into water and extracted several times with pentane. The combined pentane solution was washed with water and dried. Concentration afforded 8.9 mg (91%) of a clear oil: IR 3040, 2950, 1640 cm^{-1}; NMR δ 0.74 and 0.78 (d, J = 7 Hz, 2.9 Hz, 1_a and 30_a), 0.90 (m, 1.1 H, 1_b, 30_b, 31_b, and 31_a), 1.10–1.80 (6 H), 1.61 (s, 3 H), 1.69 (s, 6 H), 2.00 (m, 8 H), 2.37 (m, 1 H), 4.55 (br s, 0.6 H, 1_c), 4.58 (br s, 0.4 H, 30_c and 31_c), 4.66 (br s, 1 H), 5.09 and 5.12 (two overlapping t, 1 H), 5.52 (br s, 1 H).

Separation of 1 from 30 and 31. A mixture of **1**, **30**, and **31** from several experiments was subjected to flash chromatography (hexane).

More mobile fractions, **30** and **31**: NMR δ 0.78 (d, J = 7 Hz, 2.7 H, 30_a), 0.90 (br d, J = 7 Hz, 1.3 H, 30_b, 31_b, and 31_a), 1.10–2.10 (6 H), 1.60 (s, 3 H), 1.69 (s, 6 H), 2.00 (m, 8 H), 2.39 (m, 1 H), 4.58 (br s, 1 H), 4.65 (br s, 1 H), 5.09 (br t, J = 6 Hz, 1 H), 5.53 (br s, 1 H); ^{13}C NMR BB 13.6, 17.6, 23.8, 25.5, 25.7, 26.3, 26.4, 31.0, 31.6, 31.7, 36.0, 39.6, 43.0, 43.8, 106.5, 124.5, 125.1, 130.9, 133.8, 154.3. This material also contained approximately 20% of the natural product (**1**) as determined by 250-MHz ^1H and ^{13}C NMR.

Less mobile fraction, **1**: NMR δ 0.74 (d, J = 7 Hz, 3 H, 1_a), 0.89 (m, 1 H, 1_b), 1.10–1.80 (6 H), 1.61 (s, 3 H), 1.69 (s, 6 H), 2.00 (m, 8 H), 2.36 (m, 1 H), 4.55 (s, 1 H), 4.66 (s, 1 H), 5.12 (br t, J = 7 Hz, 1 H), 5.53 (br s, 1 H); ^{13}C NMR BB 13.4, 17.7, 23.8, 25.7, 25.9, 26.4, 27.0, 30.6, 31.3, 36.0, 36.5, 44.4, 45.0, 45.3, 103.2, 122.5, 125.0, 131.1, 134.7, 153.3.

Biflora-4,10(19),15-trienes 1 and 30 (9:1) from 2 and 28 in THF. Methyltriphenylphosphonium bromide (65.3 mg, 0.18 mmol) was added to 5.0 mL of dry THF and cooled to 0 °C. *n*-Butyllithium (0.12 mL, 1.5 M in hexanes, 0.18 mmol) was added and then the reaction mixture was stirred at 25 °C for 45 min. To 9.0 mg (0.03 mmol) of ketones **2**, **28**, **29** (from equilibration) in 1 mL of THF was added 2.5 mL of the cloudy, yellow ylide solution. After 1 h the reaction mixture was brought to 25 °C and after 2 h the remainder of the ylide solution was added to the reaction mixture. After being stirred overnight, the reaction mixture was quenched with water and extracted 5× with pentane. The combined organic solution was washed with water, dried, and concentrated. The residue was subjected to flash chromatography (10 mm i.d., pentane only) and afforded 5.3 mg (59%) of a clear oil: IR 3040, 2950, 1640 cm^{-1}; NMR δ 0.74 (d, J = 7 Hz, approximately 2.7 H) and 0.78 (d, J = 7 Hz, approximately 0.3 H), 0.90 (m, 1 H), 1.20–1.80 (6 H), 1.61 (s, 3 H), 1.69 (s, 6 H), 2.00 (m, 8 H), 2.37 (m, 1 H), 4.54 (br s, 0.9 H, 1_c), 4.58 (br s, 0.1 H, 30_c), 4.65 (br s, 1 H), 5.12 (br t, J = 6 Hz, 1 H), 5.53 (br s, 1 H).

Acknowledgment. This work was supported by the National Science Foundation (Grant No. CHE-8306687). K.A.P. is grateful for a Camille and Henry Dreyfus Teacher–Scholar Award and for an unrestricted grant from Merck, Sharp, and Dohme. The bruker WM-250 NMR spectrometer used in this work was purchased with funds provided by the NSF and the Montedison Group of Milan. We are grateful to Professor David F. Wiemer for copies of the ^1H and ^{13}C NMR spectra of **1** and to Professor Glenn Prestwich for samples of the crude termite secretion and gas chromatography traces.

Registry No. (±)-**1**, 95910-64-8; (±)-**2**, 104195-69-9; **10**, 64841-44-7; **11**, 54911-85-2; **12**, 104155-98-8; **13**, 66084-36-4; **14**, 98076-79-0; **15**, 104155-99-9; **16**, 24286-45-1; **17**, 104156-00-5; (±)-**18**, 104156-01-6; (±)-**19**, 104195-63-3; (±)-**19** (methyl ester), 104195-64-4; **20**, 104156-02-7; **20** (methyl ester), 104156-04-9; (±)-**21**, 104156-03-8; (±)-**22**, 104156-05-0; (±)-**23a**, 104156-06-1; (±)-**23b**, 104156-07-2; (±)-**24**, 104156-08-3; (±)-**25**, 104195-65-5; (±)-**26**, 104195-66-6; **27**, 89272-53-7; (±)-**28**, 104195-67-7; (±)-**29**, 104195-68-8; (±)-**30**, 104195-70-2; (±)-**31**, 104195-71-3; 4-penten-1-ol, 821-09-0; (carbethoxymethylene)triphenylphosphorane, 1099-45-2; 2-lithiopropene, 6386-71-6.

Supplementary Material Available: Proton NMR spectra (250-MHz) for **1**, **30**, and the 1:1 mixture of **1** and **30**; 62.8-MHz carbon-13 NMR spectrum for **1**; 250-MHz proton NMR spectrum for Claisen rearrangement product mixture, **18** containing 5% **19** and 5% **20** (6 pages). Ordering information is given on any current masthead page.

Synthesis of Allylic Alcohol Single-Chain PGH Analogues. A Synthetic Application of the Argon Laser

R. Marshall Wilson,* Karlyn A. Schnapp, Richard K. Merwin, Revathi Ranganathan, David L. Moats, and Tod T. Conrad

Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221

Received January 28, 1986

Hydroformylation of either the diethyl azodicarboxylate or *N*-phenyltriazolinedione–cyclopentadiene Diels–Alder adducts provides ready access to 5-substituted-2,3-diazabicyclo[2.2.1]hept-2-enes. Single-chain azo prostaglandin analogues have been prepared by this route and their argon laser initiated, sensitized photodecomposition affords substituted cyclopenta-1,3-diyls which are easily trapped by molecular oxygen to form single-chain prostaglandin endoperoxide analogues. In the case of the allylic alcohol single-chain endoperoxide analogue, both the natural exo side chain and the unnatural endo side chain configuration are obtained by this method in quantities which are useful for the study of their chemistry.

The prostaglandin endoperoxide PGH_2 (**1**) plays a pivotal role in the biosynthesis of the prostaglandins, prostacyclin (PGI_2, **2**)[1] and thromboxane A_2 (TXA_2, **3**),[2] as shown in Scheme I. In view of the strategic biosynthetic importance of PGH_2 (**1**), it is surprising that so little is known about the chemical factors which influence its partitioning between these various pathways. Several studies seem to indicate that the side chains of PGH_2 may play an important role in governing the mode of endoperoxide decomposition. The parent unsubstituted endoperoxide **4** undergoes β-scission of the one-carbon bridge to the exclusion of the alternative β-scission of the two-carbon bridge, pathways a and b in Scheme II, respec-

(1) Dusting, G. J.; Moncada, S.; Vane, J. R. *Advances in Prostaglandin, Thromboxane, and Leukotriene Research*; Oates, J. A., Ed.; Raven Press: New York, 1982; Vol. 10, p 59.

(2) Granstrom, E.; Diazfalusy, V.; Hamberg, M.; Hausson, G.; Malmsten, C.; Samuelsson, B. *Advances in Prostaglandin, Thromboxane, and Leukotriene Research*; Oates, J. A., Ed.; Raven Press: New York, 1982; Vol. 10, p 15.

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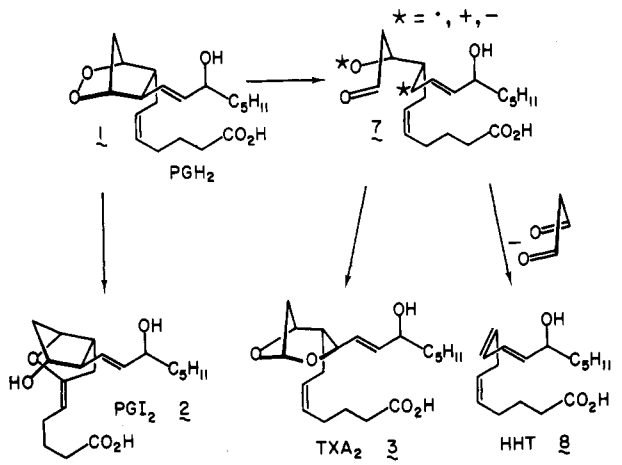
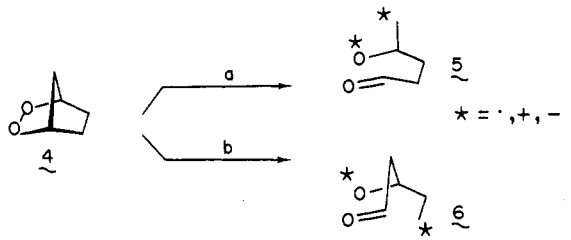
Scheme I



Scheme II

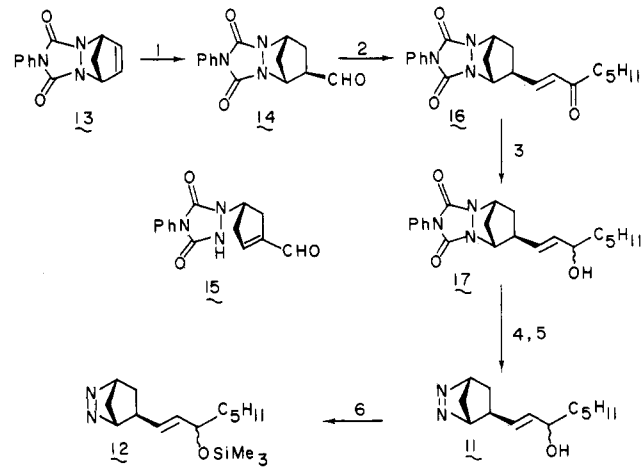


tively.[3] This propensity of **4** and closely related endoperoxides to undergo highly selective β-scission of the smaller bridge has been attributed to the more favorable overlap between the peroxide bond and the adjacent carbon–carbon bond of the smaller bridge.[4] Of course this correlation is based upon the formation of about equally unstabilized carbon centers such as those in **5** and **6**. Apparently, the introduction of the allylic alcohol side chain of PGH_2 (**1**) can alter the mode of endoperoxide fragmentation such that β-scission of the larger bridge can predominate under certain conditions.[5,6] It seems reasonable to assume that this effect may be due to the stabilizing influence of the side-chain allylic alcohol unit as indicated by **7** in Scheme I. Even if **7** is not a true intermediate but only a point on a concerted reaction surface, its collapse to either TXA_2 (**3**) or HHT (**8**) apparently is subject to some degree of control by external chemical factors.[5]

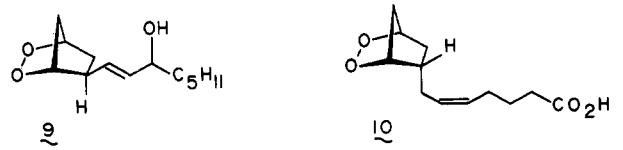
In contrast to this rather subtle effect of the allylic alcohol side chain on PGH_2 (**1**) decomposition, the effect of the carboxylic acid side chain is much more conspicuous as this side chain participates directly in the formation of PGI_2 (**2**).[7]

Thus, it would seem that the side chains of PGH_2 (**1**) do play a significant but as yet rather ill-defined role in the regulation of the modes of PGH_2 (**1**) decomposition. Our understanding of these decomposition modes and the factors which regulate them might be enhanced substantially if there were convenient methods available for the preparation of less complex single-chain analogues of PGH_2 (**1**) such as **9** and **10**. Toward this end, we would like to report a particularly facile method for the synthesis of derivatives of this type in quantities that are suitable for the further study of their chemistry.

Scheme III[a]



[a] (1) $Rh_2(CO)_4Cl_2$, H_2, CO, 2000 psi, 120–130 °C, toluene; (2) NaH, $(MeO)_2P(O)CH_2COC_5H_{11}$, THF, −78 to −35 °C; (3) $NaBH_4$, $CeCl_3$, MeOH; (4) KOH, i-C_3H_7OH; (5) $CuCl_2$, H_2O, MeOH; (6) Me_3SiCl, imidazole, DMF. The diethyl azodicarboxylate series directly parallels the triazolinedione series outlined above. In the Experimental Section, the diethyl azodicarboxylate analogues of **14**, **16**, and **17** are referred to as **14a**, **16a**, and **17a**.



The key step in this approach involves the generation of an appropriately substituted triplet 1,3-cyclopentadiyl biradical from the corresponding azoalkane and the trapping of this triplet biradical with molecular oxygen. This technique has been shown to be quite effective when an argon ion laser is used to initiate photosensitized decomposition of 2,3-diazabicyclo[n.2.1]alkanes and has been used in the preparation of a number of unusual bicyclic endoperoxides.[4a,8]

The requisite azoalkane biradical precursors **11** and **12** may be prepared in large quantities as outlined in Scheme III. This sequence was originally conducted by starting with the diethyl azodicarboxylate adduct of cyclopentadiene. The steps in this original sequence have been optimized and all proceed in good to excellent yields as described in the Experimental Section. However, all of the intermediates in this azodicarboxylate series are viscous oils and can only be purified by chromatography. In contrast the N-phenyltriazolinedione derivatives shown in Scheme III are all crystalline substances which are more easily purified. Thus, once the presently lower yields of this triazolinedione sequence have been optimized, this recently developed approach may represent a significant improvement over the diethyl azodicarboxylate pathway.

The key step in this synthesis is the hydroformylation

(3) Salomon, R. G.; Salomon, M. F.; Coughlin, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 660.

(4) (a) Wilson, R. M.; Rekers, J. W. *J. Am. Chem. Soc.* **1981**, *103*, 206. (b) Bloodworth, A. J.; Eggelte, H. J. *Tetrahedron Lett.* **1984**, *25*, 1525.

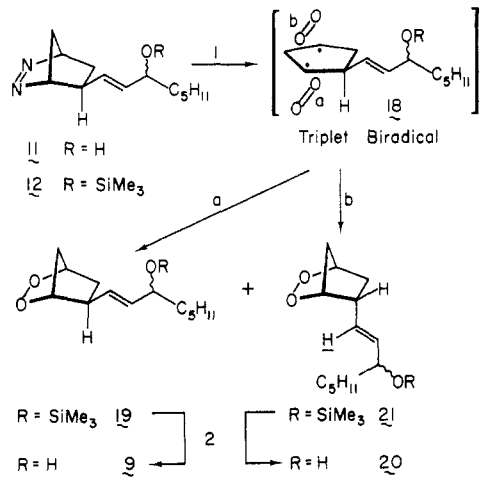
(5) Suzuki, M.; Noyori, R.; Hamanaka, N. *J. Am. Chem. Soc.* **1982**, *104*, 2024.

(6) Even when the exo allylic alcohol side chain is present some conditions still lead to preferential cleavage of the one-carbon bridge: Salomon, R. G.; Miller, D. B.; Zagorski, M. G.; Coughlin, D. J. *J. Am. Chem. Soc.* **1984**, *106*, 6049.

(7) Porter, N. A.; Mebane, R. C. *Tetrahedron Lett.* **1982**, *23*, 2289.

(8) (a) Wilson, R. M.; Geiser, F. *J. Am. Chem. Soc.* **1978**, *100*, 2225. (b) Adam, W.; Hannemann, K.; Wilson, R. M. *J. Am. Chem. Soc.* **1984**, *106*, 7646. (c) Wilson, R. M. *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker; New York, 1985, Vol. 7, p 340. (d) Adam, W.; Hannemann, K.; Hössel, P. *Tetrahedron Lett.* **1984**, *25*, 181. (e) Adam, W.; Hannemann, K.; Wilson, R. M. *Angew Chem.* **1985**, *97*, 1072; *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1071. (f) Adam, W.; Hannemann, K.; Wilson, R. M. *J. Am. Chem. Soc.* **1986**, *108*, 929.

Scheme IV[a]



[a] (1) *hν* (351.1, 351.4, and 363.8 nm argon ion laser lines), O_2 (10 atm), Ph_2CO for **11** (R = H) and $(C_6F_5)_2CO$ for **12** (R = $SiMe_3$), $CFCl_3$, −16 °C; (2) $(n\text{-Bu})_4NF$, CH_2Cl_2:MeOH (1:1), 0 °C, 20 min.

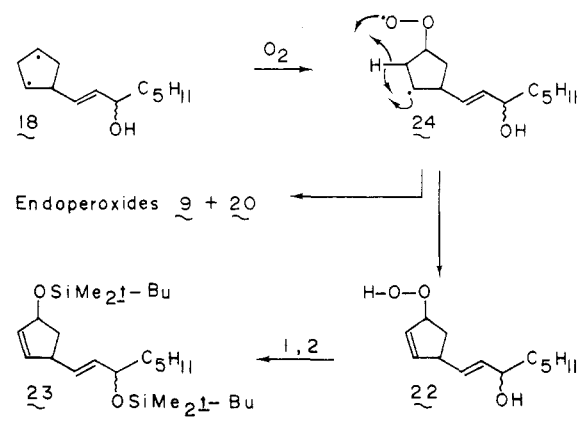
of **13** to form the exo aldehyde **14**. This aldehyde is rather labile. Upon treatment with base above about −20 °C, prolonged exposure to silica gel, or heating above about 140 °C, **14** undergoes epimerization to the endo aldehyde and ring cleavage to the α,β-unsaturated aldehyde **15**. In spite of this lability, **14** smoothly undergoes Horner–Emmons chain extension at −78 °C to the enone **16** provided that the reaction mixture is quenched at or below about −30 °C.

Reduction of the enone **16** provides a mixture of allylic alcohol epimers **17**. These epimers may be partially resolved by HPLC but are not separable by preparative column chromatography. This behavior contrasts with that of the double-chain allylic alcohols of the parent prostaglandin series where the epimeric allylic alcohols are readily resolved by column chromatography. Apparently, the buttressing effect of the second side chain in the parent series markedly affects the chromatographic behavior of these allylic alcohol epimers. Since the epimeric alcohols **17** as well as a number of their silyl derivatives behave chromatographically and spectroscopically (see Experimental Section) as an essentially pure substance, they were carried forward in the synthesis as a mixture of epimers. It should be mentioned at this point that at no point in the subsequent transformations described here has an opportunity presented itself for the column chromatographic resolution of these epimers. The conversions of the alcohol **17** to the azoalkane **11** and its TMS derivative **12** are unexceptional (Scheme III).

These azoalkanes can be converted to the desired endoperoxides and hydroperoxide isomers through the photosensitized extrusion of nitrogen in the presence of oxygen (Schemes IV and V, respectively). Freon-11 solutions of the azoalkanes and an appropriate photosensitizer (vide infra) were equilibrated at −16 °C for about one hour in Griffin–Worden tubes pressurized to about 10 atm with oxygen.[9] The sensitizer was then selectively excited by using the 351.1, 351.4, and 363.8 nm lines (ca. 1.8 W) of an argon ion laser,[8f] and the resulting peroxides were isolated by silica gel chromatography at −16 °C. The sensitizers used in these reactions (Scheme IV) were selected on the basis of the ease of their chromatographic separation from the endoperoxide products. They performed

(9) Wilson, R. M.; Wunderly, S. W.; Walsh, T. F.; Musser, A. K.; Outcalt, R.; Geiser, F.; Gee, S. K.; Brabender, W.; Yerino, L., Jr.; Conrad, T. T.; Tharp, G. A. *J. Am. Chem. Soc.* **1982**, *104*, 4429.

Scheme V[a]



[a] (1) Excess Me_2S, 24 h, room temperature; (2) *t*-$BuMe_2SiCl$, imidazole, DMF.

their photosensitization roles with comparable efficiencies.

Since the triplet cyclopentadiyl species **18** generated in this fashion are planar species on the time average,[8f] and since the side chain apparently does not provide much steric shielding of the *syn*-cyclopentadiyl face, two endoperoxide isomers result from the attack of oxygen on the *syn*- and *anti*-cyclopentadiyl faces (Scheme IV). The endoperoxides with the side chain in the natural exo configuration, **9** and **19**, arise from oxygen attack on the anti-biradical face, process a in Scheme IV, and the endoperoxides with the side chain in the unnatural endo configuration, **20** and **21**, arise from oxygen attack on the syn-biradical face, process b in Scheme IV. The unmasked alcohol **11** affords a ratio of the exo to endo side-chain isomers, **9**:**20**, of ca. 65:35 as determined by NMR analysis of the peroxide chromatography fraction.

In both the free and silylated alcohol series the yields of endoperoxides are about 26–27%. As would be expected when azoalkanes **11** and **12** are irradiated in the absence of oxygen, a mixture of substituted bicyclo[2.1.0]pentanes results in quantitative yield. Since these hydrocarbons are stable to the aerobic photolysis conditions and are only detected in trace quantities when the reactions are conducted under high pressure oxygen atmospheres, it would appear that the oxygen trapping of these 1,3-cyclopentadiyl triplets can occur with nearly quantitative efficiencies. Furthermore, quantitative oxygen trapping studies with the parent 1,3-cyclopentadiyl triplet indicate that under the conditions employed here there is virtually no oxygen-catalyzed intersystem crossing of the 1,3-cyclopentadiyl triplet and that oxygen trapping occurs with efficiencies in the range of 98% to 100%.[8f] Therefore, the reduced endoperoxide yields observed in these preparative reactions do not arise from an inefficient trapping of the 1,3-cyclopentadiyl triplets but rather seem to be due to the photolability of the endoperoxides and to the formation of hydroperoxides from alternative trapping pathways (vide infra). Therefore, the yields of endoperoxides realized by this procedure are critically dependent upon irradiation times (see Experimental Section). Excessive irradiation leads to drastically reduced peroxide yields.

The contrast between the photooxidations of the free alcohol **11** and its silylated derivatives such as **12** is quite striking. The irradiation of the free alcohol **11** is a tedious affair, since substantial polymer formation is encountered and this polymer tends to coat the inside wall of the Griffin–Worden tube at the point of entry of the laser beam. Therefore, in order to optimize endoperoxide yields in these reactions, the Griffin–Worden tube must be ro-

tated in the laser beam at frequent intervals. This troublesome problem does not occur with the silylated derivatives such as **12**. Furthermore, the endo and exo side chain isomers of the endoperoxides with the free alcohol group, **20** and **9**, respectively, have very similar chromatographic behavior on silica gel and are only resolved with great difficulty by extended cold column chromatography. In contrast, the silylated derivatives such as **19** and **21** are easily separated by cold column chromatography on silica gel. Consequently, for purposes of characterization in this work, the silyl groups were removed from the pure silylated endoperoxides **19** and **21** as indicated in Scheme IV to obtain the pure endoperoxides with unmasked allylic alcohol side chains, **9** in 16% and **20** in 25% yield.

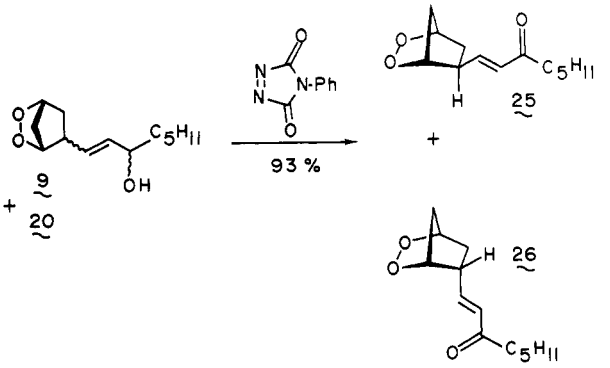
Finally, it should be mentioned that of the endoperoxides reported here the exo side chain allylic alcohol **9** is significantly more labile than the others. Furthermore, an interesting facet of the decomposition of **9** is that it seems to be associated with the formation of a transient indigo blue intermediate. Thus, upon warming concentrated solutions of **9** to room temperature or upon silica gel chromatography at room temperature an indigo blue color develops and persists for a few minutes to several hours depending upon the conditions. While this intriguing phenomenon has not been investigated in detail, it does not seem to be due to an impurity in the endoperoxide, since it occurs with **9** that has been prepared directly from **11** and via the desilylation route through **19**. This unusual phenomenon certainly warrants further quantitative study.

The structure assignments for these endoperoxides are readily derived from 300-MHz NMR data. The preservation of the bicyclic ring systems in the endoperoxides is confirmed by the presence of the characteristic bridgehead proton singlets at δ 4.4–4.5 and 4.7 ppm. These signals are shifted upfield by about 0.3 to 0.5 ppm relative to those in the starting azoalkanes. The stereochemistry of the side-chain double bond is trans in all cases as evidenced by the 15–16-Hz coupling constants between the olefinic protons. The exo chain endoperoxides **9** and **19** display NMR spectra that differ significantly from those of the azoalkanes only in the upfield shifts of the bridgehead proton signals. In contrast the NMR spectra of the endo side chain endoperoxides differ substantially from those of the starting azoalkanes. Most notably the olefinic protons adjacent to the bicyclic system (*H* in **20** and **21** in Scheme IV) are substantially deshielded ($\Delta\delta$ = 0.24 ppm) relative to the analogous protons in the exo side chain isomers. Similar deshielding due to the proximity of the peroxide linkage to endo olefinic side chains of bicyclic[2.2.1]endoperoxides has been observed by O'Connor, Mihelich, and Coleman.[10] Indeed this deshielding effect of the peroxide unit provides an extremely convenient means of distinguishing between endo and exo side chains in prostaglandin endoperoxide systems.

Finally, the aforementioned endoperoxides are accompanied by hydroperoxide isomers. In the photooxidation of the azo alcohol **11**, one of these hydroperoxides (**22** in Scheme V) can be isolated in yields (ca. 10%) that are comparable to those of the endoperoxides. Due to its extreme instability this substance was reduced and characterized as the di-TBDMS derivative **23**. The structure assignment for **23** is based upon a consistent set of ^{1}H-decoupling data and the observation of four olefinic doublets in the undecoupled ^{13}C NMR spectrum (see Experimental Section).

(10) O'Conner, D. E.; Mihelich, E. D.; Coleman, M. C. *J. Am. Chem. Soc.* **1984**, *106*, 3577.

Scheme VI



The formation of hydroperoxides such as **22** can be most easily rationalized as arising from the disproportionation of peroxy biradicals such as **24** in Scheme V. This in turn implies that **24** and related peroxy biradicals may be common intermediates in the formation of both the hydroperoxides and endoperoxides. Indeed, on the basis of spin statistics considerations about 75% of the trapping events would be expected to proceed in a stepwise fashion through intermediates such as **24**.[8f] Unfortunately, the spectroscopic data presently available for **22** and **23** do not permit the assignment of the relative stereochemistry of the cyclopentene ring substituents. Consequently, it is not possible to evaluate the factors which might influence the partitioning of the peroxy biradicals between cyclization to the endoperoxides and disproportionation to the hydroperoxides.

One further transformation of the peroxy alcohols **9** and **20** is particularly interesting from a synthetic standpoint. When a mixture of these endo and exo peroxy alcohols **9** and **20** is treated with *N*-phenyltriazolinedione, the allylic alcohols are oxidized to the enones **25** and **26** (Scheme VI) in an extremely clean and high yield reaction. Furthermore, since these enones are readily separated by low temperature (−16 °C) chromatography on silica gel, this method provides access to endoperoxides with enone side chains in quantities sufficient for further study. The stereochemistries of these two isomeric enones also are readily assigned on the basis of the deshielded β-hydrogen in the enone with the endo side chain, for **25** δ = 6.59 ppm and for **26** δ = 6.98 ppm. Finally, it should be mentioned that there are a few cases in which triazolinediones have been used to oxidize hydrazo to azo compounds[11] and alcohols to ketones.[12] However, considering the ease with which this reagent converts the allylic alcohol moieties of **9** and **20** to the respective enones, it is rather surprising that this method is not utilized more widely in synthesis.

In summary, the trapping of argon laser generated triplet 1,3-cyclopentadiyl biradicals with molecular oxygen has proven to be a viable method for the preparation of endoperoxides closely related to PGH_2. Given the availability of a suitable argon ion laser, this method offers one of the most facile routes to these highly reactive substances. Furthermore, this approach affords not only substituted endoperoxides with the natural PGH_2 side chain stereochemistry but also the little known side chain epimers with the unnatural stereochemistry. The availability of these endoperoxides provided by this method should signifi-

(11) Gisin, M.; Wirz, J. *Helv. Chim. Acta* **1976**, *59*, 2273. Hasler, E.; Gassmann, E.; Wirz, J. *Helv. Chim. Acta* **1985**, *68*, 777.

(12) Cookson, R. C.; Stevens, I. D. R.; Watts, C. T. T. *Chem. Commun.* **1965**, 259. Makay, D.; Marx, U. F.; Waters, W. A. *J. Chem. Soc.* **1964**, 4797. Dao, L. H.; Mackay, D. *Can. J. Chem.* **1979**, *57*, 2727. Yoneda, F.; Suzuki, K.; Nitta, Y. *J. Org. Chem.* **1967**, *32*, 727.

cantly enhance the ease with which the chemistry of these fascinating systems can be studied.

Experimental Section

General Procedures. Melting points were determined on a Mel-Temp capillary melting point apparatus and are uncorrected. Proton NMR and ^{13}C NMR spectra were recorded on a Nicolet NT300 300-MHz spectrometer. Spectra were recorded in $CDCl_3$ and chemical shifts are reported in parts per million (δ units) relative to tetramethylsilane as an internal standard. The abbreviations s, d, t, q, m, cm, dd, and ddd refer to singlet, doublet, triplet, quartet, multiplet, complex multiplet, doublet of doublets, and doublet of doublets of doublets, respectively. Coupling constants are in hertz. Infrared spectra were recorded on a Perkin-Elmer 599 infrared spectrometer in chloroform and were calibrated with polystyrene. Mass spectra were obtained with a Kratos MS801-DS55 spectrometer. A Coherent CR-18 Supergraphite argon ion laser was used as the ultraviolet light source for the biradical trapping reactions.

HPLC analyses were performed with an IBM LC9533 Ternary Gradient HPLC with a silica gel column (standard, 250 mm). Analtyical thin-layer chromatography was conducted on E. Merck silica gel 60 F_{254} precoated plates, and the resolved components were visualized either by UV light at 254 nm, I_2 vapor, or $KMnO_4$ stain. For preparative thick-layer chromatography, 20 × 20 EM 60 F_{254} 2-mm and 0.5-mm precoated silica gel plates were used. Column chromatographic separations utilized either EM silica gel 60, finer than 230 mesh, or for flash chromatography, EM silica gel 60, 230–400 mesh as described by Still.[13] Low temperature chromatography was performed on a jacketted chromatography column maintained at −16 °C by means of a circulating methanol refrigeration bath (Haake Model A182).

Solvents and reagents were purchased from Aldrich Chemical Co. or Fisher Chemical Co. and were used without further purification unless otherwise specified. Tetrahydrofuran was freshly distilled from benzophenone ketyl. Benzene and toluene were dried over Na ribbon. All reactions were conducted under an atmosphere of either nitrogen or argon in flame-dried flasks unless stated otherwise.

Preparation of Diethyl *exo*-5-Formyl-1,2,3-diazabicyclo-[2.2.1]heptane-2,3-dicarboxylate (14a). The Diels–Alder adduct between diethyl azodicarboxylate and cyclopentadiene[14] (15.0 g, 62.5 mmol) was dissolved in 87 mL of dry benzene. To this solution were added triphenylphosphine (0.804 g, 3.06 mmol) and tetracarbonylbis(μ-chloro)dirhodium(I) (0.119 g, 0.306 mmol). This mixture was placed in a stainless steel, 300 mL, autoclave (Autoclave Engineers ABP-300 magnedrive packless autoclave) and the system pressurized to 2000 psi with a 50:50 mixture of H_2 and CO. The autoclave was slowly heated (0.5 h) to 109 °C. At this temperature an exotherm was observed and the temperature increased rapidly to 118 °C over a period of 4 min, accompanied by a drop in pressure ($\Delta p \approx 170$ psi). Upon cooling to room temperature, the pressure was released. The reaction mixture was filtered and the filtrate evaporated to dryness. This viscous oil was chromatographed through 150 g of 230–400-mesh silica gel, eluting with a solvent gradient of dichloromethane to 96:4 dichloromethane–methanol to afford 13.4 g (49.8 mmol, 79.7%) of the desired aldehyde **14a** as a pale yellow viscous oil. Due to the instability of the aldehyde on silica gel (epimerization and/or fragmentation), it was usually used without further purification: IR ($CHCl_3$) 3035, 1729 (b), 1380, 1330 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (55 °C)[15] δ 1.29 (t, J = 7.2 Hz, 3 H), 1.30 (t, J = 7.2 Hz, 3 H), 1.7–2.4 (cm, 4 H), 3.06 (dd, J = 7.2, 7.2 Hz, 1 H), 4.24 (q, J = 7.2 Hz, 2 H), 4.26 (q, J = 7.2 Hz, 2 H), 4.64 (bs, 1 H), 4.87 (bs, 1 H), 9.74 (s, 1 H); MS (M^+) calcd for $C_{12}H_{18}N_2O_5$ 270.1215, found 270.1215.

Preparation of *exo*-8-Formyl-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-dione (14). The bicyclic olefin **13**[16] (10.17 g, 42.20 mmol) was dissolved in 85 mL of dry toluene. To this solution was added triphenylphosphine (0.807 g, 3.05 mmol) and tetracarbonylbis(μ-chloro)dirhodium(I) (0.0807 g, 0.208 mmol). This mixture was placed in an autoclave (see previous procedure for a description) and the system pressurized to 2000 psi with a 50:50 mixture of H_2 and CO. The autoclave was slowly heated over a period of 40 min to 113 °C. At this temperature, an exotherm was observed and the temperature rapidly increased to 124 °C over 4.5 min, with an accompanying drop in pressure ($\Delta p \approx 160$ psi). Upon cooling to room temperature, the pressure was released, and the reaction mixture was concentrated in vacuo, redissolved in 50 mL of dichloromethane, and filtered through Celite. The filtrate was treated with decolorizing carbon. The aldehyde **14** was recrystallized from warm diethyl ether-dichloromethane to afford 7.09 g (26.16 mmol, 62%) as a colorless solid: mp 160–160.8 °C; IR ($CHCl_3$) 3070, 1730, 1510, 1405 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.8–2.3 (cm, 4 H), 3.25 (dd, J = 5.4, 8.6 Hz, 1 H), 4.76 (s, 1 H), 4.98 (s, 1 H), 7.52 (cm, 5 H), 9.86 (s, 1 H); MS (M^+) calcd for $C_{14}H_{13}N_3O_3$ 271.0957, found 271.0951.

Preparation of Diethyl *exo*-5-(3-Oxooct-1-enyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (16a). Sodium hydride (1.18 g, 49.3 mmol) as a 50% oil dispersion was slurried in 120 mL of THF. The solution was cooled to 0 °C and a solution of dimethyl (2-oxoheptyl)phosphonate (6.33 g, 28.5 mmol) in 30 mL of THF was added dropwise over 20 min. The slurry was warmed to room temperature and upon completion of hydrogen evolution cooled to −78 °C. To this cold slurry was added a solution of the dicarbethoxy aldehyde **14a** (7.000 g, 25.9 mmol) in 50 mL of THF with vigorous mechanical stirring. After the addition was complete the mixture was warmed to −33 °C and quenched with 75 mL of saturated aqueous sodium chloride. The aqueous layer was extracted with 3 × 50 mL portions of dichloromethane. The combined organic layers were dried over magnesium sulfate and evaporated to dryness. The resulting oil was chromatographed through a column of 230–400-mesh silica gel (45% ethyl acetate in hexanes) to yield 7.68 g (20.9 mmol, 81%) of the dicarbethoxy enone **16a** as a pale yellow oil: IR ($CHCl_3$) 1745, 1700, 1630 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (55 °C)[15] δ 0.89 (t, J = 7.0 Hz, 3 H), 1.28 (t, J = 7.0 Hz, 3 H), 1.29 (t, J = 7.0 Hz, 3 H), 1.25–1.35 (cm, 4 H), 1.60 (ctt, J = 7.0, 7.0 Hz, 3 H), 1.72 (s, 2 H), 2.17 (dd, J = 9.0, 13.5 Hz, 1 H), 2.50 (t, J = 7.0 Hz, 2 H), 2.86 (dd, J = 6.5, 12.5 Hz, 1 H), 4.21 (q, J = 7.0 Hz, 2 H), 4.22 (q, J = 7.0 Hz, 2 H), 4.45 (s, 1 H), 4.60 (s, 1 H), 6.13 (d, J = 15.5 Hz, 1 H), 6.63 (dd, J = 7.0, 15.5 Hz, 1 H); MS (M^+) calcd for $C_{19}H_{30}N_2O_5$ 366.2154, found 366.2151.

Preparation of *exo*-8-(3-Oxooct-1-enyl)-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-dione (16). Sodium hydride (0.653 g, 28.3 mmol) as a 50% oil dispersion was slurried in 95 mL of THF. The mixture was cooled to 0 °C and a solution of dimethyl (2-oxoheptyl)phosphonate (3.62 g, 16.3 mmol) in 25 mL of dry THF was added dropwise over a period of 10 min. The reaction was warmed to room temperature and upon the completion of hydrogen evolution became a gelatenous mixture which was subsequently cooled to −78 °C. To this mixture was added a solution of the aldehyde **14** (4.00 g, 14.8 mmol) in 39 mL of THF with periodic shaking and mechanical stirring. The reaction was then warmed to −35 °C and quenched with 50 mL of saturated aqueous sodium chloride. The aqueous layer was extracted with 3 × 30 mL portions of dichloromethane, dried (magnesium sulfate), and evaporated to dryness. The resulting pale yellow solid was chromatographed through a column of 230–400-mesh silica gel (60% ethyl acetate in hexanes) to yield 3.36 g (9.15 mmol, 62%) of **16** as a colorless solid: mp 113.2–114 °C; IR ($CHCl_3$) 3050, 1720, 1510, 1407 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 7.2 Hz, 3 H), 1.2–1.4 (cm, 4 H), 1.63 (ctt, J = 6.9, 14.1 Hz, 3 H), 1.94 (s, 2 H), 2.33 (dd, J = 9, 13.5 Hz, 1 H), 2.52 (t, J = 7.2 Hz, 2 H), 3.04 (dd, J = 7.2, 12.5 Hz, 1 H), 4.57 (s, 1 H), 4.79 (s, 1 H), 6.21 (d, J = 15.6 Hz, 1 H), 6.62 (dd, J = 7.2, 15.6 Hz, 1 H), 7.44 (cm, 5 H); MS (M^+) calcd for $C_{21}H_{25}N_3O_3$ 367.1896, found 367.1887.

Preparation of Diethyl *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (17a) as a Mixture of Epimeric Alcohols. The dicarbethoxy enone **16a** (5.00 g, 13.7 mmol) was dissolved in a 0.4 M methanolic solution

(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(14) Gassman, P. G.; Mansfield, K. T. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. 5, p 96.
(15) The 300-MHz ^1H NMR of all synthetic intermediates containing carbethoxy groups were run at 55 °C. The room temperature spectra of these compounds display substantial line broadening due to the dynamic exchange between different conformations of the carbethoxy groups.
(16) Cookson, R. C.; Gupte, S. S.; Stevens, I. D. R.; Watts, C. T. *Org. Synth.* **1971**, *51*, 121.

of $CeCl_3 \cdot 7H_2O$ (109 mL). Sodium borohydride (1.65 g, 43.7 mmol) was added over a period of 2 min to the magnetically stirred mixture. After 75 min, the reaction was quenched with 40 mL of saturated aqueous sodium chloride and the aqueous phase extracted with 3 × 100 mL portions of dichloromethane. The combined organic extracts were dried (magnesium sulfate) and concentrated in vacuo to give a yellow oil which was chromatographed through a column of 230–400-mesh silica gel (70% ethyl acetate in hexanes) to yield 4.67 g (12.7 mmol, 93%) of the mixture of epimeric allylic alcohols: IR ($CHCl_3$) 3500, 1745, 1705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (55 °C)[15] δ 0.89 (t, J = 6.5 Hz, 3 H), 1.27 (t, J = 7.0 Hz, 3 H), 1.28 (t, J = 7.0 Hz, 3 H), 1.25–1.32 (cm, 8 H), 1.49 (m, 2 H), 1.67 (s, 2 H), 2.09 (dd, J = 9.5, 12.0 Hz, 1 H), 2.72 (m, 1 H), 4.05 (dd, J = 5.0, 11.0 Hz, 1 H) 4.21 (q, J = 7.2 Hz, 2 H), 4.21 (q, J = 7.2 Hz, 2 H), 4.35 (s, 1 H), 4.55 (s, 1 H), 5.51–5.53 (cm, 2 H); MS (M^+) calcd for $C_{19}H_{32}N_2O_5$ 368.2311, found 368.2316.

Preparation of *exo*-8-(3-Hydroxyoct-1-enyl)-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-dione (17) as a Mixture of Epimeric Alcohols. The enone 16 (3.00 g, 8.17 mmol) was dissolved in a 0.4 M methanolic solution of $CeCl_3 \cdot 7H_2O$ (65 mL). Sodium borohydride (0.989 g, 26.1 mmol) was added over a period of 3 min. This mixture was stirred at room temperature until TLC analysis (60% ethyl acetate in hexanes) showed no remaining enone. After 65 min, the reaction was quenched with 30 mL of saturated aqueous sodium chloride and the aqueous phase extracted with 3 × 50 mL portions of dichloromethane. The combined organic extracts were dried (magnesium sulfate) and concentrated in vacuo to afford a pale yellow solid which was filtered through a column of 230–400-mesh silica gel (ethyl acetate), yielding 2.00 g (5.42 mmol, 65%) of a mixture of epimeric allylic alcohols (17) as a colorless solid: mp 100.7–102.0 °C; HPLC analysis indicated that this material was a ca. 50:50 mixture of two epimers which under the conditions employed (see General Section) were only very poorly resolved; IR ($CHCl_3$) 3500, 3100, 1720, 1505, 1410 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J = 6.5 Hz, 3 H), 1.25–1.62 (cm, 9 H), 1.92 (s, 2 H), 2.25 (dd, J = 8.7, 13.7 Hz, 1 H), 2.91 (m, 1 H), 4.09 (dd, J = 5.7, 12.2 Hz, 1 H), 4.48 (s, 1 H), 4.69 (s, 1 H), 5.59 (cm, 2 H), 7.47 (m, 5 H); MS (M^+) calcd for $C_{21}H_{26}N_3O_3$ 369.2052, found 369.2052.

Preparation of the *tert*-Butyldimethylsilyl (TBDMS) Derivative of *exo*-8-(3-Hydroxyoct-1-enyl)-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-dione as a Mixture of Silyl Ether Epimers. The alcohol 17 (0.500 g, 1.36 mmol) was dissolved in 1.5 mL of dry DMF. To this solution was added *tert*-butyldimethylsilyl chloride (0.266 g, 1.76 mmol) and imidazole (0.120 g, 1.76 mmol). This mixture was stirred for 18 h at room temperature. The reaction mixture was extracted with hexanes, and the extracts were washed with 3 × 20 mL portions of saturated aqueous sodium chloride, dried (magnesium sulfate), and chromatographed through a column of 230–400-mesh silica gel (20% ethyl acetate in petroleum ether, bp 32.7–57.2 °C) to afford the TBDMS derivatives of 17 (0.706 g, 1.46 mmol, 83%) as a colorless solid: mp 58.0–59.2 °C. HPLC analysis indicated that this material was a ca. 50:50 mixture of two epimers. While this material could be resolved more completely than the unsilylated alcohols, the best resolution that could be obtained under the conditions employed (see General Section) was ca. $^2/_3$ of the peak heights: IR ($CHCl_3$) 3020, 2955, 1720, 1510, 1410 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 6 H), 0.86 (s, 9 H), 1.2–1.9 (cm, 14 H), 2.22 (dd, J = 9.0, 13.4 Hz, 1 H), 2.90 (dd, J = 6.0, 12.3 Hz, 1 H), 4.08 (dd, J = 6.0, 11.7 Hz, 1 H), 4.40 and 4.65 (2s, 1 H) (bridgehead protons of the epimeric silyl ethers), 4.68 (s, 1 H), 5.46 (dd, J = 6.3, 15.6 Hz, 1 H), 5.55 (dd, J = 5.7, 15.6 Hz, 1 H), 7.45 (cm, 5 H); MS (M^+) calcd for $C_{27}H_{41}N_3O_3Si$ 483.2917, found 483.2911.

Preparation of *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-diazabicyclo[2.2.1]hept-2-ene as a Mixture of Epimeric Alcohols 11 from Diethyl *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (17a). To a magnetically stirred solution of KOH (8.54 g, 152 mmol) in 110 mL of degassed 2-propanol was added the dicarbethoxy allylic alcohol 17a (4.00 g, 10.9 mmol) in 50 mL of 2-propanol. This mixture was heated at reflux for 4 h, cooled, and stirred at room temperature for an additional 15 h. The solution was taken to a pH of 6 with 10% HCl and made basic with concentrated NH_4OH. The yellow reaction mixture was vacuum filtered to remove solids. To this clear solution was added in portions a cupric chloride solution (3.65 g, 27.2 mmol, in 15 mL H_2O) with stirring. The solution initially bleached the cupric chloride solution from deep blue to yellow orange. Addition of the cupric chloric solution was stopped when the blue color persisted for 0.5 h. The reaction mixture was diluted with 50 mL of dichloromethane and extracted with 3 × 30 mL portions of saturated aqueous sodium chloride. The organic phase was dried (magnesium sulfate) and concentrated in vacuo to afford a yellow-brown oil which was chromatographed through a column of 230–400-mesh silica gel (80% ethyl acetate in dichloromethane) to yield 11 (2.20 g, 9.91 mmol, 91%) as a yellow oil: IR ($CHCl_3$) 3420, 975 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J = 6.0 Hz, 3 H), 1.2–1.4 (cm, 10 H), 1.50 (cm, J = 6.0 Hz, 2 H), 1.90 (dd, J = 6.5, 13.0 Hz, 1 H), 2.39 (bs, 1 H), 4.06 (dd, J = 5.5, 11.5 Hz, 1 H), 4.93 and 4.94 (2s, 1 H) (bridgehead protons of epimeric alcohols), 5.16 (s, 1 H), 5.49 and 5.50 (2dd's, J = 6.5, 15.0 Hz, 1 H), 5.57 and 5.56 (2 dd's, J = 5.5, 15.0 Hz, 1 H) [The overlapping double doublets in the latter signals are due to the two epimeric alcohols present in the sample.]; MS (M^+ + 1) calcd for $C_{13}H_{23}N_2O$ 223.1810, found 223.1812; CI MS (M^+ + 1), 223.

Preparation of *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-diazabicyclo[2.2.1]hept-2-ene as a Mixture of Epimeric Alcohols 11 from *exo*-8-(3-Hydroxyoct-1-enyl)-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-dione (17). To a magnetically stirred solution of KOH (0.470 g, 8.38 mmol) in 6 mL of degassed 2-propanol was added the allylic alcohol 17 (0.221 g, 0.599 mmol) in 5 mL of 2-propanol at 0 °C. The reaction was subsequently warmed to room temperature and stirred for 3 h. The solution was taken to a pH of 6 with 10% HCl and made basic with concentrated NH_4OH. The reaction mixture was vacuum filtered to remove any solids, and solvent was removed under reduced pressure to yield a yellow oil which was dissolved in 10 mL of methanol. To this solution was added in portions an aqueous solution of 2 N cupric chloride. Addition was stopped when the blue color persisted for 0.5 h. The reaction mixture was diluted with 20 mL of dichloromethane and extracted with 3 × 10 mL portions of saturated aqueous sodium chloride. The organic phase was dried (magnesium sulfate) and concentrated in vacuo to afford a yellow-brown oil which was chromatographed through a column of 230–400-mesh silica gel (80% ethyl acetate in dichloromethane) to yield 11 (0.074 g, 59%).

Preparation of the Trimethylsilyl (Me_3Si) Derivative of *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-diazabicyclo[2.2.1]hept-2-ene as a Mixture of Silyl Ether Epimers 12. To a slurry of the azo alcohol 11 (2.20 g, 9.91 mmol) in 7.5 mL of dry DMF was added chlorotrimethylsilane (1.40 g, 12.9 mmol) and imidazole (0.878 g, 12.9 mmol). The reaction was stirred at room temperature for 18 h, extracted with hexanes, and washed with 3 × 30 mL portions of saturated aqueous sodium chloride. The combined organic extracts were dried (magnesium sulfate) and concentrated in vacuo. The resulting yellow oil was chromatographed through a column of 230–400-mesh silica gel (30% ethyl acetate in hexanes) to yield 12 (2.59 g, 8.20 mmol, 89%) as a pale yellow oil: IR ($CHCl_3$) 3000, 1490, 1460, 1250, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 9 H), 0.80 (t, J = 6 Hz, 3 H), 1.15 (m, 8 H), 1.35 (m, 4 H), 1.80 (m, 1 H), 3.93 (dt, J = 6.3, 6.0 Hz, 1 H), 4.81 and 4.83 (2s, 1 H), 5.05 (s, 1 H), 5.32 (dd, J = 15.6, 6.9 Hz, 1 H), 5.42 (dd, J = 15.6, 5.7 Hz, 1 H) [The signals at 4.81 and 4.83 are due to a single bridgehead proton of the epimeric silyl ethers.]; MS (M^+ − 15) calcd for $C_{15}H_{27}N_2OSi$ 279.1892, found 279.1945.

General Procedure for Laser Photolysis. A Coherent Supergraphite (Model CR-18) argon ion laser fitted with a selected UV tube was used as the irradiation source. The UV lines (ca. 1.8 W) of the laser were dispersed with a quartz prism and front-surface aluminum mirror. The 351.1, 351.4, and 363.8 nm lines were isolated and used in all photoreactions described here.[17]

The azoalkane (ca. 0.200 g per run) and photosensitizer were

(17) While the 1,3-cydopentadiyl trapping with oxygen of the type described here can be realized with an extensively filtered broad spectrum source, irradiation times are increased drastically (ca. 100 times) and peroxide yields suffer accordingly.[8a] Unfiltered broad spectrum sources are completely unsuitable for 1,3-cyclopentadiyl trapping as only traces of peroxides are produced. For a detailed quantitative treatment of this type of reaction, see ref 8f.

dissolved in 10 mL of trichlorofluoromethane (Freon-11) and transferred to the Griffin–Worden tube by means of a cannula. The Griffin–Worden tube was pressurized to about 140 psig with oxygen, cooled to −16 °C in a refrigerated methanol bath, and equilibrated with magnetic stirring or agitation for 0.5–1.0 h before beginning the irradiation. Irradiation was continued until about 50–60% of the azoalkane had been consumed, usually about 40 min at this laser power level. Irradiation for longer periods of time and higher azo conversions leads to drastic reductions in peroxide yields. Apparently the starting azoalkanes tend to protect the peroxide products from sensitized decomposition. The reaction mixture was transferred to a pear-shaped flask and the Freon-11 was evaporated and replaced with the solvent to be used in the chromatography. Care must be exercised never to allow the concentrate to warm to room temperature at this stage and in the subsequent removal of solvent from peroxide chromatography fractions. The appearance of a deep blue color during these operations signals the rapid destruction of the endoperoxide. This irradiation procedure is typically repeated two to four times using a total of 0.400 to 0.800 g of azoalkane and the photolysis products from these reactions combined and separated in a single low temperature chromatography.

Photolysis of *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-diazabicyclo[2.2.1]hept-2-ene (11). Two portions of the azo alcohol **11** (0.215 g, 0.967 mmol and 0.209 g, 0.942 mmol) were each dissolved in 10 mL of trichlorofluoromethane (Freon-11) along with the photosensitizer, benzophenone (0.266 g, 1.464 mmol, and 0.263 g, 1.442 mmol, respectively). The irradiations were conducted as described in the previous section. During irradiation a polymer film forms on the inner wall of the Griffin–Worden tube where the laser beam enters the solution. Consequently, the tube must be repositioned in the laser beam every 5 min for optimum results. Toward the end of this reaction, the solution becomes cloudy and a dark oil precipitates. Upon careful evaporation of the solvent from the photolysis solution, the residual oil (ca. 0.400 g) was purified by chromatography through a column of 50 g of finer than 230-mesh silica gel (15% ethyl acetate in dichloromethane) at −16 °C. The fractions isolated in order of increasing polarity were a mixture of **9** and **20** (0.052 g, 0.232 mmol, 26.5%) which occurred in a ratio of 65:35 based upon integration of the olefinic region of the ^{1}H NMR spectrum and **22** (0.018 g, 0.077 mmol, 8.9%) based on 0.230 g of recovered azo alcohol **11**. All attempts to resolve mixtures of **9** and **20** by preparative chromatography led to only partial separation.

Photolysis of the Trimethylsilyl (Me_3Si) Derivative of *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-diazabicyclo[2.2.1]hept-2-ene (12). The trimethylsilyl azoalkane **12** (0.800 g, 2.72 mmol) and the photosensitizer, decafluorobenzophenone (0.983 g, 2.72 mmol), were dissolved in 30 mL of trichlorofluoromethane (Freon-11). This solution was irradiated in three 10-mL portions as described in the Laser Photolysis Section. In this system no polymer film if formed on the Griffin–Worden tube walls and the solution remains clear throughout the irradiation. Upon careful evaporation of the solvent from the photolysis solution, the residual oil (ca. 0.800 g) was purified by chromatography through a column of 65 g of finer than 230-mesh silica gel (6% ethyl acetate in hexanes) at −16 °C to afford **19** and **21** in yields comparable to those of **9** and **20**. In this reaction, the endo and exo isomers, **21** and **19**, respectively, are easily separated by column chromatography.

Trimethylsilyl (Me_3Si) derivative of *exo*-5-(3-hydroxyoct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane (19): isolated as a colorless viscous oil; IR ($CHCl_3$) 3000, 2490, 1250, 840 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.01 (s, 9 H), 0.88 (t, J = 6.3 Hz, 3 H), 1.20–1.40 (c, 6 H), 1.39–1.51 (m, 3 H), 2.14 (dd, J = 10.5, 10.5 Hz, 1 H), 2.19 (bs, 2 H), 2.78 (cdd, J = 6.6, 12.9 Hz, 1 H), 4.01 (dt, J = 6.0, 6.0 Hz, 1 H), 4.46 and 4.48 (2s, 1 H), 4.72 (s, 1 H), 5.35 (dd, J = 7.2, 15.5 Hz, 1 H), 5.47 (dd, J = 6.0, 15.6 Hz, 1 H); the signals at 4.46 and 4.48 are due to a single bridgehead proton of the epimeric silyl ethers; MS (M^+ − 15) calcd for $C_{15}H_{27}O_3Si$ 283.1729, found 283.1723.

Trimethylsilyl (Me_3Si) derivative of *endo*-5-(3-hydroxyoct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane (21): isolated as a colorless viscous oil; IR ($CHCl_3$) 2990, 1250, 835 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.1 (s, 9 H), 0.90 (t, J = 6.6 Hz, 3 H), 1.20–1.55 (c, 8 H), 1.61 (cd, J = 12.0 Hz, 1 H), 1.92 (dd, J = 11.1, 12.0 Hz, 1 H), 2.20 (d, J = 9.9 Hz, 1 H), 2.32 (ddd, J = 2.4, 4.5, 10.2 Hz, 1 H), 2.57 (cdd, J = 9.6, 9.6 Hz, 1 H), 4.04 (dt, J = 5.7, 7.2 Hz, 1 H), 4.50 and 4.49 (2s, 1 H), 4.66 (s, 1 H), 5.51 and 5.50 (2dd, J = 7.2, 15.6 Hz, 1 H), 5.82 (dd, J = 8.7, 15.6 Hz, 1 H); the signals at 4.50, 4.49 and 5.51, 5.50 are due to a single bridgehead and olefinic proton of the epimeric silyl ethers; MS (M^+) calcd for $C_{16}H_{30}O_3Si$ 298.1965, found 298.1986.

Preparation of *exo*-5-(3-Hydroxyoct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane as a Mixture of Epimeric Alcohols 9. The exo side chain silylated endoperoxide **19** (0.016 g, 0.054 mmol) was dissolved in 1.5 mL of a 50:50 mixture of dichloromethane and methanol. This solution was cooled to 0 °C and tetra-*n*-butylammonium fluoride (0.015 g, 0.075 mmol) was added slowly with stirring. After 20 min, 1 mL of carbon tetrachloride was added to the reaction. This mixture was chromatographed directly through a column of 230–400-mesh silica gel (20% ethyl acetate–hexanes) at −16 °C to yield **9** (0.002 g, 0.0088 mmol, 16%) as a pale yellow oil: IR ($CHCl_3$) 3360 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J = 6.9 Hz, 3 H), 1.20–1.60 (cm, 10 H), 2.13 (dd, J = 10.5, 10.5 Hz, 1 H), 2.19 (s, 2 H), 2.81 (cm, 1 H), 4.06 (dt, J = 6.0, 6.0 Hz, 1 H), 4.39 and 4.41 (2s, 1 H), 4.73 (s, 1 H), 5.46 (dd, J = 6.3, 15.3 Hz, 1 H), 5.54 (dd, J = 5.7, 15.3 Hz, 1 H); the signals at 4.39 and 4.41 are due to a single bridgehead proton of the epimeric alcohols; MS (M^+ − 18) calcd for $C_{13}H_{20}O_2$ 208.1463, found, 208.1456.

Preparation of *endo*-5-(3-Hydroxyoct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane as a Mixture of Epimeric Alcohols 20. The endo side chain silylated endoperoxide **21** (0.011 g, 0.035 mmol) was dissolved in 1.5 mL of a 50:50 mixture of dichloromethane and methanol. This solution was cooled to 0 °C and tetra-*n*-butylammonium fluoride (0.021 g, 0.045 mmol) was added slowly with stirring. After 20 min, 1 mL of carbon tetrachloride was added to the reaction. This mixture was chromatographed directly through a column of 230–400-mesh silica gel (35% ethyl acetate in hexanes) at −16 °C to yield **20** (0.002 g, 0.0088 mmol, 25%) as a pale yellow oil: IR ($CHCl_3$) 3440 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 6.6 Hz, 3 H), 1.20–1.55 (cm, 9 H), 1.63 (ddd, J = 2.4, 4.5, 13.8 Hz, 1 H), 1.92 (ddd, J = 2.1, 12.3, 12.3 Hz, 1 H), 2.23 (d, J = 9.9 Hz, 1 H), 2.32 (ddd, J = 2.1, 4.7, 10.5 Hz, 1 H), 2.56 (m, 1 H), 4.05 (dt, J = 6.0, 6.0 Hz, 1 H), 4.46 and 4.49 (2s, 1 H), 4.65 (s, 1 H), 5.50 (dd, J = 6.8, 15.8 Hz, 1 H), 5.82 (dd, J = 8.6, 15.5 Hz, 1 H); the signals at 4.46 and 4.49 are due to a single bridgehead proton of the epimeric alcohols; MS (M^+) calcd for $C_{13}H_{22}O_3$ 226.1568, found 226.1568.

Preparation of the Bis(*tert*-butyldimethylsilyl) Derivative of 4-(3-Hydroxyoct-1-enyl)cyclopent-2-en-1-ol as a Mixture of Silyl Ether Epimers 23. The hydroperoxide **22** (0.029 g, 0.129 mmol) was mixed with 5 mL of methanol and a large excess of dimethyl sulfide and stirred for 12 h at room temperature. The solvent was then removed and the oil combined with *tert*-butyldimethylsilyl chloride (0.079 g, 0.523 mmol), imidazole (0.040 g, 0.592 mmol), and 1 mL of dry DMF. The reaction was stirred overnight, diluted with hexane, washed with saturated aqueous sodium chloride, and dried (magnesium sulfate) and the solution evaporated to dryness. The resulting oil was purified by preparative thick-layer chromatography (3% ethyl acetate in hexanes) to yield **23** (0.020 g, 0.044 mmol, 34.5%) as a colorless oil: IR ($CHCl_3$) 2960, 3940, 1370, 1150, 840 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80–1.65 (cm, 42 H), 2.47 (ddd, J = 7.7, 7.2, 12.3 Hz, 1 H), 3.11 (dddd, J = 7.8, 7.8, 7.4, 5.7 Hz, 1 H), 4.00 (dt, J = 5.7, 5.4 Hz, 1 H), 4.84 (dd, J = 4.8, 7.5 Hz, 1 H), 5.43 (dd, J = 6.0, 15.3 Hz, 1 H), 5.51 (dd, J = 7.4, 15.6 Hz, 1 H), 5.72 (cm, 2 H); assignments of signals based upon a self-consistent set of double resonance experiments. ^{13}C NMR (75.5 MHz, $CDCl_3$) (proton decoupled) δ 73.61, 77.60, 133.11, (133.28, 133.35), (134.61, 134.61, 134.66), (135.80, 135.86), signals in parentheses are doubled due to epimeric silyl ethers; ^{13}C NMR (75.5 MHz, $CDCl_3$) (proton coupled) δ 73.61 (d, J = 132.4 Hz), 77.58 (d, J = 132.4 Hz), 133.11 (d, J = 154.5 Hz), 133.28 and 133.35 (2d, J = 153.6 Hz), 134.61 and 134.66 (2d, J = 163.9 Hz), 135.80 and 135.86 (2d, J = 166.3 Hz). MS m/e 381 (M^+ − t-Bu).

Preparation of *exo*-5-(3-Oxooct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane (25) and *endo*-5-(3-Oxooct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane (26). A mixture of the exo and endo peroxy alcohols **9** and **20** (0.50 g, 0.210 mmol) was dissolved in 1.5 mL of a 1:1 mixture of dichloromethane and acetonitrile. To

this solution was added 4-phenyl-1,2,4-triazoline-3,5-dione (0.110 g, 0.630 mmol) and the mixture was stirred for 3 h at room temperature. The reaction was chromatographed directly through a column of 230–400-mesh silica gel (30% ethyl acetate in hexanes) at −16 °C to yield **25** and **26** (0.020 g, 0.026 g, respectively, combined yield of 93%) as yellow oils.

***exo*-5-(3-Oxooct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane (25)**: IR ($CHCl_3$) 3010, 1760, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J = 6.6 Hz, 3 H), 1.20–1.40 (m, 4 H), 1.55–1.70 (m, 4 H), 2.21 (d, J = 11.1 Hz, 1 H), 2.28 (cd, J = 9.6 Hz, 1 H), 2.51 (t, J =7.4 Hz, 2 H), 2.96 (m, 1 H), 4.59 (s, 1 H), 4.79 (s, 1 H), 6.13 (dd, J = 1.5, 15.6 Hz, 1 H), 6.59 (dd, J = 7.8, 15.9 Hz, 1 H); MS (M^+) calcd for $C_{13}H_{20}O_3$ 224.1412, found 224.1457.

***endo*-5-(3-Oxooct-1-enyl)-2,3-dioxabicyclo[2.2.1]heptane (26)**: IR ($CHCl_3$) 3010, 2920, 1740, 1260 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.80 (t, J = 6.7, 3 H), 1.20–1.40 (m, 5 H), 1.50–1.70 (m, 2 H), 2.04 (cdd, J = 11.4, 11.4 Hz, 1 H), 2.31 (d, J = 10.5 Hz, 1 H), 2.42 (ddd, J = 10.2, 4.5, 2.1 Hz, 1 H), 2.60 (t, J = 7.5 Hz, 2 H), 2.74 (m, 1 H), 4.64 (s, 1 H), 4.77 (s, 1 H), 6.11 (d, J = 15.6 Hz, 1 H), 6.98 (dd, J = 15.9, 9.0 Hz, 1 H); MS (M^+) calcd for $C_{13}H_{20}O_3$ 224.1412, found 224.1433.

Acknowledgment. We thank the National Science Foundation for financial support (CHE-8004235 and CHE-8312691) and for financial assistance in the purchase of a 300-MHz NMR (CHE-8102974) and a high resolution mass spectrometer (PCM-8219912).

Catalysis by Undissociated H_3PO_4 in Aqueous $H_2PO_4^-/HPO_4^{2-}$ Buffer Solutions: Dependence on the Magnitude of the Brønsted Exponent

Y. Chiang, A. J. Kresge,* S. Van Do, and D. P. Weeks†

Department of Chemistry, University of Toronto, Toronto, Ontario M5S 1A1, Canada

Received June 16, 1986

An expression is derived which relates catalysis by undissociated H_3PO_4 in aqueous $H_2PO_4^-/HPO_4^{2-}$ buffer solutions of pH ~7 to buffer ratio and the Brønsted exponent α for the system. This expression predicts that H_3PO_4 catalysis will be significant when α is near unity but will have reached negligible proportions by the time α has dropped to 0.6–0.7. These predictions are borne out by experimental data for the hydrolysis of several 2-alkoxy-2-phenyl-1,3-dioxolanes.

Aqueous biphosphate buffer solutions of pH ~7 are frequently used in studies of acid–base catalysis and chemical and biological reaction mechanisms. The principal catalytically active acidic species present in such buffers, in addition to the hydronium ion, is $H_2PO_4^-$. These solutions, however, also contain very small amounts of undissociated phosphoric acid, H_3PO_4, which, because it is a much stronger acid, may compete effectively with $H_2PO_4^-$ as a general acid catalyst. Catalysis by undissociated phosphoric acid in biphosphate buffers has in fact already been detected in at least one typical acid-catalyzed reaction.[1] We present here a general analysis of this phenomenon, which allows prediction of the conditions under which it will be important, plus the results of an empirical test of that prediction.

Consider a general acid catalyzed reaction taking place in biphosphate buffers. The rate law for this process, eq 1, consists of terms for catalysis by each of the four acidic species H_2O (k_0), H_3O^+ (k_{H^+}), H_3PO_4 ($k_{H_3PO_4}$), and $H_2PO_4^-$ ($k_{H_3PO_4^-}$). The concentration of H_3PO_4 may be related to those of $H_2PO_4^-$ and H_3O^+ through the equilibrium expression for the first ionization of phosphoric acid, eq 2, and combination of eq 1 and 2 leads to eq 3. This expression shows that observed rate constants will be linear functions of the concentration of $H_2PO_4^-$, but the gradient of k_{obsd} upon $[H_2PO_4^-]$ will be equal to $k_{H_2PO_4^-}$ only when catalysis by undissociated H_3PO_4 makes an insignificant contribution, i.e., only when the second term of eq 4 is negligible.

$$k_{obsd} = k_0 + k_{H^+}[H^+] + k_{H_3PO_4}[H_3PO_4] + k_{H_2PO_4^-}[H_2PO_4^-] \quad (1)$$

$$K_1 = [H_2PO_4^-][H^+]/[H_3PO_4] \quad (2)$$

$$k_{obsd} = k_0 + k_{H^+}[H^+] + (k_{H_2PO_4^-} + k_{H_3PO_4}[H^+]/K_1)[H_2PO_4^-] \quad (3)$$

$$(\Delta k_{obsd}/\Delta[H_2PO_4^-])_{[H^+]} = k_{H_2PO_4^-} + k_{H_3PO_4}[H^+]/K_1 \quad (4)$$

Insight into the circumstances under which this might be so may be gained by expressing $k_{H_3PO_4}$ in terms of $k_{H_2PO_4^-}$ and the first (K_1) and second (K_2) dissociation constants of H_3PO_4 through use of the Brøsted relation, as in eq 5.

$$k_{H_3PO_4} = k_{H_2PO_4^-}(K_1/K_2)^{\alpha} \quad (5)$$

Substitution of eq 5 into eq 4 then gives eq 6. It is convenient also to express $[H^+]$ in terms of the buffer ratio,

$$(\Delta k_{obsd}/\Delta[H_2PO_4^-])_{[H^+]} = k_{H_2PO_4^-}(1 + [H^+]K_1^{\alpha-1}/K_2^{\alpha}) \quad (6)$$

Table I. Evaluation of the Term of Equation 8 Representing Catalysis by H_3PO_4 for Aqueous $H_2PO_4^-/HPO_4^{2-}$ Buffer Solutions with Buffer Ratio = 1.00

α	$(K_1/K_2)^{\alpha-1}$ [a]	α	$(K_1/K_2)^{\alpha-1}$ [a]
1.0	1.00	0.7	0.031
0.9	0.31	0.6	0.0095
0.8	0.098	0.5	0.0030

[a] K_1 = 7.14 × 10^{-3} M (ref 2) and K_2 = 6.31 × 10^{-8} M (ref 3).

† Present address: Department of Chemistry, Northwestern University, Evanston, IL 60201.

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