

Figure 3. Contour Plot of the HOESY experiment for 0.5 M ATP in phosphate buffer (100% D₂O, repeated lyophilizations). Acquisition parameters, same as figure 2.

the cross peaks between phosphorus and protons in the solvent disappear (there is no significant concentration of water protons remaining). Cross peaks arising from H-5' sugar and H-8 base protons to α -phosphorus and from H-5' to β -phosphorus are easily observed.

The heteronuclear 2D NOE experiment presented here provides information to analyse the dipolar relaxation behavior of the nonprotonated phosphorus atoms in ATP. This HOESY experiment should prove useful for evaluation of molecular conformation and also for studies of solvent-solute interactions. The observed nucleus is of course not restricted to phosphorus, and this technique is expected to have significant potential in studies of peptides (¹⁵N, ¹³C), metalloenzymes (M), and metabolic studies (³¹P, ¹³C).

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Registry No. Phosphate, 14265-44-2; phosphorus, 7723-14-0; hydrogen ion, 12408-02-5; adenosine triphosphate, 56-65-5.

Selective Intramolecular [6 + 4] Cycloadditions of Aminodienylfulvenes

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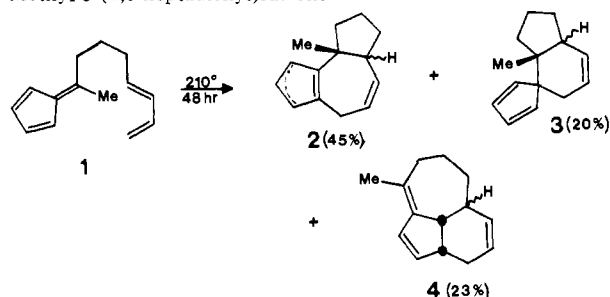
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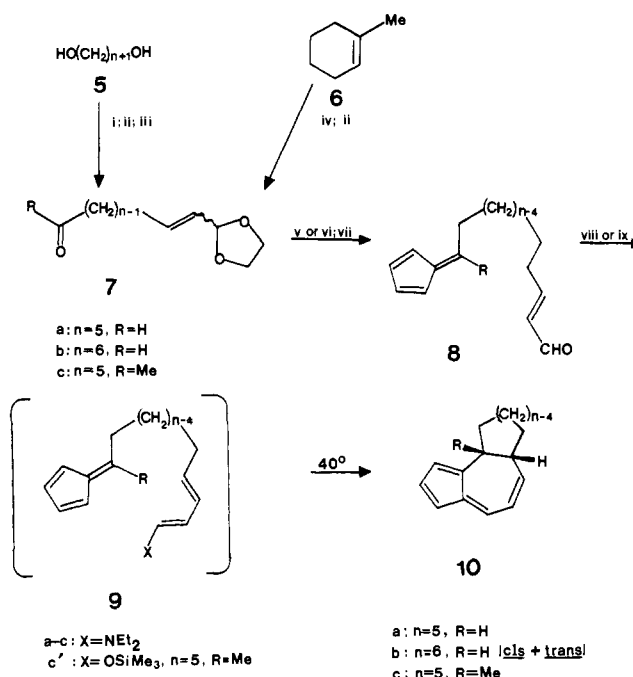
We recently reported several intramolecular [6 + 4] cycloadditions involving fulvenes as the 6 π electron components and *o*-xylylenes as the 4 π components.¹ We have now investigated similar reactions involving acyclic dienes as 4 π electron components and have found that predictable substituent effects transform a despicably unselective reaction into a delightfully specific [6 + 4] cycloaddition.

The hydrocarbon dienylfulvene **1** was prepared in 74% yield by the reaction of sodium cyclopentadienide with 6,8-nonadien-2-one.² Thermolysis of a 1% solution of **1** in toluene at 210 °C for 48 h produces the complex mixture of thermally allowed cycloadducts shown in Scheme I. The different types of adducts were separated chromatographically, but the stereoisomers have

Scheme I. Intramolecular Cycloadditions of 6-Methyl-6-(4,6-heptadienyl)fulvene



Scheme II. Preparation and Cycloadditions of Fulvenes Linked to Electron-Rich Dienes^a



^a Reagents (yields): (i) PCC, CH₂Cl₂ (a, 62%; b, 41%); (ii) Ph₃P⁺CH₂CH(OCH₂CH₂O)Br⁻, *t*-BuOK, THF (a, 47%; b, 43%; c, 53%); (iii) PCC, CH₂Cl₂ (a, 81%; b, 72%); (iv) O₃, then KI, HOAc (30%); (v) C₅H₆, Et₃NH, MeOH (a, 50%; b, 72%); (vi) C₅H₆, KOH, THF, MeOH (c, 41%); (vii) 5% aqueous HCl, THF (a, 85%; b, 85%; c, 81%); (viii) Et₃NH, K₂CO₃, PhH, 5A molecular sieves (a, 55%; b, 46%; c, 54%);¹⁴ (ix) Me₃SiCl, ZnCl₂, Et₃N (c).

not been separated.³ The trimethylene connecting chain can be seen to promote the [6 + 4] and spiro-[4 + 2] cycloaddition modes, since the intermolecular reactions of alkyl-substituted dienes with fulvenes give only Diels-Alder adducts analogous to **4**.⁴

Theoretical predictions and experimental studies⁵ of intermolecular cycloadditions of dienes to fulvenes have shown that an electron donor at one terminal carbon of the diene provides sufficient nucleophilicity at the other diene terminus to promote

(3) The product compositions were determined by NMR spectroscopy. The [6 + 4] adduct **2** is a mixture of *cis* and *trans* isomers and cyclopentadiene isomers,¹ while the [4 + 2] adducts are *cis-trans* mixtures. Details will be reported in a full paper.

(4) Houk, K. N.; Luskus, L. J. *J. Org. Chem.* **1973**, *38*, 3836.

(5) Houk, K. N.; Sims, J.; Watts, C. R.; Luskus, L. J. *J. Am. Chem. Soc.* **1973**, *95*, 7301. Houk, K. N.; George, J. K.; Duke, R. E., Jr. *Tetrahedron* **1974**, *30*, 523. Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361. Dunn, L. C.; Chang, Y.-M.; Houk, K. N., *J. Am. Chem. Soc.* **1976**, *98*, 7095. Dunn, L. C.; Houk, K. N. *Tetrahedron Lett.*, **1978**, 3411. Mukherjee, D.; Dunn, L. C.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 251. Gupta, Y. N.; Mani, S. R.; Houk, K. N. *Tetrahedron Lett.* **1982**, *23*, 495. Bimanand, A. Z.; Gupta, Y. N.; Doa, M. J.; Eaton, T. A.; Houk, K. N.; Fronczek, F. R. *J. Org. Chem.* **1983**, *48*, 403.

(6) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(1) Gupta, Y. N.; Doa, M. J.; Houk, K. N. *J. Am. Chem. Soc.*, **1982**, *104*, 7336.

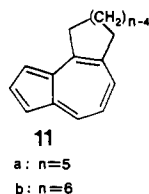
(2) Gras, J.-L.; Bertrand, M. *Tetrahedron Lett.* **1979**, 4549.

the [6 + 4] cycloaddition. In order to test the efficacy of this substituent effect in intramolecular reactions, we prepared the dienamines **9a-c** and the silyl dienol **9c'** according to the procedures outlined in Scheme II.

The oxidation of the diols **5a** or **5b** with 1 equiv of PCC⁶ afforded the corresponding hydroxyaldehydes⁷ which undergo the Wittig reaction with 1,3-dioxolan-2-ylmethyltriphenylphosphonium bromide⁸ and potassium *tert*-butoxide in THF to produce **7a** or **7b**.⁹ The synthesis of **7c** begins with ozonolysis of 1-methylcyclohexene (**6**) to produce 6-oxoheptanal; reaction of this ketoaldehyde with the same reagent occurs selectively at the aldehyde moiety to give **7c**. The Wittig reaction gives a mixture of cis and trans alkenes, **7** in each case. The fulvenes **8a** or **8b** were formed from **7a** or **7b** with cyclopentadiene-diethylamine,¹⁰ while the fulvene **8c** was produced from **7c** and cyclopentadiene by using KOH in MeOH-THF.¹¹ Hydrolysis of the fulvene ketals gives unsaturated aldehydes **8a-c**. The trans isomer of **8** is produced exclusively, even though the cis, trans mixture **7** was used in these reactions. These unsaturated aldehydes can be converted into dienamines **9a-c** with diethylamine and K₂CO₃.¹² The siloxy diene **9c'** was prepared from the aldehyde **8c** with trimethylsilyl chloride and ZnCl₂.¹³

The electron-rich dienamines, **9a-c**, were not isolated, but warming solutions of these dienes overnight at 40 °C causes intramolecular cycloadditions, followed by spontaneous elimination of diethylamine, to produce the orange-red⁵ dihydroazulenes **10a-c** in good yields (Scheme II).^{14,15} The siloxy diene **9c'** produces both the dihydroazulene **10c** and rearrangement products containing the trimethylsilyloxy group. These rearrangement products have not yet been characterized.

The carbon skeletons of **10a** and **10b** were verified by dehydrogenation with sulfur in triglyme to give brilliant blue azulenes **11a** and **11b**, in 85% and 38% yields, respectively. The cis



stereochemistry of **10a** was indicated by NMR spectroscopy: the protons at the saturated 5-7 fusion are coupled by 6.3 Hz. Dihydroazulene **10b** is a 1:1 mixture of cis and trans isomers which has not surrendered to chromatographic coaxing. The stereochemistry of **10c** was not determined, but a single isomer is formed in the reaction.

Thus, the intramolecular [6 + 4] cycloadditions of suitably activated dienyfulvenes can be used to assemble hydroazulenes fused to a third ring. Applications to synthesis and comparisons of stereochemistries to those of analogous Diels-Alder reactions will be forthcoming.

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(7) A more elegant route to appropriate terminally differentiated compounds involves the modified ozonolysis of alkenes: Schreiber, S.; Claus, R. E.; Reagan, J. *Tetrahedron Lett.* **1982**, 23, 3867.

(8) Cresp, T. M.; Sargent, M. V.; Vogel, P. *J. Chem. Soc., Perkin Trans. I* **1974**, 37.

(9) New compounds were characterized by spectral methods and by high-resolution mass spectrometry.

(10) Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1979**, 101, 7129.

(11) Yates, P. *Adv. Alicyclic Chem.* **1968**, 2, 70.

(12) Hunig, S.; Kahanek, H. *Chem. Ber.* **1957**, 90, 238.

(13) Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc.* **1974**, 96, 7807.

(14) Yields given are for the overall conversion of **8** to **10**. The analogous reaction using pyrrolidine in place of diethylamine is unsuccessful.

(15) Compare the couplings observed for cis- and trans-fused hydrindan systems of 4-6 and ~11 Hz, respectively: Roush, W. R.; Hall, S. E. *J. Am. Chem. Soc.* **1981**, 103, 5200.

Transition Structure for the Reaction of a Carbenoid, LiCH₂F, with Ethylene

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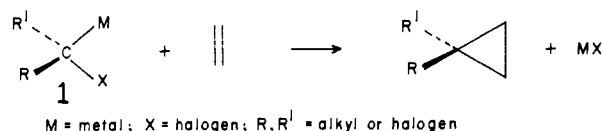
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Carbenoids,¹ **1**, are organometallic species that transfer a carbene unit, CRR', to alkenes to form cyclopropanes.² The



structures and reactions of carbenoids have been the subject of theoretical³⁻⁸ and experimental studies,^{1,2,9-15} but the transition structures of carbenoid reactions remain only the subject of speculation. We wish to report a computational investigation of the reaction of the simplest carbenoid, LiCH₂F, with ethylene, and to compare our results with previous proposals^{1,9-14} and computed carbene cycloaddition transition structures.¹⁶⁻²¹

For the Simmons-Smith reaction,^{10,11} in which the carbenoid is IZnCH₂I, or a solvated or aggregated version thereof, the "butterfly" transition structure, **2**, has been proposed.¹⁰ Here, L and L' represent "passive" ligands in the reaction. A three-dimensional representation, **3**, was proposed later,¹¹ in which in-

(1) Closs, G. L.; Closs, L. E. *Angew. Chem., Int. Ed. Engl.* **1962**, 1, 334. Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, 86, 4042.

(2) Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971; pp 83-128. Marchand, A. P. In "The Chemistry of Double-Bonded Functional Groups"; Patai, S., Ed.; Wiley-Interscience: New York, 1977; Supplement A, Part 1, pp 553-557, 585-587. Gilchrist, T. L.; Rees, C. W. "Carbenes, Nitrenes, and Arynes"; Thomas Nelson and Sons, Ltd.: London, 1969; pp 85-128. Recent reviews: Siegel, H., *Top. Curr. Chem.* **1982**, 106, 55. Taylor, K. G. *Tetrahedron* **1982**, 38, 2752. Moss, R. A.; Jones, M., Jr. "Reactive Intermediates"; Wiley-Interscience: New York, 1981; Vol. 2, p 796. Wulfman, D. S.; Polling, B. "Reactive Intermediates"; Plenum Press: New York, 1980; Vol. 1, Chapter 5. Krief, A. *Tetrahedron* **1980**, 36, 2531.

(3) Clark, T.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1979**, 883.

(4) Clark, T.; Schleyer, P. v. R. *Tetrahedron Lett.* **1979**, 4963.

(5) Clark, T.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1979**, 101, 7747.

(6) Vincent, M. A.; Schaefer, H. F., III. *J. Chem. Phys.* **1982**, 77, 6103.

(7) Rohde, C.; Clark, T.; Kaufman, E.; Schleyer, P. v. R., *J. Chem. Soc., Chem. Commun.* **1982**, 882.

(8) Luke, B. J.; Pople, J. A.; Schleyer, P. v. R.; Clark, T. *Chem. Phys. Lett.*, submitted for publication.

(9) Moss, R. A. In "Carbenes, Vol. I"; Jones, M., Jr., Moss, R. A., Ed.; Wiley-Interscience: New York, 1973.

(10) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, 80, 5323. See also: Doering, W. v. E.; LaFlamme, P. M. *Tetrahedron* **1958**, 2, 75. Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, 81, 4256.

(11) Simmons, H. E.; Blanchard, E. P.; Smith, R. D. *J. Am. Chem. Soc.* **1964**, 86, 1347.

(12) Köbrich, G. *Angew. Chem. Int. Ed. Engl.* **1967**, 6, 41. Köbrich, G.; Flory, K.; Drischel, W. *Angew. Chem., Int. Ed. Engl.* **1964**, 3, 513.

(13) Hoes, D. F.; Lusk, D. I.; Crumbliss, A. L. *J. Am. Chem. Soc.* **1965**, 87, 4147.

(14) Moser, W. R. *J. Am. Chem. Soc.* **1969**, 91, 1135, 1141.

(15) Seebach, D.; Hassig, R.; Gabriel, J. *Helv. Chim. Acta* **1983**, 66, 303 and references therein.

(16) Hoffmann, R. *J. Am. Chem. Soc.* **1968**, 90, 1475. Hoffmann, R., Hayes, D. M.; Skell, P. S., *J. Phys. Chem.* **1972**, 76, 664.

(17) Rondan, N. G.; Houk, K. N.; Moss, R. A. *J. Am. Chem. Soc.* **1980**, 102, 1770.

(18) Houk, K. N.; Rondan, N. G.; Mareda, J., submitted for publication.

(19) Schoeller, W. W. *Angew. Chem., Int. Ed. Engl.* **1981**, 20, 698.

(20) Bodor, N.; Dewar, M. J. S.; Wasson, J. S. *J. Am. Chem. Soc.* **1972**, 94, 9095.

(21) Zurawski, B.; Kutzelnigg, W. *J. Am. Chem. Soc.* **1978**, 100, 2654.