Studies for Control of the $Ni(CO)_4$-Promoted Carbonylative Cycloaddition of Allyl Halides and Acetylenes

Francisco Camps, Josep Coll, Josep M. Moretó,* and Josep Torras

Department of Biological Organic Chemistry, C.I.D. (CSIC) Jordi Girona, 18-26, 08034-Barcelona, Spain

Received August 10, 1988

The influence of solvent and substitution in either acetylenes or allyl halides on the title reaction has been studied. Whereas in the reaction with monosubstituted acetylenes acetone favors the formation of cyclic derivatives, methanol leads mainly to 3-allylacrylic esters. For disubstituted acetylenes the role played by the solvent seems to be irrelevant, and cyclopentenones are generally obtained. In all cases, provided that steric effects were not very strict, the regioselectivity of the reaction was controlled by the triple-bond polarization, the allyl group being inserted at the negative end of the acetylene dipole. From these results, the influence of chelation and electronic and steric factors on the reaction mechanism is discussed.

Introduction

The cobalt-mediated carbonylative cycloaddition of olefins with acetylenes ("Pauson–Khand" reaction), initially reported to work satisfactorily only with strained alkenes,[1] has been recently extended to other olefins and found remarkably regioselective.[2,3] The current interest of this procedure has increased after its successful application to the synthesis of several bioactive compounds, such as methylenomycin A, sarkomycin, coriolin, and hirsutic acid.[4-6]

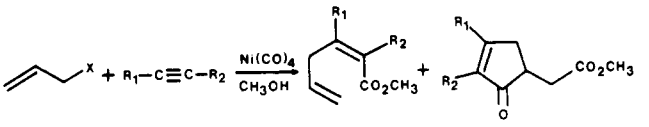
A closely related reaction, using $Ni(CO)_4$, under very mild conditions, was reported some time ago by G. P. Chiusoli (Scheme I).[7] However, this reaction has been heretofore scarcely applied in organic synthesis, despite having exhibited some degree of stereoselectivity in the formation of 5-substituted cyclopentenones.[8] Two reasons may be responsible for this lack of attention:

(a) The yields in cycloadducts are generally low. Linear products usually accompany cyclopentenone and cyclohexenone formation, although it has been observed that the amount of cycloadduct formed increases with the length of the acetylenic chain.[9] In this context, it should be pointed out that linear products that originate from formal addition of the olefins on acetylenes are also found in the Pauson–Khand reaction, but their formation only becomes important with olefins bearing strongly electron withdrawing substituents.[2]

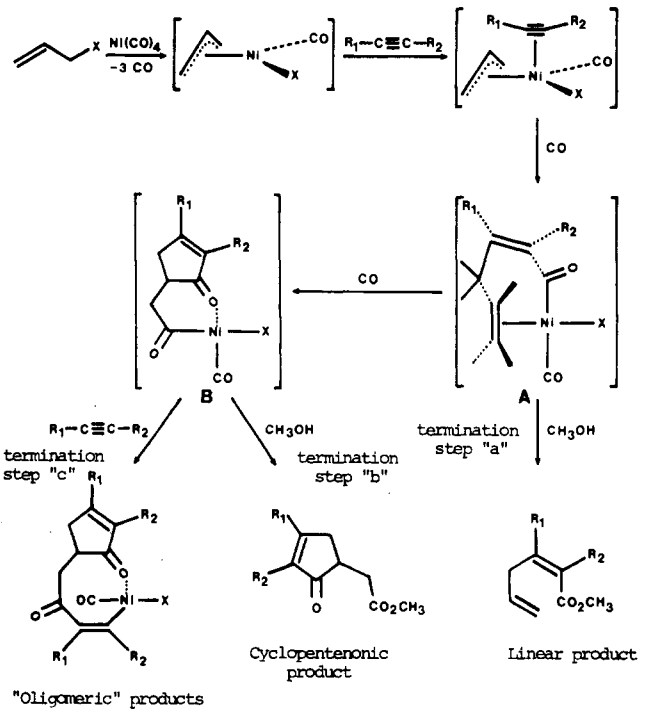
(b) Even in cases when cycloaddition is prevalent, it is difficult to preclude further attack of acetylenes on the cyclic intermediates postulated in this reaction, and, consequently, very often a mixture of cyclopentenone derivatives are obtained.

As shown in Scheme II, according to Chiusoli's rationalization all products found in the reaction could be derived from only two intermediates, A and B. The course of the reaction was found to be much dependent on the solvent, but, in some cases, by proper choice of the reaction conditions good yields of cyclopentenone derivatives could be attained.[8,10]

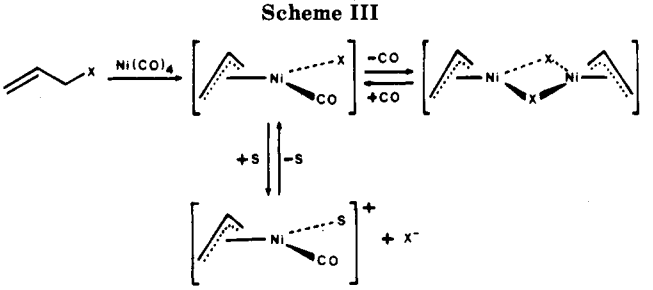
Scheme I



Scheme II



Scheme III

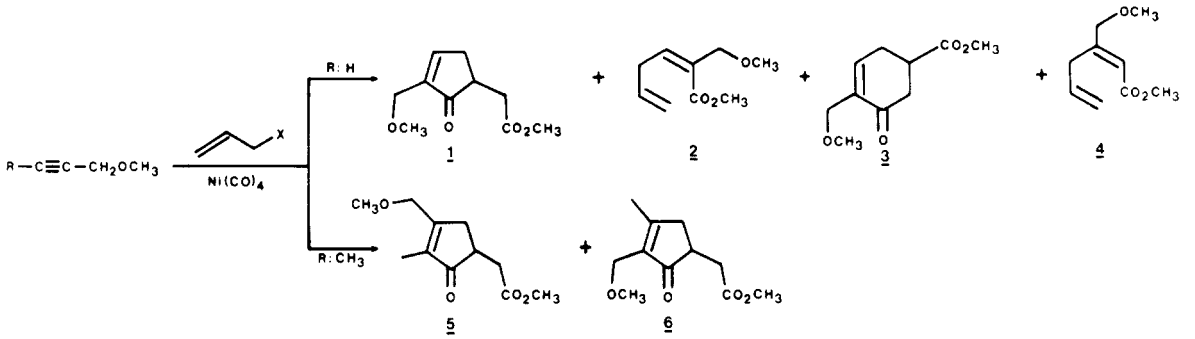


Recently, the potential utility of this reaction in organic synthesis has been demonstrated in our laboratory in straightforward syntheses of methylenomycin B[11] and

(1) Khand, J. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977.
(2) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855.
(3) Krafft, M. E. *J. Am. Chem. Soc.* **1988**, *110*, 968.
(4) Billington, D. C. *Tetrahedron Lett.* **1983**, *24*, 2905.
(5) Exon, C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2477.
(6) Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861.
(7) (a) Chiusoli, G. P. *XXIII Int. Congress Pure Applied Chem.* **1971**, *6*, 169. (b) Chiusoli, G. P. *Acc. Chem. Res.* **1973**, *6*, 422. (c) Chiusoli, G. P.; Cassar, L. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 124.
(8) Cassar, L.; Chiusoli, G. P. *Tetrahedron Lett.* **1965**, 3295. Also ref 32, p 385.
(9) Cassar, L.; Chiusoli, G. P.; Guerrieri, F. *Synthesis* **1973**, 509.
(10) Cassar, L.; Chiusoli, G. P. *Chim. Ind. Milan* **1966**, *48*, 323.

0022-3263/89/1954-1969$01.50/0

Table I. Product Distribution in Different Solvent Systems[a]



solvent system	acetylene RC≡CCH2OMe R	cyclic products 1	3	5	6	total cyclic products	linear products 2	4	total linear products
acetone–MeOH (9:1)	H	1.5	22.5			24	15	4	19
THF–MeOH (9:1)	H	5	11			16	22	5	27
methanol	H	9	7			16	20	7	27
acetone–MeOH (9:1)	CH_3			7	1.5	8.5			
THF–MeOH (9:1)	CH_3			11	2	13			
methanol	CH_3			55	11	66			

[a] The figures shown correspond to isolated yields calculated from the starting acetylene. When propargyl methyl ether was used some losses in linear products during workup could have occurred as indicated from GLC peak areas. These losses could not be completely supressed due to the high volatility of the products and the considerable amount of solvent used for flash chromatography separation. However, conclusions drawn would be much the same.

bicyclo[3.3.0]octenone derivatives.[12] These preliminary promising results have prompted us to carry out a systematic study on the influence of the solvent system and substitution in both allyl and acetylenic derivatives on product distribution, in an attempt to understand the factors ruling the mechanism and selectivity of this reaction.

Results and Discussion

Influence of the Solvent. The important role played by the solvent in this carbonylative cycloaddition was attributed by Chiusoli to its ability to stabilize the acyl–Ni bond in intermediate A.[8,10] However, we anticipated that other effects could be also operative.

Polar solvents, such as methanol, with a well-known capability to break acyl–metal bonds,[7b] can also promote the dissociation of the coordination complex after the occurrence of the oxidative addition. In this context, it is well established that π-allyl–nickel complexes in methanol are extensively ionized[9,13] (cf. Scheme III). Consequently, a higher reactivity toward nucleophiles, such as acetylenes, should be expected in polar solvents.

As shown in Scheme II, it is noteworthy that the cleavage of the acyl–Ni bond by methanol can be either unfavorable, leading to linear compounds from intermediate A (cf. termination step a), or advantageous for the formation of the desired cyclopentenone derivatives from intermediate B, thus preventing further reaction of this species with additional acetylene moieties to afford oligomeric products (cf. termination steps b and c, respectively) as has been found in other reactions.[14]

Likewise, in intermediate A methanol could coordinate the metal favoring π-back donation from metal to olefin

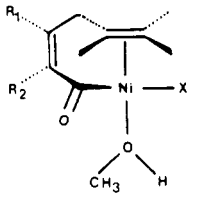


Figure 1.

and, hence, the nucleophilic attack of this moiety on the nearby acyl–nickel bond. A similar facilitating role has been reported for carboxylate groups in nucleophilic attack of Ni-coordinated allyl by amino[15] and acetylene[16] compounds.

From these considerations, it is apparent that a careful choice of the amount of methanol present in the reaction mixture would be required to favor the formation of cyclopentenone derivatives. In the present study, three different solvent systems were used, namely, 9:1 acetone–methanol, 9:1 tetrahydrofuran–methanol, and methanol.

Furthermore, it was anticipated that the presence of a methoxy substituent in the acetylene substrate might also play a beneficial role by chelation to the metal, as it has been reported in related reactions.[17] Consequently, two model acetylenes, prop-2-ynyl methyl ether and but-2-ynyl methyl ether were selected to react with allyl chloride and $Ni(CO)_4$ in the three different solvent systems mentioned above. The results of these reactions, summarized in Table I, showed that the solvent had a marked influence in the case of the terminal acetylene. Thus, while THF and MeOH promoted predominantly the formation of linear products, acetone did not favor the cyclization as extensively as reported previously.[8,10]

In contrast, but-2-ynyl methyl ether afforded exclusively cyclopentenone derivatives in all instances, but the yield

(11) Camps, F.; Coll, J.; Moretó, J. M.; Torras, J. *Tetrahedron Lett.* **1985**, *26*, 6397.
(12) Camps, F.; Coll, J.; Moretó, J. M.; Torras, J. *Tetrahedron Lett.* **1987**, *28*, 4745.
(13) Guerrieri, F. *J. Chem. Soc., Chem. Commun.* **1968**, 983.
(14) Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65.
(15) Yamamoto, T.; Ishizu, I.; Yamamoto, A. *J. Am. Chem. Soc.* **1981**, *103*, 6863.
(16) Castellani, M.; Chiusoli, G. P.; Salerno, G. *J. Organomet. Chem.* **1978**, *146*, C-19.
(17) Jackson, W. R.; Perlmutter, P. *Chem. Brit.* **1986**, *22*, 338.

Table II. Product Distribution from Terminal Acetylenes[a]

entry	acetylene	main products (yield)[b]			
a	$HC{\equiv}CCH_2OCH_3$	1 (9)	2 (20)	3 (7)	4 (7)
b	$HC{\equiv}CCH_2OH$	1 (3)	3 (6)	7 (24)	8 (4)
		9 (4)			
c	$HC{\equiv}CCH_2CH_2OH$	10 (11)	11 (65)	12 (8)	
d	$HC{\equiv}CCOCH_3$	13 (16)	14 (10)		
e	$HC{\equiv}CCO_2CH_3$	15 (19)	16 (12)	17 (11)	

[a] Yields of isolated product based on starting acetylene. Reaction carried out in methanol with a 2/1 molar ratio nickel/acetylene and a 1/1 molar ratio nickel/allyl halide. [b] In all cases, it was observed the formation of substantial amounts of cooligomeric compounds, which was not further investigated.

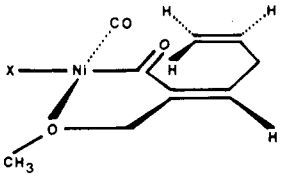


Figure 2.

(66%) obtained with pure methanol was much higher than in the other solvent systems. As depicted in Figure 1, the simplest explanation for this preference would invoke the favorable conformation of intermediate A for cyclization to cyclopentenone derivatives, in which the nucleophilicity of the coordinated olefin would be enhanced by ligand to metal σ-donation of methanol at the trans position. In addition, the presence of the nearby substituents (Me or CH_2OMe) would hinder the formation of linear products by direct attack of methanol on the acyl group and also may favor the coordination of the olefin to the metal to avoid steric congestion.

Similarly, as shown in Figure 2, the corresponding putative conformation of intermediate A in the case of prop-2-ynyl methyl ether, with a very stable five-member ring chelation of the propargyl ether group to the metal would explain the preferential formation of linear adduct **2** and the relative high amount of cyclohexenone **3** from this acetylene. On the other hand, the results observed in the presence of acetone confirmed the stabilization of the acyl–nickel bond by this solvent.[8,10]

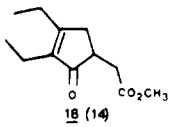
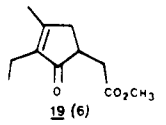
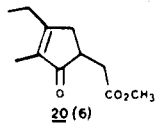
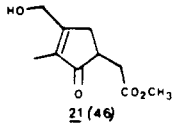
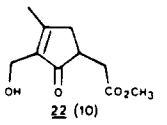
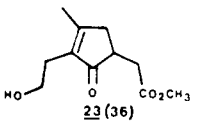
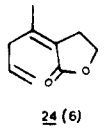
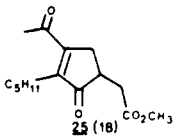
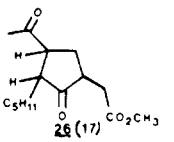
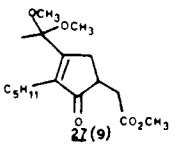
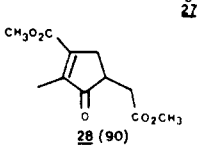
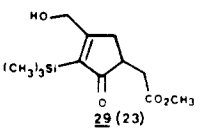
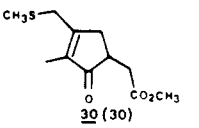
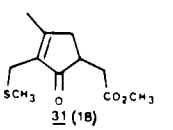
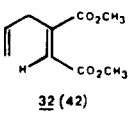
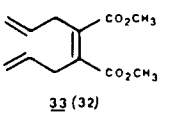
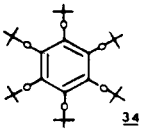
Influence of the Acetylene Substitution. To assess the influence of electronic and/or steric factors derived from acetylenic substitution, a systematic study of the reaction of allyl chloride with different mono- and disubstituted acetylenes in the presence of $Ni(CO)_4$ in methanol was carried out. The results with monosubstituted acetylenes, summarized in Table II, show that in all cases linear adducts were predominant. Almost the same product distribution was obtained with propargyl alcohol and its methyl ether (cf. entries a and b). Unexpectedly, with but-3-yn-1-ol, a very high yield of methylene lactones was found (cf. entry c), plausibly, due to the appropriate location of the hydroxyl moiety in this case for five-member ring lactone formation. Although addition of the allyl group at the unsubstituted acetylenic carbon atom seems to be a general rule for all monoalkyl- and monoarylacetylenes,[18] the presence of a strongly electron withdrawing substituent can decrease or reverse this trend (cf. entries d and e).

As shown in Table III, both yields and regioselectivities in the formation of cyclopentenones were generally increased, when the cycloaddition was performed with disubstituted functionalized acetylenes. However, in the case of dialkyl substituents with similar steric requirements yields were very low, and, as expected, no regioselectivity in the cycloaddition was observed. (cf. entries b and c). Remarkably, dramatic improvements were obtained with but-2-yn-1-ol (cf. entry d). As mentioned above, these results were initially associated with the chelating properties of the hydroxyl group.[17,19] However, while the corresponding methyl ether afforded better yields than the parent but-2-yn-1-ol (entry a), the thia analogue a priori a better σ-donor, gave inferior results compared to the alcohol specially in selectivity (cf. entry i).

These results indicate that the polarization of the triple bond might be also an important factor in the outcome of this reaction as the suggested explanation for the regioselectivity observed in the metal-catalyzed carbonylative cycloaddition of acetylenes to quinones.[20] In the present study, this effect is spectacularly apparent in the reaction with methyl 2-butynoate, where an almost quantitative yield of cyclopentenone **28** was obtained (cf. entry g). On the other hand, the presence of a ketone carbonyl group led to a mixture of cyclopentenone **25** and its dihydro and

(18) Chiusoli, G. P.; Bottaccio, G. *Chim. Ind. Milan* **1965**, *47*, 165.
(19) Tanase, T.; Shimizu, F.; Kuse, M.; Yano, Sh.; Yoshikawa, S.; Hidai, M. *J. Chem. Soc., Chem. Commun.* **1987**, 659.
(20) Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Iyer, S.; Leeds, J. P. *Tetrahedron* **1985**, *41*, 5839.

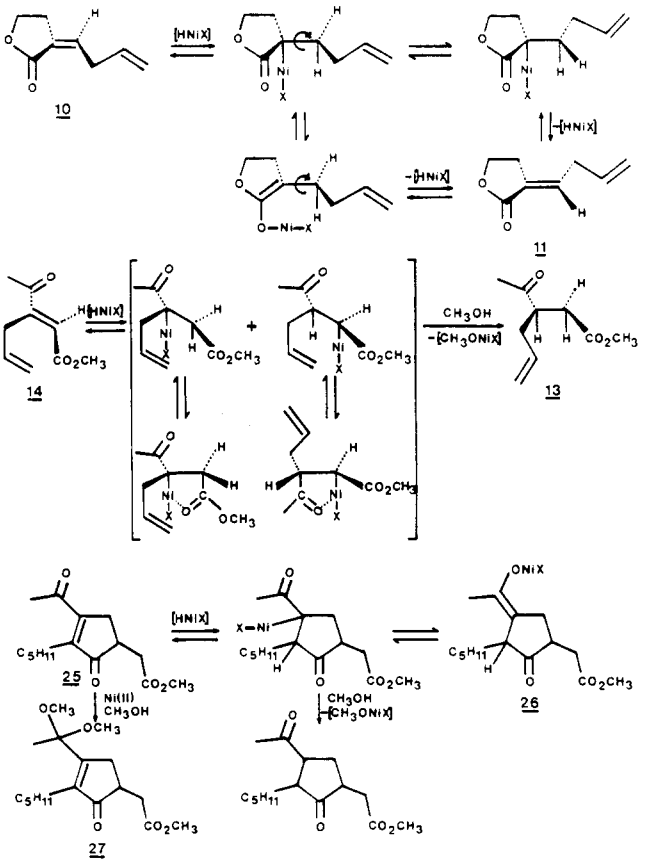
Table III. Product Distribution from Disubstituted Acetylenes[a]

entry	acetylene	main products (yield)[b]	
a	$CH_3C{\equiv}CCH_2O$-CH_3	5 (55)	6 (11)
b	$CH_3CH_2C{\equiv}CCH_2$-CH_3	 18 (14)	
c	$CH_3C{\equiv}CCH_2CH_3$	 19 (6)	 20 (6)
d	$CH_3C{\equiv}CCH_2OH$	 21 (46)	 22 (10)
e	$CH_3C{\equiv}CCH_2CH_2$-OH	 23 (36)	 24 (6)
f	n-$C_5H_{11}C{\equiv}C$-$COCH_3$	 25 (18)	 26 (17)
		 27 (9)	
g	$CH_3C{\equiv}CCO_2CH_3$	 28 (90)	
h	$Me_3SiC{\equiv}C$-CH_2OH	 29 (23)	
i	$CH_3C{\equiv}CCH_2S$-CH_3	 30 (30)	 31 (18)
j	$CH_3O_2CC{\equiv}C$-CO_2CH_3[c]	 32 (42)	 33 (32)
k	t-BuOC$\equiv$C-O-t-Bu	 34 (60)	

[a] Yields of isolated product based on starting acetylene. Reaction performed in methanol using a 2/1 molar ratio nickel/acetylene and a 1/1 molar ratio nickel/allyl chloride. [b] In all cases, except f, g, j, and k, the presence of unchanged acetylene was detected in the reaction crude. [c] Yields were dependent upon the excess of allyl halide used. Those reported are for the conditions described above.

dimethyl acetal derivatives **26** and **27**, respectively. This double bond hydrogenation, which has also been observed with the corresponding terminal acetylene (cf. Table II, entry d), is thought to occur through nickel hydride addition on the conjugated double bond. As has been reported in related processes,[21] this rationale would also account for the formation of trans addition lactone **11** as the main product in the reaction with but-3-yn-1-ol (cf. Scheme IV).

Scheme IV



It is noteworthy to compare the results of cycloadditions with but-2-yn-1-ol and pent-3-yn-1-ol (cf. Table III, entries d and e). While in the first case an excellent yield of cyclopentenones was obtained, in the second one reduction in yield and regiochemistry reversal in the cycloaddition were observed. However, with pent-3-yn-1-ol steric factors also promoted the formation of lactone **24**, to a much lesser extent than that of lactone **11** obtained from the corresponding terminal acetylene, but-3-yn-1-ol (cf. Table II, entry c).

As it has been reported for electron-deficient olefins in related reactions,[22] dimethyl acetylenedicarboxylate did not undergo carbonylative cycloaddition but led instead to the formation of mono- and diallyl adducts **32** and **33**. On the other hand, electron-rich di-*tert*-butoxyacetylene, under the present reaction conditions, trimerized to the hexasubstituted arene **34** (cf. Table III, entry k).

For correlation of the regioselectivity observed in the cycloaddition with the triple bond polarization, the ^{13}C chemical shifts of the acetylenic carbons were used as an approximate measure of the zonal charge density,[23] that should be related to that polarization.

The assignment of these chemical shifts was made in monosubstituted acetylenes by direct identification of the

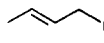
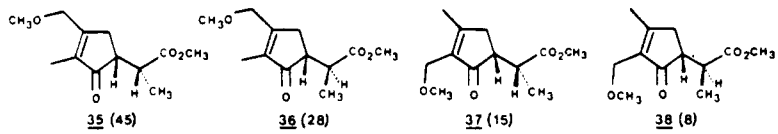
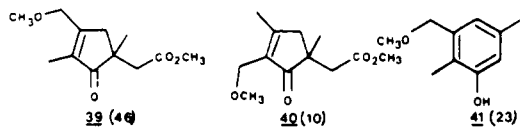
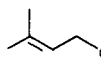
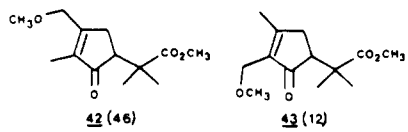
(21) (a) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 5268. (b) Semmelhack, M. F.; Brickner, S. J. *J. Org. Chem.* **1981**, *46*, 1723.
(22) Browning, J.; Cook, D. J.; Crudy, C. S.; Green, M.; Stone, F. G. A. *J. Chem. Soc., Chem. Commun.* **1968**, 929.
(23) Meier, H.; Estravridon, E.; Storek, C. *Angew Chem., Int. Ed. Engl.* **1986**, *25*, 809.

Table IV. ^{13}C Chemical Shifts of Acetylenic Carbon Atoms

monosubstituted acetylenes $\overset{\beta}{H}C\equiv\overset{\alpha}{C}R$				disubstitued acetylenes $CH_3\overset{\beta}{C}\equiv\overset{\alpha}{C}R$			
R	δ_α	δ_β	$\Delta\delta_{(C\equiv C)}$	R	δ_α	δ_β	$\Delta\delta_{(C\equiv C)}$
n-C_4H_9[a]	83.0	66.0	−17	CO_2CH_3	72.8	85.6	13.8
CH_2CH_2OH	81.8	70.5	−11.3	$COCH_3$[b]	81.7	93.6	11.9
CH_2OH	82.5	74.4	−8.1	CH_2OH	78.5	81.6	3.1
$COCH_3$	82.2	79.4	−2.8	CH_2SCH_3	80.1	82.5	2.4
CO_2CH_3	75.0	76.0	1	CH_2CH_2OH	76.6	77.3	0.7
				$\overset{\beta}{Me_3Si}C\equiv\overset{\alpha}{C}CH_2OH$	104.9	89.4	−15.5
Ph[a]	83.3	77.7	−5.6	$MeO_2CC\equiv CCO_2Me$	75.1	75.1	0
				t-BuOC≡CO-t-Bu	56.1	56.1	0

[a] Reported to give cyclopentenonic products with the expected regioselectivity in ketonic solvents.[18] [b] The substituent C_5H_{11} replaced methyl for this particular acetylene.

Table V. Product Distribution from Different Allyl Halides[a]

entry	allyl halide	regioisomeric ratio	main products[c] (yield)
a		3.9	**5** (62) **6** (16)
b	 [b]	3.3	 **35** (45) **36** (28) **37** (15) **38** (8)
c		4.6	 **39** (46) **40** (10) **41** (23)
d		3.8	 **42** (46) **43** (12)

[a] Yields of isolated product based on starting acetylene (2-butynyl methyl ether). Reactions were performed in methanol. [b] Three different isomeric allyl mixtures were used with the same results: (i) 85% *trans*-crotyl bromide, 15% 3-bromo-1-butene; (ii) 70% *trans*-crotyl chloride, 25% *cis*-crotyl chloride; (iii) 85% 3-chloro-1-butene, 10% *trans*-crotyl chloride. [c] Diasteromeric pairs **35–36** and **37–38** are mutually interchangeable.

H–^{13}C coupling of the terminal carbon atom by comparison of broad-band and SFORD spectra, whereas for disubstituted acetylenes each residual coupling was established by selective proton decoupling.

In Table IV are summarized δ ^{13}C values and chemical shift differences $\Delta\delta$ (C≡C) for the studied acetylenes, as a rough index of triple-bond polarization.

From comparison of this data with the results depicted in Tables I–III, it can be concluded that in all cases when chemical shift differences are large enough ($\Delta\delta > 3$), the allyl moiety and the carbonyl group will predominantly add as electrophile and nucleophile to the more shielded and deshielded carbon atom, respectively. However, as we have mentioned above, the occurrence of severe competitive steric or chelating effects can reverse this regioselectivity (cf. Table III, entry h).

Influence of Allyl Substitution. The reaction of different alkyl substituted allyl halides with 1-methoxybut-2-yne was carried out to clarify the possible steric influence of this substitution on the outcome of the carbonylative cycloaddition. From the results depicted in Table V, several conclusions can be drawn. The acetylene derivative always attacks the allyl group at the less substituted site as has been reported for reactions with π-allyl metal systems.[24-26] Remarkably, from crotyl bromide two pairs of diastereoisomers were isolated, each pair in a 1.7/1 relative ratio. Although it was not further investigated, a priori it might be expected that replacement of the methyl by a bulkier group would increase this ratio. Surprisingly, in contrast to previous studies,[27] in our case the overall yield is not markedly influenced by allyl substitution. This was also observed in the regioisomeric ratio.

Considerations on the Reaction Mechanism. As we have pointed out above, our results would agree with an electrophilic behavior of the allyl group rather than with the nucleophilic character commonly accepted for this moiety in related reactions.[28] In fact, this discrepancy has already been implicit in the reported replacement of the allyl group in this type of reaction by such an electrophile as acyl chloride in the reaction with acetylenes.[29,30] Likewise, along the same line it is possible to include the

(24) Hegedus, L. S.; Varaprath, S. *Organometallics* **1982**, *1*, 259.
(25) Chiusoli, G. P.; Bottaccio, G.; Venturello, C. *Chim. Ind. Milan* **1966**, *48*, 107.
(26) Chiusoli, G. P.; Bottaccio, G.; Venturello, C. *Tetrahedron Lett.* **1965**, 2875.
(27) Allyl halides add oxidatively to nickel carbonyl with some differences in rate (see: Semmelhack, M. F. In *Formation of Carbon-Carbon bonds via π-allyl-nickel* compounds; Wiley: New York, 1972; Organic Reactions, Vol. 19, p 161.
(28) For reviews see: (a) Billington, D. C. *Chem. Soc. Rev.* **1985**, *14*, 93. (b) Baker, R. *Chem. Rev.* **1973**, *73*, 487. (c) Tsuji, J. *Tetrahedron* **1986**, *42*, 4361. (d) Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic Press: New York, 1974. (e) Semmelhack, M. F. in ref 27.
(29) Cassar, L.; Chiusoli, G. P.; Foa, M. *Chim. Ind. Milan* **1968**, *50*, 515.
(30) Cassar, L.; Foa, M. *Chim. Ind. Milan* **1969**, *51*, 673. See also ref 32, p 355.

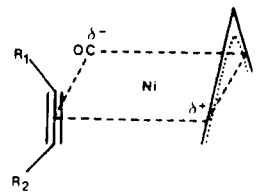


Figure 3.

addition of allyl moieties to quinones and electronically poor olefins or acetylenes mediated by Ni complexes without concurrent carbonylation.[22,27,31]

On the other hand, the regioselectivities observed in the present reaction were similar to those found for the Ni-mediated alkyne carbonylation[32] and the Pd(II)-catalyzed addition of allyl halides to alkynes.[33] The fact that these reactions are reported to proceed through cis metalated intermediates led us to propose an analogous mechanism in the present case, where the first step would be the carbometalation of the acetylene (cf. Scheme V). The regioselectivity of the addition of the Ni–CO bond can be predicted from theoretical calculations, which assign a neat positive charge to the nickel atom and a negative one for the carbonyl group.[34]

In a second step the resulting metallacycle in disubstituted acetylenes might preferentially insert an allyl moiety or, alternatively, in terminal acetylenes, methanol would attack on the acyl–nickel bond to yield vinylnickel species, which, eventually, by further reaction with allyl or acetylene moieties, would be transformed into the final products. However, all our attempts to trap the putative nickel acyclobutenone intermediate with different electrophiles failed and led to almost complete acetylene recovery.

On the other hand, IR spectroscopy comparative studies on the disappearance of the CO stretching triple bond absorption band at 2030 cm^{-1} in binary mixtures of either propargyl methyl ether, 2-butynyl methyl ether, or allyl chloride with $Ni(CO)_4$ and in ternary mixtures of those acetylenes with allyl chloride and $Ni(CO)_4$ in 1:1 THF–EtOH at room temperature, revealed that the above absorption faded very sluggishly in the absence of allyl halide, although it has been reported that the carbonylation of terminal acetylenes in the presence of protic acids is a fast reaction.[35] In contrast, a significant decrease of this band was observed in all cases when allyl chloride was present, indicating a stronger interaction of this moiety with $Ni(CO)_4$.

Finally, the formation of a π-allyl complex as the initial intermediate was conclusively proved by carrying out the reaction of 2-butynyl methyl ether with different allyl derivatives, such as 3-chloro-1-butene, *trans*-crotyl bromide and a mixture of *cis*- and *trans*-crotyl chloride, in the presence of $Ni(CO)_4$. In all cases, the same distribution of four different isomers was found, indicating that the reaction occurred through a common π-allyl intermediate. As shown in Figure 3, plausibly, the electrophilicity of this intermediate might be conferred by the presence of the very π-acidic carbonyl, trans to the allyl moiety. After a quasi-concerted double insertion or an alternative two-step process, this assembly might lead to the same intermediate A depicted in Scheme V, common to both mechanisms.

Conclusions

As it has been shown, by adequate choice of the reaction conditions, cyclopentenone derivatives can be obtained in satisfactory yields in the $Ni(CO)_4$-promoted carbonylative cycloaddition of allyl halides and acetylenes. It is noteworthy that, in the reaction with monosubstituted acetylenes, methanol leads mainly to the formation of 3-allyl acrylic esters and acetone to cyclic derivatives, whereas for disubstituted acetylenes cyclopentenones are generally produced. The reason for this different behavior seems to be associated with steric and electronic factors due to acetylene disubstitution, which may facilitate the coordination of the olefin onto the metal and/or the stabilization by the substituents of the resulting acyl–nickel bond, favoring the cyclization in both regioisomers.

The regioselectivity of the reaction was dependent on triple-bond polarization in all cases where steric factors were not very demanding. The influence of additional electronic or chelative control effects by incorporation of substituents in the allyl moiety is presently being investigated.

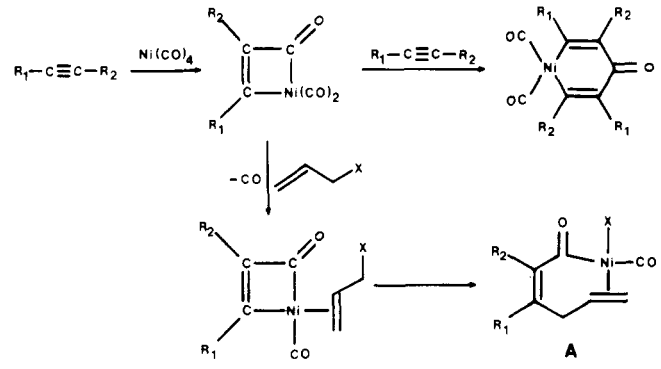
Experimental Section

IR spectra were recorded with a Perkin-Elmer 399B spectrometer. ^1H NMR and ^{13}C NMR were recorded with WP-80 SY Bruker and XL-200 Varian machines. Elemental analyses were performed with Carlo Erba apparatus (1107 and 1500 Models). Mass spectra were taken with a VG-updated AEI MS-902 instrument. GLC analyses were performed with a Carlo Erba Fractovap Series 2350 instrument, fitted with a 2-m column, type OV-101, and a Shimadzu Chromatopac C-R1B recorder and flame ionization detector. HPLC analyses were carried out on a Waters 510 Model, using a Spherisorb 10-OD S-2 25 × 0.46 cm Tracer column, a Waters 740 recorder, a Waters 450 UV detector, and a Waters R-401 RI detector. TLC was run on Merck 60 F_{254} silica gel plates, with ethyl acetate–hexane mixtures as eluent. Flash chromatography was performed on 230–400 mesh Merck 60 silica gel. $Ni(CO)_4$ was supplied by Merck A.G., unless otherwise stated. Acetylenes were furnished by Aldrich, but 1-methoxybut-2-yne, non-3-yn-2-one, 3-(trimethylsilyl)prop-2-yn-1-ol, 1-(methylthio)-but-2-yne and di-*tert*-butoxyacetylene were prepared in our laboratory by conventional procedures.[36,37] Allyl chloride and bromide were purchased from Merck A.G. and the other allyl halides from Fluka. All these compounds were distilled prior to use and the isomeric composition was determined by GLC.

A. Reactions in Different Solvent Systems. (A.1) 1-Methoxyprop-2-yne in Acetone–Methanol. A solution of nickel(0) tetracarbonyl (5.2 mL, 40 mmol) in dry acetone (5 mL) was added dropwise at 15 °C into a solution of the alkyne (1.4 g, 20 mmol) and allyl chloride (3.0 g, 40 mmol) in acetone–methanol (40 mL:5 mL) placed in a thermostated reaction flask, equipped with magnetic stirrer, dropping funnel, thermometer, gas inlet, and mercury valve, which had been previously purged with argon, and the reaction mixture was kept for 15 h at 14 °C. Then, the temperature was raised to 40 °C and after one additional hour a stream of nitrogen was passed through the mixture for 5 h, keeping the temperature at 40 °C, to remove any unreacted nickel(0) tetracarbonyl and most of the solvent. The remaining solvent was removed under vacuum, and the crude reaction product was treated with water (40 mL) and repeatedly extracted with dichloromethane. The extract was dried over $MgSO_4$, and, after removal of the solvent, flash chromatography (silica gel; hexane–ethyl acetate, 1:1) of the residue afforded cyclopentenone 1 and cyclohexenone 3 in 1.5% and 22.5% yield, respectively. Also

(31) Chiusoli, G. P. *Chim. Ind. Milan* **1961**, *43*, 365.
(32) See Carbon Monoxide addition to Acetylenic Substrates by Pino, P.; Braca, G. In *Organic Synthesis via Metal Carbonyls*; Wender, I., and Pino, P., Eds.; Wiley: New York, 1977; Vol. II, p 419. Also ref 28d, Vol. II, p 294.
(33) Kaneda, K.; Uchiyama, T.; Fujiwara, Y.; Imanaka, T.; Teranishi, S. *J. Org. Chem.* **1979**, *44*, 55.
(34) Reference 28d, Vol. I, p 8.
(35) Reference 32, p 447.
(36) Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: Amsterdam, 1971. Brandsma, L.; Verkruijsee, A. D. *Synthesis of Acetylenes, Alkenes and Cumulenes*; Elsevier: Amsterdam, 1981.
(37) Pericàs, M. A.; Serratosa, F. *Tetrahedron Lett.* **1977**, 4433.

Scheme V



isolated from the crude was a mixture of methyl 2- and 3-(methoxymethyl)hexa-2,5-dienoate **2** and **4** (15% and 4% yield respectively).

1: IR ($CHCl_3$) 1730, 1700, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.3–2.9 (5 H, =CCH_2, =CCH), 3.35 (3 H, s, OMe), 3.65 (3 H, s, COOMe), 4.1 (2 H, q, J = 1 Hz, CH_2O), 7.5 (1 H, br s, HC=); ^{13}C NMR ($CDCl_3$) δ 30.2 (t), 33.6 (t), 41.5 (d), 51.4 (q), 59.5 (q), 67.3 (t), 142.5 (s), 156.7 (d), 172.3 (s), 208.8 (s).

2: IR ($CHCl_3$) 1710, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.25 (2 H, ddt, J_a = 8.0 Hz, J_b = 6.0 Hz, J_c = 1.0 Hz, =CCH_2C=), 3.3 (3 H, s, OMe), 3.8 (3 H, s, COOMe), 4.2 (2 H, s, CH_2O), 4.9–5.2 (2 H, =CH_2), 5.85 (1 H, ddt, J_a = 20.0 Hz, J_b = 10.0 Hz, J_c = 6.0 Hz, HC=), 6.25 (1 H, tt, J_a = 8.0 Hz, J_b = 1.0 Hz, HC=).

3: IR ($CHCl_3$) 1730, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.5–2.8 (5 H, =CCH_2, =CCH), 3.4 (3 H, s, OMe), 3.7 (3 H, s, COOMe), 4.1 (2 H, br s, CH_2O), 7.0 (1 H, br s, HC=); ^{13}C NMR ($CDCl_3$) δ 27.8 (t), 39.5 (t), 39.5 (d), 51.9 (q), 58.6 (q), 68.6 (t), 136.1 (s), 143.3 (d), 173.2 (s), 195.7 (s). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.34; H, 7.28.

4: IR ($CHCl_3$) 1710, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.3 (3 H, s, OMe), 3.35 (2 H, d, J = 8 Hz, =CCH_2C=), 3.7 (3 H, s, COOMe), 4.2 (2 H, br s, CH_2O), 4.9–5.3 (2 H, =CH_2), 5.75 (1 H, ddt, J_a = 20 Hz, J_b = 10 Hz, J_c = 8 Hz, HC=), 6.0 (1 H, br s, HC=).

(A.2) 1-Methoxyprop-2-yne in Tetrahydrofuran–Methanol. To nickel(0) tetracarbonyl (5.2 mL, 40 mmol) in THF (25 mL) was added the alkyne (1.4 g, 20 mmol) in this solvent (5 mL) and allyl chloride (3.0 g, 40 mmol) in THF–methanol (15 mL:5 mL). After 14 h, the reaction was warmed to 35 °C, and nitrogen flushing was started. The same mixture of products but in different ratios was obtained on workup (5% of cyclopentenone, 11% cyclohexenone, and 27% mixture of the two dienoates).

(A.3) 1-Methoxyprop-2-yne in Methanol. To a mixture of the alkyne (0.7 g, 10 mmol) and allyl chloride (1.5 g, 20 mmol) in methanol (25 mL) was added nickel(0) tetracarbonyl (2.6 mL, 20 mmol), under the same procedure described above, to give 0.83 g of crude reaction product, showing one major and three minor peaks on GLC and HPLC analysis. Flash chromatography eluting with a 1:1 mixture of hexane–ethyl acetate afforded a 20:7 mixture of methyl (*Z*)-2-(methoxymethyl)hexa-2,5-dienoate (**2**) and methyl (*E*)-3-(methoxymethyl)hexa-2,5-dienoate (**4**) (460 mg, 27% global yield), the cyclohexenone **3** (142 mg, 7%), and the cyclopentenone **1** (171 mg, 9%).

(A.4) 1-Methoxybut-2-yne in Acetone–Methanol. The reaction was carried out as in A.1, replacing 1-methoxypropyne by 1-methoxybut-2-yne. The reaction mixture afforded the cyclopentenone **5** in 7% yield as the only pure material, as well as a 1.5% of the regioisomer **6**.

(A.5) 1-Methoxybut-2-yne in Tetrahydrofuran–Methanol. Similar treatment in this solvent system led to isolation of the same compounds as above in 13% total yield.

(A.6) 1-Methoxybut-2-yne in Methanol. From this alkyne (0.84 g, 10 mmol) and allyl chloride (1.5 g, 20 mmol) in 35 mL of methanol, when allowed to react under the standard reaction conditions with nickel(0) tetracarbonyl (2.6 mL, 20 mmol) in hexane (10 mL), 2.11 g of crude material were obtained. Flash chromatography (hexane–ethyl acetate, 2.5:1) afforded a 55% yield of 5-[(methoxycarbonyl)methyl]-3-(methoxymethyl)-2-methylcyclopent-2-enone **5** [IR ($CHCl_3$) 1730, 1690, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.7 (3 H, s, CH_3C=), 2.1–3.0 (5 H, =CCH_2, =CCH), 3.4 (3 H, s, OMe), 3.7 (3 H, s, COOMe), 4.3 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 8.1 (q), 34.0 (t), 35.1 (t), 41.0 (d), 51.1 (q), 59.0 (q), 70.2 (t), 135.1 (s), 167.2 (s), 172.0 (s), 209.2 (s). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.26; H, 7.55. Found: C, 62.22; H, 7.43] and an 11% yield of the regioisomer **6** [IR ($CHCl_3$) 1730, 1690, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.2 (3 H, s, CH_3C=), 2.3–3.1 (5 H, =CCH_2, =CCH), 3.3 (3 H, s, OMe), 3.7 (3 H, s, COOMe), 4.1 (2 H, s, CH_2O)]. Substituting allyl bromide (2.42 g, 20 mmol) for the chloride led to 61% and 17% yields, respectively.

On air exposure **5** was slowly transformed into 3-(methoxycarbonyl)-5-[(methoxycarbonyl)methyl]-2-methylcyclopent-2-enone (**28**). The isomer **6** was not oxidized under these conditions.

B. Reaction of Nickel(0) Tetracarbonyl and Allyl Chloride with Different Acetylenes in Methanol as Solvent. (B.1) Reaction with Prop-2-yn-1-ol. Under the general reaction conditions described above, propargyl alcohol (1.1 g, 20 mmol) as substrate yielded 3.0 g of a crude material, showing one major and four minor components by GLC and HPLC analysis. Flash chromatography (hexane–ethyl acetate, 3:1 for the 20 early fractions and 3:2 for the following 15) gave methyl (*Z*)-2-(hydroxymethyl)hexa-2,5-dienoate (**7**) (0.76 g, 24%) [IR ($CHCl_3$) 3620–3200, 1710, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) identical signals as found for **2** but the OMe absorption (δ 3.30) is replaced by an OH signal (δ 2.8); ^{13}C NMR ($CDCl_3$) δ 34.1 (t), 52.0 (q), 66.5 (t), 118.3 (t), 131.7 (s), 136.9 (d), 143.8 (d), 168.2 (s)]. The minor compounds were identified on spectroscopic grounds as 5-furfuryl-2-(methoxymethyl)cyclopent-2-enone (**8**) (0.17 g, 4%) [IR ($CHCl_3$) 1700, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.4–2.9 (5 H, =CCH_2, =CCH), 3.4 (3 H, s, OMe), 4.1 (2 H, br s, CH_2O), 6.05 (1 H, br s, HC=), 6.3 (1 H, t, J = 2 Hz, HC=), 7.3 (1 H, br s, HC=), 7.6 (1 H, br s, HC=); ^{13}C NMR ($CDCl_3$) δ 29.0 (t), 32.7 (t), 45.1 (d), 58.9 (q), 67.8 (t), 106.8 (d), 110.1 (d), 141.5 (d), 142.1 (s), 153.5 (s), 158.7 (d), 209.1 (s)], methyl (*E*)-3-(hydroxymethyl)hexa-2,5-dienoate (**9**) (0.12 g, 4%) [IR ($CHCl_3$) 3620–3200, 1710, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) identical signals as found for **4** but the OMe absorption (δ 3.30) is replaced by an OH signal (δ 1.7); ^{13}C NMR ($CDCl_3$) δ 33.8 (t), 51.0 (q), 65.1 (t), 113.9 (d), 116.5 (t), 134.6 (d), 158.6 (s), 166.8 (s). Anal. Calcd for $C_8H_{12}O_3$: C, 61.54; H, 7.69. Found: C, 61.49; H, 7.67], 5-(methoxycarbonyl)-2-(methoxymethyl)cyclohex-2-enone (**3**) (0.24 g, 6%), and 5-[(methoxycarbonyl)methyl]-2-(methoxymethyl)cyclopent-2-enone (**1**) (0.12 g, 3%).

(B.2) Reaction with But-3-yn-1-ol. From 0.7 g (10 mmol) of this ynol, and 1.5 g of allyl chloride (20 mmol) in methanol (40 mL), the reaction with nickel(0) tetracarbonyl (2.6 mL, 20 mmol) in hexane (5 mL) yielded 1.7 g of crude material, comprised of one major and two minor compounds. On flash chromatographic separation (hexane–ethyl acetate, 4:1), the three compounds were isolated and identified as (*Z*)-2-(but-3-enylidene)-4-butanolide (**10**) (11% yield) [IR ($CHCl_3$) 1750, 1670, 1635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.9 (2 H, tdt, J_a = 8 Hz, J_b = 2 Hz, J_c = 1 Hz, =CCH_2), 3.5 (2 H, ddt, J_a = 8 Hz, J_b = 6 Hz, J_c = 1 Hz, =CCH_2C=), 4.3 (2 H, t, J = 8 Hz, CH_2OCO), 4.9–5.3 (2 H, =CH_2), 5.75 (1 H, ddt, J_a = 16 Hz, J_b = 9 Hz, J_c = 6 Hz, =CH), 6.25 (1 H, tt, J_a = 8 Hz, J_b = 2 Hz, =CH); ^{13}C NMR ($CDCl_3$) δ 29.0 (t), 31.5 (t), 65.2 (t), 116.0 (t), 124.1 (s), 135.0 (d), 140.3 (d), 169.7 (s)], (*E*)-2-(but-3-enylidene)-4-butanolide **11** (65% yield) [IR ($CHCl_3$) 1750, 1670, 1635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.8–3.1 (4 H, =CCH_2), 4.4 (2 H, t, J = 8 Hz, CH_2O) 4.9–5.3 (2 H, =CH_2), 5.75 (1 H, ddt, J_a = 16 Hz, J_b = 9 Hz, J_c = 6 Hz, =CH), 6.75 (1 H, tt, J_a = 8 Hz, J_b = 1.6 Hz, =CH); ^{13}C NMR ($CDCl_3$) δ 24.6 (t), 33.6 (t), 65.1 (t), 116.3 (t), 126.2 (s), 133.0 (d), 136.7 (d), 170.6 (s). Anal. Calcd for $C_8H_{10}O_2$: C, 69.56; H, 7.24. Found: C, 69.24; H, 7.55], and methyl (*E*)-2-(2-hydroxyethyl)hexa-2,5-dienoate (**12**) 8% yield) [IR ($CHCl_3$) 3600, 3600–3250, 1710, 1635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.6 (2 H, t, J = 8 Hz, =CCH_2), 2.7 (1 H, s, OH), 2.9 (2 H, ddt, J_a = 8 Hz, J_b = 6 Hz, J_c = 1 Hz, =CCH_2C=), 3.65 (2 H, t, J = 8 Hz, CH_2O), 3.75 (3 H, s, COOMe), 4.8–5.2 (2 H, =CH_2), 5.8 (1 H, ddt, J_a = 16 Hz, J_b = 9 Hz, J_c = 6 Hz, =CH), 6.9 (1 H, t, J = 8 Hz, =CH)].

(B.3) Reaction with But-3-yn-2-one. This ketone (0.68 g, 10 mmol) under the above conditions [1.5 g (20 mmol) of allyl chloride in 40 mL of methanol and 2.6 mL (20 mmol) of nickel(0) tetracarbonyl in 5 mL of hexane] yielded 2.2 g of crude reaction mixture. The two major components were isolated by flash chromatography (hexane–ethyl acetate, 10:1) and characterized

as methyl (*E*)-3-acetylhexa-2,5-dienoate (**14**) (170 mg, 10%) [IR ($CHCl_3$) 1720, 1685, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.35 (3 H, s, CH_3CO), 3.55 (2 H, d, J = 7 Hz, $=CCH_2C=$), 3.8 (3 H, s, COOMe) 4.9–5.2 (2 H, $=CH_2$), 5.8 (1 H, ddt, J_a = 17 Hz, J_b = 10 Hz, J_c = 7 Hz, =CH), 6.6 (1 H, s, =CH); ^{13}C NMR ($CDCl_3$) δ 26.2 (q), 30.4 (t), 51.5 (q), 116.3 (t), 125.9 (d), 134.2 (d), 151.9 (s), 165.9 (s), 198.7 (s)] and methyl 3-allyllevulinate (3-allyl-4-oxopentanoate) (**13**) (270 mg, 16%) [IR ($CHCl_3$) 1730, 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.2 (3 H, s, CH_3CO), 2.1–3.4 (5 H, $=CCH_2$, =CCH), 3.65 (3 H, s, COOMe), 4.9–5.2 (2 H, $=CH_2$), 5.4–6.0 (1 H, =CH); ^{13}C NMR ($CDCl_3$) δ 29.3 (q), 34.4, (t), 35.3 (t), 47.4 (d), 51.4 (q), 117.7 (t), 134.15 (d), 172.5 (s), 209.5 (s)].

(B.4) Reaction with Methyl Propiolate. The acetylenic ester (0.84 g, 10 mmol) was reacted as above to afford 2.0 g of crude material yielding after flash chromatography (hexane–ethyl acetate, 5:1) dimethyl allylfumarate (**17**) (0.2 g, 11%) [^1H NMR ($CDCl_3$) δ 3.6 (2 H, d, J = 6 Hz, $=CCH_2C=$), 3.75 (3 H, s, COOMe), 3.8 (3 H, s, COOMe), 4.9–5.3 (2 H, $=CH_2$), 5.85 (1 H, ddt, J_a = 16 Hz, J_b = 9 Hz, J_c = 6 Hz, =CH), 6.8 (1 H, s, =CH); ^{13}C NMR ($CDCl_3$) δ 31.6 (t), 51.6 (q), 52.4 (q), 116.6 (t), 126.7 (d), 134.1 (d), 145.3 (s) 165.7 (s), 166.85 (s)], dimethyl but-2-enylidenemalonate (**15**) (0.36 g, 19%) [^1H NMR ($CDCl_3$) δ 1.9 (3 H, d, J = 6 Hz, $CH_3C=$), 3.75 (3 H, s, COOMe), 3.8 (3 H, s, COOMe), 6.1–6.6 (2 H, HC=), 7.35 (1 H, d, J = 10 Hz, HC=); ^{13}C NMR ($CDCl_3$) δ 18.8 (q), 52.0 (q, double intensity), 122.7 (s), 127.2 (d), 144.6 (d), 145.8 (d), 165.0 (s), 165.5 (s). Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.52. Found: C, 58.77; H, 6.59], and dimethyl (3-methoxybutylidene)malonate (**16**) (0.26 g, 12%) [IR ($CHCl_3$) 1730, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (3 H, d, J = 8 Hz, CH_3CO), 2.5 (2 H, dd, J_a = 8 Hz, J_b = 7 Hz, $CH_2C=$), 3.3 (3 H, s, OMe), 3.6–3.9 (1 H, CHO), 3.77 (3 H, s, COOMe), 3.82 (3 H, s, COOMe), 7.1 (1 H, t, J = 8 Hz, HC=); ^{13}C NMR ($CDCl_3$) δ 19.1 (q), 36.1 (t), 52.0 (q), 52.1 (q), 56.0 (q), 75.3 (d), 129.2 (s), 146.6 (d), 164.2 (s), 165.5 (s)].

(B.5) Reaction with Hex-3-yne. The acetylene (0.82 g, 10 mmol) was reacted under the same conditions as in B.2 to afford 1.17 g of crude material yielding, after flash chromatography (hexane–ethyl acetate, 5:1), 2,3-diethyl-5-[(methoxycarbonyl)-methyl]cyclopent-2-enone (**18**) (300 mg, 14%) [IR ($CHCl_3$) 1740, 1690, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (3 H, t, J = 8 Hz, CH_3), 1.1 (3 H, t, J = 8 Hz, CH_3), 2.0–3.0 (5 H, $=CCH_2$, =CCH), 2.15 (2 H, q, J = 8 Hz, $CH_2C=$), 2.4 (2 H, q, J = 8 Hz, $CH_2C=$), 3.8 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 11.7 (q), 12.9 (q), 16.1 (t), 23.65 (t), 35.1 (t), 35.5 (t), 41.1 (d), 51.3 (q), 140.1 (s), 172.4 (s), 172.6 (s), 208.7 (s)].

(B.6) Reaction with Pent-2-yne. The acetylene (0.68 g, 10 mmol) was reacted as above to afford 1.1 g of crude material, yielding, after flash chromatography (hexane–ethyl acetate, 3:1), a mixture of 2-ethyl-5-[(methoxycarbonyl)methyl]-3-methylcyclopent-2-enone (**19**) and 3-ethyl-5-[(methoxycarbonyl)-methyl]-2-methylcyclopent-2-enone (**20**) (0.24 g, 12% yield of a 1:1 mixture; only partially separated into the pure compounds). **19**: ^1H NMR ($CDCl_3$) δ 1.0 (3 H, t, J = 8 Hz, CH_3), 2.05 (3 H, s, $CH_3C=$), 2.2 (2 H, q, J = 8 Hz, $CH_2C=$), 2.0–3.2 (5 H, $=CCH_2$, =CCH), 3.7 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 10.2, 16.3, 30.0, 33.6, 34.6, 41.0, 51.8, 143.0, 158.9, 172.0, 209.7. **20**: ^1H NMR ($CDCl_3$) δ 1.1 (3 H, t, J = 8 Hz, CH_3), 1.7 (3 H, s, $CH_3C=$), 2.3 (2 H, q, J = 8 Hz, $CH_2C=$), 1.9–3.0 (5 H, $=CCH_2$, =CCH), 3.7 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 8.0, 11.1, 24.0, 36.2, 37.1, 41.0, 52.1, 134.0, 172.2, 173.1, 209.2.

(B.7) Reaction with But-2-yn-1-ol. To this ynol (1.4 g, 20 mmol) and allyl chloride (3 g, 40 mmol) in methanol (40 mL) was added nickel(0) tetracarbonyl (5.2 mL, 40 mmol), and the reaction was treated under the standard conditions to yield a crude residue (3.4 g). Flash chromatography (ethyl acetate) afforded 3-(hydroxymethyl)-5-[(methoxycarbonyl)methyl]-2-methylcyclopent-2-enone (**21**) (1.82 g, 46%) [IR ($CHCl_3$) 3660, 3600–3200, 1730, 1690, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7 (3 H, s, $CH_3C=$), 2.1–3.3 (6 H, $=CCH_2$, =CCH, OH), 3.7 (3 H, s, OMe), 4.6 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.6, 33.8, 34.7, 40.7, 51.3, 60.0, 134.1, 170.4, 172.3, 209.8], as well as a minor amount of the regioisomer **22** (0.40 g, 10%) [IR ($CHCl_3$) 3660, 3600–3200, 1730, 1690, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1 (3 H, s, $CH_3C=$), 2.3–3.0 (6 H, $=CCH_2$, =CCH, OH), 3.7 (3 H, s, OMe), 4.3 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 16.8 (q), 34.6 (t), 38.8 (t), 41.3 (d), 51.5 (q), 54.6 (t), 137.6 (s), 171.9 (s), 172.2 (s), 204.2 (s)].

(B.8) Reaction with Pent-3-yn-1-ol. The reaction was performed as above with pent-3-yn-1-ol (1.7 g, 20 mmol) as substrate to afford 3.8 g of crude material, which yielded 2-(2-hydroxyethyl)-5-[(methoxycarbonyl)methyl]-3-methylcyclopent-2-enone (**23**) (1.53 g, 36%) on chromatographic separation [IR ($CHCl_3$) 3700–3150, 1725, 1685, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1 (3 H, s, $CH_3C=$), 2.3–3.2 (8 H, $=CCH_2$, =CCH, OH), 3.7 (3 H, s, OMe), 3.7 (2 H, t, J = 6.0 Hz, CH_2O); ^{13}C NMR ($CDCl_3$) δ 17.0 (q), 27.1 (t), 34.8 (t), 38.7 (t), 41.0 (d), 51.5 (q), 60.7 (t), 136.8 (s), 171.4 (s), 172.3 (s), 210.0 (s). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.26; H, 7.55. Found: C, 61.92; H, 7.71] and (*Z*)-2-(1-methylbut-3-enylidene)-4-butanolide (**24**) (0.18 g, 6%) [IR ($CHCl_3$) 1750, 1670, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 (3 H, br s, $CH_3C=$), 2.9 (2 H, t, J = 8 Hz, $=CCH_2$), 3.5 (2 H, d, J = 7 Hz, $=CCH_2C=$), 4.3 (2 H, t, J = 8 Hz, CH_2O), 4.9–5.3 (2 H, $=CH_2$), 5.8 (1 H, m, HC=)].

(B.9) Reaction with Non-3-yn-2-one. From this ketone (2.76 g, 20 mmol) under the above conditions resulted 4.78 g of a three compound mixture, which on flash chromatography (hexane:ethyl acetate 9:1) afforded 3-(1,1-dimethoxyethyl)-5-[(methoxycarbonyl)methyl]-2-pentylcyclopent-2-enone (**27**) (0.54 g, 9%) [IR ($CHCl_3$) 1730, 1700, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3 H, t, J = 8 Hz, CH_3), 1.1–1.7 (6 H, CH_2), 1.5 (3 H, s, CH_3CO), 2.0–2.6 (7 H, $=CCH_2$, =CCH), 3.2 (6 H, s, OMe), 3.7 (3 H, s, COOMe)] and a mixture of 3-acetyl-5-[(methoxycarbonyl)methyl]-2-pentylcyclopent-2-enone (**25**) and the corresponding cyclopentanone **26** (1.85 g, 35%). It was possible to isolate minor amounts of both pure compounds to fully characterize spectroscopically each one. **25**: IR ($CHCl_3$) 1740, 1710, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3 H, t, J = 8 Hz, CH_3), 1.1–1.7 (6 H, CH_2), 2.4 (3 H, s, CH_3CO), 2.1–3.1 (7 H, $CH_2C=$, CCH=), 3.7 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 13.7 (q), 22.2 (t), 24.2 (t), 28.1 (t), 29.5 (q), 31.8 (t), 33.7 (t), 34.5 (t), 41.1 (d), 51.7 (q), 147.1 (s), 158.9 (s), 171.9 (s), 199.0 (s), 209.4 (s). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.6; H, 8.27. Found: C, 67.42; H, 8.44. **26**: IR ($CHCl_3$) 1740, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (3 H, t, J = 8 Hz, CH_3), 1.1–1.7 (8 H, CH_2), 2.3–3.0 (7 H, $CH_2C=$, CHC=), 2.3 (3 H, s, CH_3CO), 3.7 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.3, 26.4, 29.0, 29.6, 31.7, 33.7, 45.8, 50.3, 51.7, 52.9, 172.1, 207.9, 216.9. Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.16; H, 8.95. Found: C, 66.82; H, 8.99.

(B.10) Reaction with Methyl But-2-ynoate. From this ester (0.28 g, 10 mmol), under the same conditions as in B.2, was isolated, after flash chromatography purification (hexane–ethyl acetate, 3:1), 2.04 g (90% yield) of 3-(methoxycarbonyl)-5-[(methoxycarbonyl)methyl]-2-methylcyclopent-2-enone (**28**) was obtained: IR ($CHCl_3$) 1730, 1710, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.05 (3 H, t, J = 2 Hz, $CH_3C=$), 2.3–3.1 (5 H, $=CCH_2$, =CCH), 3.7 (3 H, s, COOMe), 3.9 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 9.5 (q), 33.1 (t), 34.2 (t), 40.8 (d), 51.4 (q), 51.6 (q), 146.2 (s), 152.3 (s), 165.2 (s), 171.6 (s), 209.0 (s). Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.19. Found: C, 58.40; H, 6.14.

(B.11) Reaction with 3-(Trimethylsilyl)prop-2-yn-1-ol. Nickel(0) tetracarbonyl (30 mmol) was condensed[38] into a solution of the starting alkyne (1.92 g, 15 mmol) and allyl chloride (0.2 g, 30 mmol) in methanol (35 mL). The reaction was kept at 40 °C for 2 h and then worked up to afford 3-(hydroxymethyl)-5-[(methoxycarbonyl)methyl]-2-(trimethylsilyl)cyclopent-2-enone (**29**) (0.6 g, 23%; yield) after purification by flash chromatography (hexane–ethyl acetate 2:1): IR ($CHCl_3$) 3700–3200, 3600, 1735, 1690, 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.2 (9 H, s, MeSi), 2.3–3.1 (6 H, $=CCH_2$, =CCH, OH), 3.7 (3 H, s, COOMe), 4.65 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ –0.5 (q, triple intensity), 35.1 (t), 37.2 (t), 42.4 (d), 51.8 (q), 62.4 (t), 138.6 (s), 172.9 (s), 185.4 (s), 213.3 (s). Anal. Calcd for $C_{12}H_{20}O_4Si$: C, 56.20; H, 7.86. Found: C, 56.54; H, 7.82.

(B.12) Reaction with 1-(Methylthio)but-2-yne. Nickel(0) tetracarbonyl (20 mmol) was allowed to react with the thioalkyne (1.0 g, 10 mmol), allyl chloride (1.53 g, 20 mmol), and methanol (40 mL), under the standard conditions, to afford a 1.24 g of a crude mixture of two major components. Flash chromatography (hexane–ethyl acetate, 3:1) led to the isolation of 5-[(methoxycarbonyl)methyl]-2-methyl-3-[(methylthio)methyl]cyclopent-2-enone (**30**) (0.66 g, 30%) [IR ($CHCl_3$) 1730, 1695, 1640 cm^{-1}; ^1H

(38) Boix, F.; Camps, F.; Coll, J.; Moretó, J. M.; Torras, J. *Synth. Commun.* **1987**, *17*, 1149.

NMR ($CDCl_3$) δ 1.71 (3 H, s, CH_3C=), 1.95 (3 H, s, CH_3S), 2.1–2.9 (5 H, CH_2C=, CHC=), 3.35 (2 H, s, =CCH_2S), 3.6 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 8.2 (q), 15.1 (q), 32.8 (t), 34.9 (t), 35.3 (t), 41.2 (d), 51.6 (q), 136.8 (s), 165.9 (s), 172.2 (s), 209.0 (s). Anal. Calcd for $C_{11}H_{16}O_3S$: C, 57.87; H, 7.07; S, 14.04. Found: C, 57.54; H, 7.38; S, 13.88] and the regioisomer **31** (0.43 g, 18%) [IR ($CHCl_3$) 1730, 1695, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0 (3 H, s, CH_3S), 2.05 (3 H, s, CH_3C=), 2.2–2.9 (5 H, CH_2C=, CHC=), 3.2 (2 H, s, =CCH_2S), 3.65 (3 H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ 15.8 (t), 17.3 (q), 25.0 (t), 35.0 (t), 38.7 (q), 41.3 (d), 51.7 (q), 136.7 (s), 170.8 (s), 172.3 (s), 207.5 (s). Anal. Calcd for $C_{11}H_{16}O_3S$: C, 57.87; H, 7.07; S, 14.04. Found: C, 57.81; H, 7.05; S, 14.12].

(B.13) Reaction with Dimethyl But-2-yne-1,4-dioate. From dimethyl acetylenedicarboxylate (2.85 g, 20 mmol) and other conditions as in B.1., a 4.25 g of crude material was obtained, showing the presence of two major peaks on GLC in a ratio close to 1:1. On flash chromatography (hexane–ethyl acetate, 7:1), separation was achieved and the products identified as dimethyl diallylmaleate (**33**) (1.43 g, 32%) [IR ($CHCl_3$) 1720, 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.1 (4 H, dt, J_a = 5.6 Hz, J_b = 1.4 Hz, =CCH_2C=), 3.7 (6 H, s, COOMe), 5.1 (2 H, dt, J_a = 16.8 Hz, J_b = 1.4 Hz, =CH_2), 5.2 (2 H, dt, J_a = 8.4 Hz, J_b = 1.4 Hz, =CH), 5.8 (2 H, ddt, J_a = 16.8 Hz, J_b = 8.4 Hz, J_c = 5.6 Hz, =CH); ^{13}C NMR ($CDCl_3$) δ 33.1 (t), 52.0 (q), 117.1 (t), 132.9 (d), 136.3 (s), 168.4 (s). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.28; H, 7.14. Found: C, 63.89; H, 7.37] and dimethyl allylmaleate (**32**) (1.55 g, 42%) [IR ($CHCl_3$) 1725, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.1 (2 H, d, J = 5.6 Hz, =CCH_2C=), 3.7 (3 H, s, COOMe), 3.8 (3 H, s, COOMe), 5.0–5.3 (2 H, =CH_2), 5.5–6.1 (1 H, HC=), 5.85 (1 H, br s, HC=); ^{13}C NMR ($CDCl_3$) δ 39.0 (t), 51.1 (q), 51.5 (q), 119.5 (t), 120.6 (d), 131.1 (d), 149.0 (s), 166.1 (s), 169.0 (s)]. With use of a 1:4:2 ratio of the acetylene, allyl chloride, and nickel compound, the same products were found in a 7:3 ratio.

(B.14) Reaction with Di-*tert*-butoxyacetylene. Under the standard reaction conditions, this substrate reacted immediately to a cyclotrimer (60% yield of hexa-*tert*-butoxybenzene, mp 223–4 °C, as already reported in the literature).[37]

C. Reaction of 1-Methoxybut-2-yne with Different Alkyl-Substituted Allyl Moieties. (C.1) Reaction with *trans*-1-Bromobut-2-ene (Crotyl bromide). The reaction was performed by dropwise addition of a solution of nickel(0) tetracarbonyl (3 mL, 23 mmol) in hexane (4 mL) to 1-methoxybut-2-yne (0.84 g, 10 mmol) and *trans*-1-bromobut-2-ene, containing 15% of 3-bromo-1-butene, (2.7 g, 20 mmol) in methanol (40 mL). HPLC analyses of the resulting crude mixture with both RI and UV (240 nm) detectors and isocratic mode (44:56 MeOH–H_2O) revealed the presence of four different compounds with retention times of 9, 10, 12, and 15 min, in a 8:16:29:46 ratio, respectively. Flash chromatography separation of this mixture using a 1:2.5 EtOAc–hexane mixture, allowed the isolation of two pairs of regioisomers in 22% and 73%, which by further TLC isolation as pure compounds were identified as **35** + **36** and **37** + **38**, respectively. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.72; H, 7.96. Found: C, 63.58; H, 8.12.

35: IR ($CHCl_3$) 1730, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (3 H, d, J = 8 Hz, CH_3), 1.7 (3 H, s, CH_3C=), 2.3–3.2 (4 H, =CCH_2, =CCH), 3.4 (3 H, s, OMe), 3.7 (3 H, s, COOMe), 4.3 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.9 (q), 11.8 (q), 30.5 (t), 39.2 (d), 46.4 (d), 51.7 (q), 58.8 (q), 70.1 (t), 136.6 (s), 167.3 (s), 175.4 (s), 208.9 (s).

36: IR ($CHCl_3$) 1730, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (3 H, d, J = 8 Hz, CH_3), 1.75 (3 H, s, CH_3C=), 2.3–3.2 (4 H, =CCH_2, =CCH), 3.4 (3 H, s, OMe), 3.6 (3 H, s, COOMe), 4.3 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.9 (q), 14.8 (q), 31.6 (t), 39.5 (d), 47.2 (d), 51.4 (q), 58.6 (q), 69.9 (t), 136.3 (s), 165.8 (s), 174.3 (s), 208.9(s).

37: IR ($CHCl_3$) 1730, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (3 H, d, J = 8 Hz, CH_3), 2.2 (3 H, s, CH_3C=), 2.3–3.2 (4 H, =CCH_2, =CCH), 3.3 (3 H, s, OMe), 3.7 (3 H, s, COOMe), 4.1 (2 H, br s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 11.6 (q), 17.3 (q), 35.0 (t), 38.9 (t), 46.8 (d), 51.7 (q), 58.35 (q), 63.0 (t), 136.8 (s), 175.1 (s), 175.5 (s), 207.5 (s).

38: IR ($CHCl_3$) 1730, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (3 H, d, J = 8 Hz, CH_3), 2.15 (3 H, s, CH_3C=) 2.3–3.2 (4 H, =CCH_2, =CCH), 3.3 (3 H, s, OMe), 3.6 (3 H, s, COOMe), 4.1 (2 H, br s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 15.1 (q), 17.4 (q), 36.4 (t), 39.6 (d), 47.9 (d), 51.6 (q), 58.4 (q), 63.1 (t), 136.0 (s), 173.6 (s), 174.6 (s), 207.55 (s).

(C.2) Reaction with a Mixture of *cis*- and *trans*-1-Chlorobut-2-ene. The reaction in this case was carried out as in C.1, replacing *trans*-crotyl bromide by a mixture of 25% *cis*- and 70% *trans*-crotyl chloride. HPLC analyses of the crude product (2.5 g) exhibited the same peak sequence in a 7:16:29:47 ratio.

(C.3) Reaction with 3-Chlorobut-1-ene. The reaction was performed as above with a mixture of 85% of 3-chlorobut-1-ene and 10% *trans*-crotyl chloride. HPLC analyses of the crude product (2.5 g) gave the same peak profile in a 7:15:25:43 ratio.

(C.4) Reaction with 1-Chloro-2-methylprop-2-ene (2-Methylallyl chloride). As above, with 1-chloro-2-methylprop-2-ene as allyl reagent (1.81 g, 20 mmol), flash chromatography with hexane–ethyl acetate (2:1) gave 3-(methoxymethyl)-2,5-dimethylphenol (0.465 g, 23%) [IR ($CHCl_3$) 3600, 3100, 1710, 1625, 1590, 910, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.15 (3 H, s, CH_3Ar), 2.2 (3 H, s, CH_3Ar), 3.4 (3 H, s, OMe), 4.45 (2 H, s, CH_2O), 6.45 (1 H, s, HAr), 6.7 (1 H, s, HAr); ^{13}C NMR ($CDCl_3$) δ 10.2 (q) 20.5 (q), 57.5 (q), 73.0 (t), 115.5 (d), 119.9 (s), 121.7 (d), 135.5 (s), 136.5 (s), 154.0 (s)], 5-[(methoxycarbonyl)methyl]-3-(methoxymethyl)-2,5-dimethylcyclopent-2-enone (**39**) (1.03 g, 46%) [IR ($CHCl_3$) 1735, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1 (3 H, s, CH_3), 1.8 (3 H, s, CH_3C=), 2.5 (2 H, s, CH_2C=), 2.1–3.1 (2 H, CH_2C=), 3.4 (3 H, s, OMe), 3.6 (3 H, s, COOMe), 4.3 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.9, 24.1, 40.8, 41.4, 43.6, 51.0, 58.4, 69.7, 133.9, 164.9, 171.2, 211.2. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.72; H, 7.96. Found: C, 63.65; H, 8.14], and 5-[(methoxycarbonyl)-methyl]-2-(methoxymethyl)-3,5-dimethylcyclopent-2-enone (**40**) (0.22 g, 10%) [IR ($CHCl_3$) 1735, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1 (3 H, s, CH_3), 2.2 (3 H, s, CH_3C=), 2.5 (2 H, s, CH_2C=), 2.1–3.1 (2 H, CH_2C=), 3.3 (3 H, s, OMe), 3.6 (3 H, s, COOMe), 4.1 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 17.4 (q), 24.3 (q), 41.0 (t), 44.6 (s), 46.4 (t), 51.45 (q), 58.4 (q), 63.3 (t), 134.3 (s), 171.8 (s), 173.1 (s), 210.3 (s)].

(C.5) Reaction with 1-Bromo-3-methylbut-2-ene (3,3-Dimethylallyl bromide). As above but with 1-bromo-3-methylbut-2-ene (3.0 g, 20 mmol) as allyl reagent, the resulting crude mixture, subjected to flash chromatography (hexane–ethyl acetate, 2.5:1), afforded 5-[1-(methoxycarbonyl)-1-methylethyl]-3-(methoxymethyl)-2-methylcyclopent-2-enone (**42**) (1.11 g, 46% yield) [IR ($CHCl_3$) 1725, 1695, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2 (6 H, s, CH_3), 1.7 (3 H, s, CH_3C=), 2.2–3.0 (3 H, =CCH_2, =CCH), 3.35 (3 H, s, OMe), 3.7 (3 H, s, COOMe), 4.3 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.8 (q), 21.6 (q), 22.7 (q), 31.3 (t), 44.0 (s), 51.1 (d), 51.8 (q), 58.7 (q), 70.0 (t), 137.0 (s), 165.6 (s), 177.1 (s), 208.7 (s)] and 5-[1-(methoxycarbonyl)-1-methylethyl]-2-(methoxymethyl)-3-methylcyclopent-2-enone (**43**) (0.29 g, 12% yield) [IR ($CHCl_3$) 1725, 1695, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2 (6 H, s, CH_3), 2.2 (3 H, s, CH_3C=), 2.2–3.0 (3 H, CH_2C=, CHC=), 3.35 (3 H, s, OMe), 3.75 (3 H, s, COOMe), 4.05 (2 H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ 17.1 (q), 21.7 (q), 22.5 (q), 36.0 (t), 43.9 (s), 51.4 (q), 51.7 (d), 58.2 (q), 62.9 (t), 137.1 (s), 173.2 (s), 177.0 (s), 207.1 (s)].

Acknowledgment. Financial support from CAICYT (Grant 84-0087) and CSIC (Pr. 263-85) is gratefully acknowledged.

Registry No. **1**, 118891-01-3; **2**, 118891-02-4; **3**, 118891-03-5; **4**, 118891-04-6; **5**, 118891-05-7; **6**, 118891-06-8; **7**, 118891-07-9; **8**, 118891-08-0; **9**, 118891-09-1; **10**, 118891-10-4; **11**, 118891-11-5; **12**, 118891-12-6; **13**, 118891-14-8; **.14**, 118891-13-7; **15**, 50984-35-5; **16**, 118891-16-0; **17**, 118891-15-9; **18**, 118891-17-1; **19**, 118891-18-2; **20**, 118891-19-3; **21**, 103633-24-5; **22**, 103633-23-4; **23**, 118891-20-6; **24**, 118891-39-7; **25**, 118891-22-8; **26**, 118891-23-9; **27**, 118891-21-7; **28**, 118891-24-0; **29**, 118891-25-1; **30**, 118891-27-3; **31**, 118891-28-4; **32**, 119009-92-6; **33**, 118891-29-5; **35**, 118891-30-8; **36**, 118891-31-9; **37**, 118891-32-0; **38**, 118891-33-1; **39**, 118891-35-3; **40**, 118891-36-4; **42**, 118891-37-5; **43**, 118891-38-6; nickel(0) tetracarbonyl, 13463-39-3; 1-methoxyprop-2-yne, 627-41-8; allyl chloride, 107-05-1; 1-methoxybut-2-yne, 2768-41-4; allyl bromide, 106-95-6; prop-2-yn-1-ol, 107-19-7; but-3-yn-1-ol, 927-74-2; but-3-yn-2-one, 1423-60-5; methyl propiolate, 922-67-8; hex-3-yne, 928-49-4; pent-2-yne, 627-21-4; but-2-yn-1-ol, 764-01-2; pent-3-yn-1-ol, 10229-10-4; non-3-yn-2-one, 27259-09-2; methyl but-2-ynoate, 23326-27-4;

3-(trimethylsilyl)prop-2-yn-1-ol, 5272-36-6; 1-(methylthio)but-2-yne, 118891-26-2; dimethyl but-2-yne-1,4-dioate, 762-42-5; di-*tert*-butoxyacetylene, 66478-63-5; *trans*-1-bromobut-2-ene, 29576-14-5; 3-bromo-1-butene, 22037-73-6; *cis*-crotyl chloride, 4628-21-1; *trans*-crotyl chloride, 4894-61-5; 3-chlorobut-1-ene, 563-52-0; 1-chloro-2-methylprop-2-ene, 563-47-3; 3-(methoxymethyl)-2,5-dimethylphenol, 118891-34-2; 1-bromo-3-methylbut-2-ene, 870-63-3.

Interannular Diastereoselectivity in the Hydroboration of Functionalized 1-Cyclohexylcyclohexenes

Thomas W. Bell,* J. Ramón Vargas, and Gerard A. Crispino

Department of Chemistry, State University of New York, Stony Brook, New York 11794-3400

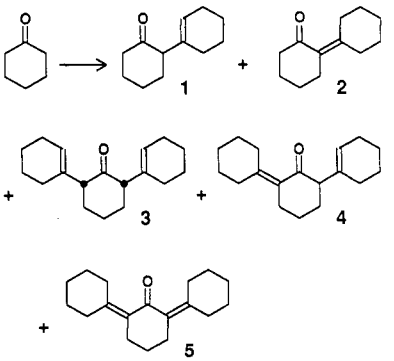
Received December 16, 1988

The reactions of thexylborane with 2-(1-cyclohexen-1-yl)cyclohexanone, *cis*-2,6-di(1-cyclohexen-1-yl)cyclohexanone, and related alcohols and ketals were investigated. All reactions are selective for products with erythro linkages between cyclohexyl rings, diastereoselectivities ranging from 66 to 97%. Greatest erythro selectivities were observed for equatorial homoallylic alcohols and ethylene ketals. The configurations of all products were unambiguously assigned by correlation with [1,1′-bicyclohexyl]-2,2′-diones and an erythro,erythro triketone (**25**), the configuration of which was determined by X-ray crystallography. The diastereoselectivities of these hydroborations and related examples from the literature can be qualitatively rationalized by the Houk transition structure model.

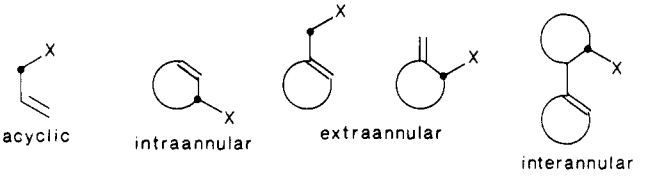
Hydroboration has proven to be extraordinarily useful in the stereoselective synthesis of complex organic molecules.[1] Good stereoselectivity may be achieved either by enantioselective reaction of optically active boranes with achiral alkenes[2] or by diastereoselective hydroboration of chiral alkenes.[3] In the latter case, stereoselection may be described as either "cyclic" or "acyclic", depending on whether the reactive double bond and the chiral center (stereogenic unit) are located within a ring. Cyclic diastereoselection is often high, presumably because the orientation of a polar functional group or a steric barrier is constrained relative to the diastereotopic faces of the double bond. Even in acyclic systems diastereoselective hydroboration may be controlled by allylic[4] or homoallylic[5] chiral centers.

The classification of diastereoselection as either cyclic or acyclic does not fully take into account the various possible conformational relationships between interacting centers in cyclic alkenes. Cyclic diastereoselectivity is more exactly described as "intraanular", since the reactive group and chiral center are in the same ring. Alternatively, two types of "extraannular" relationships may exist in which either the double bond or the chiral center is outside the ring (exocyclic), resulting in very different diastereoselectivities.[4e] Finally, when the carbon–carbon double bond

Scheme I



and chiral center are situated in separate rings "interannular" diastereoselectivity may result.[6]



Previous studies on bicyclohexyl systems revealed diastereoselective hydroboration of cyclohexenes in which boron or oxygen substituents are situated on the adjacent ring.[6] The large selectivities observed could not easily be rationalized by conventional mechanistic models. The current study was undertaken to further explore interannular diastereoselectivity in bicyclohexyls and 1,3-dicyclohexylcyclohexanes and to provide synthetic access to stereochemically defined polyalcohols and polyketones that might be of interest as ionophores. These new results, along with a configurational reassignment of [1,1′-bi-

(1) Houk, K. N.; Rondan, N. G.; Wu, Y.-D.; Metz, J. T.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257–2274.
(2) See Brown, H. C.; Jadhav, P. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, pp 1–43.
(3) (a) Klein, J.; Dunkelblum, E.; Avrahami, D. *J. Org. Chem.* **1967**, *32*, 935–939. (b) Pasto, D.; Klein, F. M. *Ibid.* **1968**, *33*, 1468–1476. (c) Gordon, M. H.; Robinson, M. J. T. *Tetrahedron Lett.* **1975**, 3867–3870. (d) Brener, L.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 2702–2704.
(4) (a) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487–2489. (b) Heathcock, C. H.; Jarvi, E. T.; Rosen, T. *Tetrahedron Lett.* **1984**, *25*, 243–246. (c) Tsai, D. J.-S.; Midland, M. M. *J. Am. Chem. Soc.* **1985**, *107*, 3915–3918. (d) McGarvey, G. J.; Bajwa, J. S. *Tetrahedron Lett.* **1985**, *26*, 6297–6300. (e) Birtwistle, D. H.; Brown, J. M.; Foxton, M. W. *Tetrahedron Lett.* **1986**, *27*, 4367–4370.
(5) (a) Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P. *J. Am. Chem. Soc.* **1982**, *104*, 2027–2029. (b) Evans, D. A.; Bartroli, J.; Godel, T. *Tetrahedron Lett.* **1982**, *23*, 4577–4580.
(6) (a) Bell, T. W. *Tetrahedron Lett.* **1980**, *21*, 3443–3446. (b) Bell, T. W. *J. Am. Chem. Soc.* **1981**, *103*, 1163–1171. (c) Jennings, P. W.; Gingerich, S. B. *J. Labelled Compd. Radiopharm.* **1983**, *20*, 591–603.

0022-3263/89/1954-1978$01.50/0