taken as the binuclear radical-cation VIII, formed via precursor complex VII (which cannot be chelated), the latter is present only at small steady-state concentrations, whereas conversion to VIII is very nearly complete. Intermediate VIII appears then, in the presence of excess Cr^{2+} , to be attacked by a second Cr^{2+} (very probably at one of the ring nitrogens).⁵

Complex VI is thus similar to I in that both heterocyclic systems readily accept an electron from Cr^{2+} to form a moderately stable radical-cation which can undergo internal electron transfer with reduction of Co(III). The cinnoline reduction is, however, complicated by the availability of an additional site at which further rapid external reductive attack may occur. Work is continuing in an effort to define the structural features within the ligand which favor one or the other type of behavior.^{7,9}

Acknowledgments. Sponsorship of the Petroleum Research Fund, administered by the American Chemical Society under Grant 2868-A3, is gratefully acknowledged. Thanks go also to Professor William Movius for valuable discussions.

(5) Further elaboration of Scheme II is necessary to accommodate the earlier finding^{1b} that when oxidant VI is in excess, just 1 equiv of Co^{2+} is eventually produced for each equivalent of Cr^{2+} taken. The alternatives appear to be a second, intramolecular path for reduction of Co(III) in VIII, which becomes important when only a deficiency of Cr^{2+} is taken, or, less likely, a slow reduction of Co(III) in VI by radical cation IX, in a manner similar to that proposed for radical-cations in the pyridine series.⁶

(6) C. Norris and F. R. Nordmeyer, J. Amer. Chem. Soc., 93, 4044 (1971); J. R. Barber, Jr., and E. S. Gould, *ibid.*, 93, 4045 (1971).

(7) Although the rates of formation of the strongly absorbing intermediates derived from oxidants I and VI are independent of acidity in the (H⁺) range 0.12–1.20 *M*, the rates of disappearance of these species are acid-dependent but in opposite directions. The fading of the intermediate from I is 0.7 times as rapid in 0.12 *M* HClO₄ ($\mu = 1.22$) as in 1.2 *M* HClO₄, whereas the intermediate from VI disappears about twice as rapidly at the lower acidity. These trends correspond to those observed in the Cu⁺ reductions of these complexes⁸ and are in accord with the suggestion that protonation of the 4-nitrogen in the pyrazine complex facilitates electron transfer to Co(III) within a dinuclear intermediate, whereas with the cinnoline complex, H⁺ and the reducing metal center compete for a basic "lead-in" site.

(8) E. R. Dockal, E. T. Everhart, and E. S. Gould, J. Amer. Chem. Soc., 93, 5661 (1971).

(9) A similar, but much more short-lived, Co(III)-bound radicalcation intermediate has recently been characterized in the e_{aq} reduction of *p*-nitrobenzoatopentaamminecobalt(III) by M. Z. Hoffman and M. Simic, *ibid.*, 94, 1757 (1972). These authors report a specific rate of 2600 sec⁻¹ for internal electron transfer, at pH 5.5–7.7, but there is evidence¹⁰ that this radical-cation may be greatly stabilized by conversion to its conjugate acid in 1.2 *M* HClO₄.

(10) E. S. Gould, ibid., 88, 2983 (1966).

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Synthesis of an Optically Active α -Aminophosphonic Acid

Sir:

Although various syntheses for α -aminophosphonic acids have been known for several years, ¹⁻³ an optically active acid has not been reported to date. We wish to report the synthesis of the first optically active α -aminophosphonic acid. We have succeeded in preparing

(1) M. E. Chalmers and G. M. Kosolapoff, J. Amer. Chem. Soc., 75, 5278 (1953).

(2) K. D. Berlin, R. T. Claunch, and E. T. Gaudy, J. Org. Chem., 33, 3090 (1968).

(3) J. R. Chambers and A. F. Isbell, ibid., 29, 832 (1964).

both enantiomers of α -aminobenzylphosphonic acid and we wish in further work to develop this synthesis into a general procedure for preparing the optically active phosphonic acid analogs of various amino acids.

The α -aminobenzylphosphonic acid enantiomers 5 were prepared by condensing benzaldehyde with either (R)-(+)- or (S)-(-)- α -methylbenzylamine (1) to form the respective Schiff's base 2. The diethyl ester 3 was prepared by heating a mixture of 2 with diethyl hydrogen phosphonate at 140° for 1 hr.⁴ The ester was hydrolyzed in concentrated HCl and evaporated to dryness. Treatment of the hydrochloride salt dissolved in a minimum amount of water with propylene oxide⁵ gave 4. The final product 5 was obtained by hy-



drogenolysis of the α -methylbenzyl group on a lowpressure Paar hydrogenator using 10% Pd(OH)₂/C⁶ in glacial acetic acid at room temperature. Removal of the acetic acid gave a solid mass which was recrystallized from water-ethanol. Physical properties of both enantiomers were identical with the known racemic acid.^{4°} Synthesis of **5** with (S)-(-)- α -methylbenzylamine gave the dextrorotatory enantiomer, $[\alpha]^{25}D$ +18.1° (c 2.0, 1 N NaOH), and the (R)-(+)-amine gave the levorotatory enantiomer, $[\alpha]^{25}D$ -18.1° (c 2.0, 1 N NaOH). Preliminary testing of each isomer with D-amino acid oxidase has failed to give an indication of absolute configuration.

Acknowledgment. We are grateful to the American Foundation for Pharmaceutical Education and the Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, for their support of this work.

(4) (a) E. K. Fields, J. Amer. Chem. Soc., 74, 1528 (1952); (b) A.
N. Pudovik, Dokl. Akad. Nauk SSSR, 83, 865 (1952); Chem. Abstr., 47, 4299 (1953); (c) R. Tyka, Tetrahedron Lett., 677 (1970).

(5) K. D. Berlin, N. K. Roy, R. T. Claunch, and D. Bude, J. Amer. Chem. Soc., 90, 4494 (1968).
(6) W. M. Pearlman in "Reagents for Organic Synthesis," L. F.

(6) W. M. Pearlman in "Reagents for Organic Synthesis," L. F. Fieser and M. Fieser, Ed., Wiley, New York, N. Y., 1967, p 782.

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Biogenetically Patterned Approaches to Eudesmane Sesquiterpenes. A Total Synthesis of (\pm) -Junenol

Sir:

Nonenzymic cationic cyclizations of farnesol derivatives have been extensively investigated as a means for accomplishing biogenetic-type syntheses of sesquiterpenes.¹ While several representatives of sesquiterpene

(1) E. E. van Tamelen, Fortschr. Chem. Org. Naturst., 19, 242 (1961), and references therein.



The generally accepted biogenesis of eudesmane sesquiterpenes involves first cyclization of farnesyl pyrophosphate to a cyclodecadiene (germacrane class), followed by further cationic cyclization to the required skeleton⁴ (Scheme I, path a). Although the second



step of this sequence has been demonstrated⁵ to proceed nonenzymically with great facility, our efforts to duplicate the initially required cyclization have proved futile.6 We therefore examined the feasibility of an alternate approach to the eudesmane skeleton as outlined in path b of Scheme I.

The stereoisomeric mixture of methyl farnesates (2) was obtained from commercial farnesol by oxidation and esterification. Cationic cyclization of 2 initiated at the central double bond⁷ was smoothly effected by treatment of it with excess Lucas reagent⁸ (ZnCl₂-HCl, no cosolvent, vigorous stirring, 5 hr at 25°). The crude product, containing primarily the *tert*-chloride 3,^{9a} was treated sequentially with $ZnCl_2$ in water (12 hr at reflux) and anhydrous $ZnCl_2$ in benzene (4.5 hr at reflux with a water separator) to give after chromatographic separation the desired monocyclic ester 49 (54% from 2), its double bond isomer 5^{98} (16% from 2),

(2) (a) Y. Kitahara, T. Kato, T. Suzuki, S. Kanno, and M. Tane-mura, *Chem. Commun.*, 342 (1969); (b) S. Kanno, T. Kato, and Y. Kitahara, *ibid.*, 1257 (1967); (c) E. E. van Tamelen and R. M. Coates, ibid., 413 (1966); (d) W. Rittersdorf and F. Cramer, Tetrahedron, 24, 43 (1968).

(3) (a) V. Herout, O. Motl, and F. Sorm, Collect. Czech. Chem. Commun., 22, 785 (1957); (b) A. M. Shaligram, A. S. Rao, and S. C.

Bhattacharyya, *Tetrahedron*, **18**, 969 (1962). (4) J. B. Hendrickson, *ibid.*, **7**, 82 (1959); W. Parker, J. S. Roberts,

and R. Ramage, *Quart. Rev., Chem. Soc.*, 21, 331 (1967). (5) See, for example: T. W. Sam and J. K. Sutherland, *Chem. Commun.*, 970 (1971).

(6) M. A. Schwartz and T. J. Dunn, J. Amer. Chem. Soc., 94, 4205 (1972).

(7) Previous acid-catalyzed cyclization studies in this series have been reported to give solely products resulting from protonation of the terminal double bond.1,2

(8) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964, p 132.

(9) (a) Infrared, nmr, and mass spectral data for this compound were consistent with the assigned structure; (b) satisfactory combustion analytical or high-resolution mass spectral data were obtained for this compound.

and the bicyclic ester 6^{9a} (17% from 2).¹⁰ Reduction of 4 with LiAlH₄ (THF, 24 hr at reflux) afforded a 1:1 mixture of the epimeric monocyclofarnesols 7.9,11

The epimeric alcohols 7 could be separated by pre-



parative thin-layer chromatography (tlc) either before or after oxidation with $CrO_3 \cdot 2C_5H_5N$,¹³ to give the monocyclic aldehydes 11a^{9a} and 11b.^{9a} Cyclization of 11a and 11b separately with 0.35 mol equiv of SnCl₄ in benzene¹⁴ (1 hr at 25°) unfortunately proceeded without stereospecificity,¹⁴ giving the epimeric mixtures 12a and 12b, respectively; there was no indication that cyclization of 11a gave rise to any epimers of the cis series (12b) or that 11b gave any epimers of the trans series (12a). The desired isomer $12c^{9a}$ was isolated (18 % from 11a) by preparative tlc separation of mixture 12a. The assigned stereochemistry of 12c was verified by nmr analysis (δ 3.33 (t, J = 9.5 Hz, H-6)) and by catalytic hydrogenation (10% Pd/C) of it to (\pm) -dihydro-

(10) Direct dehydrohalogenation of 3 with KOH-CH₃OH afforded primarily the unwanted isomer 5; the above procedure involving conversion of 3 first to the corresponding tertiary alcohol and then to the alkene was therefore adopted.

(11) We initially prepared the epimeric monocyclofarnesols 7 by an alternate procedure. In view of the previous work,7 it at first seemed necessary to block the terminal double bond of 2 in order to realize the desired mode of cyclization. Consequently methyl farnesate mono-bromohydrin (8) was prepared¹² and submitted to the Lucas reagent; the resulting mixture of monocyclic dihalide 99a and vinyl bromide 109a was then treated with zinc dust in acetic acid-ether followed by LiAlH4 in refluxing THF to give 7 (54% from 8). However, subsequent consideration of a likely mechanism for the $ZnCl_2$ -HCl cyclization of 8 made it apparent that direct cyclization of 2 would be feasible. (12) E. E. van Tamelen, M. A. Schwartz, E. J. Hessler, and A. Storni,

Chem. Commun., 409 (1966); E. J. Hessler, Ph.D. Dissertation, Stan-(13) R. Ratcliffe and R. Rodehorst, J. Org. Chem., 35, 4000 (1970).

(14) J. A. Marshall, N. H. Andersen, and P. C. Johnson, ibid., 35. 186 (1970).

junenol (13), mp 90-92°, identical by spectral and chromatographic comparison with an authentic¹⁵ sample of 13. Selective hydrogenation of the isopropenyl group of 12c [(Ph₃P)₃RhCl in benzene], followed by photoisomerization (450-W medium-pressure lamp, unfiltered, 40 hr in degassed benzene) of the endocyclic double bond,¹⁷ gave (\pm) -junenol⁹ (1), mp 77.5-79°, in 65% overall yield. The synthetic material was indistinguishable from authentic¹⁶ (+)-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 equilibration¹⁸ (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 (sodiumethanol) of the resulting saturated ketone¹⁸ afforded (\pm) -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.

(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. (17) F. J. McQuillin and J. D. Parrack, J. Chem. Soc., 2973 (1956).

(18) D. W. Theobald, Tetrahedron, 20, 2593 (1964).

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Copper-Induced Coupling of Vinyl Halides. Stereochemistry of the Ullmann Reaction¹

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 activated³ copper powder, we have found that cis- and trans-bromostilbene, diethyl bromoand iodomaleate,⁴ and diethyl bromo- and iodofumarate⁴ 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-1,2,3,4tetracarbethoxy-1,3-butadiene (2).6 At 100°, the cou-

(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).

pling 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.



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 intermediates² rather than of radicals.⁸ The stereochemical instability of the latter¹⁰ 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 guinoline 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-

(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) Fanta⁹ 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.