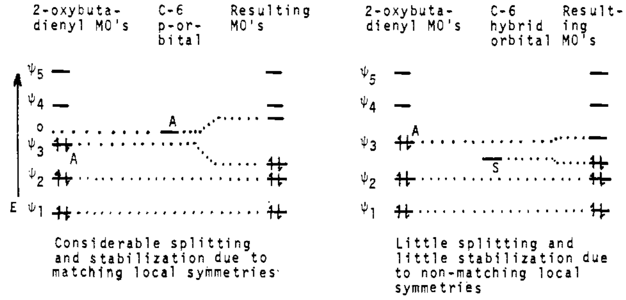
$\psi_3$ and p-orbital of 14i $\psi_3$ and sp$^2$ orbital of 13



E represents energy in units of |β|. S and A refer to local symmetry.

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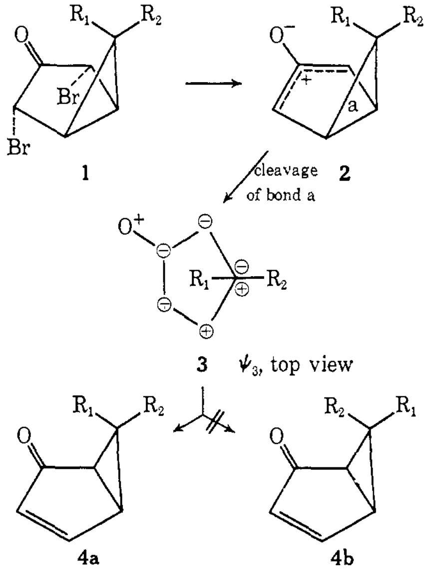
## Stereochemistry of a 1,4-Sigmatropic Rearrangement[1]

*Sir:*

Insight into the mechanism of thermal unimolecular reactions has been enormously increased by the concept of conservation of orbital symmetry, introduced by Woodward and Hoffmann.[2] In one group of reactions, defined as sigmatropic transformations, a σ-bonded atom or group migrates from one end of a conjugated chain to the other. When the highest occupied molecular orbital of the conjugated system across which migration occurs is antisymmetric, conservation of orbital symmetry in a concerted reaction requires that the migrating group must also undergo an antisymmetric transformation. The group either transverses the nodal plane of the skeleton (antarafacial motion) or suffers an inversion of configuration above the nodal plane (suprafacial motion).[3] No examples of antarafacial migration have yet been observed, but recently Berson and Nelson[4] reported a suprafacial 1,3-sigmatropic rearrangement which proceeded with inversion of configuration in the asymmetric migrating group. We report here a stereochemical study of a 1,4-sigmatropic rearrangement in which migrating carbon also undergoes inversion of configuration.

The system under investigation is the symmetrical Favorskii-like intermediate, usually depicted as the zwitterion 2, derived from bicyclo[3.1.0]hexan-3-ones (1). This species, suggested earlier as an intermediate in the photochemical rearrangement of cyclohexadienones, has been generated recently by nonphotochemical methods (treatment of the bromo ketone with base or of the dibromo ketone with zinc) and shown to rearrange[5] to bicyclo[3.1.0]hex-3-en-2-ones (4). The conjugated system over which migration occurs may be considered a 2-oxobutadiene skeleton. Calculation of the symmetry properties of the Hückel molecular orbitals of 3 shows that, whether or not the effect of the oxygen is included, the highest occupied molecular orbital ($\psi_2$ of butadiene or $\psi_3$ of 2-oxobutadiene) is antisymmetric. Thus a concerted suprafacial rearrangement requires *inversion* of configuration of the migrating group, leading to **4a**.

Experimental verification of this predicted mode of rearrangement has been achieved by stereospecific synthesis of one isomer of type 1 ($R_1$ = $CH_2C_6H_5$; $R_2$ = $C_6H_5$) and of reduced derivatives of product **4a**. Diazo ester 5, prepared by treatment of cyclopent-3-en-1-ol with the *p*-toluenesulfonylhydrazone of phenylglyoxalyl chloride in the presence of triethylamine,[6] was cyclized (by a catalytic mixture of copper, cuprous oxide, and cupric sulfate in refluxing toluene) to lactone 6, mp 120–121°; ν 1710 cm$^{-1}$. Reaction with phenyllithium gave hemiketal 7, mp 152–154°, which was reduced with $LiAlH_4$ to ether 8, mp 75–78°, and further by sodium–ethanol in liquid ammonia to alcohol 9, mp 102–105°. Chromic acid oxidation gave the requisite ketone 10, ν 1740 cm$^{-1}$, of unambiguous stereochemistry. Bromination in acetic acid gave dibromide 11,[7] which rearranged almost quantitatively to 12, ν 1690 cm$^{-1}$, on treatment with zinc in refluxing dioxane. The product was judged homogeneous by the appearance of only one spot in several tlc systems and particularly by the single sharp benzyl methylene absorption in the nmr spectrum of the total crude product.



**4a**
(inversion)

**4b**
(retention)

To facilitate comparison, 12 was hydrogenated over Raney nickel to the corresponding saturated ketone, ν 1720 cm$^{-1}$, and then reduced to the crystalline alcohol

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(1) This work was supported in part by a research grant (GP-3811) from the National Science Foundation, to whom the authors express their thanks.

(2) R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87**, 2511 (1965). For recent surveys, see (a) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968); (b) R. B. Woodward, "Aromaticity," Special Publication No. 21, The Chemical Society, London.

(3) For a detailed discussion of this question, see J. A. Berson, *Accounts Chem. Res.*, **1**, 152 (1968).

(4) J. A. Berson and G. L. Nelson, *J. Am. Chem. Soc.*, **89**, 5503 (1967).

(5) H. E. Zimmerman, D. Döpp, and P. S. Huyffer, *ibid.*, **88**, 5352 (1966).

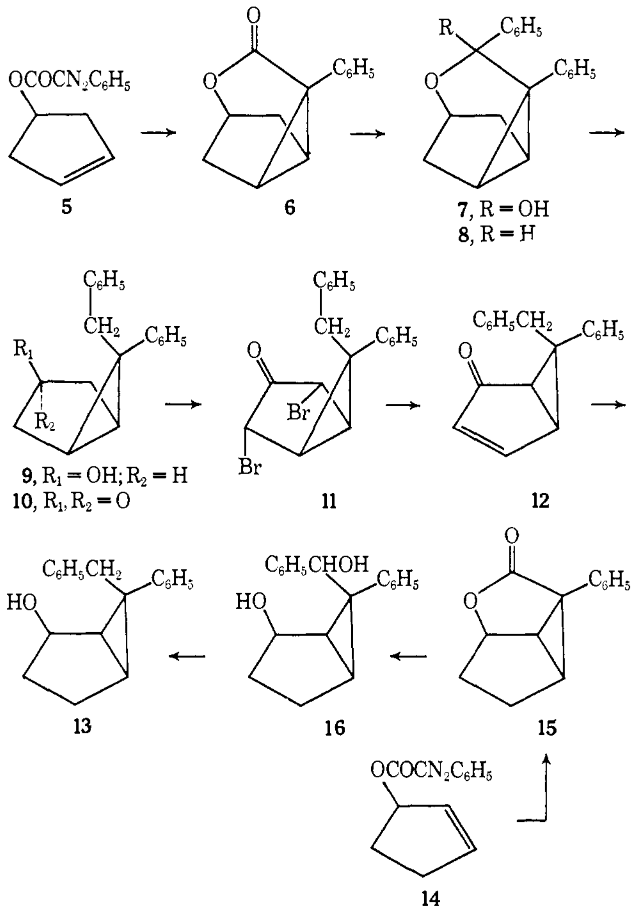
(6) This synthesis was patterned after the method developed by H. O. House and C. J. Blankley, *J. Org. Chem.*, **33**, 53 (1968).

(7) Both bromines are assigned *exo* configurations because of nmr identity of protons at $C_2$ and $C_4$ and the lack of coupling between protons at $C_1$ and $C_2$.

**13**, mp 104–106°, with lithium tri-*t*-butoxyaluminum hydride. This alcohol was synthesized independently by an analogous route, involving cyclization of the diazo ester **14** derived from cyclopent-2-en-1-ol to lactone **15**, $\nu$ 1760 cm$^{-1}$, reaction with phenyllithium, $LiAlH_4$ reduction to diol **16**, mp 146–148°, and finally sodium-ammonia reduction to **13**. The samples of **13** produced by these two routes showed no melting point depression on admixture and had identical infrared and nmr spectra.

In agreement with the configurations assigned to these compounds is the downfield shift of the benzylic methylene group in the nmr spectra of alcohols **9** ($\delta$ 3.21) and **13** ($\delta$ 3.40) relative to its position in ketones **10** ($\delta$ 2.85) and **12** ($\delta$ 3.05).

The inversion of configuration at migrating carbon in this 1,4-sigmatropic shift provides yet another example in a previously unstudied system of the predictive powers of orbital symmetry correlations.



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## Carbon–Carbon Bond Formation by Selective Coupling of *n*-Alkylcopper Reagents with Organic Halides

*Sir:*

Two new methods for carbon–carbon bond formation between unlike groups derived from an organic halide and an organo–transition metal derivative have recently been described.[1,2] One of these is generally effective for allyl-nonallyl coupling and involves the use of $\pi$-allylhalonickel complexes;[1] the other utilizes as reagent the product from the interaction of an alkyllithium compound with cuprous iodide in a molar ratio 2:1.[3,4] The copper method was shown to have broad applicability for a wide variety of halides of the C(sp$^2$)–Hal as well as C(sp$^3$)–Hal type, using the reagent derived from methyllithium. This communication is concerned with the extension of the coupling reaction to *n*-alkylcopper reagents which demonstrates generality for the primary alkyl organometallic class.

Addition of *n*-butyllithium (Foote Mineral Co., hexane solution) to an ethereal suspension of cuprous iodide[5] at −20° leads to formation of a dark insoluble product at a 1:1 molar ratio which by analogy with previous work probably corresponds to $(RCu)_n$. The precipitate dissolves upon addition of a second equivalent of *n*-butyllithium to give a brown-black solution probably containing a solvated complex species; both this reagent (arbitrarily described below as $R_2CuLi$) and the insoluble 1:1 mixture respond negatively in the test for free alkyllithium using Michler's ketone.[6] In the butyl series, as found previously for the methyl series,[2] $R_2CuLi$ is considerably *more* reactive toward organic halides than is $(RCu)_n$ and also much more efficient in cross-coupling. Dark 2:1 complexes of type $R_2CuLi$ have also been prepared from ethyllithium and *n*-heptyllithium in a manner analogous to the butyl case. Since the reactions of these three reagents with halides have been found to be closely similar, one case, R = *n*-butyl, was selected for intensive study.

The reaction of lithium di-*n*-butyl- or diethylcopper[7] reagents (*ca.* 0.25 *M*, 5 molar equiv) with a number of halides in ether as solvent led to efficient cross-coupling as indicated, for example, by eq 1–11, which also summarize experimental conditions.[8]

In general, the lithium di-*n*-alkylcopper reagents react more rapidly with halides than does lithium dimethylcopper, but they are also less stable thermally. They are also more apt to produce halogen–copper exchange as a side reaction (*i.e.*, R–Hal → R–Cu) than is lithium dimethylcopper. Such exchange, especially serious with the starting halides of eq 8, 9, and 11, can be nullified by a subsequent addition to the reaction mixture of an excess of the alkyl halide corresponding to the *n*-alkylcopper reagent. Without such treatment the

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(1) E. J. Corey and M. F. Semmelhack, *J. Am. Chem. Soc.*, **89**, 2755 (1967).

(2) E. J. Corey and G. H. Posner, *ibid.*, **89**, 3911 (1967).

(3) H. Gilman, R. G. Jones, and L. A. Woods, *J. Org. Chem.*, **17**, 1630 (1952).

(4) H. Gilman and J. M. Straley, *Rec. Trav. Chim.*, **55**, 821 (1936).

(5) All reactions involving organometallic reagents were carried out with the usual precautions for rigorous exclusion of air and moisture.

(6) H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, 47, 2002 (1925).

(7) The use of this designation is not intended to carry structural implications. One intriguing possibility is that the dimeric species $[R_4Cu_2Li_2]$ might predominate because it can adopt a tetrahedral structure analogous to that of $[CH_3Li]_4$ with two Li being replaced by two Cu (for $[CH_3Li]_4$ see E. Weiss and E. A. C. Lucken, *J. Organometal. Chem.*, **2**, 197 (1964)). If the dominant species is the monomeric complex $[R_2CuLi]^-$, a structure analogous to $[C_2H_5Li]_2$ (H. Dietrich, *Acta Cryst.*, **16**, 681 (1963)) would appear to be plausible. Clearly, physical studies on these copper reagents in solution are in order.

(8) In all cases products were analyzed by gas chromatography (gc), isolated, and characterized. Previously described compounds were compared by gc and nmr and infrared spectroscopy with authentic samples. New compounds were purified by gc and characterized by nmr, infrared, and mass spectroscopy.