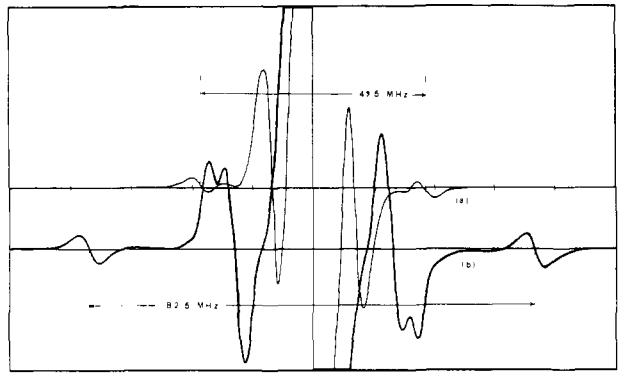

Figure 1. ESR hyperfine spectra of $PTBT^{+\cdot}$ (a) and $PTM\cdot$ (b).

Table I. ESR Parameters

	^{13}C coupling constants, MHz			
radical	α	bridgehead	ortho	g value
$PTBT^{+\cdot}$	41.5	17.9	14.8	2.0026
$PTM\cdot$[1a,5]	82.5	35.5	30.0	2.0026

phenylbi-*p*-tolyl), elemental analyses, and IR and UV-vis spectra.

Registry No. PTBT:, 33135-34-1; $PTBT^{2+}$, 89959-10-4; $PTBT^{+\cdot}$, 89959-12-6; $PTBT^{2+}\cdot 2SbCl_6^-$, 89959-11-5; $PTBT^{+\cdot}\cdot SbCl_6^-$, 89959-13-7; perchloro-$\alpha'$-(4-oxocyclohexadienylidene)-α,α,α'-triphenylbi-*p*-tolyl, 89959-14-8; perchloro-α,α'-bis(4-oxacyclohexadienylidene)-α,α'-diphenylbi-*p*-tolyl, 89959-15-5.

Diels-Alder Reaction of Protonated Azo Compounds. Isolation of a Tetraalkyldiazenium Dication

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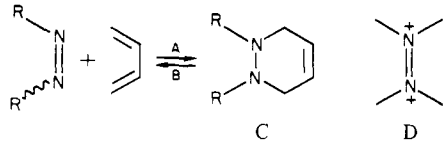
Although 1,2-diacyldiimides such as triazolinedione derivatives are among the most potent of isolable dienophiles, the Diels-Alder addition of dialkyldiimides to dienes (reaction A) has not been

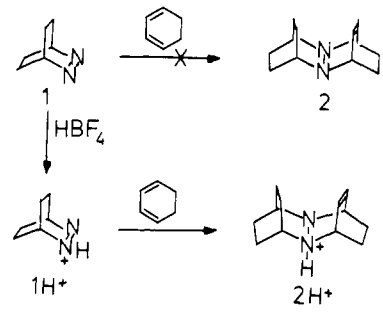


C D

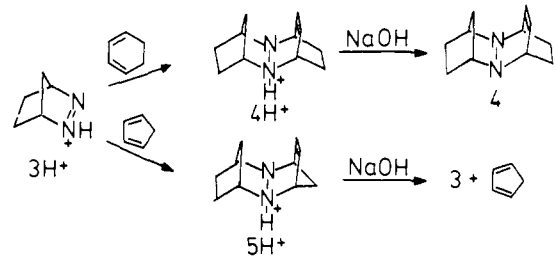
reported. The reverse reaction, retro Diels-Alder cleavage of 1,2,3,6-tetrahydropyridazines (C) is known to be an easy reaction.[1] We report here that protonation of bicyclic azo compounds makes equation A a high-yield reaction and use it to prepare the first example of an isolably stable tetraalkyldiazenium dication (D).

It was easily predictable that protonation at nitrogen would greatly increase the dienophilicity of the azo linkage. Protonated 1,1-dimethyldiazene was shown to be a dienophile by Urry and co-workers over 25 years ago.[2] Acids rapidly rearrange azo compounds with removable α-hydrogens to hydrazones, but bicyclic azo compounds such as **1** are protected against this rearrangement (the hydrazone would have its C=N bond too twisted for appreciable double-bond character), and Heyman and Snyder[3] showed that $\mathbf{1H^+}ClO_4^-$ is isolable. Protonated **1** adds 1,3-cyclohexadiene in Diels-Alder fashion (Scheme I). The reaction proceeds slowly at room temperature, but we obtained a better conversion at 45 °C (97% $\mathbf{2H^+}BF_4^-$ isolated by crystallization). A slight excess of diene is required for complete $\mathbf{1H^+}$ consumption because of polymerization, and it is necessary to avoid excess HBF_4, which polymerizes cyclohexadiene rapidly. Deprotonation of $\mathbf{2H^+}$ gives **2**, which undergoes retro Diels-Alder cleavage slowly at room temperature (half-life of about 7 h). Similarly, protonated 2,3-diazabicyclo[2.2.1]hept-2-ene $\mathbf{3H^+}$ adds to both cyclohexadiene and cyclopentadiene to give $\mathbf{4H^+}$ and $\mathbf{5H^+}$ (Scheme II). The major products have the stereochemistry shown, because there is a strong upfield shift of one of the protons on the CH_2 bridge ($\mathbf{4H^+}$, δ 1.38; **4**, δ 0.64; $\mathbf{5H^+}$, δ 1.26) as expected for the proton held in the shielding cone of the double bond. Although this is the geometry for endo addition of the dienophile, Allinger MM2 calculations[4] on the related hydrocarbons (both N atoms replaced by CH) show that it is also the thermodynamic product. Deprotonation of $\mathbf{4H^+}$ gives **4**, which undergoes retro Diels-Alder cleavage more slowly than **2**, but deprotonation of $\mathbf{5H^+}$ at room temperature gives the cleaved products, cyclopentadiene and **3**, so the retro Diels-Alder cleavage clearly increases in rate in the order **4** < **2** < **5**.

Scheme I



Scheme II



The facile cleavage of Diels-Alder adducts **2**, **4**, and **5** demonstrates that the problem with Diels-Alder addition of cyclic dienes to **1** and **3** is not kinetic, but thermodynamic. Diels-Alder addition causes overall conversion of π(C=C) and π(N=N) bonds to two σ(C—N) bonds, which is certainly exothermic. Steric strain is obviously increased in the products compared to the starting materials, and the σ(NN) bond formed is certainly unusually weak because of large lone pair, lone pair interactions in the adducts, which have the lone pairs held at a nearly 0° dihedral angle. We have been unable to detect any **2** or **4** by NMR upon mixing neat cyclohexadiene with **1** or **3**, either at room temperature or upon mild heating. All three Diels-Alder reactions appear to be endothermic. The reason protonation makes the reaction proceed, then, is not kinetic, but thermodynamic. Azo compounds are exceedingly weak bases,[5] but hydrazines are strongly basic, so the product is more stabilized by protonation than is the starting

(1) Nelsen, S. F. *J. Am. Chem. Soc.* **1974**, *96*, 5669.
(2) (a) Urry, W. H.; Kruse, H. W.; McBride, W. R. *J. Am. Chem. Soc.* **1957**, *79*, 6568. (b) Urry, W. H.; Szecsi, P.; Ikoku, C.; Moore, D. W. *Ibid.* **1958**, *80*, 2224. (c) For a review of diazenium salt chemistry, see: Kuznetsov, M. A. *Russ. Chem. Rev.* (*Engl. Transl.*) **1979**, *48*, 563.
(3) Heyman, M. L.; Snyder, J. P. *J. Am. Chem. Soc.* **1975**, *97*, 4416.
(4) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127; Quantum Chemistry Program Exchange, Program 395.
(5) (a) Haselbach, E. *Helv. Chim. Acta.* **1970** *53*, 1526. (b) pK_a for protonated di-*tert*-butyldiimide is −0.05; Scherer, K., private communication.

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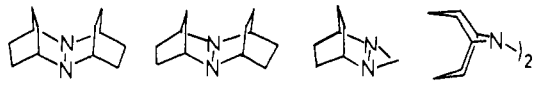
azo compound. If the azo compound were 10 pK_a units less basic than the product hydrazine, which seems entirely reasonable, this would provide 7 kcal/mol of exothermicity in the reaction with protonated azo compound compared to the reaction with unprotonated material at room temperature, which we propose is the reason for facile addition of the protonated azo compounds to cyclic dienes.

Hydrogenation of **2** and **4** to **6** and **7** using palladium on barium



6 7 8 9

carbonate in the presence of added potassium carbonate proceeds in excellent yield, although overreduction is a problem with more active catalysts. The four-step sequence reported here makes **6** available in 93% overall yield from **1**.

6 is the most easily oxidized hydrazine known; cyclic voltammetry measurements give $E^{\circ\prime}(\mathbf{6},\mathbf{6}^+) = -0.53$ V,[6] making electron removal 0.60 V (13.8 kcal/mol) thermodynamically easier than oxidation of its monobicyclic analogue **8**.[7] We attribute its easy oxidation principally to strain relief upon removal of an antibonding electron. Hydrazines with 180° lone pair, lone pair dihedral angles such as **9** are known to have their nitrogens bent past tetrahedral geometry (average of the CNC and CNN angles less than 109.5°[8]), and we expect a 0° dihedral angle hydrazine like **6** to also electronically prefer very bent nitrogens. Such bending is resisted by methylene, methylene steric interaction in **6**, which makes neutral **6** quite strained. The radical cation $\mathbf{6}^+$ will have flattened nitrogens, relieving the steric interactions of the neutral form. As expected from the behavior of **9**, **6** shows a reversible second oxidation wave, $E^{\circ\prime}(\mathbf{6}^+,\mathbf{6}^{2+}) = 0.95$ V, making **6** 7.6 kcal/mol easier to oxidize to its dication than is **9**. $AgNO_3$ oxidation of **6** gives $\mathbf{6}^+NO_3^-$ in 97% yield as a faintly yellow solid, although other hydrazine radical cations we have worked with are distinctly yellow. $\mathbf{9}^+PF_6^-$ has a UV spectrum (CH_3CN) λ_m 340 (ϵ 4000), sh 260 nm (ϵ 1300),[9] while $\mathbf{6}^+PF_6^-$ absorbs at significantly shorter wavelength: (CH_3CN) λ_m 266 (ϵ 1700), 244 (ϵ 1700), 218 nm (ϵ 1800).[10] Two moles of $NOPF_6$ mixed with **6** in CH_3CN give $\mathbf{6}^{2+}(PF_6^-)_2$, isolated as the CH_3CN solvate after precipitation by vapor diffusion of ether in 81% yield.[11] $\mathbf{6}^{2+}$ has ^1H NMR (CD_3CN) δ 6.23 (m, bridgehead), 2.73, and 2.11 (2m, CH_2) and ^{13}C NMR (CD_3CN) δ 81.4 and 30.3. Interestingly, the dication has longer wavelength absorption than the monocation radical: (CH_3CN) λ_m 317 (ϵ 2600), 227 nm (ϵ 8400); the same λ_m values are observed for $\mathbf{6}^{2+}(BF_4^-)_2$. **6** is the first hydrazine for which three oxidation states are isolable, and structural data for these compounds will be reported when available. $\mathbf{6}^{2+}$ is remarkably kinetically stable and does not react rapidly with water. Its reactions with nucleophiles should prove interesting.

Acknowledgment. We thank the National Science Foundation for support of this work under Grant CHE-8026111.

Supplementary Material Available: Preparation of $\mathbf{2H}^+$, **2**, **6**, $\mathbf{6}^+NO_3^-$, and $\mathbf{6}^{2+}(PF_6^-)_2$ (3 pages). Ordering information is given on any current masthead page.

(6) Cyclic voltammetry conditions: 0.1 M tetra-*n*-butylammonium perchlorate in acetonitrile, 23 ± 1 °C, 200 mV/s scan rate, Pt or Au working electrode, reported vs. a saturated calomel reference electrode.

(7) Nelsen, S. F.; Parmelee, W. P. *J. Org. Chem.* **1981**, *46*, 3453.

(8) (a) Nelsen, S. F.; Hollinsed, W. C.; Calabrese, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 4461. (b) Nelsen, S. F.; Hollinsed, W. C.; Kessel, C. R.; Calabrese, J. C. *Ibid.* **1978**, *100*, 7876.

(9) Nelsen, S. F.; Teasley, M. F.; Kapp, D. L.; Kessel, C. R.; Grezzo, L. A. *J. Am. Chem. Soc.* **1984**, *106*, 791.

(10) Interestingly, the UV of $\mathbf{6}^+$ is rather anion sensitive. The BF_4^- salt has λ_m 264 (ϵ 1600), 243 nm (ϵ 1500), and NO_3^- salt λ_m 267 (ϵ 1600), 203 nm (ϵ 9600), both in acetonitrile.

(11) NMR measurements make it likely that there are two CH_3N molecules per $\mathbf{6}^{2+}(PF_6^-)_2$. The crystals lose solvent rapidly upon removal from CH_3CN, and our analysis corresponded to $\mathbf{6}^{2+}(PF_6^-)_2 \cdot 1.8CH_3CN$. We have not obtained crystals with well-developed faces without CH_3CN present.

Steric Course of the 5-Enolpyruvylshikimate-3-phosphate Synthetase and Anthranilate Synthetase Reactions

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The reactions of the shikimate pathway of aromatic biosynthesis[1,2] pose a number of mechanistic and stereochemical problems. Three unanswered stereochemical questions center around the formation and further conversions of the key intermediate chorismate (**3**) and its immediate precursor, 5-enolpyruvylshikimate-3-phosphate (ESP) (**2**). These deal with the steric course of the conversion of phosphoenolpyruvate (**1**) into the enolpyruvyl side chain of **2** and with the direction of attack on the side-chain methylene group of **3** in the chorismate mutase and anthranilate synthetase reactions. Elucidation of these questions requires the generation of **2** and **3** labeled asymmetrically in the side-chain methylene group and is complicated by the fact that ESP synthetase operates by an addition/elimination mechanism.[3,4] We now report a solution to this problem.

An addition/elimination mechanism as shown in Scheme I will place a single, stereospecific tritium label from phosphoenolpyruvate evenly into the *E* and *Z* positions of the side chain of **2**. However, if every tritiated substrate molecule also carries deuterium in the other methylene position, the addition reaction will generate a chiral methyl group, which in the elimination step will produce two tritiated species, e.g., **2a** and **2b**, one containing deuterium and tritium and the other tritium and a normal hydrogen. Conversion of the methylene group of **2a** + **2b** into a methyl group by stereospecific introduction of ^1H will generate a "racemic" $C^1H_2{}^3H$ group from **2b** and a chiral methyl group from **2a**. The configuration of the latter will reveal the configuration of **2a**.[5]

To implement this approach (Scheme II) we synthesized (1*R*,2*R*)-[1-$^2H_1$,$^3H_1$]glycerol by equilibration of (2*R*)-2,3-isopropylidene-[1-$^2H_2$]glycerol[7] with alcohol dehydrogenase and [1-^3H]ethanol followed by acid hydrolysis.[9] The product was fed, together with excess unlabeled shikimate, to cultures of *Klebsiella pneumoniae* mutant 62-1 accumulating chorismic acid, using a modification of the conditions of Gibson.[10,11] The endogenously formed **1** will have *E* configuration;[12] it should produce **3** in which the molecules carrying ^2H and ^3H in the side chain have *Z* configuration if addition and elimination proceed with the

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(1) Haslam, E. "The Shikimate Pathway"; Wiley: New York, 1974.

(2) Weiss, U.; Edwards, J. M. "The Biosynthesis of Aromatic Compounds"; Wiley: New York, 1980.

(3) Levin, J. G.; Sprinson, D. B. *J. Biol. Chem.* **1964**, *239*, 1142.

(4) Ife, R. J.; Ball, L F.; Lowe, P.; Haslam, E. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1776.

(5) If, as has since been demonstrated by Knowles and co-workers,[6] the ESP synthetase reaction involves a significant deuterium isotope effect, species **2a** will be formed in excess over **2b**, potentially allowing other strategies of analysis. Our approach, however, was designed to provide answers regardless of whether or not the elimination step proceeds with an isotope effect.

(6) Grimshaw, C. E.; Sogo, S. G.; Knowles, J. R. *J. Biol. Chem.* **1982**, *257*, 596.

(7) Obtained by $LiAlD_4$ reduction of the ethyl ester prepared from diisopropylidene-D-mannitol.[8]

(8) Baer, E.; Fischer, H. O. L. *J. Biol. Chem.* **1939**, *128*, 463.

(9) The presence of a large amount of unreacted dideuterated species is immaterial for the subsequent analysis.

(10) Gibson, F. *Biochem. Prep.* **1968**, *12*, 94.

(11) Earlier work[4] had suggested the possibility that **2** might bind to ESP synthetase and undergo reversible protonation/deprotonation. The in vivo approach was chosen to minimize this problem by tightly coupling the formation of **2** to its further conversion into **3**.

(12) Cohn, M.; Pearson, J. E.; O'Connell, E. L.; Rose, I. A. *J. Am. Chem. Soc.* **1970**, *92*, 4095.

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