

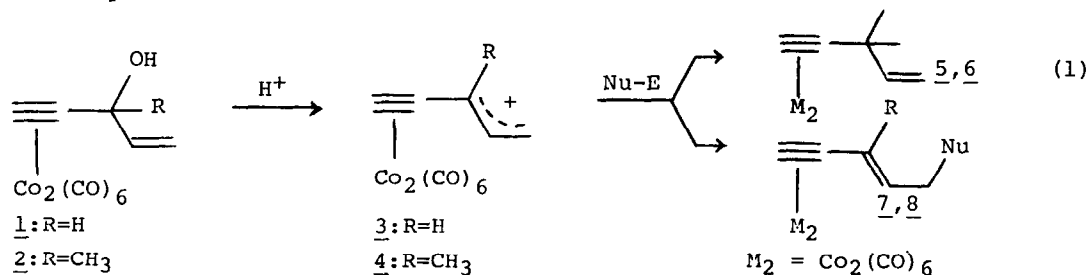
REGIO- AND STEREOSELECTIVE SYNTHESIS OF E-1,3-ENYNES  
 VIA COUPLING OF NUCLEOPHILES WITH  
 1-[(ALKYNYL)DICOBALT HEXACARBONYL]ALLYL CATIONS

S. Padmanabhan and K.M. Nicholas  
 Chemistry Department  
 Boston College  
 Chestnut Hill, MA 02167 U.S.A.

**ABSTRACT:** Reactions of the title complexes with the nucleophiles anisole, allyl silanes, isopropenyl acetate, and ethanol have been examined. The carbon nucleophiles react regio- and stereoselectively to give E-1,3-enyne derivatives.

In previous reports we have described the remarkable stabilizing and directing effect of the  $-\text{Co}_2(\text{CO})_6$  group when coordinated to propargyl cations, i.e.  $(\text{RC}\equiv\text{CCR}_2)\text{Co}_2(\text{CO})_6^{+1}$ . Exploitation of these features has led to the development of synthetically useful methods for the propargylation of aromatics,<sup>2a</sup>  $\beta$ -dicarbonyls,<sup>2b</sup> ketones and enol derivatives,<sup>2c,d</sup> allyl silanes,<sup>2e</sup> and methyl organometallics,<sup>2f</sup> free from the classic problem of acetylene/allene isomerization.<sup>3</sup>

In order to further elucidate the steric and electronic properties of the carbonium ion-stabilizing (alkynyl) $\text{Co}_2(\text{CO})_6$  group and to seek prospective synthetic applications, we have begun to examine the reactions of various nucleophiles with the vinylogous cations 3, 4 derived from vinyl ethynyl carbinol complexes (eq. 1).



We report herein preliminary findings showing that cations 3 and 4 are attacked regio- and selectively by selected nucleophiles to efficiently produce complexes of conjugated E-enyne (7,8), intermediates of considerable importance for the synthesis of insect pheromones,<sup>4</sup> vitamin A derivatives, and carotenes.<sup>5</sup>

The cations 3 and 4 were generated in situ upon treatment of the alcohol pre-

cursors in  $\text{CH}_2\text{Cl}_2$  with  $\text{HBF}_4 \cdot \text{Me}_2\text{O}$  or  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ <sup>6</sup> at  $-78^\circ$ . Subsequent addition of nucleophilic substrates resulted in reactions which were complete within 1-5 hours (TLC monitoring). The product complexes were conveniently isolated following addition of solid  $\text{NaHCO}_3$  and  $\text{MgSO}_4$ , filtration, solvent evaporation, and preparative TLC over silica gel.<sup>7</sup> Results are presented in the Table.

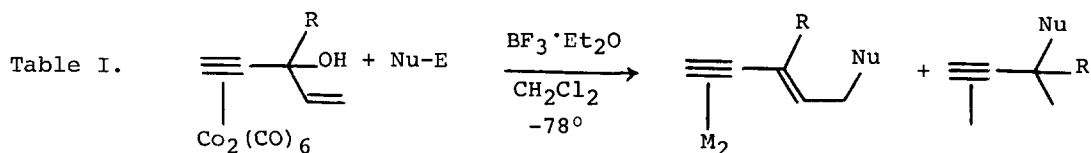
Of the important features to be noted from Table I, we first point out the high (>90%)<sup>8</sup> regio- and selectivity for the production of E-enynne complexes from the coupling of both 1 and 2 with anisole and the allyl silanes. This E-selectivity contrasts with acid-catalyzed<sup>9</sup> and Claisen<sup>10</sup> rearrangements of free ene-yne-ol derivatives and ethynylcyclopropyl carbinols<sup>11</sup> in which the free  $\text{RC}\equiv\text{C}$ -group exhibits a steric demand comparable to  $-\text{H}$  and less than  $-\text{CH}_3$ ; e.g. isomeric mixtures ranging from largely E to roughly equal proportion of E and Z for  $\text{R} = \text{H}$  and the Z-isomer dominating when  $\text{R} = \text{CH}_3$  have been reported. The considerable steric bulk of the  $(-\text{CO}_2)\text{CO}$ <sub>6</sub> moiety clearly plays a critical role in determining the stereochemical course of the present reactions.<sup>13</sup>

In those instances in which mixtures of regioisomers were obtained ( $\text{Nu} = \text{CH}_2\text{C}(\text{CH}_3)\text{OAc}$ ,  $\text{EtOH}$ ), it was established that thermodynamic control was operative, i.e. coupling is reversible under the reaction conditions. Thus when a single regioisomer, e.g. 7d or 5e, was contacted with additional substrate [ $\text{CH}_2\text{C}(\text{CH}_3)\text{OAc}$  for 7d,  $\text{EtOH}$  for 5e] and  $\text{HBF}_4$  in  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ$  (1-2hrs), equilibration to a regioisomeric mixture was found to occur by TLC and <sup>1</sup>H NMR monitoring. We ascribe the reversibility in these cases to the presence of easily protonated oxygen centers in the products, providing a ready pathway to cation re-formation. The free enynols,<sup>9</sup> on the other hand, rearrange exclusively to conjugated 2-en-4-yne derivatives. These results suggest that a stabilizing conjugative interaction between the C-C double bond and coordinated alkyne is negligible. Further, a comparison of the rates of acid-catalyzed isomerization of 1-penten-4-yn-3-ol<sup>9b</sup> and the conversion of its complex 1 to 5e + 7e,  $k_{\text{rel}} \sim 10^5$ , attests once again to the powerful activating effect of the cobalt carbonyl moiety.

As we have reported previously, the  $-\text{Co}_2(\text{CO})_6$  group is conveniently removed oxidatively.<sup>14</sup> For example, treatment of complex 7d with excess  $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$  in ethanol at  $0^\circ$  (3 hrs) gave E-5-octen-7-yn-2-one [91% yield; IR (Smear):  $1715 \text{ cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ ):  $\delta 2.1(\text{s}, 3\text{H})$ ,  $2.3-2.7(\text{m}, 4\text{H})$ ,  $2.85(\text{d}, 1\text{H})$ ,  $5.3-6.4(\text{m}, 2\text{H})$ ] after standard aqueous workup.

The methodology described herein coupled with the ready availability of vinyl ethynyl carbinols provides an attractive and flexible route to conjugated E-enynnes.<sup>15</sup> We are currently exploring the utilization of this chemistry in natural product synthesis.

We are grateful for financial support provided by the National Institutes of Health (GM 26760) and the Alfred P. Sloan Foundation (1980-1982).



Complex	Substrate	Products (% yield)
<u>1</u>	   	<u>7a</u> (82) <sup>a</sup> <u>7b</u> (81) <u>7c</u> (80) <u>7d</u> (76) <sup>a</sup> + <u>5d</u> (6)
<u>2</u>	  	<u>7e</u> (5-10) <sup>a, b</sup> + <u>5e</u> (60-70) <sup>b</sup> <u>8a</u> (73) <sup>c</sup> <u>8b</u> (76) <u>8d</u> (68)

a)  $J_{\text{H-H}}(\text{trans}) = 12 - 14 \text{ Hz}$

b)  $\text{HBF}_4 \cdot \text{Me}_2\text{O}$  catalyst;  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  gave only 7e.

c) Stereochemistry assigned on the basis of  $J[^{13}\text{CH}_3/\text{H}(\text{ol})] = 10.4 \text{ Hz}$  (ref. 9).

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6. Yields with  $\text{HBF}_4 \cdot \text{Me}_2\text{O}$  averaged 10-20% lower than with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ .
7. All new compounds were characterized by IR, and  $^1\text{H}$  NMR spectroscopy and gave satisfactory elemental analyses.
8. Only a single isomer was detectable in each case by TLC,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR (e.g. for 7a:  $\delta(\text{CDCl}_3)$  158.0(C9), 137.0(C3), 131.0(C6), 129.0(C8), 127.5(C4), 114.5(C7), 81.0(C2), 73.0(C1), 54.5(C10) and 38.5(C5)). Regiochemistry was clearly established from  $^1\text{H}$  NMR spectra, the presence or absence of a methine resonance at ca.  $\delta$ 4.0 or terminal vinylic resonances at ca.  $\delta$ 5.0 being diagnostic. Stereochemistry was determined as indicated in footnotes a,c in Table I.
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(Received in USA 26 February 1982)