ORGANIC LETTERS

2006
Vol. 8, No. 22
5125−5128

Intramolecular Arene Epoxidation by Phosphadioxiranes

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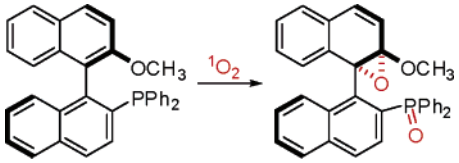
Received September 5, 2006

ABSTRACT



Singlet oxygen reacts with binaphthyl phosphine derivatives such as 1,1′-binaphthyl di-*tert*-butyl phosphine to form the corresponding binaphthyl-2-oxide phosphine oxides. This new intramolecular arene epoxidation reaction proceeds with complete retention of stereochemistry. The binaphthyl-2-oxide di-*tert*-butyl phosphine oxide undergoes a slow "NIH-rearrangement" to form the corresponding hydroxylated product. A transient phosphadioxirane intermediate has been directly observed by low-temperature NMR. Kinetic analyses show that all of the phosphadioxirane intermediate is converted to product.

Phosphadioxiranes are the primary adducts formed during the reaction of singlet dioxygen with trivalent arylphosphines.[1,2] They are highly unstable species, and have been shown to undergo a variety of reactions, including epoxidation of unfunctionalized olefins, reaction with alcohols to form hydroperoxy phosphoranes,[1] oxidation of phosphites and sulfides,[3] and intramolecular oxygen atom insertion into phosphorus−carbon single bonds.[3,4] Phosphadioxiranes are also key transient intermediates during the antioxidant activity of bulky phosphines used as jet-fuel stabilizers.[5] Ab initio calculations have indicated that they should be electrophilic oxidants, consistent with the observed reactivity.[6] However, to date there have been no reports of hydroxylation and/or arene epoxidation by a phosphadioxirane.[7] Furthermore, rapid reactivity of phosphadioxiranes with the starting arylphosphines from which they are derived usually precludes their direct observation even at very low temperatures, except when bulky electron-rich substituents in the ortho position are used.[1] We now report the direct observation of a new phosphadioxirane derived from a

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(6) (a) Nahm, K.; Li, Y.; Evanseck, J. D.; Houk, K. N.; Foote, C. S. *J. Am. Chem. Soc.* **1993**, *115*, 4879. (b) A very recent paper by Weinhold et al. suggests an unusual cyclic three center/four electron (3c/4e) bonding mode for phosphadioxiranes; this is also consistent with their observed electrophilic reactivity: Wilke, J. J.; Weinhold, F. *J. Am. Chem. Soc.* **2006**, *128*, 11850.
(7) Several transition-metal-catalyzed routes to arene epoxides have recently been reported: (a) Villeneuve, K.; Tam, W. *J. Am. Chem. Soc.* **2006**, *128*, 3514. (b) Hashmi, A. S. K.; Rudolph, M.; Weyrauch, J. P.; Woelfle, M.; Frey, W.; Bats, J. W. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 2798.

10.1021/ol0622007 CCC: $33.50
Published on Web 09/26/2006

binaphthyl system, and its ability to undergo intramolecular arene epoxidation.

Photooxidation of 1,1′-binaphthyl di-*tert*-butyl phosphine (**1**) at room temperature in toluene, acetonitrile, or methylene chloride leads to formation of binaphthyl-2-oxide di-*tert*-butyl phosphine oxide (**2**) and 1,1′-binaphthyl di-*tert*-butyl phosphine oxide (**3**). Compound **2** is relatively unstable at room temperature (see below), but we were able to establish its identity by an X-ray molecular structure at − 20 °C; the ORTEP diagram of **2** is shown in Figure 1. If the naphthalene

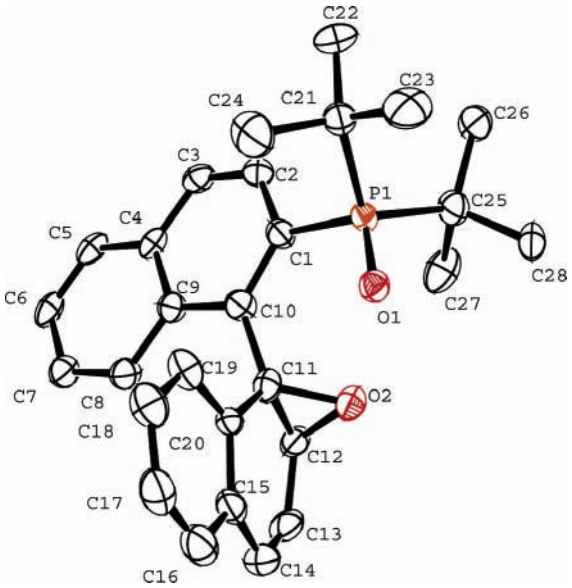


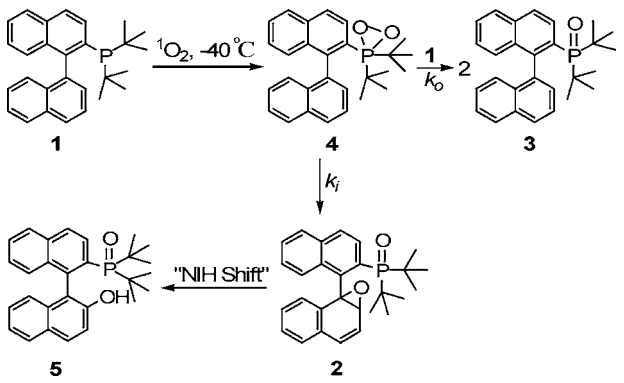
Figure 1. ORTEP diagram of **2**. Solvent molecules and hydrogen atoms have been omitted for clarity.

epoxide **2** is indeed formed by intramolecular oxidation from a phosphadioxirane intermediate while the phosphine oxide is formed via intermolecular attack of the same intermediate on unreacted starting material, the following relationship must hold (at low conversion of **1**; where k_i is the rate constant for the intramolecular oxidation and k_o is the rate constant for intermolecular oxidation):

$$\frac{[\mathbf{3}]}{[\mathbf{2}]} = \frac{2k_o[\mathbf{1}]}{k_i}$$

Plots of the product ratio[**3**]/[**2**] vs [**1**] are indeed linear (conversion of **1** was limited to less than 20%), with a slope of 14 ± 2. The ratio of inter- vs intramolecular oxidation is thus 7 ± 1. This implies that the naphthalene epoxide formation predominates if the starting material concentration is kept sufficiently low (i.e., 10 mmol or less). The naphthalene epoxide **2** is unstable at room temperature in toluene and slowly rearranges to the hydroxylated product **5**, via one observable intermediate. At room temperature, this conversion takes approximately 2 days to go to completion. The mechanism of this conversion is most likely the

Scheme 1. Reaction of 1,1-Binaphthyl Di-tert-butyl Phosphine (**1**) with Singlet Oxygen



well-known "NIH-Shift mechanism",[8] which implies that the intermediate is the enone tautomer of the final hydroxylated product. Support for this hypothesis is derived from the ^{1}H NMR signal of the intermediate at 4.54 ppm, presumably due to the proton on the bridgehead carbon adjacent to the carbonyl moiety. If the photooxidation of **1** is carried out in toluene, the hydroxylated product **5** readily precipitates from the product mixture. The identity of **5** was confirmed by an X-ray molecular structure. The ORTEP diagram of compound **5** is shown in Figure 2.

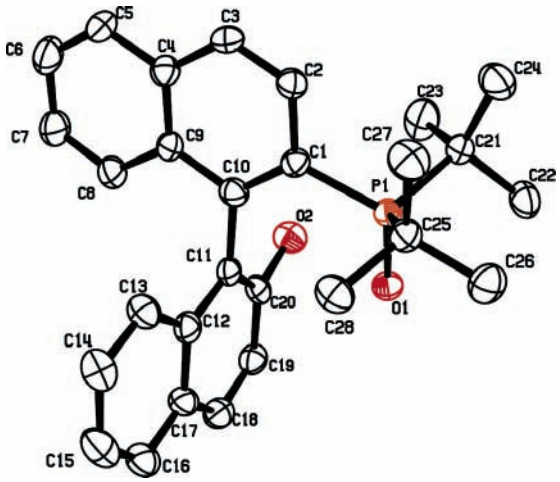


Figure 2. ORTEP diagram of **5**. Solvent molecules and hydrogen atoms have been omitted for clarity.

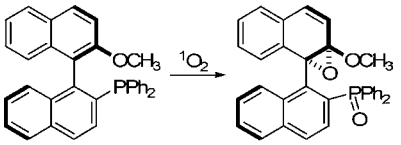
Low-temperature photooxidation of 1,1′-binaphthyl di-*tert*-butyl phosphine (**1**) in toluene at temperatures of −40 to −80 °C leads to formation of a peroxidic species with a ^{31}P NMR signal peak at −18.6 ppm. The shift difference relative to the starting compound **1**, as well as the absolute position of the ^{31}P NMR signal, is similar to that of the tris(*o*-

(8) Guroff, G.; Daly, J. W.; Jerina, D. M.; Renson, J.; Witkop, B.; Udenfriend, S. *Science* **1967**, *157*, 1524.

methoxyphenyl)phosphadioxirane previously reported by our group.[1] We therefore formulate this new species as the phosphadioxirane derived from compound **1**, namely 1,1′-binaphthyl di-*tert*-butyl phosphadioxirane (**4**). Further support for this assignment is derived from the observations that the new species oxidizes phosphines to the corresponding phosphine oxides and cyclohexene to cyclohexene oxide, albeit in relatively poor yield (generally less than 50%). The low yields may be due to the steric bulk of the binaphthyl system. Warming phosphadioxirane **4** to room temperature initially leads to formation of the epoxide **2**, confirming that this species is indeed obtained by intramolecular arene epoxidation. Formation of the phosphadioxirane **4** from a racemic mixture of **1** is first order throughout the entire photooxidation.

Since phosphadioxiranes are electrophilic oxidants,[1−4] addition of electron-donating groups to the binaphthyl moiety should favor intramolecular arene oxidation over reaction with unreacted phosphine. We therefore investigated the reaction of 2-(diphenylphosphino)-2′-methoxy-1,1′-binaphthyl (**6**) with singlet oxygen. Indeed, phosphine **6** reacts with singlet oxygen to produce exclusively 2-(diphenylphosphine oxide)-2′-methoxy-2′-epoxy-1,1′-binaphthyl (**7**) in quantitative yield, as determined by ^{31}P NMR. This is the first example where reaction of a phosphadioxirane with unreacted starting material phosphine to form phosphine oxide is completely outcompeted by a kinetically faster process. Intramolecular arene epoxidation is so rapid that we were unable to detect the phosphadioxirane derived from compound **6** at temperatures as low as −80 °C; only the epoxide **7** is observed when the reaction is carried out and products are analyzed at this temperature. The initial attack of the singlet oxygen molecule must have been exclusively at the phosphorus atom since no endoperoxide (which would result from attack of singlet oxygen on the naphthalene ring)[9] was observed. To further investigate the unusually efficient

Scheme 2. Reaction of (*R*)-(+)-2-(Diphenylphosphino)-2′-methoxy-1,1′-binaphthyl (**6**) with Singlet Oxygen



6 **7**

oxygen atom transfer, we investigated the kinetic activation barrier for the conversion of **6** to **7** with density functional theory methods at the B3LYP/6-311G** level. Structural ensembles of **6** and **7** were generated (1.2 Å rmsd) and subjected to all atom minimization. Truncated models were created, minimized, and used to locate the transition state (DMol3) for the oxygen insertion reaction. Successive geometry optimizations were performed with a scan parameter (C−O bond formation), with a final single point frequency calculated for the optimized transition state. Multiple iterations and subsequent optimizations yielded a transition state barrier of 6.63 ± 1.91 kcal relative to the starting conformation of **6**, consistent with the rapid oxygen atom transfer at −80 °C.

PM3 calculations show that the barrier of rotation of the starting phosphine **6** is 147 ± 3 kcal/mol. There is thus no interconversion between the R and S isomers of starting material **6**. Indeed, formation of **7** proceeds with complete retention of stereochemistry. (*R*)-(+)-2-(Diphenylphosphino)-2′-methoxy-1,1′-binaphthyl produces the corresponding R-isomer of **7**, and using the S-isomer of **6** likewise only produces the S-isomer of product **7**. Products for both isomers were characterized by ^{1}H and ^{31}P NMR as well as CD spectroscopy. In particular, the ^{1}H NMR showed characteristic doublets for the vinylic protons of the epoxidized ring at 6.27 and 6.57 ppm. The CD values of both isomers of compounds **6** and **7** in acetonitrile ((*R*)-2-(diphenylphosphino)-2′-methoxy-1,1′-binaphthyl: $\Delta\epsilon_{220}$ −6.1, $\Delta\epsilon_{232}$ +43.6, $\Delta\epsilon_{240}$ −94.6; (*R*)-2-(diphenylphosphine oxide)-2′-methoxy-2′-epoxy-1,1′-binaphthyl: $\Delta\epsilon_{214}$ +49.9, $\Delta\epsilon_{240}$ −89.9; (*S*)-2-(diphenylphosphino)-2′-methoxy-1,1′-binaphthyl: $\Delta\epsilon_{220}$ +9.0, $\Delta\epsilon_{232}$ −41.5, $\Delta\epsilon_{240}$ +95.8; (*S*)-2-(diphenylphosphine oxide)-2′-methoxy-2′-epoxy-1,1′-binaphthyl: $\Delta\epsilon_{214}$ −49.2, $\Delta\epsilon_{240}$ +97.1) are also consistent with complete retention of stereochemistry. Furthermore, kinetic analysis shows that each isomer reacts with singlet oxygen at the same rate: Singlet oxygen luminescence quenching experiments yield a total rate k_T of singlet oxygen removal (i.e., via physical quenching and chemical reaction) for the R-isomer of 1.0 ± 0.1 × 10^7 M^{-1} s^{-1}, and 1.1 ± 0.1 × 10^7 M^{-1} s^{-1} for the S-isomer. Competition experiments carried out with 9,10-dimethylanthracene gave values of 1.1 ± 0.1 × 10^7 M^{-1} s^{-1} for the rate formation (k_r) of both products. Since the values of k_r and k_T are identical, there is no physical quenching of singlet oxygen by either isomer, as has been reported for other electron-rich arylphosphines.[3]

In conclusion, we have established that singlet oxygen can be used to epoxidize binaphthyl phosphines via transient phosphadioxirane intermediates. The reaction proceeds with retention of configuration, and there is no physical quenching of singlet oxygen. Functionalized binaphthyl phosphines such as 2-(di-*tert*-butylphosphine)-2′-hydroxy-1,1′-binaphthyl have recently been found to be highly effective catalysts for stereoselective Bayliss−Hillman reactions,[10] and the process reported here may represent a convenient entry into this type of substituted binaphthyl phosphine. Further experiments to explore the diverse chemistry of phosphadioxiranes are in progress.

Acknowledgment. This research was supported by a Henry Dreyfus Teacher-Scholar Award. Support by the NIH-NIGMS MBRS program (Award no. GM08101) is also gratefully acknowledged.

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Supporting Information Available: Experimental procedures for photooxidation and characterizations (^{1}H NMR and ^{31}P NMR), CD spectra, as well as CIF files for the crystal structures of **2** and **5**, and Cartesian coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0622007