Synthetic Studies on Insect Hormones. VIII.[1,2] A New Stereospecific Synthesis of Trisubstituted Olefins from Organocopper Reagents and Acetylenes

Sir:

Considerable effort in devising methods[3] for the stereospecific synthesis of trisubstituted double bonds has been prompted by recent interest in the insect juvenile hormones[4] I and II and in polyolefinic precursors for cyclization to condensed terpenes and steroids.[5] We wish to report a new stereospecific one-step synthesis[6] of trisubstituted olefins by alkylation of conjugated acetylenic esters with organocopper reagents.

Injection of ethereal methyl pent-2-ynoate (IV) (4.5 mmol, 0.22 *M*) into a clear solution of lithium dimethylcopper[7] (4.75 mmol, 0.06 *M*) in ether under an argon atmosphere affords in high yield two isomeric olefinic esters[8] (V)[9b] and (VI)[9b] whose proportions are dependent on time and temperature of reaction and on the method of work-up (See Table I).

Table I. Reaction of Lithium Dimethylcopper (4.75 mmol) in Ether (20 ml) with IV (4.5 mmol) in Ether (8 ml)

Temp, °C	Time, min	Ratio V:VI	Yield[9a] of V + VI, %	Notes
0	5	39:61	35	
0	360	38:62	44	
−78	60	85:15	90	Quenched by water at −78°
−78	2	92:8	92.5	Quenched by water at −78°
−100	2	97:3	95[9c]	Quenched by water at −100°

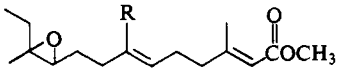
The highest degree of stereospecificity (*cis*:*trans* 97:3) in the reaction of IV with lithium dimethylcopper was observed when this transformation was carried out at −100° in ether–hexane (2:1).

Attempts to trap the suspected intermediates IX or X by co-injection of IV with either trimethylchlorosilane or acetic anhydride led to no new products but did *not* impede formation of V and VI.

Deuterium oxide quenching (at −78°) of the products from reaction of lithium dimethylcopper and IV gave the monodeuterated olefin XI (85%)[9b] containing 88% deuterium located exclusively[10] at C_2, but a reaction in the presence of added excess hexadeuterioacetone led to no significant deuteration of V (95%,[9c] 88%[9b]) or VI (5%[9c]). Alkylation of the anion X by methyl iodide gave the tetrasubstituted olefin XII[11] and its geometrical isomer in 25% yield, but only at temperatures which also allowed isomerization of X.

A simple direct synthesis of 1,5- (isoprenoid) diene systems is achieved by using the previously unknown homoallylcopper reagents for alkylation of acetylenic esters. Preliminary experiments with the ethereal Grignard reagent[12] from 4-methylpent-3-enyl bromide and 1.5 equiv of the copper complex[13] (VIII) were successful when (i) a molar excess of tri-*n*-butylphosphine was present and (ii) the reaction was carried out below −50°, preferably at −80° for 1.5 hr before injection of the acetylenic ester III at −90°.

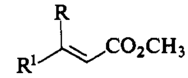
Efficient[14] synthesis of methyl *trans*-3,7-dimethylocta-2,6-dienoate[15] (VII) [*trans*:*cis* 96:4, 52%[9b] from 4-methylpent-3-enyl bromide] was carried out under the above



I, R = CH_3
II, R = C_2H_5

$RC{\equiv}CCO_2CH_3$

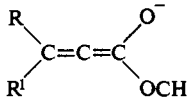
III, R = CH_3
IV, R = C_2H_5



V, R = C_2H_5; R^1 = CH_3
VI, R = CH_3; R^1 = C_2H_5
VII, R = CH_3; R^1 = $(CH_3)_2C{=}CHCH_2CH_2$

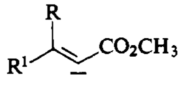
$[CuI\{n\text{-}(C_4H_9)_3P\}]_4$

VIII

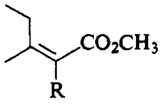


$$\begin{matrix} R & & & & O^- \\ & C{=}C{=}C & & & \\ R^1 & & & & OCH_3 \end{matrix}$$

IX



X



XI, R = D
XII, R = CH_3

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[1] Part VII: see R. Zurflüh, E. N. Wall, J. B. Siddall, and J. A. Edwards, *J. Am. Chem. Soc.*, **90**, 6224 (1968).

[2] Contribution No. 356 from the Syntex Institute of Organic Chemistry.

[3] (a) E. J. Corey, J. A. Katzenellenbogen, and G. H. Posner, *J. Am. Chem. Soc.*, **89**, 4245 (1967); (b) S. F. Brady, M. A. Ilton, and W. S. Johnson, *ibid.*, **90**, 2882 (1968).

[4] (a) R. Zurflüh, E. N. Wall, J. B. Siddall, and J. A. Edwards, *ibid.*, **90**, 6224 (1968); (b) W. S. Johnson, T.-Y. Li, D. J. Faulkner, and S. F. Campbell, *ibid.*, **90**, 6225 (1968); (c) E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman, and B. W. Erickson, *ibid.*, **90**, 5618 (1968).

[5] W. S. Johnson, M. Semmelhack, M. V. S. Sultanbawa, and L. A. Dolak, *ibid.*, **90**, 2994 (1968).

[6] We have learned, by private communication, of a similar synthesis developed in the laboratories of Professor E. J. Corey.

[7] N. Gilman, R. G. Jones, and L. A. Woods, *J. Org. Chem.*, **17**, 1630 (1952); also see N. Gilman and J. M. Straley, *Rec. Trav. Chim.*, **55**, 821 (1936).

[8] Identified by comparison of observed nmr spectra with the data of K. H. Dahm, B. M. Trost, and H. Röller, *J. Am. Chem. Soc.*, **89**, 5292 (1967). Nmr spectra were measured on a Varian HA-100 spectrometer using tetramethylsilane as internal standard in deuteriochloroform solution.

[9] (a) Isolated by fractional distillation; (b) isolated by distillation and preparative gas–liquid partition chromatography; (c) yield calculated by gas chromatography using naphthalene (as internal standard) co-injected with the acetylenic ester.

[10] Within the limits of error in determination by integration of nmr spectra.

[11] Structure assigned by mass spectrometry and chemical shift (δ 1.80 m) of the β-methyl. The isomer showed a doublet, J = 1.52 Hz at δ 1.97.

[12] M. Julia, S. Julia, and R. Guegan, *Bull. Soc. Chim. Fr.*, 1072 (1960).

[13] H. O. House and W. F. Fischer, Jr., *J. Org. Chem.*, **33**, 949 (1968), and references therein.

conditions. Quenching of the intermediate anion with deuterium oxide led to incorporation of deuterium (91% d, < 1% d_2) at C_2 in the product VII.

Complete utilization of the alkenyl or alkyl group attached to copper is permitted by use of 1 equiv of tri-*n*-butylphosphine or pyrrolidine as a solubilizing ligand in contrast to the lithium dialkylcopper reagents which transfer only one of their two alkyl groups to acetylenic esters. The stereospecificity of these alkylations appears to approach 99% with pyrrolidine as ligand.

Analogous alkylations of α,β-acetylenic amides by primary and tertiary alkylcopper reagents have been carried out in this laboratory and will be reported subsequently.

Since neither Grignard nor alkyllithium reagents effect these transformations, the results described above provide a new and useful stereospecific synthesis of trisubstituted olefins from readily available acetylenes.

(14) Efficiency appears to be limited only by the relatively difficulty of forming homoallylic Grignard reagents.

(15) Characterized by bp 118–119° (14 mm); ν_{max}^{film} 1650, 1720 cm^{-1}; nmr (δ, ppm) 1.62 (s, 7-CH_3), 1.69 (s, 7-Me), 2.17 (d, $J = 1.5$ Hz, 3-CH_3), 3.69 (s, OCH_3), 5.11 (m, 6-H), and 5.70 (m, 2-H); mass spectra, *m/e*, 182 (M^+).

(16) Syntex Postdoctoral Fellow, 1967–1968.

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The Effect of Free Radicals on Superconductors. Nitric Oxide on Aluminum

Sir:

In previous work, the idea of "conductive conjugation" has been introduced in theoretical discussions of the possible effects of molecules on the superconductivity of metals.[1-3] The essential point is that under favorable circumstances molecules may interact so strongly with conducting metals that some of the molecular electrons become part of the Fermi sea. Unfortunately, it is difficult to test the conductive conjugation picture experimentally. However, for odd-electron free radicals, the absence of conductive conjugation should manifest itself by a strong depression of the superconducting transition temperature, since localized unpaired spins can break up the Cooper pairs of the superconducting state.[4] This absence of conductive conjugation is demonstrated in the present work for nitric oxide deposited on superconducting aluminum films.

The films were prepared as follows. A 15-20-Å film of silicon monoxide was evaporated onto a quartz crystal held at 4.2°K. The aluminum was then deposited on the silicon monoxide, and the critical temperature (T_c^0) was determined by a four-point resistivity measurement.[5] In these experiments, T_c^0 is defined as that temperature at which the resistance of the pure aluminum film equals one-half of the resistance change observed in the transition. The film was exposed to nitric oxide at a pressure of 6×10^{-8} Torr for a measured period of time, typically 10–60 sec. The new critical temperature, T_c, was measured over a period of 0.25–0.5 hr, and then more nitric oxide was added. This process was repeated until the supply of liquid helium in the cryostat became exhausted.

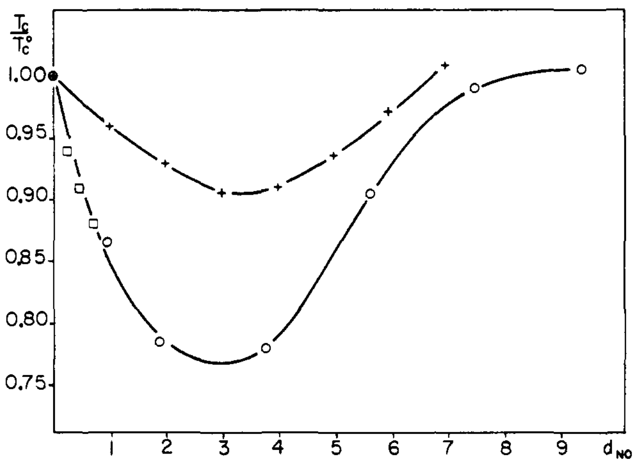

Figure 1. Reduced critical temperature, T_c/T_c^0, *vs.* thickness of nitric oxide, d_{NO}, in monolayers for superimposed aluminum and nitric oxide films. (○) 24-, (□) 28-, and (+) 117-Å aluminum films.

Figure 1 gives the reduced critical temperature, T_c/T_c^0, as a function of the nitric oxide thickness in "monolayers" for 24-, 28-, and 117-Å aluminum films. The initial effect of one monolayer of nitric oxide is to depress the critical temperature by approximately 12–15% for a 24-Å film. The data indicate the absence of conductive conjugation since a fraction of a monolayer also has the effect of sharply depressing the critical temperature. The efficacy of the nitric oxide in depressing the critical temperature is reduced as the thickness of the aluminum is increased. For a nitric oxide thickness of two to four monolayers, the critical temperature attains its minimum value; and, as the nitric oxide thickness is increased, the critical temperature also begins to increase. It returns to or slightly exceeds its original value for a nitric oxide thickness of seven to nine monolayers.

We interpret these results as the product of two competing effects. The first is the depression of the critical temperature due to spin-exchange interaction between the nitric oxide molecule and the metal. The second effect arises from the dimerization of nitric oxide, $2NO \rightarrow (NO)_2$. In this reaction, the unpaired electrons in the nitric oxide molecules become paired in the dimers;[6] an increase of the critical temperature results due to an elimination of the unpaired spins. The former mechanism is predominant for small concentrations of nitric oxide, while the latter dominates for thick nitric oxide films.

In further experiments, a monolayer of nitric oxide was deposted on superimposed films of aluminum and nitro-

(1) H. M. McConnell, B. Hoffman, D. D. Thomas, and F. Gamble, *Proc. Natl. Acad. Sci. U. S.*, **54**, 371 (1965).

(2) B. M. Hoffman, F. R. Gamble, and H. M. McConnell, *J. Am. Chem. Soc.*, **89**, 27 (1967).

(3) H. M. McConnell, F. R. Gamble, and B. M. Hoffman, *Proc. Natl. Acad. Sci. U. S.*, **57**, 1131 (1967).

(4) E. A. Lynton, "Superconductivity," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1964.

(5) F. R. Gamble, Ph.D. Thesis, Stanford University, 1967.

(6) W. J. Dulmage, E. A. Meyers, and W. N. Lipscomb, *J. Chem. Phys.*, **19**, 1432 (1951).