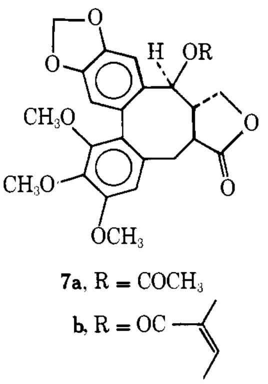

7a, R = COCH$_3$

b, R = OC

It has been demonstrated[10] that phenylcopper and deuterioiodobenzene in a coordinating solvent such as pyridine or quinoline give a nearly statistical distribution of labeled and unlabeled biphenyl, whereas, in a weakly coordinating solvent (DMF), biphenyl forms by phenylcopper disproportionation.

We have found that it is necessary for the intramolecular stabilizing ligands to be present.[11] When aryl Cu^I **1a** was treated with an equivalent of iodobenzene, unsymmetrical coupling was repressed in favor of symmetrical coupling, **5a**, by aryl Cu^I disproportionation.[12] The biaryls **5a** and **5b** were found to be by-products (<5% of the crude hydrolyzed reaction mixture, HPLC analysis) in entries 3 and 4, respectively.

The mechanism is viewed as an oxidative addition[13] of the arylimine iodide to the copper reagent to form an intermediate (arylimine)$_2$Cu^{III}I-d_8 species which collapses to product and CuI·L.[14]

Typical reaction conditions are as follows (entry 3). In a flame-dried flask equipped with a serum cap and N_2 inlet is dissolved 310 mg (1 mmol) of 6-bromopiperonalcyclohexylimine[15] in 5 ml of THF (from sodium benzophenone ketyl) followed by cooling to −78 °C (CO_2–acetone bath). To the magnetically stirred solution was added via syringe 0.52 ml (1.10 mmol) of 2.1 M BuLi in hexane (Ventron). After the yellow solution had been stirred for 15 min, addition of 535 mg (1.5 mmol) of solid CuI·$(C_2H_5O)_3P$[16] formed a homogeneous orange-red solution. After an additional 15 min, 357 mg (1 mmol) of 2-iodopiperonalcyclohexylimine[15] was added as a solid, the bath was removed, and the reaction mixture allowed to warm to room temperature while stirring was continued for 5 h. The reaction mixture was diluted with methylene chloride and washed continuously with concentrated NH_4OH (until the aqueous washes were no longer blue) followed by successive washing with water and saturated brine. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated providing 623 mg of oil which was subsequently hydrolyzed in 10 ml of CH_2Cl_2 and 10 ml of 10% aqueous HCl at reflux for 1 h. Separation of the layers followed by workup (vide supra) gave 356 mg of foam. Integration (NMR) of the aldehyde resonances (δ 9.67 and 9.73) against a known quantity of freshly distilled benzaldehyde (δ 10.00) indicated a yield of 86%. The residue was percolated through a short column of silica gel (1:1 THF/hexane) followed by HPLC purification (40% THF/hexane, E. Merck Silica Gel 60H). The combined biaryl fractions (253 mg) were crystallized from ethanol to provide 148 mg (58%) of **5c**, mp 146.5–148.5 °C (corr.).

Acknowledgment. We wish to thank the National Institutes of Health (CA 16432) and Hoffmann-La Roche for financial support of this work.

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(1) For a recent review of the Ullmann reaction and related copper chemistry, see (a) J. F. Normant, *Synthesis*, 63 (1972), and (b) P. E. Fanta, *ibid.*, 9 (1974).

(2) For related biaryl forming reactions under mild conditions, see (a) A. I. Meyers and E. D. Mihelich, *J. Am. Chem. Soc.*, **97**, 7383 (1975), and (b) T. Cohen and I. Cristea, *ibid.*, **98**, 748 (1976).

(3) Reagent **2a** failed to couple with 6-iodopiperonal and 3,4-methylenedioxy-6-iodoacetophenone. A coupling with methyl 3,4-methylenedioxy-6-iodobenzoate was partially successful (30% of aldehydo-ester isolated). The *anti-O*-methyloxime of 3,4-methylenedioxy-6-iodoacetophenone coupled efficiently on the basis of the NMR spectrum of the crude reaction mixture.

(4) All new compounds gave satisfactory combustion analyses and spectra. Known compounds were in accord with literature data.

(5) Reference **2a** and earlier papers in the series.

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(14) Cohen and Cristea[2b] have demonstrated that the formation of biaryl from *o*-bromonitrobenzene with cuprous triflate (excess) in aqueous ammonia obeys the rate equation $d[Ar_2]/dt = k_{Ar_2}[ArBr]^2[Cu^I]$, indicating that an initially formed ArCu^{III}Br species is not reduced to the Cu^I state prior to reacting with a second molecule of ArBr. This is an isoelectronic equivalent of the Ni(0) coupling of aryl halides.[6] This observation does not preclude oxidative addition to a Cu^I species from occurring when the opportunity arises.

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(17) National Institutes of Health Career Development Awardee, 1973–1978.

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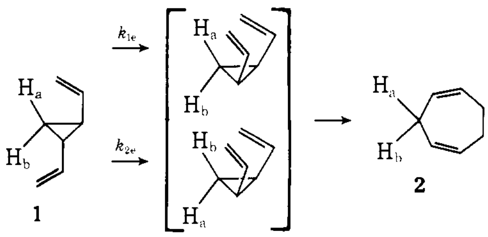
Thermal Isomerization of (−)-(1*R*,5*R*)-6-*exo*-Vinylbicyclo[3.1.0]hex-2-ene to (−)-(1*R*,5*R*)-Bicyclo[3.2.1]octa-2,6-diene: One-Center Thermal Epimerization of a Cyclopropane

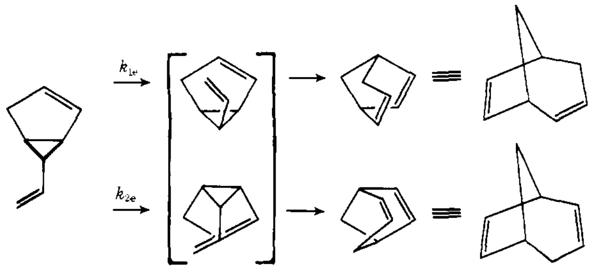
Sir:

trans-1,2-Divinylcyclopropane at 190 °C gives rise to 1,4-cycloheptadiene;[1] this net result and related data for other *trans*-1,2-dialkenylcyclopropanes have been interpreted in terms of geometrical isomerization to give short-lived *cis*-1,2-dialkenylcyclopropanes which in turn suffer rapid Cope rearrangements.[2-4] Whether the geometrical isomerization is a one-center epimerization or a two-center process has not been addressed experimentally. For *trans*-divinylcyclopropane (**1**), a two-center epimerization leading to racemization is kinetically competitive with the trans-to-cis geometrical isomerization,[4] but the latter could well be either a one-center or a two-center event.



Recent work on (+)-1,2-*trans*-dideuteriocyclopropane[5] and both antipodes of *trans*-1-phenyl-2-deuteriocyclopropane[5] indicated exclusive or nearly exclusive epimerization through two-center processes. Kinetic work on deuterium labeled and optically active versions of 1-methylspiro[2.4]hepta-4,6-diene demonstrated that one-center epimerization at the spiro carbon atom was definitely not prominent; the three experimental rate constants for distinct cyclopropane geometrical isomerizations could be accommodated with the three two-center epimerization rate constants.[6]

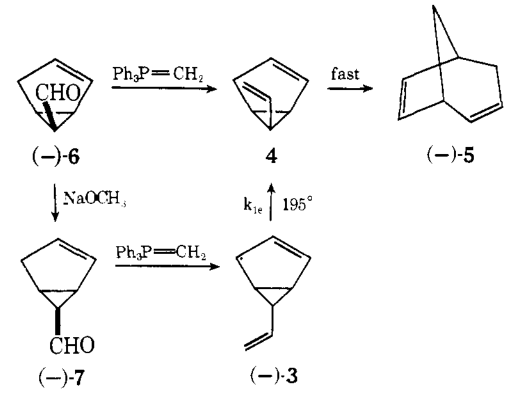
We sought to learn whether a particular *trans*-1,2-divinylcyclopropane, 6-*exo*-vinylbicyclo[3.1.0]hex-2-ene (**3**), isomerizes to the 6-endo isomer **4** through a one-center epimerization, at C(6), or a two-center epimerization, at C(1) and C(5). This choice of substrate would permit a quantitative determination of k_{1e} and k_{2e} through comparison of absolute stereochemistry and relative optical purity of substrate and final product, bicyclo[3.2.1]octa-2,6-diene (**5**).



endo-Bicyclo[3.1.0]hex-2-ene-6-carboxaldehyde (±-**6**), prepared through peracetic or *m*-chloroperbenzoic acid oxidation of norbornadiene,[7] was combined with 0.5 equiv of *l*-(−)-ephedrine. The unreacted aldehyde was recovered, purified, and found to be optically active, $[\alpha]_D$ −54.4° (*c* 1.01, $CHCl_3$). Wittig condensation[8] converted a portion of this aldehyde to bicyclo[3.2.1]octa-2,6-diene, (−)-**5**, $[\alpha]_{365}$ −77.0 ± 0.4°; another portion with sodium methoxide in methanol[9] at reflux for 1.5 h gave rise to the exo-aldehyde (−)-**7**, $[\alpha]_D$ −60.4°, which was converted to 6-*exo*-vinylbicyclo[3.1.0]hex-2-ene, (−)-**3**, $[\alpha]_{365}$ −283.1 ± 0.3°, through another Wittig reaction (see Scheme I).

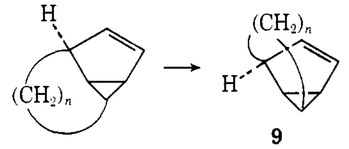
The absolute configurations for these molecules are indeed as formulated below. (−)-Bicyclo[3.2.1]octa-2,6-diene was reduced with diimide to afford (+)-(1*R*,5*R*)-bicyclo[3.2.1]oct-2-ene.[10] (−)-*exo*-6-Vinylbicyclo[3.1.0]hex-2-ene and the stereochemically analogous (−)-(1*S*,1*S*)-*trans*-divinylcyclopropane,[4,11] have very similar ORD spectra from 365 to 589 nm. In the absence of other strong chromophores in the two molecules compared, the ORD spectra should reflect absolute stereochemistry reliably.[12]

Scheme I



Pyrolysis of (−)-*exo*-6-vinylbicyclo[3.2.0]hex-2-ene at 195 °C for 1 h in a sealed, degassed ampoule gave (−)-bicyclo-[3.2.1]octa-2,6-diene, $[\alpha]_{365}$ −75.8 ± 0.3. Thus, within limits much smaller than probable experimental imprecisions, the entire reaction follows the one-center epimerization alternative; $k_{2e} = 0$.

Although bicyclo[3.1.0]hex-2-ene exhibits the two-center epimerization process along with 1,3-sigmatropic shifts of the C(1)–C(5) bond,[13] the 6-*exo*-vinyl system **3** shows only the one-center epimerization. Dauben and Kellogg[14] found that the thermal rearrangement **8** → **9**, restricted by geometrical constraints to the one-center epimerization mode, did occur, while in cyclopropane and phenylcyclopropane,[5] systems without such constraint and free to rearrange by either mode, two-center epimerization is the exclusive or nearly exclusive operative process. The present results demonstrate clearly for the first time one-center epimerization in a cyclopropane for which an alternative two-center option is geometrically feasible and gives the thermodynamically undisadvantaged, enantiomeric product.



n = 4 or 5

Similar work with other constrained *trans*-divinylcyclopropanes, monocyclic *trans*-divinylcyclopropanes, and derivatives of vinylcyclopropane itself will be needed to discover the minimal structural features facilitating kinetic dominance of one-center over two-center epimerizations in cyclopropanes.

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Structural Studies of Tautomeric Systems: the Importance of Association for 2-Hydroxypyridine–2-Pyridone and 2-Mercaptopyridine–2-Thiopyridone

Sir:

The fact that the positions of tautomeric equilibrium for hydroxypyridines–pyridones and related systems are reversed by transfer from polar solvents to the vapor has been established recently.[1] The usual procedure for eliminating solvation effects of polar solvents, and thereby to approach the vapor phase environment, is to use dilute solutions in nonpolar solvents.[2] We wish to report that due to dominating association effects this approach succeeds in the case of 2-hydroxypyridine