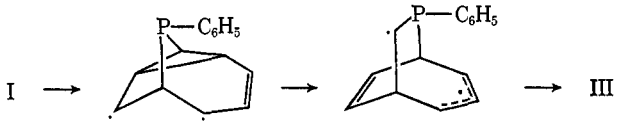
multiplets at τ 2.57, 6.12, and 6.61 in intensity ratios 4.90:1.96:6.14). Reduction with trichlorosilane in triethylamine–benzene[12] gives II (mp 58–59°) in 76% yield.[8]

In contrast, when benzene solutions of I are photolyzed through Pyrex, the major product[13] isolated (25% yield) after chromatography on silica gel is III (mp 43–45°).[8] The corresponding phosphine oxide (mp 101–102.5°),[8] formed by H_2O_2 oxidation of the crude product, was easier to isolate (30% yield), and could be reduced (Si_2Cl_6, C_6H_6)[16] back to the phosphine (III, 76% yield). The oxide shows at room temperature an nmr spectrum similar to that of the parent hydrocarbon:[5b] with the phosphorus spin decoupled, besides phenyl protons, two triplets ($|J|$ = 8.0 Hz) at τ 3.90 and 4.32, a multiplet at 5.70, and a triplet ($|J|$ = 7.2 Hz) at 7.42 in the intensity ratio 2.09:3.90:1.77. Upon cooling to −96° the pattern changes to multiplets at τ 3.89, 4.31, 7.22, and 7.84 in the intensity ratio 2:2:3:1. The kinetic parameters, estimated as E_a = 7 kcal, log A = 9, are similar to those measured for the hydrocarbon.[5b] The nmr features of the phosphine III are similar: at ambient temperature in C_6D_6 multiplets at τ 2.89, 4.47, 6.25, and 7.54 of intensities 5.12:1.95:3.88:2.05; at −92° in $CFCl_3$–CD_2Cl_2, aromatics and multiplets at τ 4.16, 4.62, 6.76, and 7.42 of intensities 3:1:1:3.

Considering what is known about related photochemical reactions, the difference between the photolyses leading to V and VI (and then to the oxide of II) and the photolysis leading to III appears to be the difference between a singlet[17] and triplet reaction.[18] The mechanism for the formation of III may[18a-c] be that indicated below.



Acknowledgments. We are grateful to N. J. Turro for advice, Badische Anilin und Sodafabrik, A.G., for gifts of cyclooctatetraene, and the National Institutes of Health (MH-08912) for its support.

(12) (a) H. Fritsche, V. Hasserodt, and F. Korte, *Chem. Ber.*, **98**, 171 (1965); (b) S. E. Cremer and R. J. Chorvat, *J. Org. Chem.*, **32**, 4066 (1967).

(13) Other chromatography fractions showed peaks attributable to 9-phenyl-9-phosphabicyclo[6.1.0]nonatriene,[1,14] and to the phosphorus epimer of I.[1,15]

(14) *Cf.* A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 762 (1967).

(15) *Cf.* K. Mislow, M. Axelrod, D. R. Rayner, H. Gotthardt, L. M. Coyne, and G. S. Hammond, *J. Amer. Chem. Soc.*, **87**, 4958 (1965).

(16) K. Naumann, G. Zon, and K. Mislow, *ibid.*, **91**, 2788 (1969).

(17) J. Saltiel, R. M. Coates, and W. G. Dauben, *ibid.*, **88**, 2745 (1966).

(18) (a) H. E. Zimmerman and P. S. Mariano, *ibid.*, **91**, 1718 (1969); (b) H. E. Zimmerman, R. W. Binkley, R. S. Givens, G. L. Grunewald, and M. A. Sherwin, *ibid.*, **91**, 3316 (1969); (c) H. E. Zimmerman, R. S. Givens, and R. M. Pagni, *ibid.*, **90**, 6096 (1968); (d) P. W. Rabideau, J. B. Hamilton, and L. Friedman, *ibid.*, **90**, 4465 (1968); (e) L. A. Paquette and G. R. Krow, *ibid.*, **90**, 7149 (1968); (f) J. P. N. Brewer and H. Heaney, *Chem. Commun.*, 811 (1967).

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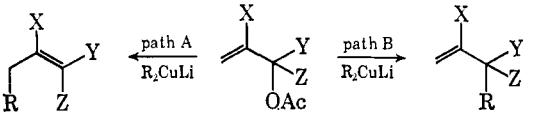
Stereoselective Synthesis of Olefins.[1] Reaction of Dialkylcopper–Lithium Reagents with Allylic Acetates

Sir:

The recently reported reaction[2] of organocopper–lithium complexes[3] with a steroidal allylic acetate to give alkylated *trans*-trisubstituted olefins in 33–40% yield suggested that such reactions might be stereospecific. We wish to report a preliminary investigation of the scope, stereoselectivity, and synthetic utility of this unusual reaction and to describe a novel application to synthesis of stereoisomers of juvenile hormone.

In reactions of dialkylcopper–lithium "ate"[4] complexes[5] with acyclic allylic acetates of type **1**, we have found that *two* alkylation paths are generally available: displacement of acetate with allylic rearrangement (path A) and direct displacement (path B). Both the olefin isomer ratio from path A and the extent of path B are highly predictable.

Scheme I



1, X, Y, Z = H or alkyl
Y > Z

Alkylations summarized in Table I indicate that *trans*-trisubstituted olefins are formed stereoselectively in high yield from **1** when (i) X is equal to or smaller than the entering alkyl of reagent and (ii) Z is hydrogen. When the substituent Y in **1** contains potential coordinating ligands for copper(I), a slight decrease in stereoselectivity is seen (**3**[6,7] and **4**[7,8] *vs.* **2**), but when Y is ethoxycarbonyl in **6**,[7,9] alkylation is completely inhibited.

Direct displacement of acetate in **2**, **3**, and **4** is a very minor reaction (**1**, Z = H) when ether is the solvent, but modification of the coordinated reagent by using tetra-

(1) Contribution No. 2 from the Research Laboratory of Zoecon Corp.

(2) P. Rona, L. Tökes, J. Tremble, and P. Crabbé, *Chem. Commun.*, 43 (1969).

(3) (a) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966); (b) H. O. House and W. F. Fischer, Jr., *ibid.*, **33**, 949 (1968); (c) H. Gilman, R. G. Jones, and L. A. Woods, *ibid.*, **17**, 1630 (1952); (d) G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1969).

(4) W. Tochtermann, *Angew. Chem. Int. Ed. Engl.*, **5**, 351 (1966); G. Wittig, *Quart. Rev.* (London), **20**, 191 (1966).

(5) Prepared by titration of cuprous iodide (1.2 equiv) with alkyllithium (2.3 equiv) in ether, avoiding excess alkyllithium by use of the Gilman I test: H. Gilman and F. Schulze, *J. Amer. Chem. Soc.*, **47**, 2002 (1925). Though represented as R_2CuLi, these reagents are probably solvated tetrahedral metal clusters.

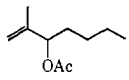
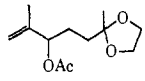
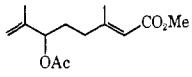
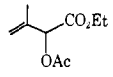
(6) Prepared from 2-methylhept-2-en-6-one by ketalization, hematoporphyrin-photosensitized oxygenation (methanol), sodium borohydride reduction, acetylation, and chromatography; *cf.* C. S. Foote, *Accounts Chem. Res.*, **1**, 104 (1968).

(7) Satisfactory elemental analyses and infrared and nmr spectra were obtained (Varian T-60 or HA-100 spectrometers using deuteriochloroform solutions with tetramethylsilane as internal reference) for this compound.

(8) Prepared from methyl *trans*-3,7-dimethylocta-2,6-dienoate by "one-flask" photosensitized oxygenation in pyridine, *in situ* reduction of hydroperoxides with trimethyl phosphite (2 equiv, 5°), and selective acetylation of the secondary allylic alcohol with acetic anhydride, followed by silica chromatography.

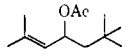
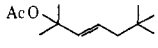
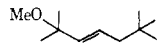
(9) Prepared in 40% yield from ethyl 3-methyl-2,3-epoxybutanoate and 15% acetic anhydride in refluxing acetic acid.

Table I[a]

Substrate	Compd no.	R_2CuLi	Products			Isolated yield, %	Time, hr
	**2**	Me_2CuLi	97[b]	2[b]	1[c]	80	0.25
	**3**	Me_2CuLi	94.3[d,7]	3.4[d]	2.3	82	0.5
		$(MeCu)_n$	93	4	3	27[e]	0.5
		Me_2CuLi[f]	47	24.5	17[g]	91	24
		$(n\text{-}Bu)_2CuLi$	92[7]	4.5[c]	1.5[c]	73	1.0
		$(C_6H_5)_2CuLi$	70[g,7]	20[g]	9[c]	77	0.5
	**4**	Me_2CuLi	87.3[g]	8[g]	3[c]	75	0.5
	**5**[h]	Me_2CuLi	63[i,7]	27[i]	8[i]	90	0.5
	**6**	Me_2CuLi	0	0	0		0.5[j]

[a] Alkylations were carried out at $-10°$ in ether under argon atmosphere. [b] Assigned by comparison with authentic samples from lithium diethylcuprate alkylation of 4-methylhex-3-enyl bromide isomers (i): K. H. Dahm, H. Röller, and B. M. Trost, *Life Sci.*, **7**, 129 (1968). [c] Tentative structure assignment. [d] Authentic samples obtained by acylation of the Grignard of i at $-78°$ and ketalization. [e] Unchanged after 0.4 hr. [f] In tetrahydrofuran. [g] Isolated by preparative glpc and characterized (ir, nmr). [h] From 5-methylhex-4-enoic acid by sequential treatment with *m*-chloroperbenzoic in dichloromethane, phosphorus oxychloride in pyridine, and selective removal of the enol lactone isomer of **5** with aqueous pyridine. [i] Isolated by glpc as the ethyl esters and characterized (ir, nmr). [j] Formation of reduction, hydrolysis, conjugation, and acylation products accounts for disappearance of **6**.

Table II[a]

Substrate	Compd no.	R_2CuLi	Products **9**	Products **10**	Isolated yield, %	Time, hr
	**7**	Me_2CuLi	81[b,7]	15[b]	57	10
		$(n\text{-}Bu)_2CuLi$	82[b,7]	18[b]	85	4
	**8**	$(n\text{-}Bu)_2CuLi$	83	17	89	0.5
	**11**[c]	Me_2CuLi	0	0		24

[a] Alkylations were carried out at $-10°$ in ether under argon atmosphere. [b] Isolated by preparative glpc and characterized (ir, nmr). [c] Prepared by acid-catalyzed methanolysis of the alcohol of **7**.

hydrofuran solvent enhances this path and markedly decreases stereoselectivity in a much slower alkylation of **3**.

Disubstituted olefin formation results from **1** when both X and Z are hydrogen and is stereospecific in the case of **7**[7,10] (see Table II), with both dimethyl- and di-*n*-butylcopper–lithium in ether. The formation of **9**[7] and **10** in almost identical ratios from butylations of **7** and its isomer **8**[7,10] suggests that transfer of acetate to copper with displacement of a weakly basic ether ligand occurs with electron transfer to the substrate forming a tightly held allyl radical. Subsequent transfer of an alkyl radical may then afford **9** and **10**. Here the predominance of direct displacement (**8** → **9**) when both Y and Z substituents in **1** are alkyl is a serious limitation for olefin synthesis but provides a useful quaternary alkylation in contrast to tertiary halides.[3d] Substituents at the double bond terminus in **7** retard but do *not* prevent alkylation with allylic rearrangement (path A).

Attempts to alkylate allylic acetates with copper reagents other than "ate" complexes were not successful. "Polymeric" methylcopper[11] with **4** gave only partial reaction (high stereospecificity), but methylcopper complexed with tributylphosphine,[3a] trimethyl phosphite,[3b] or tetramethylethylenediamine gave no reaction.

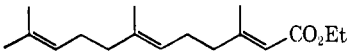
Application of this trisubstituted olefin synthesis to the insect juvenile hormone[12] skeleton involved "one-flask" conversion[8] of readily available all-*trans* ethyl

(10) Prepared by 1,4 methylation (Me_2CuLi) of phorone, sodium borohydride reduction, and acetylation of the product. Chromatography (SiO_2) affords both **7** and **8**, but these isomers are *not* interconverted during organocopper alkylation.

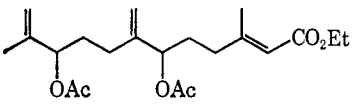
(11) Freshly generated *in situ* from methyllithium (1 equiv) and cuprous iodide (2 equiv) but not purified.[3b]

(12) H. Röller, K. H. Dahm, C. C. Sweeley, and B. M. Trost, *Angew. Chem. Int. Ed. Engl.*, 6, 179 (1967).

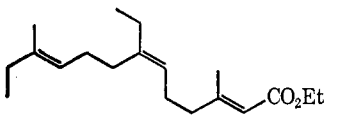
farnesoate (**12**) to the double allylic acetate **13**[7,13] in 23% yield. Methylation of **13** with ethereal[14] lithium dimethylcuprate (−10°, 0.5 hr) gave ethyl 3,11-dimethyl-7-ethyltrideca-2,6,10-trienoate in quantitative yield as a mixture of all-*trans* (14%), *trans,cis,cis* (8%), and *trans,cis,trans* **14** (76%). Thus *cis* olefins form stereoselectively from allylic acetates of type **1** when X is larger than the entering alkyl of reagent.



12



13



14

In general, lithium dialkylcuprate alkylation of **1**, Z = H, is highly stereoselective for the path A product which has alkyl groups X and Y in a *cis* relationship. Investigation of the scope[15] of this widely applicable olefin synthesis is continuing.

Acknowledgment. We thank L. Dunham and Virginia L. Spain for invaluable technical assistance.

(13) No trace of the 7,8-double bond isomer is evident from nmr spectra of **13** or the corresponding diol.

(14) Methylation of **13** in tetrahydrofuran produces appreciable amounts of *trans,trans,cis*-**14**. The corresponding methyl ester has been converted to juvenile hormone by K. H. Dahm, B. M. Trost, and H. Röller, *J. Amer. Chem. Soc.*, **89**, 5292 (1967).

(15) The requirement for 2 equiv of alkyllithium when only 1 equiv is utilized could be obviated by use of mixed reagents,[3d] such as lithium butylvinylcuprate, which are being examined.

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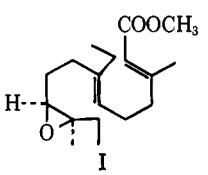
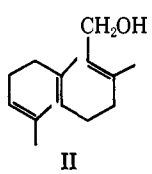
Synthesis of *Cecropia* Juvenile Hormone from *trans,trans*-Farnesol[1]

Sir:

As part of a continuing program concerned with the bioorganic chemistry of terpenoid terminal epoxides,[2] we have developed a convenient *Cecropia* juvenile hormone (I) total synthesis fundamentally different



I



II

from those approaches previously described.[3-9] This route starts with the readily available *trans,trans*-farnesol (II), a possible biochemical precursor of the hormone, and features positionally selective oxidation, elimination, and methylation processes, all carried out in tandem in the 6,7 and 10,11 environments.

trans,trans-Farnesol acetate, on treatment (15 min, 0°) with ~2 equiv of *m*-chloroperbenzoic acid in methylene dichloride, underwent exclusive oxidation at the nonallylic olefinic centers,[10] providing after saponification with aqueous–alcoholic potassium carbonate the 6,7:10,11-diepoxide III, which exhibited nmr peaks (CCl_4, 60 Mc) at δ 5.40, 4.03, 2.60, 1.67, and 1.23. Lithium diethylamide (5 equiv) in refluxing benzene during 1 hr induced in III a double, Hoffmann-like elimination[11] involving the epoxide moieties to give, of the possible trienetriols, only the desired bis(terminal methylene) case IVa, purified by silica gel chromatography. The nmr spectrum ($CDCl_3$, 60 Mc) possessed peaks at δ 5.44, 4.95, 4.13, 4.06, 1.70, and 1.66. In order to permit selectivity in the methylation phase, the trisallylic alcohol was transformed with trityl chloride–pyridine to the primary mono(trityl ether) IVb.

Conversion of IVb by means of tosyl chloride–lithium chloride (room temperature, 24 hr) to the unrearranged (nmr) bis(allyl chloride),[12] followed directly by the action of 5 equiv of lithium dimethylcopper at −5° for 1 hr,[13] led to formation of triene trityl ether Vb, isolated by column chromatography[14,15] (ether–hexane elution from silica gel). Nmr peaks (CCl_4,

Trost, and H. Röller, *J. Amer. Chem. Soc.*, **89**, 5292 (1967); (c) K. H. Dahm, H. Röller, and B. M. Trost, *Life Sci.*, 7, 129 (1968).

(4) E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman, and B. W. Erickson, *J. Amer. Chem. Soc.*, **90**, 5618 (1968).

(5) R. Zurflüh, E. N. Wall, J. B. Siddall, and J. A. Edwards, *ibid.*, **90**, 6224 (1968).

(6) W. S. Johnson, T. Li, D. J. Faulkner, and S. F. Campbell, *ibid.*, **90**, 6225 (1968).

(7) K. Mori, B. Stalla-Bourdillion, M. Ohki, M. Matsui, and W. S. Bowers, *Tetrahedron*, **25**, 1667 (1969).

(8) H. Schulz and I. Sprung, *Angew. Chem. Int. Ed. Eng.*, **8**, 271 (1969).

(9) J. A. Findlay and W. D. MacKay, *J. Chem. Soc., D*, 733 (1969).

(10) Selectivity of epoxidation is much less pronounced with farnesol itself.

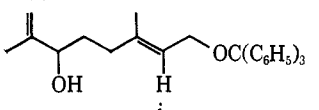
(11) Sharpless carried out (unpublished work, Stanford University) the base-induced 2-methylheptene-2 conversion to the 1-en-3-ol just prior to the appearance of the first in a series of notable publications on epoxide eliminations by Crandall and coworkers (J. K. Crandall and L. H. Chang, *J. Org. Chem.*, **32**, 435 (1967)).

(12) G. Stork, P. A. Grieco, and M. Gregson, *Tetrahedron Letters*, 1393 (1969).

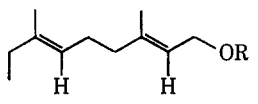
(13) E. J. Corey and G. H. Posner, *J. Amer. Chem. Soc.*, **89**, 3911 (1967).

(14) Approximately 15% substitution without allylic isomerization was observed.

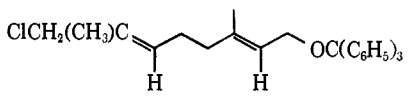
(15) Other methods of alkylation were investigated, all of which stereospecifically afforded only the *trans* isomer ii when applied to the model system i. These methods include: (1) conversion of i to the acetate followed by alkylation with lithium dimethylcopper (P. Rona, L. Tökes, J. Tremble, and P. Crabbé, *J. Chem. Soc., D*, **43** (1969)); (2) conversion to the chloride, followed by alkylation with methyllithium; and (3) conversion to the rearranged chloride iii with thionyl chloride in



i



ii



iii

ethyl ether, followed by alkylation with methyllithium. When either of the first two methods was tried on the diol IV, the seemingly exclusive product was the triene V with *trans,cis,trans* geometry. This novel stereospecific alkylation procedure deserves detailed study and should find utility in the controlled synthesis of trisubstituted olefins.