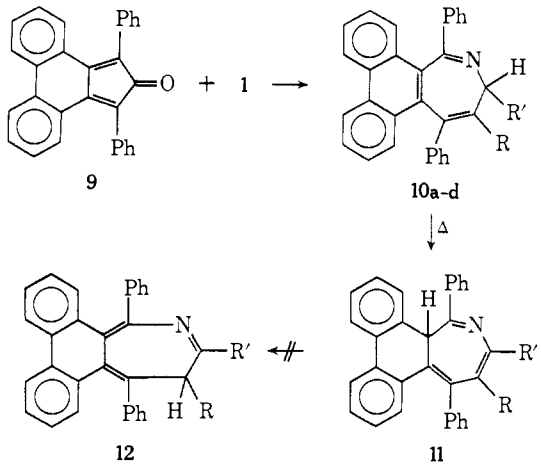
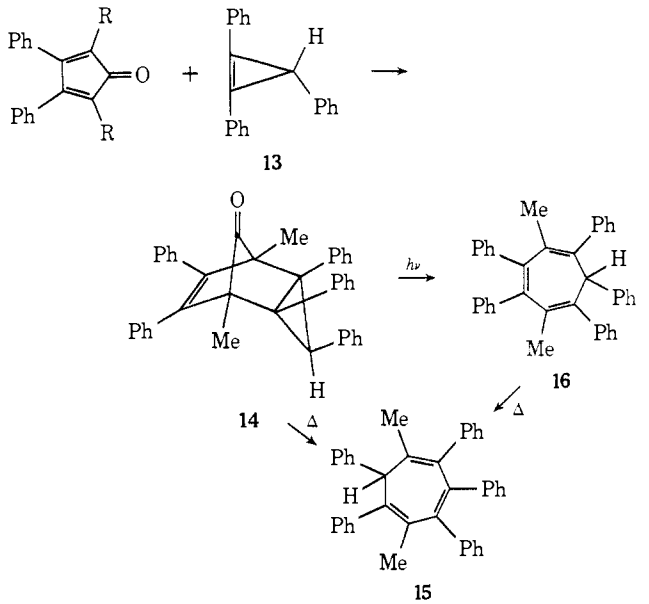


Further heating of 2*H*-azepines **10** in triglyme (or neat) afforded the 3*H*-azepines **11** *via* a symmetry-allowed 1,5-hydrogen shift. This isomerization also proceeded in the presence of potassium *tert*-butoxide in refluxing glyme. Benzoazepines **8** were inert to these conditions. The structures of **11** were evident from their nmr spectra. An isomeric 3*H*-azepine structure **12** was readily excluded, since there was no coupling of the ring proton in **11a** or **11d**.[6]

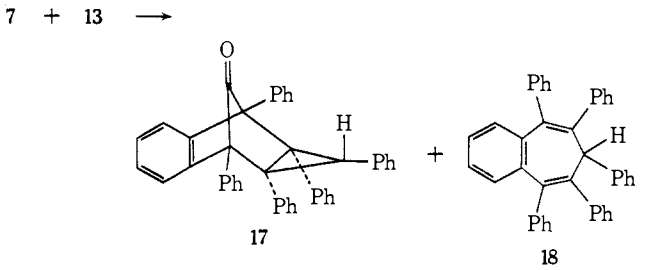
These results are consistent with pathway **3** → **5** → **6**. Additional evidence for this mechanism was obtained by further studies of analogous cyclopropene cycloadditions. The cyclopropene adduct **14**, which on heating in toluene affords cycloheptatriene **15**, produced



the symmetrical cycloheptatriene **16** (equivalent methyl groups in the nmr) on photochemical decarbonylation. Heating **16** in toluene led to formation of **15** in 75% yield, by a 1,5-hydrogen shift; hence **15** is probably a secondary thermolysis product of **14**.

On the basis of other studies[7] on the thermal decarbonylation of bridged ketocyclopropyl systems related to **14**, it is expected that for a concerted electrocyclic opening of the three-membered ring with loss of CO (step **3** → **5**), more efficient orbital overlap in the transition state is obtained with an endo rather than an exo configuration.

It is highly probable then that addition of azirines **1** to cyclopentadienones **2** occurs preferentially from the endo side. In support of this contention is our ability to isolate, in a 1:4 ratio, the exo adduct **17** and cycloheptatriene **18** from the cycloaddition of triphenyl-



cyclopropene **13** to **7**. Unlike **14**, adduct **17** is stable to 300°.

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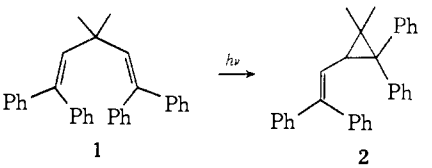
Evidence for Requirement of the Second π Bond in the Di-π-methane Rearrangement and the Observation of Excited Singlet 1,4-Phenyl Migration. Mechanistic and Exploratory Organic Photochemistry. LXXII[1]

Sir:

In our earlier efforts we uncovered a basic type of excited state behavior characteristic of molecules having two π moieties attached to an sp^3-hybridized carbon;[2] we termed this the di-π-methane rearrangement.[2b,3] Subsequently this rearrangement has proven to be of exceptional generality. Typifying the rearrangement is the transformation of 1,1,5,5-tetraphenyl-3,3-dimethyl-1,4-pentadiene (**1**)[4] (eq 1). Our mechanism



(1)

involves initial bonding between the two π moieties.

In contrast, Woodward and Hoffmann[5] have suggested that the reaction is a $_{\sigma}2_a + {}_{\pi}2_a$ or $_{\sigma}2_s + {}_{\pi}2_s$ process, a mechanism in which only one π bond plays a role.

The present report contains evidence describing (1) the necessity of the second π bond for facile rearrange-

(6) J. I. G. Cadogan and R. K. Mackie, *J. Chem. Soc. C*, 2819 (1969), showed that $J_{2,3}$ in 3*H*-azepines is *ca.* 5 Hz.

(7) B. Halton, M. A. Battiste, R. Rehberg, C. L. Deyrup, and M. E. Brennan, *J. Amer. Chem. Soc.*, **89**, 5964 (1967).

(1) For paper LXXI of the series note H. E. Zimmerman and G. A. Epling, *J. Amer. Chem. Soc.*, **94**, 7806 (1972).

(2) (a) H. E. Zimmerman and G. L. Grunwald, *ibid.*, **88**, 183 (1966); (b) H. E. Zimmerman, R. W. Binkley, R. S. Givens, and M. S. Sherwin, *ibid.*, **89**, 3932 (1967).

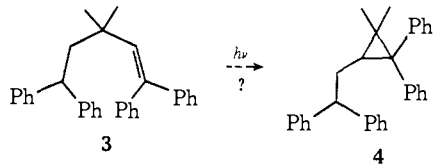
(3) H. E. Zimmerman, R. S. Givens, and R. M. Pagni, *ibid.*, **90**, 6096 (1968).

(4) H. E. Zimmerman and P. S. Mariano, *ibid.*, **91**, 1718 (1969).

(5) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970, pp 98-99.

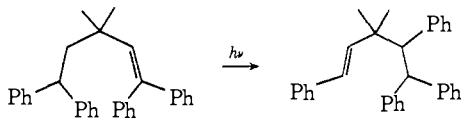
ment and (2) a novel 1,4-phenyl migration observed in the absence of the second π system.

For our study we selected the monoolefin **3** because of its close relationship to the diene **1**. If it were really correct that only σ bond 3–4 is involved in the rearrangement, then the monoolefin **3** should rearrange with greater facility than the diene **1** since in the monoolefin **3** it is a weaker sp^3–sp^3 σ bond, compared with the sp^2–sp^3 bond of the diene **1**, which would have to add across the π bond.



3 4 (2)

Photolysis of a 0.0051 *M* solution of the monoolefin **3** for 10 hr in *tert*-butyl alcohol afforded an 11% conversion to a photoproduct whose structure was assigned as 1,4,5,5-tetraphenyl-3,3-dimethyl-1-pentene (**5**) based



3 5 (3)

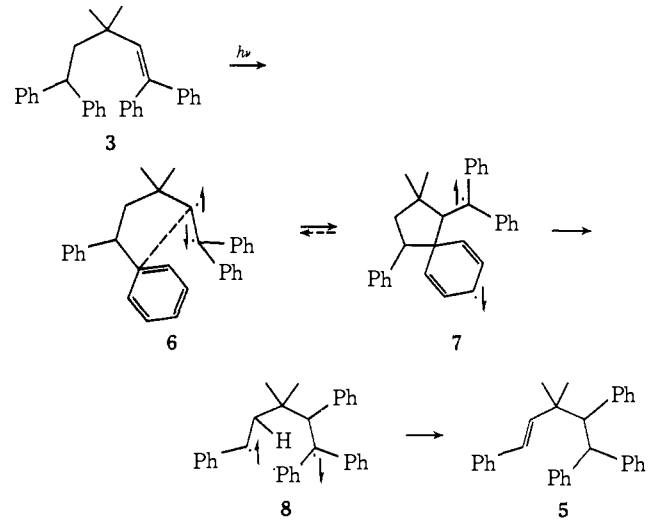
on spectral data and an independent synthesis.[6,8] The nmr spectrum of **5** is particularly instructive. It shows a 20-hydrogen multiplet centered at τ 2.84 (aromatic), a two-hydrogen singlet at 3.90 (vinyl hydrogens of the trans isomer[9]), an AB quartet with τ_A 5.51 and τ_B 6.20 (J = 11.5 Hz, benzylic and benzhydryl hydrogens), and two three-hydrogen singlets at 8.94 and 9.26 indicating that these methyl groups are bonded to a carbon atom adjacent to a diastereotopic center. Unequivocal evidence in support of the assigned photoproduct structure **5** was provided by independent synthesis.

It should be noted that **5** is not a product of a concerted $_\sigma2 + _\pi2$ reaction (*cf.* eq 2 and 3). The absence of **4** was evidenced by analytical liquid chromatography using independently synthesized **4** as a standard. In addition, the quantum yield and rate of excited state rearrangement of monoolefin **3** are considerably less than for diene **1** (*vide infra*). The quantum yield of formation of **5** on direct irradiation was found to be ϕ = 0.0008. The diene **1** rearranges with a quantum yield[4] which is 100 times greater than that of the corresponding monoolefin **3**. This comparison is justified, since both reactions of **1** and **3** are singlet processes. Thus, sensitization of monoolefin **3** under conditions where benzophenone transfers only triplet excitation gave no reaction.

The difference in quantum yields was shown to reflect a difference in the inherent rate of reaction rather than just a difference in the rate of excited state decay. Thus, using the method described by Zimmerman and Baum[10] and also by Dalton and Turro,[11] the rate of excited state rearrangement of the diene **1** was shown to be 627 times that of the monoolefin **3**.

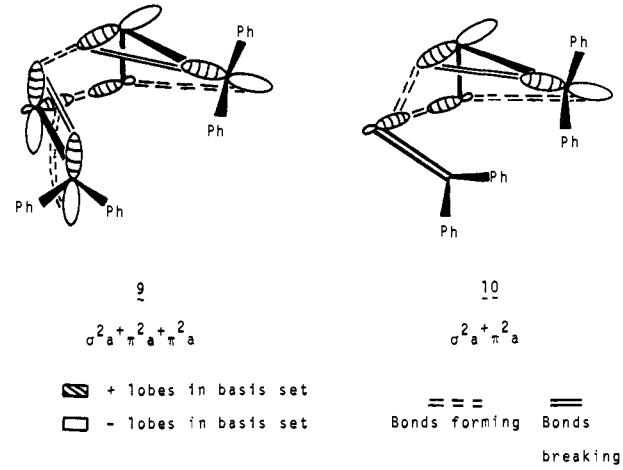
A mechanism which accounts for the formation of the observed photoproduct **5** is depicted in Chart I.

Chart I. Mechanism of Rearrangement of 1,1,5,5-Tetraphenyl-3,3-dimethyl-1-pentene (**3**)



Thus, initial excitation of **3** leads to excited state **6** which can be transformed to **7** through interaction of the C-5 phenyl group and the odd electron center at C-2. Species **7** can then either decay back to **6** or proceed to **8** thus completing the 1,4-phenyl shift. Finally, hydrogen transfer followed by demotion to the ground state leads to the observed photoproduct **5**. This rearrangement is initiated by a 1–5 π–π type interaction and is reminiscent of the recent elegant studies by Binkley.[12]

Thus it is evident that the di-π-methane rearrangement is indeed a result of the interaction of two π moieties and is best described as a $_\sigma2_a + _\pi2_a + _\pi2_a$ process[4,13] as in **9** although the $_\sigma2 + _\pi2$ mechanism (note alternative **10**) does afford the di-π product on paper.



Acknowledgment. The authors wish to thank the National Science Foundation for supporting this

(6) Photolyses were run preparatively with a 450-W apparatus and quantitative runs were with our Black Box apparatus.[7]

(7) H. E. Zimmerman, *Mol. Photochem.*, 3, 281 (1971).

(8) All compounds analyzed properly. Full synthetic and other details will be reported in our full paper.

(9) The cis isomer showed an AB quartet with τ_A 3.92 and τ_B 4.56 (J = 12.9 Hz).

(10) H. E. Zimmerman and A. A. Baum, *J. Amer. Chem. Soc.*, 93, 3646 (1971).

(11) J. C. Dalton and N. J. Turro, *ibid.*, 93, 3569 (1971).

(12) (a) W. C. Schumann, D. B. Vashi, J. A. Ross, and R. W. Binkley, *J. Org. Chem.*, 37, 21 (1972); (b) R. W. Binkley and W. C. Schumann, *J. Amer. Chem. Soc.*, 94, 1769 (1972).

(13) H. E. Zimmerman and A. C. Pratt, *ibid.*, 92, 1409 (1970).

research and Roberta L. Arnold for assistance with certain aspects of this work.

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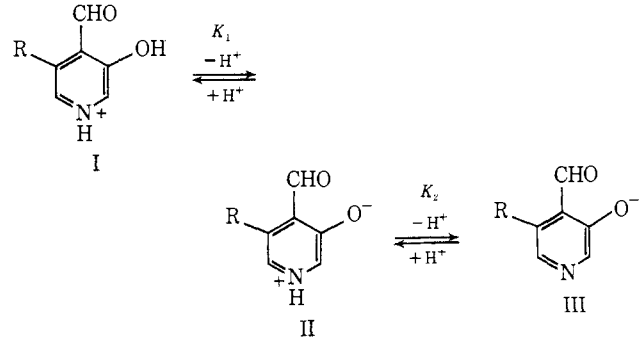
Reduction of Pyridoxal Phosphate (and Analogs) by 1,4-Dihydropyridine

Sir:

Though in enzymatic reactions nicotinamide–adenine dinucleotide (NADH) serves as a reducing agent for aldehydes, *via* direct hydrogen transfer, rather extensive search has led to no aldehyde substrate reducible by 1,4-dihydropyridine in simple model systems operating in aqueous solution at ambient temperature.[1] For horse liver alcohol dehydrogenase the Zn^{II} species present at each of the two NADH-containing active sites has been suggested to facilitate aldehyde reduction by polarization of the carbonyl group through direct interaction with the carbonyl oxygen.[2] Though Creighton and Sigman[3] have quite recently described a Zn^{II}-dependent reduction of 1,10-phenanthroline-2-carboxaldehyde by *N*-propyl-1,4-dihydronicotinamide (NPrNH), this system, being reported only in acetonitrile, is apparently restricted to aprotic solvents. Apparently searches for aldehyde substrates have never been directed to pyridoxal phosphate and analogs. This is rather surprising considering the fact that, as cofactors, NADH and pyridoxal phosphate cohabit in the same cell milieu. We report herein that pyridoxal phosphate (PLP), pyridoxal (PL), and 3-hydroxypyridine-4-aldehyde (PCHO) serve as suitable aldehyde substrates for reduction by the 1,4-dihydropyridines, NPrNH, and 2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine (Hantzsch ester). Also, we find the reductions to be facilitated by metal ions in aqueous solution. Kinetic studies were carried out spectrophotometrically under N_2 in Thunberg cuvettes employing two media: (a) neat boiling methanol (NPrNH at 354 nm, Hantzsch ester at 372 nm); and (b) 52.1 wt % aqueous methanol at 30°, μ = 0.01 with KCl (NPrNH at 362 nm, Hantzsch ester at 372 nm). Tlc and nmr studies established that the products of reaction of PCHO and NPrNH were *N*-propylnicotinamide and the carbinol formed by reduction of the aldehyde. In refluxing methanol without buffer, the predominant species of pyridine aldehydes present will be II and III. We may assume that the rate of reduction of II $\gg$ III. The second-order rate constants (M^{-1} min^{-1}) for reduction of species II are as follows: 16 [PCHO][NPrNH]; 0.74 [PCHO][Hantzsch ester]; 0.28 [PL][Hantzsch ester]. The nmr spectrum of the product from reaction of PL and Hantzsch ester in refluxing methanol-*d* had singlet peaks of almost identical integral intensities at 4.63 and 4.82 ppm (δ). This result establishes direct transfer of a hydrogen from the dihydropyridine to the 4-aldehyde of PL. In the buffered aqueous methanol solutions at pH 8.34 the following



apparent second-order rate constants were obtained employing Hantzsch ester: PCHO, no reaction; PL, 0.22; PLP, 0.48 M^{-1} min^{-1}. From the pH dependence of the reaction of PLP with NPrNH the rate constants for the ionic forms of PLP corresponding to I, II, and III could be estimated at 17, 2.7, and $\sim 10^{-1}$ M^{-1} min^{-1}, respectively. The order of reactivity of $PLP_I > PLP_{II} > PLP_{III}$ > pyridine-4-aldehyde = 0 is that previously noted for imine formation[4] and finds similar explanation.

One would anticipate enhancement in the rate of reduction of PLP, PL, and PCHO upon complexation by metal ions, much as in the transamination reaction.[5] This was found to be the case. Employing 52.1 wt % methanol–water (30°) buffered by EDTA (pH 7.05–7.10) at 0.02 *M* with metal ion at 0.015 *M*, the following order of catalysis was observed in reduction of PLP by Hantzsch ester: $Ni^{2+}(k_{rel} = 7.2) > Co^{2+}(k_{rel} = 3.4) \geq Zn^{2+}(k_{rel} = 2.8) > Mn^{2+}(k_{rel} = 1.3) = Mg^{2+}(k_{rel} = 1.2)$, and no metal ion ($k_{rel}$ = 1.0). Considering that [EDTA] slightly exceeded [metal ion] in these experiments, the metal ion enhancement of rate is appreciable.

At present, it would appear as though the only aldehydes susceptible to 1,4-dihydropyridine reductions in aqueous solutions at ambient temperatures are PLP and its analogs. Also, the metal ion promotion of these reactions apparently represents the only case of metal ion catalysis of aldehyde reduction by a 1,4-dihydropyridine in aqueous solution.

Acknowledgment. This research was supported by grants from the National Institutes of Health and the National Science Foundation.

(1) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. II, W. A. Benjamin, New York, N. Y., 1966, Chapter 9.
(2) For a review see A. S. Mildvan, *Enzymes*, **2**, 446 (1970).
(3) D. J. Creighton and D. S. Sigman, *J. Amer. Chem. Soc.*, **93**, 6314 (1971).
(4) D. S. Auld and T. C. Bruice, *ibid.*, **89**, 2083 (1967).
(5) For a review of the work of E. E. Snell, D. E. Metzler, and others, see ref 1, Chapter 8.
(6) Postdoctoral fellow, Department of Chemistry, University of California, Santa Barbara, Calif. 93106.

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Nicandrenone, an Insecticidal Plant Steroid Derivative with Ring D Aromatic

Sir:

In 1951, the isolation of a substance termed "nicandrin" from the Peruvian weed *Nicandra physalodes* was reported.[1] It was later found to possess strong insect repellent and mild insecticidal properties, and as it was

(1) F. V. Gizycki and G. Kotitschke, *Arch. Pharm. (Weinheim)*, **284** 129 (1951).