

(isomer 1), 94978-11-7; 4 (R = H, 5-[(benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl) (isomer 2), 95043-21-3; (R*)-4 (R = H, (1 α ,5 α ,6 α ,7 α)-6-(benzyloxy)-3,3-dimethyl-2,4,8-trioxabicyclo[3.3.0]octan-7-yl), 94978-03-7; 4 (R = H, 3,3-dimethyl-8-methoxy-2,4,7-trioxabicyclo[3.3.0]octan-6-yl) (isomer 1), 94978-04-8; 4 (R = H, 3,3-dimethyl-8-methoxy-2,4,7-trioxabicyclo[3.3.0]octan-6-yl) (isomer 2), 95042-59-4; *cis*-4 (R = CH₂CH₂CH(*t*-Bu)CH₂CH₂), 94956-85-1; 4 (R = Me, (CH₂)₈C(O)OEt), 94956-86-2; 5 (R = H, Ph), 80997-79-1; (S*,S*,S*)-5 (R = H, 5-[(benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl), 94956-87-3; (R*)-5 (R = H, (1 α ,5 α ,6 α ,7 α)-6-(benzyloxy)-3,3-dimethyl-2,4,8-trioxabicyclo[3.3.0]octan-1-yl), 94978-05-9; (S*)-5 (R = H, (1 α ,5 α ,6 α ,7 α)-6-(benzyloxy)-3,3-dimethyl-2,4,8-trioxabicyclo[3.3.0]octan-7-yl), 95042-61-8; (R*)-5 (R = H, (1 α ,5 α ,6 α ,8 α)-3,3-dimethyl-8-methoxy-2,4,7-trioxabicyclo[3.3.0]octan-6-yl), 94978-06-0; *cis*-5 (R = CH₂CH₂CH(*t*-Bu)CH₂CH₂), 94956-88-4; 5 (R = Me, (CH₂)₈C(O)OEt), 94956-89-5; 6 (R = R' = Ph), 94956-90-8; 6 (R = Pr, R' = Ph), 94956-91-9; 6 (R = Pr, R' = *i*-Pr), 94956-92-0; 6 (R = Me, R' = 3-pyridinyl), 94956-93-1; 7 (R = R' = Ph), 94956-94-2; 7 (R = Pr, R' = Ph), 94956-95-3; 7 (R = Pr, R' = *i*-Pr), 94956-96-4; 7 (R = Me, R' = 3-pyridinyl), 94956-97-5; PhCHO, 100-52-7; CH₃C(O)-(CH₂)₈C(O)OEt, 36651-38-4; PhCH=NPh, 538-51-2; PhCH=NPr, 6852-55-7; (CH₃)₂CHCH=NPr, 2875-39-0; CH₂=C(CH₃)CH₂OH, 513-42-8; Bu₃SnCl, 1421-22-9; BF₃·Et₂O, 109-63-7; TiCl₄, 7550-45-0; ZnCl₂, 7646-85-7; Ph₃P, 603-35-0; Pd(OAc)₂, 3375-31-3; *trans*-2,2-dimethyl-5-[(benzyloxy)methyl]-1,3-dioxolane-4-carboxaldehyde, 95042-60-7; (1 α ,5 α ,6 α ,7 α)-3,3-dimethyl-6-(benzyloxy)-2,4,8-trioxabicyclo[3.3.0]octane-7-carboxaldehyde, 87938-29-2; (1 α ,5 α ,6 α ,8 α)-3,3-dimethyl-8-methoxy-2,4,7-trioxabicyclo[3.3.0]octan-6-carboxaldehyde, 58056-24-9; 4-*tert*-butylcyclohexanone, 98-53-3; 3-[(methylimino)methyl]pyridine, 16273-54-4.

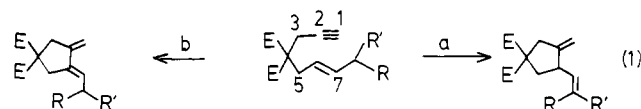
Cyclization via Isomerization: A Palladium(2+)-Catalyzed Carbocyclization of 1,6-Enynes to 1,3- and 1,4-Dienes

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The development of routes for the synthesis of five-membered rings continues to attract attention due largely to the wide variety of natural products containing this structural unit.^{1,2} As part of our continuing effort to expand the utility of transition-metal-catalyzed alkylations,³ we turned our attention to the synthesis of 1,6-enynes. Synthetic routes to such species would offer an efficient entry into highly substituted cyclopentane derivatives via thermal ene reactions.⁴ During the course of these studies, we made the unanticipated observation that palladium(2+) salts catalyze cyclizations via an isomerization to lead to related products under very mild conditions as summarized in eq 1, paths



a and b. The factors that influence the pathway traversed and

(1) For reviews, see: (a) Trost, B. M. *Chem. Soc. Rev.* **1981**, 11, 141. (b) Ramaiah, M. *Synthesis* **1984**, 529. (c) Paquette, L. A. *Top. Curr. Chem.* **1984**, 119, 1.

(2) For leading references, see: Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, 105, 2315.

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(4) For reviews on the intramolecular ene reaction, see: Taber, D. F. "Intramolecular Diels-Alder and Alder Ene Reactions"; Springer-Verlag: Berlin, 1984. Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, 17, 476. Hoffman, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, 8, 556.

the generality of this new cyclization are the subject of this communication.

The starting enynes⁵ are readily prepared by using the palladium(0)-catalyzed coupling of allylic carboxylates with dimethyl propargylmalonate anion [3-5 mol % (Ph₃P)₄Pd, NaH, THF, 1-16 h at reflux]. As seen in Table I the yields are consistently good (55-90%) with high chemo-, regio-, and stereoselectivity associated with the alkylation process. As previously noted, palladium-catalyzed allylic alkylations³ tend to favor formation of the isomer that results from attack at the less substituted terminus of the π -allylmethyl intermediate.

Carbocyclizations were conveniently carried out by heating a mixture of the enyne with a catalytic amount (3-10 mol %) of a palladium salt in a variety of organic solvents at 60-70 °C for 1-4 h.

A Pd(0) species such as (Ph₃P)₄Pd does not catalyze reaction after 12 h at reflux in THF. The effectiveness of the Pd(2+) species appears related to the Lewis acidity of the catalyst. For example, bis(acetonitrile)palladium chloride⁶ catalyzes cyclization of 3 to 4 very slowly (16% after 6.5 h in refluxing THF). On the other hand, L₂Pd(OAc)₂ effects complete reaction in THF at room temperature to reflux depending on L. Palladium acetate (5 mol %) cyclizes enyne 3 to give diene 4 in 50% yield in THF at room temperature. Best yields and cleanest reactions derive from use of preformed (Ph₃P)₂Pd(OAc)₂⁷ or [(*o*-CH₃C₆H₄)₃P]₂Pd(OAc)₂ although heating is required. Changing solvent polarity (PhH, THF, CHCl₃, or CH₃CN) does not appreciably affect the rate of the reaction. Again, yields appear maximized by use of nonpolar solvents like benzene. A phosphine to Pd ratio as high as 5-6:1 slows the reaction further but does not inhibit reaction.

Substrates containing methyl or methylene groups in allylic positions (Table I, entries 1-4) undergo the isomerization yielding 1,4-dienes. The reaction exhibits a high degree of stereoselectivity (entry 1) yielding the *trans* olefin. Furthermore, no isomerization to the α,β -unsaturated ester is observed in the preparation of 4. Examination of a case producing vicinal substituents shows the reaction is diastereoselective—producing a 3:1 *trans*/*cis* mixture of cyclopentanes (entry 3). Attempts to further improve the selectivity involving manipulation of phosphine ligands are in progress.

The cyclization of enyne 7 is somewhat puzzling. It is the only case examined to date where one of the double bonds (in this case the cyclohexenyl one) suffers further isomerization. Among several phosphines examined to minimize isomerization of the $\Delta^{6,7}$ isomer to the $\Delta^{7,8}$ one, 5 mol % of dppb with 5 mol % Pd(OAc)₂ in PhH produces the best ratio (5.7:1). In the absence of ligands or by using phosphites as ligands, extensive (25%) isomerization of the exocyclic double bond to an endocyclic position occurred.

The discovery of the cyclization process offers several advantages over simple thermal ene methodology. For example, all attempts to thermalize 3 result in the recovery of starting material (<650 °C) or decomposition (>675 °C) in contrast to normal reactivity in the palladium-catalyzed reaction. It is also possible to carry out a "one-pot" alkylation-carbocyclization by simply adding a catalytic amount (~5 mol %) of palladium acetate to the original Pd(0)-catalyzed alkylation reaction mixture. In this way, diene 4 arises directly from the allylic acetate in 68% overall yield.

Entries 5-7 reveal that an alternative pathway is possible when the allylic carbon (C-8 in eq 1) is disubstituted. NMR analysis of the crude reaction mixtures reveal that only 1,3-dienes are produced with no trace of the 1,4-diene. Again a wide variety of functional groups are tolerated and the utility of such products

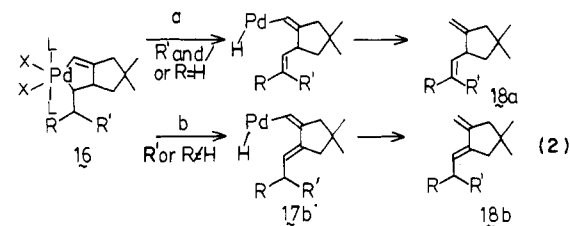
(5) All new compounds have been fully characterized by spectral means including combustion analysis and/or high-resolution mass spectroscopy.

(6) For examples of this catalyst in Cope rearrangements, see: Overman, L. E.; Jacobsen, E. J. *J. Am. Chem. Soc.* **1982**, 104, 7225 and references therein. Cyclizations of such systems to cyclohexenes are also reported: Overman, L. E.; Renaldo, A. F. *Tetrahedron Lett.* **1983**, 24, 2235.

(7) Preparation of phosphine complexes of palladium, see: Stephenson, T. A.; Morehouse, S. M.; Powell, A. R.; Heffer, J. P.; Wilkinson, G. *J. Chem. Soc.* **1965**, 3632.

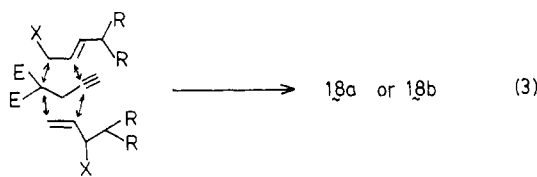
entry	allyl acetate	enyne ^{a,b}	yield ^c	cyclization conditions			product ^b	yield ^c
				solvent	temp	time, h ^d		
1				C ₆ D ₆	60 °C	1 h		71%
2			85%	THF THF C ₆ D ₆	room temp ^e reflux 60 °C	1.5 h 1.5 h		50% 70% 85%
3				C ₆ D ₆	60 °C			68%
4			87%	see text				see text
5			71%	C ₆ D ₆	66 °C			64%
6			55%	C ₆ D ₆	66 °C	1.75 h		71%
7			62%	C ₆ D ₆	66 °C			80%

15

$$L_2PdX_2 + \begin{array}{c} \text{R}' \\ | \\ \text{R}-\text{CH}=\text{CH}-\text{C}(\text{CH}_3)_2-\text{C}\equiv\text{CH} \end{array} \longrightarrow$$


(15) See: Grille, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4933. Loar, M. K.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4174. Morovskiy, A.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4182. Kurosawa, H.; Emoto, M.; Urabe, A. *J. Chem. Soc., Chem. Commun.* **1984**, 968.

diverted to other products. These possibilities in addition to mechanistic studies form the basis of current studies. Overall, the current reaction allows a novel cyclopentannulation of an allylic derivative (eq 3).



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Registry No. 1, 95123-89-0; 2, 95123-90-3; 3, 95123-91-4; 4, 95123-92-5; 5, 95123-93-6; *cis*-6, 95123-94-7; *trans*-6, 95123-95-8; 7, 95123-96-9; $\Delta^{6,7}$ -8, 95123-97-0; $\Delta^{7,8}$ -8, 95123-98-1; 9, 95123-99-2; 10, 95124-00-8; 11, 95124-01-9; 12, 95124-02-0; 13, 95124-03-1; 14, 95124-04-2; 15, 95124-05-3; (MeO)₂CH(CH₂)₉CH(OAc)CH=CH₂, 88399-89-7; (E)-CH₃CH=CHCH(OAc)CH₃, 31001-80-6; CH₃CCH₂CH(CO₂C-H₃)₂, 95124-07-5; [(*o*-CH₃C₆H₄)₃P]Pd(OAc)₂, 69073-98-9; (CH₃C-N)₂PdCl₂, 14592-56-4; (Ph₃P)₂Pd(OAc)₂, 14588-08-0; methyl *cis*-5-acetoxycyclohex-3-enecarboxylate, 60729-55-7; 1-acetoxy-2-methylenecyclohexane, 53723-50-5; (1-acetoxyprop-2-en-1-yl)cyclohexane, 95124-06-4; 4-(1-acetoxyprop-2-en-1-yl)-2,2-dimethyl-1,3-dioxolane, 18524-20-4; 22(S)-(acetyloxy)chola-4,23-dien-3-one, 85994-21-4; maleic anhydride, 108-31-6.

2-Thiabicyclo[2.2.1]hept-5-ene *endo*-2-Oxide Derivatives: Stereospecific Formation, Rearrangement to Bicyclic Sulfenes, and Conversion to (*E*)-5-Alkylidene-2-cyclopentenones¹

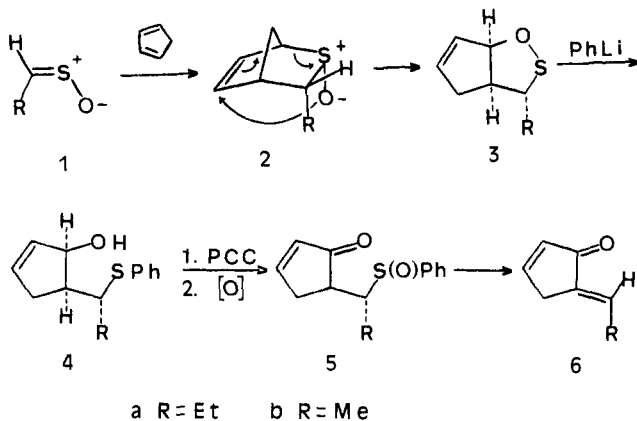
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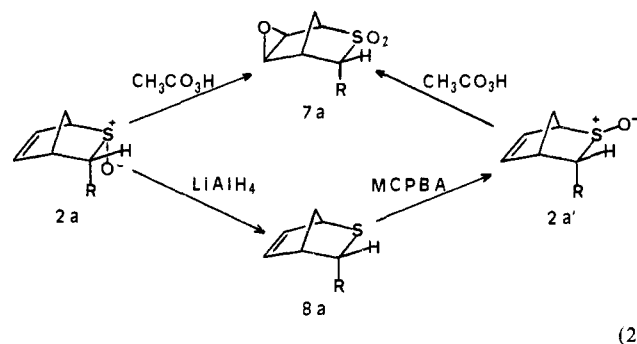
Received September 10, 1984

Diels-Alder adducts of cyclopentadiene and thiocarbonyl compounds² are attractive intermediates for the controlled synthesis of polyfunctional cyclopentanoids through sulfur-mediated transformations followed by desulfurization. We find that *endo*-sulfoxides **2**, prepared stereospecifically from cyclopentadiene and alkanethial *S*-oxides **1**, readily rearrange to bicyclic sulfenes **3**, representatives of a rare class of sulfur heterocycles, which in turn may be easily converted to various cyclopentenoids including (*E*)-5-alkylidene-2-cyclopentenones (**6**) (eq 1).

Addition of cyclopentadiene to a Freon 11 solution of (*Z*)-propanethial *S*-oxide (**1a**),³ obtained by dehydrochlorination of propanesulfinyl chloride with triethylamine, gave a single product characterized⁴ as *endo*-3-ethyl-2-thiabicyclo[2.2.1]hept-5-ene *endo*-2-oxide (**2a**) (eq 1). Thus, on the basis of an X-ray crystal structure of epoxy sulfone **7a** (R = Et),⁴ prepared by peracetic acid oxidation of **2a**, we conclude that **2a** has an *endo*-ethyl group. Reduction of **2a** to sulfide **8a** and reoxidation with MCPBA gave a different sulfoxide, **2a'**, also converted to epoxy sulfone **7a** by



oxidation (eq 2). The presence of an *exo*-sulfoxide oxygen in



2a', anticipated on the basis of the stereochemistry of oxidation of 2-thiabicyclo[2.2.1]heptane⁵ (9; *exo*-sulfoxide favored with MCPBA), was unequivocally established by Eu(fod)₃ and aromatic solvent induced shift studies giving results in good agreement with similar studies on the two *S*-oxides of **9**.⁶ The *endo*,*endo* ethyl group-sulfoxide oxygen relationship in **2a** is consistent with a stereospecific Diels-Alder reaction of (*Z*)-**1a** following the Alder *endo* rule.

Also consistent with an *endo*-sulfoxide oxygen in **2a** is the striking difference in reactivity of sulfoxides **2a** and **2a'**. While isomer **2a'** was unchanged after refluxing in toluene for 20 h, sulfoxide **2a** rearranges at room temperature, presumably via a [2,3]-sigmatropic shift,⁸ to 4-ethyl-2-oxa-3-thiabicyclo[3.3.0]oct-7-ene (**3a**) (eq 1), a rare example of an isolable sulfene.⁹ Compound **3a**, obtained in 51% yield (based on propanesulfinyl chloride) after refluxing a methylene chloride solution of **2a** for 1.5 h followed by vacuum distillation (bp 75 °C (0.05 mm)), is a pale yellow oil homogeneous by capillary GC and showing the absence of an S=O group or other functionality other than C=C in the IR.¹⁰ Similarly, 4-methyl-2-oxa-3-thiabicyclo[3.3.0]oct-

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