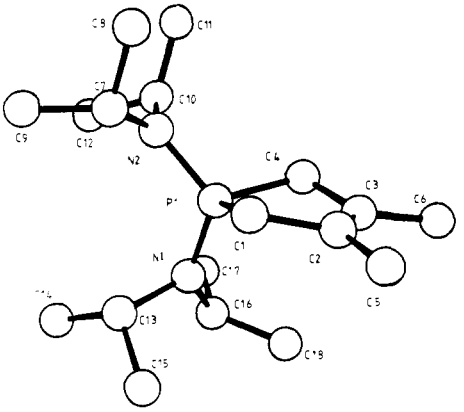

Figure 1. Structure of the 3-phospholenium cation **2a** showing the atom numbering scheme. Important parameters: C(2)-C(3) 1.313 (5), C(1)-C(2) 1.509 (5), C(3)-C(4) 1.526 (5), P(1)-N(1) 1.633 (3), P(1)-N(2) 1.620 (3) Å; N(1)-P(1)-N(2) 116.1 (2)°. The angle between the planes C(1)-P(1)-C(4) and C(1)-C(2)-C(3)-C(4) is 31.4°.

reactions of phosphenium ions with alkenes and alkynes are in progress.

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Registry No. 1, 68880-45-5; **2a**, 87712-41-2; **2b**, 87712-43-4; **2c**, 87712-45-6; **2d**, 87712-47-8; **2e**, 87712-49-0; **3a**, 87712-51-4; **3b**, 87712-53-6; **4a**, 87712-56-9; $[(Me_2N)_2P]^+$, 61788-01-0; $[(i\text{-}Pr_2N)(Cl)P]^+$, 87712-54-7; 2,3-dimethyl-1,3-butadiene, 513-81-5; isoprene, 78-79-5; 1,3-butadiene, 106-99-0; *trans*-1,3-pentadiene, 2004-70-8; *trans*-2,-*trans*-4-hexadiene, 5194-51-4.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond angles, and bond lengths for **2a** (5 pages). Ordering information is given on any current masthead page.

Electron Spin Echo Modulation Demonstrates P-450$_{scc}$ Complexation

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The initial structural information needed for understanding the chemical mechanism of an enzymatic reaction includes the topological relationship between the substrate and the protein active site. Unfortunately, most present pictures of such states come from indirect measurements: crystallographic studies of enzyme-inhibitor complexes[1] or examinations of reaction products derived enzymatically from mechanism-based inhibitors.[2] In a few cases, it has been possible to visualize enzyme-substrate complexes stabilized at low temperature, using crystallography.[3] Herein we report the first application of electron spin echo spectroscopy (ESE) to the estimation of interatomic distance in an enzyme-substrate complex.

This novel approach takes advantage of the sensitive detection of weak hyperfine interactions, between an unpaired electron and its environment, afforded by electron spin echo envelope modulation (ESEEM). In this technique, the application of an intense microwave field reorients the individual magnetic dipoles associated with an electron spin system. Sequences of pulses can be used to interrogate residual magnetic polarization after varying ensemble phase decay intervals. In rephasing after multiple perturbations the system emits an "echo" signal, which reflects the relaxation processes of the system. Thus, a plot of echo magnitude as a function of time between pulses can reveal not only the decay associated with magnetic relaxation mechanisms (T_m) but also periodic modulations resulting from coupling between the electron and neighboring nuclear spins. The depth and frequency of this modulation convey information as to the identity of nearby nuclei, their number, and the distance separating them from the electron spin. Consequently, one can probe directly the immediate magnetic environment of a paramagnet.[4]

Here we investigate the bovine adrenal side-chain cleavage enzyme, cytochrome P-450$_{scc}$. This membrane-bound hemoprotein catalyzes the transformation of cholesterol to pregnenolone via three successive hydroxylations, in the rate-determining step of adrenocorticosteroid synthesis.[5] P-450$_{scc}$ acts as well on a variety of related steroidal substrates; all of these reactions exhibit a high degree of regio- and stereospecificity.[6] We are concerned both with understanding the molecular basis for this specificity and in its implications for the mechanism of catalysis.

We examined the first step in the catalytic cycle of P-450$_{scc}$, i.e., the binding of substrates to the oxidized form of the enzyme. In order to distinguish substrate-derived modulations from those due to the proton background of solvent and protein residues, we have used steroids selectively deuterated at specific positions.[7] Our present concern has been with the initial site of cholesterol activation, carbon 22, and we have examined thus far three different substrates deuterated at that position: cholesterol-*22,22-d*$_2$, 22-hydroxycholesterol-*22-d* (the first intermediate in cholesterol turnover), and 20-azacholesterol-*22,22-d*$_2$. The results of three-pulse echo experiments[8] carried out at $g = 2.2$ for these enzyme-substrate complexes are shown in Figure 1. In the presence of unlabeled substrate, little modulation of the echo decay can be detected. A clear periodicity, however, is obvious in each of the deuterated samples. Analysis of the data for 22(*R*)-hydroxycholesterol-*22-d* (Figure 1a) is the most straightforward, since only one deuterium is involved. Fourier transformation of this spectrum reveals a modulation frequency of 1.9 MHz, well within the range expected for deuterium (with a free precession frequency of 1.93 MHz at 2950 G). Comparisons with simulated spectra,[9] as illustrated in Figure 2, imply a separation of 4 ± 1 Å between the deuteron at C22 and the unpaired spin. Inter-

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