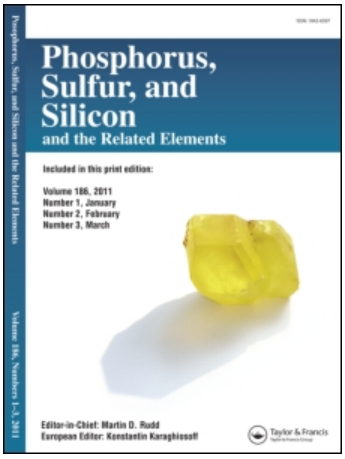

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis and Anomalous Reactivity of 5-Bromo-3,5- Di-t-Butyl-2-Phenyl-1,2-Oxaphosphol-3-Ene 2-Oxide and its 4-Bromo Analog

Roger S. Macomber[a]; Daniel E. Rardon[a]; Douglas M. Ho[a]
[a] Department of Chemistry, University of Cincinnati Cincinnati, Ohio, USA

To cite this Article Macomber, Roger S. , Rardon, Daniel E. and Ho, Douglas M.(1993) 'Synthesis and Anomalous Reactivity of 5-Bromo-3,5- Di-t-Butyl-2-Phenyl-1,2-Oxaphosphol-3-Ene 2-Oxide and its 4-Bromo Analog', Phosphorus, Sulfur, and Silicon and the Related Elements, 75: 1, 95 — 98
To link to this Article: DOI: 10.1080/10426509308037373
URL: http://dx.doi.org/10.1080/10426509308037373

Phosphorus, Sulfur, and Silicon, 1993, Vol. 75, pp. 95–98
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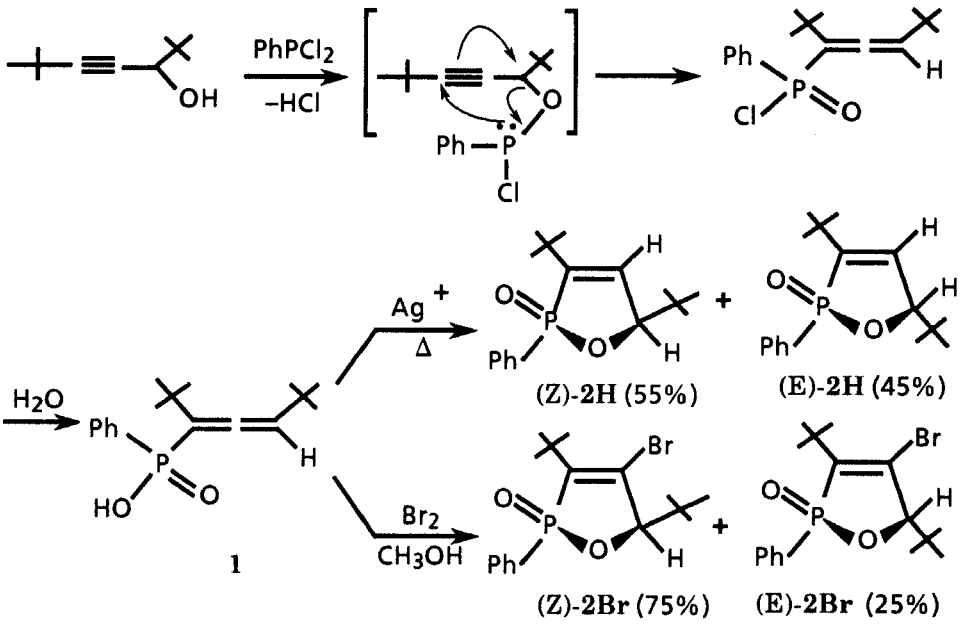
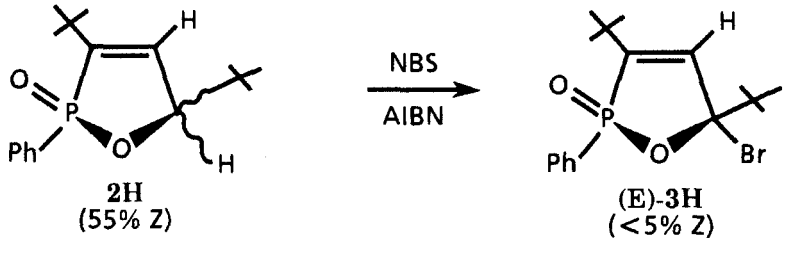
SYNTHESIS AND ANOMALOUS REACTIVITY OF 5-BROMO-3,5-DI-t-BUTYL-2-PHENYL-1,2-OXAPHOSPHOL-3-ENE 2-OXIDE AND ITS 4-BROMO ANALOG

Roger S. Macomber*, Daniel E. Rardon, and Douglas M. Ho
Department of Chemistry, University of Cincinnati
Cincinnati, Ohio USA 45221-0172

Reaction of 2,2,6,6-tetramethyl-4-heptyn-3-ol with dichlorophenylphosphine leads to 2,2,6,6-tetramethyl-3,4-heptadien-3-yl phenyl phosphinic acid (1), which undergoes Ag^+-catalyzed cyclization to 3,5-di-t-butyl-2-phenyl-1,2-oxaphosphol-3-ene 2-oxide (**2H**, 75-55% Z, 25-45% E). Electrophilic bromination of 1 affords **2Br**, the 4-bromo derivative of **2H**, as a 75% Z, 25% E diastereomer mixture from which pure (Z)-**2Br** can be isolated.



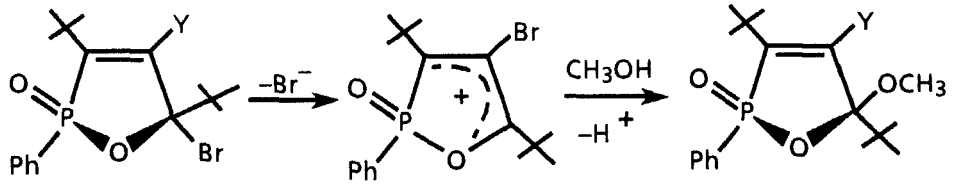
Free radical allylic bromination of (Z/E)-**2H** and (Z)-**2Br** leads to the corresponding 5-bromo derivatives **3H** and **3Br**, each as a single diastereomer. X-ray analysis proved that **3Br** has the E configuration, which is therefore also assigned to **3H**. All other diastereomeric configurations were assigned on the basis of ^{1}H NMR.



2H (55% Z) → **(E)-3H** (<5% Z)

(Z)-2Br → **(E-3Br)** (<1% Z)

Allylic bromide (E)-**3H** is at least 1700 times more reactive than (E)-**3Br** toward methanolysis, though both yield the corresponding 5-methoxy derivatives (**4H** and **4Br**) with predominant inversion of configuration. This is attributed to hydrogen bonding between the phosphoryl oxygen and the attacking methanol molecule.

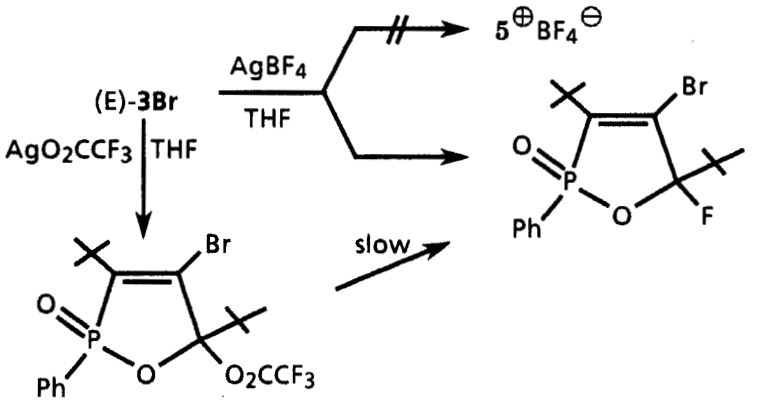


(E)-**3** → **5** → (Z)-**4**

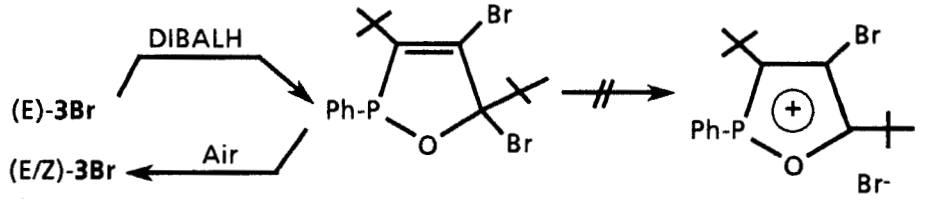
The retardation of (E)-**3Br** relative to (E)-**3H** is ascribed to steric interference between the C_4 bromine and the C_5 t-butyl group in the

(potentially anti-aromatic) methanolysis intermediate (**5**), an effect which is supported by a low-temperature ^{1}H NMR study of E-**3Br**.

Reaction of (E)-**3Br** with $AgBF_4$ or AgOTFA in THF gives the 5-fluoro and 5-trifluoroacetoxy derivatives, respectively, further indication of the instability of **5**.



^{31}P NMR indicates that the phosphoryl oxygen in (E)-**3Br** can be reductively eliminated by DIBALH, but the resulting product is quickly re-oxidized to (E/Z)-**3Br** by air, rather than ionize to form potentially heteroaromatic ion **6**. Reaction of (E)-**3Br** with $NaBH_4$ results in reductive



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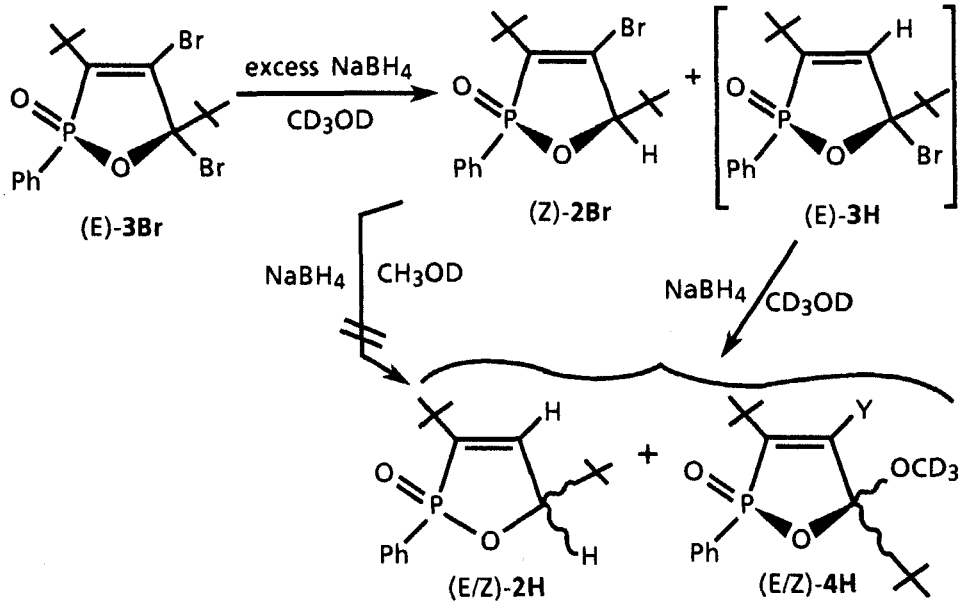
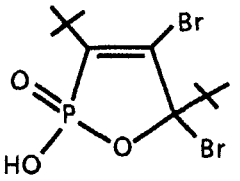
cleavage of the C_4-bromine as well as the C_5 bromine, leading to the formation of (E/Z)-**2H**, (Z)-**2Br**, and (E/Z)-**4H**. (Z)-**2Br** is inert under these conditions.

Extended Huckel calculations are in agreement with the stereochemical preferences observed in this work, as well as the solvolysis-rate-retarding



effect of the phosphoryl oxygen. In view of the dramatic solvolysis rate reduction caused by the 4-bromo group in (E)-**3Br**, the previously noted (Rardon, D.; Macomber, R.S. *J. Org. Chem.* **1990**, *55*, 1493) high solvolytic reactivity of **7**, the 2-hydroxy analog of **3Br**, is ascribed to a mechanism involving reversible opening of the 5-membered ring.



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