junenol (**13**), mp 90–92°, identical by spectral and chromatographic comparison with an authentic[15] sample of **13**. Selective hydrogenation of the isopropenyl group of **12c** [$(Ph_3P)_3RhCl$ in benzene], followed by photoisomerization (450-W medium-pressure lamp, unfiltered, 40 hr in degassed benzene) of the endocyclic double bond,[17] gave (±)-junenol[9] (**1**), mp 77.5–79°, in 65% overall yield. The synthetic material was indistinguishable from authentic[16] (+)-junenol in its ir, nmr, and mass spectra, as well as in tlc and gas chromatographic behavior.

The mixed bicyclic alcohols **12a** and **12b** were subjected to selective reduction of the isopropenyl group, Jones oxidation, and base-catalyzed equilibration[18] (KOH in aqueous ethanol, 37 hr at 25°) to give a mixture containing 42% of the α,β-unsaturated ketone **14**,[9a] 26% of its C-7 epimer **15**,[9a] and 32% of epimeric β,γ-unsaturated ketones (determined by gas chromatography). Resubmission of **15** to the equilibration conditions gave the same mixture. Catalytic hydrogenation (10% Pd/C) of **14** and reduction (sodium–ethanol) of the resulting saturated ketone[18] afforded (±)-dihydrojunenol (**13**),[9] indistinguishable from the material prepared above.

We are continuing investigations into the utilization of this general approach in the synthesis of other eudesmanoid sesquiterpenes.

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[15] Prepared by catalytic reduction[3a] of authentic (+)-junenol.[16]

[16] We thank Professor S. C. Bhattacharyya, Indian Institute of Technology, Bombay, and Professor N. H. Andersen, University of Washington, Seattle, for providing us with authentic samples of (+)- and (−)-junenol, respectively.

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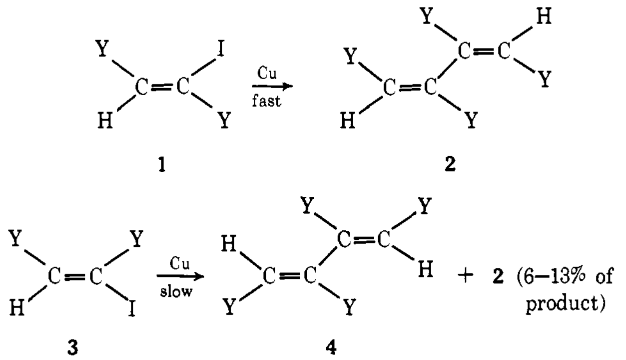
Copper-Induced Coupling of Vinyl Halides. Stereochemistry of the Ullmann Reaction[1]

Sir:

Evidence has been presented that organocopper compounds are intermediates in the copper-induced coupling of aryl halides.[2] We now report the Ullmann coupling of vinyl halides and the stereochemistry of this reaction. Utilizing activated[3] copper powder, we have found that *cis*- and *trans*-bromostilbene, diethyl bromo- and iodomaleate,[4] and diethyl bromo- and iodofumarate[4] couple in the melt. The most stereochemical information was derived from the iodo esters which are stereochemically stable to the reaction conditions.

Coupling of the iodofumarate (**1**) at 100° was complete in 12 hr and led, after work-up, to a 96% isolated yield of gas chromatographically pure *trans,trans*-1,2,3,4-tetracarbethoxy-1,3-butadiene (**2**).[6] At 100°, the coupling of the iodomaleate (**3**) was complete at the end of 48 hr and yielded 89% of pure tetraester which consisted of 87% *cis,cis*-butadiene (**4**)[6] and 13% of the trans,trans isomer **2**.[7] At 75°, the iodomaleate coupling gave a product which contained 94% of **4** and 6% of **2**, while the iodofumarate gave pure **2**. The cis,cis isomer **4** underwent 15% isomerization to the trans,trans product **2** when heated at 100° for 24 hr, but only in the presence of the iodo ester **3**; it is probable that the **2** produced from **3** results from such product isomerization.



Y = CO_2Et

When two parts of iodomaleate (**3**) and one part of iodofumarate (**1**) were heated at 75° with copper until the **1** had nearly completely reacted, the product was pure trans,trans ester **2**.

These results support the concept that the products are formed by coupling of organocopper intermediates[2] rather than of radicals.[8] The stereochemical instability of the latter[10] renders unlikely their intermediacy in such highly stereoselective reactions. On the other hand, simple vinylic organocopper compounds have been shown to be fairly stable stereochemically and to couple stereospecifically with configurational retention at temperatures of 25–90°.[10] The self-coupling of the iodofumarate in the presence of an excess of the slower reacting iodomaleate indicates that in this case, as in the coupling of *p*-iodotoluene in quinoline solution,[11] the organocopper intermediate probably undergoes self-coupling rather than coupling with unreacted organoiodide.

When diethyl iodofumarate (**1**) and diethyl iodomaleate (**3**) were separately heated with copper and benzoic acid, the major products were stereochemically pure diethyl fumarate and diethyl maleate, respectively. If, as seems likely, these diesters are produced by pro-

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[1] This work was supported by Grant No. GP-22955 from the National Science Foundation.

[2] A. H. Lewin and T. Cohen, *Tetrahedron Lett.*, 4531 (1965).

[3] A. H. Lewin, M. J. Zovko, W. H. Rosewater, and T. Cohen, *Chem. Commun.*, 80 (1967).

[4] Diethyl iodomaleate was prepared from iodomaleic anhydride which was very conveniently obtained by treatment of bromomaleic anhydride (Aldrich) with sodium iodide in acetone. Diethyl iodofumarate was prepared by esterification of the acid which was obtained by the addition of HI to acetylenedicarboxylic acid.[5]

[5] J. Thiele and W. Peter, *Justus Liebigs Ann. Chem.*, 369, 119 (1909).

[6] (a) The gross structures of the tetraesters were adduced from elemental analysis and mass and pmr spectra and their stereochemistry was assigned on the basis of the latter. The vinyl protons of the trans,trans ester 2 absorb at τ 3.17 and those of the cis,cis isomer 4 at τ 4.00. These chemical shifts are identical within experimental error with those reported for a mixture of the stereoisomers[6b] and they correspond to the absorptions at τ 3.22 and 3.77 for the vinyl protons of diethyl fumarate and diethyl maleate, respectively. (b) A mixture of two or possibly three isomers of this compound has been prepared in very poor yield by a long synthetic sequence: H. Hopff and R. V. Rütte, *Helv. Chim. Acta*, 49, 329 (1966).

[7] The absence of the (unavailable) cis–trans isomer in the product is surmised from the two, sharp, widely separated gas chromatographic peaks (corresponding to 2 and 4) which were exhibited on five different columns.

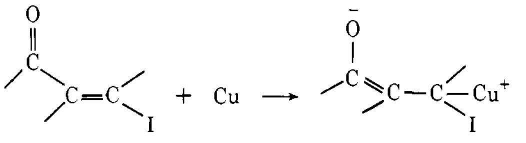
[8] Fanta[9] has reviewed the arguments for both types of mechanism.

[9] P. E. Fanta, *Chem. Rev.*, 64, 613 (1964).

[10] G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Amer. Chem. Soc.*, 93, 1379 (1971).

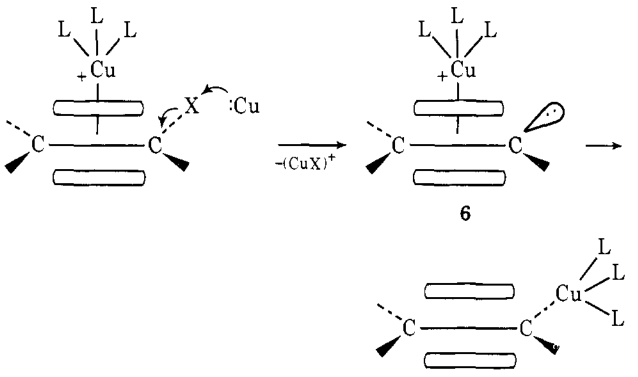
[11] A. H. Lewin and T. Cohen, unpublished results.

tolysis of an organocopper intermediate,[2] then formation and protolysis of the latter must occur with complete retention of configuration; the alternative hypothesis, that both processes occur with inversion, is unlikely in view of the coupling results. The stereospecific conversion of the iodides to organocoppers renders unlikely not only a radical course[12] for the first stage in the reaction but also a mechanism involving nucleophilic displacement of the iodide by a copper atom,[9] since the resulting intermediate (5) would presumably be capable of rotation about the single bond with consequent loss of stereochemistry.



5

A close similarity exists between the Ullmann coupling and the copper–quinoline decarboxylation.[13] The rates of both reactions are enhanced by most substituents on the benzene ring,[9,14] strong electron-attracting ortho substituents such as the nitro group being most effective.[9,13-15] Both reactions appear to involve organocopper intermediates[2,13-15] and they proceed with a high degree of retention of configuration when applied to vinyl systems.[14] Cuprous ion is the catalyst in the decarboxylation and, although copper metal is usually used in the Ullmann coupling, cuprous oxide has frequently been found effective;[16] when copper is used in the coupling it is strongly activated by washing it with complexing agents, a procedure which is thought to result in a copper surface coated with readily accessible cuprous oxide.[3] Both reactions are strongly promoted by heterocyclic complexing agents such as quinoline and pyridine when used as solvents.[2,14-16] All this suggests that the mechanism previously proposed for the decarboxylation[14] may by suitable modification be applicable to the conversion of the aryl or vinyl halide to an organocopper.



6

L = ligand

The π complexing of a cuprous ion may inductively increase the stability of the σ anion 6 and thereby increase its rate of formation. In the decarboxylation, the carboxylate group (X) can readily eject carbon dioxide, leaving behind the electron pair, whereas halogen, which is very unstable as the cation, must accept a pair of electrons from a copper atom or cuprous ion before it can generate the anion 6.

The synthetic potential of the coupling of vinyl halides is obvious.[17] A further attractive feature of this reaction is the potential utilization of the vinylcopper intermediates in some of the wide variety of carbon–carbon bond forming reactions which have recently been discovered for organocopper compounds.[18] Those vinyl halides which would most readily undergo the copper–halogen exchange are just those (bearing groups such as carbethoxy and nitro) which cannot be converted to organocopper compounds by the standard procedure *via* organolithium or Grignard reagents.

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(19) National Defense Education Act Fellow.

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Chloroperoxidase. IX. The Structure of Compound I[1]

Sir:

The nature of peroxidase and catalase compound I (I), the initial intermediate observed spectrally in the reaction of these heme enzymes with hydrogen peroxide, has been the subject of intense research for many years.[2-15] In this communication, we report ^{18}O studies with chloroperoxidase (CPO) and a peracid substrate which allow us to suggest a definite chemical composition for I.

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