diaminobutyric acid) lactam (VII): 38%; mp 145–149°; $[\alpha]^{20}D$ −25.3° (*c* 0.94, methanol). *Anal.* Calcd for $C_{31}H_{46}N_6O_7$ (614.7): C, 60.6; H, 7.54; N, 13.6. Found: C, 60.4; H, 7.82; N, 13.6.

The benzyloxycarbonyl group was removed by catalytic hydrogenolysis[16] and condensed with the symmetrical anhydride of 2-nitro-3-benzyloxy-4-methylbenzoic acid[17] giving, after purification (as described for VII), N^{α}-(2-nitro-3-benzyloxy-4-methylbenzoyl)-L-*threo*-α,β-diaminobutyryl-D-valyl-L-prolylsarcosyl-L-*N*-methylvalyl(N^{β}-diaminobutyric acid) lactam (VIII) in crystalline form: 74%; mp 164–168°; $[\alpha]^{20}D$ −35.3° (*c* 1, methanol). *Anal.* Calcd for $C_{38}H_{51}N_7O_9$ (749.9): C, 60.9; H, 6.86; N, 13.1. Found: C, 60.7; H, 7.18; N, 12.91.

Catalytic hydrogenation of VIII followed by oxidation in the presence of potassium ferricyanide[18] in a 1:1 mixture of methanol and 0.066 *M* phosphate buffer, pH 7.1, gave actinomycin D lactam which was purified by column chromatography on Sephadex LH-20 in ethanol. Crystallization was achieved from ethyl acetate–methanol–hexane giving actinomycin D lactam (XI) (Chart I) as orange red needles: 18%; mp 260–267°; $[\alpha]^{20}D$ −206.5 ± 3° (*c* 0.23, methanol). *Anal.* Calcd for $C_{62}H_{87}N_{13}O_{15}\cdot H_2O$ (1272.6): C, 58.5; H, 7.14; N, 15.4. Found: C, 58.7; H, 6.98; N, 15.1.

Microbiological assays using *Lactobacillus arabinosus* (ATCC 8014) and *L. casei* in pantothenate- and thiamine-dependent systems, respectively,[19] showed IX to possess high antibacterial activity [ID_{50} 0.5 μg/ml and 0.25–0.5 μg/ml, respectively].[20] Preliminary toxicity studies, in AKD_2F_1 male mice, indicate an LD_{50} of approximately 1.5 mg/kg. Suppression of ROS mouse tumor growth[21] was observed at daily doses of 0.6–1.2 mg/kg.

Acknowledgments. We wish to thank Dr. G. F. Foley for microbiological assay, Miss B. L. Brown for toxicity and antitumor studies, and Dr. S. Sengupta for a generous supply of 2-nitro-3-benzyloxy-*p*-toluic acid.

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Phenylphosphinidene Oxide. Thermal Decomposition of 2,3-Benzo-1,4,5,6,7-pentaphenyl-7-phosphabicyclo-[2.2.1]hept-5-ene Oxide

Sir:

The generation of phosphinidene and phosphinidene oxide, analogs of carbene, is of interest because of their possible intermediacy and synthetic value in the formation of phosphorus heterocycles. In particular, the addition of phosphinidene to acetylene could afford phosphacyclopropene, a heterocycle π isoelectronic with cyclobutadiene. Although much attention has been given to the generation and intermediacy of phosphinidenes,[1–5] there is little information on phosphinidene oxides. A possible route to these species is the thermal decomposition of bicyclic compounds containing a phosphorus bridge. One such compound with a trivalent phosphorus atom, 9-phenyl-9-phosphabicyclo[4.2.1]nonatriene, has been prepared,[4] but no phosphinidene was detected on its thermolysis. Although the Diels–Alder adduct of pentaphenylphosphacyclopentadiene and maleic anhydride has been reported,[6] other phosphine-bridged compounds in the bicyclo [2.2.1] series could not be prepared.[7]

Bicyclic compounds with a bridged phosphine oxide group are more stable, however, and can be isolated.[8,9] Thus, 2,3-benzo-1,4,5,6,7-pentaphenyl-7-phosphabicyclo[2.2.1]hept-5-ene oxide (**2**) was prepared in 92% yield by the addition of benzyne,[10] generated *in situ* at 40°, to pentaphenylphosphacyclopentadiene oxide.[11] All attempts to reduce **2** to **1** afforded only tetraphenylnaphthalene (**3**). Decomposition of **2** at 155° also gave a quantitative yield of tetraphenylnaphthalene and a polymer which analyzed for $(C_6H_5PO)_n$, poly(phenylphosphinidene oxide) (**4**), mol wt 1770. The mass spectrum of **2** (70 eV) showed *m/e* 432 (tetraphenylnaphthalene) and *m/e* 124 (C_6H_5PO), indicating that the bridge portion of **2** cleaves completely and exists independently for a finite period before polymerization occurs.

The thermal decomposition of **2** in a sealed tube in the presence of diethyl disulfide afforded *S,S*-diethyl phenyldithiophosphonate (**5**) which was identified by comparison with an authentic sample obtained from the oxidation of *S,S*-diethyl phenyldithiophosphonite:[12] nmr δ 7.6 (5 H, aromatic), 2.92 (s, 4 H, J = 7 Hz), and 1.35 (t, 6 H, J = 7 Hz). When **2** was thermally decomposed in the presence of methanol, methyl phenylphosphinate (**6**) was obtained; nmr δ 7.1 (5 H, aromatic), 3.4 (d, 3 H, J_{H-P} = 11 Hz), and 7.0 (d, 1 H, J_{H-P} = 520 Hz). Thermal decomposition of **2** in a sealed tube in the presence of ketene diethylacetal (**7**), an electron-

$$\underset{\mathbf{7}}{CH_2{=}C(OCH_2CH_3)_2} + \underset{\mathbf{9}}{(C_6H_5P)_n} \xrightarrow[2.\ O_2]{1.\ \Delta} \underset{\mathbf{8}}{C_6H_5\overset{\overset{O}{\uparrow}}{P}(OCH_2CH_3)_2}$$

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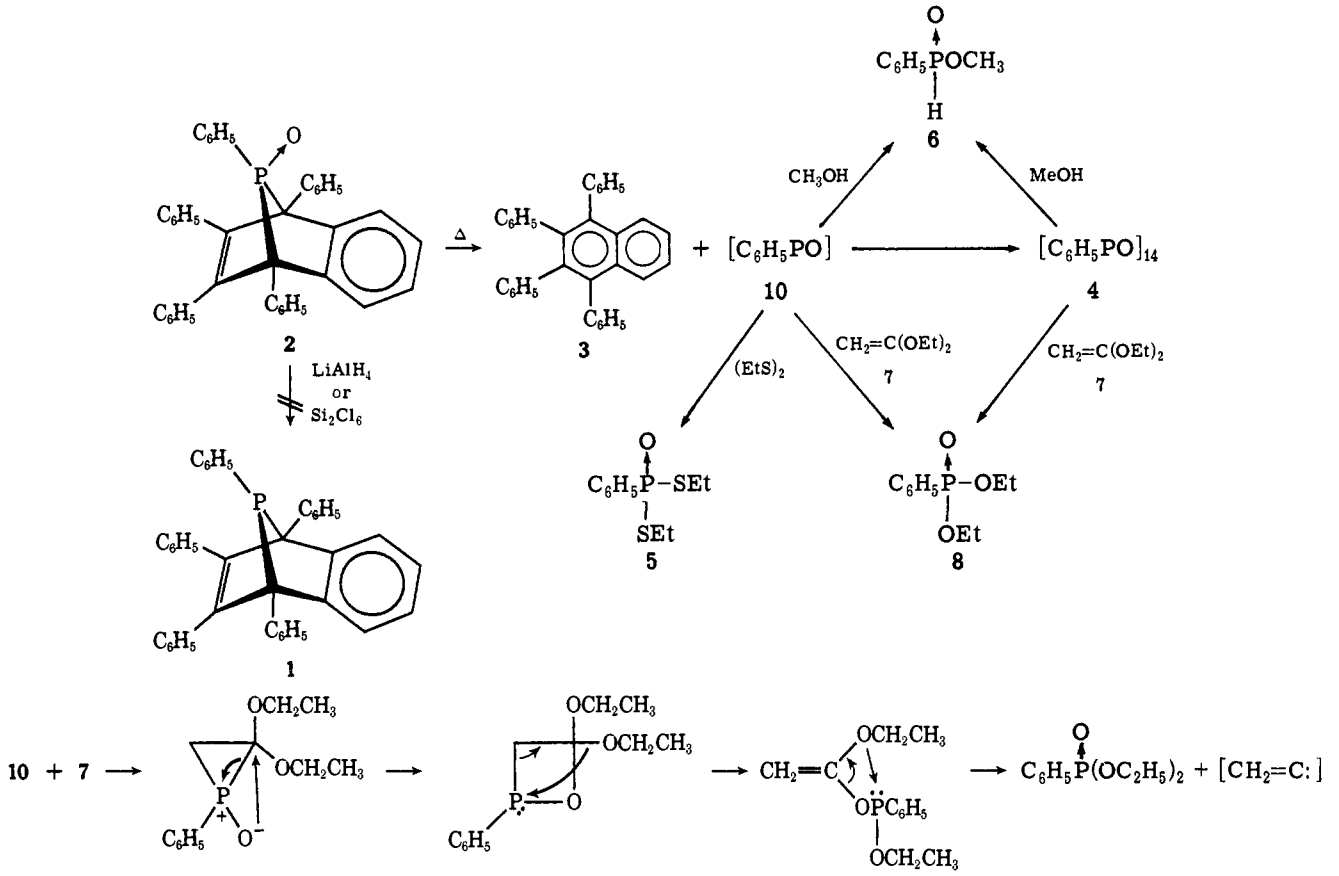
Scheme I



rich carbene trapping agent,[13,14] gave diethyl phenylphosphonate (**8**) in high yield. Also, the thermolysis of cyclopolyphenylphosphine (**9**)[15] with **7** followed by oxidation by air gave **8** as the major product; nmr δ 7.68 (m, 5 H), 4.06 (2 q, 4 H), 1.19 (t, 6 H); ir (neat) 1430 (C_6H_5P), 1260 (P→O), 1030 (POC) cm^{-1}; mass spectrum *m/e* 214 (parent), 186 ($C_8H_{11}O_3P$), 169 ($C_8H_{10}O_2P$), 159 ($C_6H_8O_3P$), 141 ($C_6H_6O_2P$), 125 (C_6H_6PO). The retention time determined by glc analysis was identical with that of an authentic sample. Ethylene and ethyl acetate were also isolated from the product mixture obtained from the thermolysis of **2** in the presence of **7**, but these compounds are products of the decomposition of **7** alone.[16] No acetylene or other volatiles could be detected in the reaction products. It was shown by nmr, infrared, and glc analysis of separate reactions that neither **2** nor **9** reacts with ethyl acetate to give **8**. Unfortunately, efforts to trap the intermediate, **10**, by a variety of acetylenes and by other olefins did not yield any identifiable product except **3** and **4**.

In one experiment, isoprene was coated on a cold finger inside a vacuum reaction vessel at −196° at a distance less than a mean free path from a thin layer of **2** coated on the outside wall of the reaction vessel. The entire apparatus was evacuated to a pressure of 10^{-5} mm and was plunged into an oil bath at 170°. Decomposition occurred and within a few minutes all of the material transferred to the cold finger. Isoprene and **3** were recovered, but no other new products containing carbon–phosphorus bonds were observed. When the mixture was extracted with methanol, a reaction occurred with the phenylphosphinidene oxide polymer **4** to give methyl phenylphosphinate (**6**). Thus, neither the reactive phenylphosphinidene oxide (**10**) nor its polymer **4** reacted with isoprene.

In a similar experiment, ketene diethylacetal (**7**) was coated on the cold finger. No reaction was apparent between **7** and **10** at −196° but, near room temperature as the material melted, a reaction occurred as evidenced by a color change. Diethyl phenylphosphonate (**8**) was identified from the reaction mixture. It is evident that phosphorus products of the thermal decomposition of **2** transferred to the cold finger as **10**, since polymer would not be expected to be instantly volatile. At −196°, **10** either reacted with itself to form the polymer **4**, which subsequently reacted with **7**, or remained as **10** at the lower temperature and reacted with **7** at elevated temperatures.

The results obtained from the flash pyrolysis of **2** and transfer of the products to the liquid nitrogen cold finger supports the existence of a discrete phenylphosphinidene oxide species **10**. Most of the chemical evidence, however, shows that this species does not behave like a conventional neutral electron-deficient intermediate characterized by carbene. It is possible that the formation of **5** occurred *via* an attack of ethyl sulfide radical on **2** (Scheme I): it is also possible that methanol added to phosphorus in **2** before decomposition. However, the addition of phosphinidene oxide (**10**) across the olefinic bond of **7** followed by rearrangement to give **8** is a probable mechanism for the forma-

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tion of **8**. Radical intermediates were evidently not involved in this reaction, since radicals are known to add to the terminal olefinic carbon of **7**.[17]

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Interpretation of Linear Hammett Constant Correlations in Substituted *ms*-Tetraphenylporphins

Sir:

The biological significance of porphyrins is well known, but their usefulness as model compounds in empirically discovering or exploring structure–reactivity or structure–property relationships has only been recently emphasized.[1] Below we give a preliminary report showing one of each of these types of relationships in terms of the well-known Hammett constants.[2,3]

Pseudo-first-order reaction rate constants for the reaction[4]

$$\mathrm{T}(p\text{-X})\mathrm{PP} + \mathrm{CuCl_2} \longrightarrow \mathrm{CuT}(p\text{-X})\mathrm{PP} + 2\mathrm{HCl}$$

in dimethylformamide at various controlled temperatures, with a copper chloride concentration of 1.6×10^{-3} M and initial porphyrin concentration of 3.2×10^{-5} M, were obtained by spectrophotometric monitoring with time of the free base porphyrin peaks at about 510 nm and their copper derivatives at about 540 nm. ΔG^* was obtained by conventional methods.[5] Plots of ΔG^* *vs.* Hammett's σ and σ^+ parameters[2] exhibit reasonable linearity with σ^+, while considerable deviation from linearity is seen for the σ plot, especially for the T(*p*-OH)PP and T(*p*-OCH_3) derivative (*cf.* Figure 1). In substituted benzenoid compounds such behavior is characteristic of reactions proceeding through electron-deficient intermediates and is usually ascribed to resonant electron donation from these substituents to the reactive center by some conjugated path.[6,7]

Visible absorption spectra of the dications, T(*p*-X)PPH_2^{2+}, prepared by saturating 10^{-5} M solutions of these bases in dimethylformamide with dry gaseous HCl at 298°K, were obtained on a Coleman-Hitachi 124 double-beam spectrophotometer. Spectroscopic energy shifts of the Q band, π–π transitions,[8] relative to $TPPH_2^{2+}$ at 7511 cm^{-1}, are plotted *vs.* the Hammett σ, σ^+ and ($\sigma^+ - \sigma$) constants of the respective *p*-X substituents (*cf.* Figure 2). No linear correlations with σ and σ^+ themselves are observed, while the observed frequency shift yields a good linear correlation with ($\sigma^+ - \sigma$). Similar spectral shifts, though of much smaller magnitude, and similar correlations were also observed in the free base spectra.

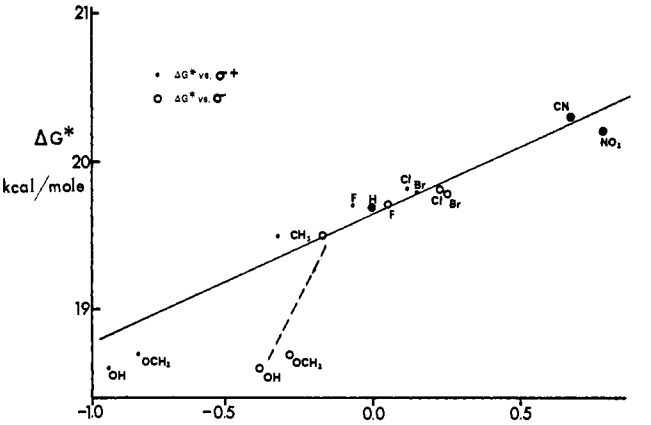

Figure 1. Free energy of activation for binding of Cu^{2+} in *N,N*-dimethylformamide by various para-substituted *ms*-tetraphenylporphyrins correlated to Hammett's σ and σ^+ constants. Note superimposed points for CN, NO_2, and H.

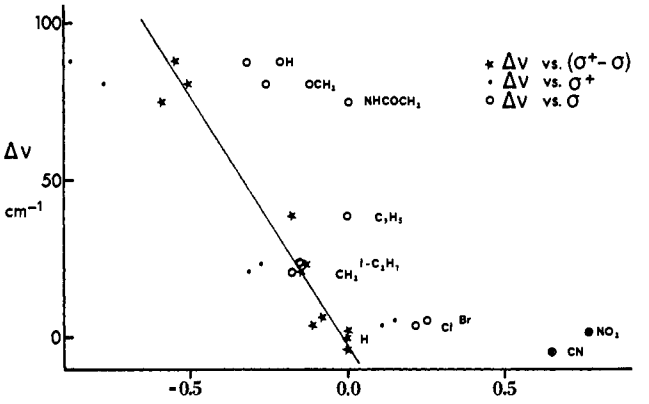

Figure 2. Frequency difference between the acid forms of *ms*-tetraphenylporphin as reference and various of its para-substituted derivatives in the 600–700-nm region correlated to Hammett's σ, σ^+, and ($\sigma^+ - \sigma$) constants. Note superimposed points for H, CN, NO_2, C_6H_5, and $NHCOCH_3$.

Such energy shifts by substituents are usually ascribed to inductive σ and π effects and to resonant π effects.[3,6,7] The differences from σ to σ^+ are conventionally explained[3] by an additional conjugation between filled substituent p orbitals and an electron-deficient center *via* some aromatic π system.

The difference $\sigma^+ - \sigma$ is thus expected to be mainly indicative of the presence in such resonance effects of electron-deficient intermediates.[6]

However, to get such resonance forms with strong conjugation in these macrocyclic ring systems would require either considerable coplanarity of the phenyl and porphin π systems or a breakup of the conjugative bonding in the porphin system itself. The present X-

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